**Committee of Experts on the Transport of Dangerous Goods
and on the Globally Harmonized System of Classification
and Labelling of Chemicals**

**Sub-Committee of Experts on the Globally Harmonized
System of Classification and Labelling of Chemicals**

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Item 4 (a) of the provisional agenda
**Development of guidance on the application of the
Globally Harmonized System of Classification
and Labelling of Chemicals: Alignment of Annex 9 (section A9.7)
and Annex 10 with the criteria in Chapter 4.1**

Status update on the on-going work of the informal correspondence group on the alignment of Annex 9 (section 9.7) and Annex 10 (on metals and metal compounds) to the criteria in Chapter 4.1 and the generic environmental hazard guidance

Transmitted by the International Council on Mining and Metals (ICMM) on behalf of the correspondence group

Background

1. In 2018, at its thirty-sixth session, the Sub-Committee reconfirmed the mandate of a correspondence group to amend the strategy for metals and metal compounds to align the long-term aquatic assessment with the third revised edition of the GHS (ref: informal document INF.25 (24th session)). Following the work item being approved to continue in the 2021-2022 biennium, the group has carried on with its work towards proposing amendments to the GHS to the Sub-Committee for consideration at a forthcoming session.

2. This information document is intended to present the proposed changes agreed within the correspondence group to date as an initial step towards formally presenting an official document with proposed changes at the 43rd session of the Sub-Committee for its consideration.

Scope of work

3. The correspondence group is reviewing Annex 9 section A9.7 (Environmental Classification of metals and metal compounds) as well as Annex 10 (Transformation-Dissolution of metals and metal compounds in aqueous media) for inclusion under the tenth revised edition of the GHS. This would ensure the classification strategy, guidance and tools on metals and metal compounds are in line with the long-term aquatic classification scheme introduced by the third revised edition.

4. The main changes that are being considered to amend the basis for hazard categories towards the long-term aquatic classification endpoint for metals and metal compounds include:

    (a)   For Annex 9, section A9.7:

        (i)   extension of the classification strategy and guidance for metals, and poorly soluble metal compounds towards the long-term aquatic classification endpoint

(ii)   extension of the effects data interpretation for data rich substances, to the long-term aquatic classification endpoint

(iii)   review of the application of M factors for the acute and long-term aquatic classification endpoint

(b)   For Annex 10: extension of the Transformation/Dissolution protocol (TDp) to lower doses (0.1 and 0.01 mg/L at 28 days) - which could include testing and modelling guidance

Status of the work

5.   At its thirty-ninth session, the Sub-Committee agreed to keep this item on the 2021-2022 biennium work programme. Since the thirty-ninth session, the group was invited to review and provide additional comments to the set of documents developed by ICMM to capture and inform the group's progress on three occasions. After each consultation round and follow-up call, ICMM proceeded to reflect the comments received from the correspondence group by integrating the changes that had been agreed and by identifying remaining issues in annexes 9 and 10 of the GHS text.

6. Following the progress report submitted to the Sub-Committee under INF.17 (41st session), members were invited during March 2022 to consider further revisions to the text reflecting comments received, to ensure the proposed revised wording is in line with the GHS text. This was followed up by a call on 31 March 2022.

7.   Based on the additional feedback from members, potential solutions were put forward to address the four remaining open issues identified. These open issues include considering:

(a)   The primary role of the screening test for metal compounds (with reference to A9.7.2.2.3, A9.7.5.3, A10.2.2.1 and A10.5.3.1.2)

(b)   Linked to the conclusions of the discussions outlined in 7. (a) of this document, the approach to be followed when it comes to a default classification category (with reference to A 9.7.5) for chronic 4 classifications

(c)   Whether the text in Annex 9.7 is sufficiently clear when it comes to the correlation between the Transformation/Dissolution and toxicity at varying pH (with reference to A9.7.2.1.2.1 and A9.7.2.2.4)

(d)   Whether there is a need to improve the consistency in the way ecotoxicity reference values are defined throughout the annexes

8.   During the March 2022 call, the group considered the amendments proposed to address open issues 7 (a) to 7 (d) in more details. Alternative text for all open issues was agreed, with the exception of one remaining element of open issue 7 (b). This relates to how to address missing Transformation/Dissolution data in the acute classification of metals and poorly soluble metal compounds. The correspondence group is looking on how to progress it further and will propose further amendments with respect to A 9.7.5 in due course, as may be appropriate.

9.   In light of the extent of the proposed changes to both GHS annexes and to allow the Sub-Committee the necessary time to consider them, the proposed amendments agreed to date can be found under Annex I of this information document with respect to the changes put forward for Annex 9 (Guidance on hazards to the aquatic environment) relevant to metals and metals compounds and under Annex II of this information document with respect to the changes put forward for Annex 10 (Transformation/Dissolution of metals and metal compounds in aqueous media).

10. In earlier discussions of the correspondence group, some issues of further interest to the group were identified. These are out of scope of the current work item. Subject to further discussions, these could be brought forward for the consideration of the Sub-Committee as a potential new work item in the future.

11. The correspondence group hopes to have a set of recommendations and proposed amendments to the GHS ready to be submitted, as an official document to the Sub-Committee for consideration at its next session.

Requested action

12. The Sub-Committee is invited to consider the changes proposed to the annexes to date and to provide feedback to the correspondence group on any of the proposed changes to inform any additional amendments to the correspondence group's next submission.

ANNEX I

Proposed amendments to Annex 9 "GUIDANCE ON HAZARDS TO THE AQUATIC ENVIRONMENT"

A9.1 to A9.6 [*unchanged*]

A9.7   Classification of metals and metal compounds

A9.7.1   *Introduction*

A9.7.1.1   The harmonized system for classifying substances is a hazard-based system, and the basis of the identification of hazard is the aquatic toxicity of the substances, and information on the degradation and bioaccumulation behaviour (OECD 1998). Since this document deals only with the hazards associated with a given substance when the substance is dissolved in the water column, exposure from this source is limited by the solubility of the substance in water and bioavailability of the substance in species in the aquatic environment. Thus, the hazard classification schemes for metals and metal compounds are limited to the hazards posed by metals and metal compounds when they are available (i.e. exist as dissolved metal ions, for example, as M^+ when present as $M\text{-}NO_3$), and do not take into account exposures to metals and metal compounds that are not dissolved in the water column but may still be bioavailable, such as metals in foods. This section does not take into account the non-metallic ion (e.g. CN-) of metal compounds which may be toxic ~~or which may be organic and may pose bioaccumulation or persistence hazards~~. For such metal compounds the hazards of the non-metallic ions must also be considered.

Organometallic compounds (OM) (e.g. methyl mercury or tributyltin,…) and Organo Metallic Salts (OMS) may also be of concern given that they may pose bioaccumulation or persistence hazards in case they do not quickly dissociate or dissolve in water. Unless they act as a significant source of the metal ion (as a result of the dissociation and/or degradation processes), the organic moieties and the inorganic components should be assessed individually (OECD 2015). They are therefore excluded from the guidance of this section and should be classified according to the general guidance provided in section 4. Alternatively, those metal compounds that contain an organic component but that dissociate or dissolve easily in water as the metal ion should be treated in the same way as metal compounds and classified according to this annex (e.g. Zinc acetate, ...).

A9.7.1.2   The level of the metal ion which may be present in solution following the addition of the metal and/or its compounds, will largely be determined by two processes: the extent to which it can be dissolved, i.e. its water solubility, and the extent to which it can react with the media to transform to water soluble forms. The rate and extent at which this latter process, known as "transformation" for the purposes of this guidance, takes place can vary extensively between different compounds and the metal itself, and is an important factor in determining the appropriate hazard class. Where data on transformation are available, they should be taken into account in determining the classification. The Protocol for determining this rate is available in Annex 10.

A9.7.1.3   Generally speaking, the rate at which a substance dissolves is not considered relevant to the determination of its intrinsic toxicity. However, for metals and many poorly soluble inorganic metal compounds, the difficulties in achieving dissolution through normal solubilization techniques is so severe that the two processes of solubilization and transformation become indistinguishable. Thus, where the compound is sufficiently poorly soluble that the levels dissolved following normal attempts at solubilization do not exceed the available $L(E)C_{50}$, it is the rate and extent of transformation, which must be considered. The transformation will be affected by a number of factors, not least of which will be the properties of the media with respect to pH, water hardness, temperature etc. In addition to these properties, other factors such as the size and specific surface area of the particles which have been tested, the length of time over which exposure to the media takes place and, of course the mass or surface area loading of the substance in the media will all play a part in determining the level of dissolved metal ions in the water. Transformation data can generally, therefore, only be considered as reliable for the purposes of classification if conducted according to the standard Protocol in Annex 10.

A9.7.1.4   This Protocol aims at standardizing the principal variables such that the level of dissolved ion can be directly related to the loading of the substance added. It is this loading level which yields the level of metal ion equivalent to the available $L(E)C_{50}$ that can then be used to determine the hazard category appropriate for classification. The testing methodology is detailed in Annex 10. The strategy to be adopted in using the data from the testing protocol, and the data requirements needed to make that strategy work, will be described.

A9.7.1.5   In considering the classification of metals and metal compounds, both readily and poorly soluble, recognition has to be paid to a number of factors. As defined in Chapter 4.1, the term "degradation" refers to the decomposition of organic molecules. For inorganic compounds and metals, clearly the concept of degradability, as it has been considered and used for organic substances, has limited or no meaning. Rather, the substance may be transformed by normal environmental processes to either increase or decrease the bioavailability of the toxic species. Equally, the log K_{ow} cannot be considered as a measure of the potential to accumulate. Nevertheless, the concepts that a substance, or a toxic metabolite/reaction product may not be rapidly lost from the environment and/or may bioaccumulate are as applicable to metals and metal compounds as they are to organic substances.

A9.7.1.6   Speciation of the soluble form can be affected by pH, water hardness and other variables, and may yield particular forms of the metal ion which are more or less toxic. In addition, metal ions could be made non-available from the water column by a number of processes (e.g. ~~mineralization and~~ partitioning or chemical speciation to a non-soluble and hence not-bioavailable form). Sometimes these processes can be sufficiently rapid to be analogous to degradation in assessing long-term (chronic) classification. However, partitioning of the metal ion from the water column to other environmental media does not necessarily mean that it is no longer bioavailable, nor does it mean that the metal has been made permanently unavailable.

A9.7.1.7   Information pertaining to the extent of the partitioning of a metal ion from the water column, or the extent to which a metal has been or can be converted to a form that is less toxic or non-toxic is frequently not available over a sufficiently wide range of environmentally relevant conditions, and thus, a number of assumptions will need to be made as an aid in classification. These assumptions may be modified if available data show otherwise. In the first instance it should be assumed that the metal ions, once in the water, are not rapidly partitioned from the water column and thus these compounds do not meet the criteria. Underlying this is the assumption that, although speciation can occur, the species will remain available under environmentally relevant conditions. This may not always be the case, as described above, and any evidence available that would suggest changes to the bioavailability over the course of 28 days, should be carefully examined. The bioaccumulation of metals and inorganic metal compounds is a complex process and bioaccumulation data should be used with care. The application of bioaccumulation criteria will need to be considered on a case-by-case basis taking due account of all the available data.

A9.7.1.8   A further assumption that can be made, which represents a cautious approach, is that, in the absence of any solubility data for a particular metal compound, either measured or calculated, the substance will be sufficiently soluble to cause toxicity at the level of the ~~L(E)C50,~~ ecotoxicity reference value (ERV), being the acute ERV (expressed as L(E)C50), and/or the chronic ERV (expressed as the NOEC/ECx), and thus may be classified in the same way as other soluble salts. Again, this is clearly not always the case, and it may be wise to generate appropriate solubility data.

A9.7.1.9   This section deals with metals and metal compounds. For how this guidance applies to OMs and OMSs, see A9.7.1.1. Within the context of this guidance document, metals and metal compounds are characterized as follows~~, and therefore, organo-metals are outside the scope of this section~~:

  (a)   metals, M^0, in their elemental state are not soluble in water but may transform to yield the available form. This means that a metal in the elemental state may react with water or a dilute aqueous electrolyte to form soluble cationic or anionic products, and in the process the metal will oxidize, or transform, from the neutral or zero oxidation state to a higher one;

  (b)   in a simple metal compound, such as an oxide or sulphide, the metal already exists in the oxidized state, so that further metal oxidation is unlikely to occur when the compound is introduced into an aqueous medium.

However, while oxidization may not change, interaction with the media may yield more soluble forms. A sparingly soluble metal compound can be considered as one for which a solubility product can be calculated, and which will yield a small amount of the available form by dissolution. However, it should be recognized that the final solution concentration may be influenced by a number of factors, including the solubility product of some metal compounds precipitated during the T~~t~~ransformation/D~~d~~issolution test, e.g. aluminium hydroxide.

A9.7.2   *Application of aquatic toxicity data and solubility data for classification*

A9.7.2.1   *Interpretation of aquatic toxicity data*

A9.7.2.1.1   Aquatic toxicity studies carried out according to a recognized protocol should normally be acceptable as valid for the purposes of classification. Section A9.3 should also be consulted for generic issues that are common to assessing any aquatic toxicity data point for the purposes of classification.

Ecotoxicity data of soluble inorganic compounds are used and combined to derive the acute and chronic ecotoxicity reference value of the dissolved metal ion (ERV or ERV_{ion}). The ecotoxicity of soluble inorganic metal compounds is dependent on the physico-chemistry of the medium, irrespective of the original metal species released in the environment.

When evaluating ecotoxicity data and deriving ERVs, the general "weight of evidence" principle is also applicable to metals (see section A9.3.4).

The ecotoxicity data selected should be evaluated for their adequacy. Adequacy covers here both the reliability (inherent quality of a test relating to test methodology and the way that the performance and results of a test are described) and the relevance (extent to which a test is appropriate to be used for the derivation of an ecotoxicity reference value) of the available ecotoxicity data (see section A9.2.6 and A9.3.6). Under the reliability criteria, metal specific considerations include the description of some abiotic parameters in the test conditions for enabling the consideration of the bioavailable metal concentration and free metal ion concentration:

- Description of the physical test conditions: in addition to the general parameters (O_2, T°, pH, …), measurements of abiotic parameters such as dissolved organic carbon (DOC), hardness, alkalinity of the water that govern the speciation and hence the metal bioavailability are recommended.

- Description of test materials and methods: to calculate the free metal ion concentration with speciation models the concentrations of dissolved major ions and cations (e.g. aluminium, iron, magnesium, and calcium) are recommended.

- Concentration-effect relationship; hormesis: sometimes an increased performance in growth or reproduction is seen at low metal doses that exceed the control values, referred to as hormesis. Such effects can occur especially with major trace nutrients such as iron, zinc and copper but can also occur with a wide variety of non-essential substances. In such cases, positive effects should not be considered in the derivation of acute ERVs and especially chronic ERVs. Other models than the conventional log-logistic dose-response model should be used to fit the dose-response curve and consideration should be given to the adequacy of the control diet/exposure. Due to the essential nutritional needs, caution is needed with regards to extrapolation of the dose-response curve (e.g. to derive an acute or chronic ERV) below the lowest tested concentration.

Under the relevancy criteria, certain considerations need to be made, related to the relevancy of the test substance and to acclimatisation/adaptation:

- Relevance of the test substance: tests conducted with soluble metal salts should be used for the purpose of deriving acute and chronic ERVs. The ecotoxicity adapted from organic metal compounds exposure should not be used.

- Acclimatisation/adaptation: For essential metals, the culture medium should contain a minimal concentration not causing deficiency for the test species used. This is especially relevant for organisms used for chronic toxicity tests where the margin between essentiality and toxicity may become small. For this reason a proper description of culture conditions related to the level of essential metals is required.

A9.7.2.1.2   Metal complexation and speciation

A9.7.2.1.2.1   The toxicity of a particular metal in solution, appears to depend primarily on (but is not strictly limited to) the level of dissolved free metal ions. Abiotic factors including alkalinity, ionic strength and pH can influence the toxicity of metals in two ways: (i) by influencing the chemical speciation of the metal in water (and hence affecting the availability) and (ii) by influencing the uptake and binding of available metal by biological tissues. For the classification of metals and metal compounds, Transformation/Dissolution (T/D) testing is carried out over a pH range (see A10.2.3.2). If evidence is available that the aquatic toxicity of the dissolved metal depends on pH, then T/D data and aquatic toxicity are compared at a similar pH. If such evidence is not available, then the aquatic toxicity cannot be grouped according to pH. The highest aquatic toxicity observed is then compared to the T/D data obtained at the pH which causes maximum transformation and dissolution.

A9.7.2.1.2.2   Where speciation is important, it may be possible to model the concentrations of the different forms of the metal, including those that are likely to cause toxicity. Analysis methods for quantifying exposure concentrations,

which are capable of distinguishing between the complexed and uncomplexed fractions of a test substance, may not always be available ~~or economic~~.

A9.7.2.1.2.3   Complexation of metals to organic and inorganic ligands in test media and natural environments can be estimated from metal speciation models. Speciation models for metals, including pH, hardness, DOC, and inorganic substances such as MINTEQ (Brown and Allison, 1987), WHAM (Tipping, 1994; Tipping et al., 2011) and CHESS (Santore and Driscoll, 1995) can be used to calculate the uncomplexed and complexed fractions of the metal ions. Alternatively, the Biotic Ligand Model (BLM)~~,~~ allows for the calculation of the concentration of metal ion responsible for the toxic effect at the level of the organism, which may be affected by the DOC concentration, the pH, and the concentrations of competing ions such as calcium and magnesium. Such models may be investigated to better understand the impact of test medium composition on metal toxicity. The BLM model has at present ~~only~~ been validated for ~~a limited number of~~ specific metals, organisms, and end-points (Santore and Di Toro, 1999; Garman et al., 2020). The models and formula used for the characterization of metal complexation in the media should always be clearly reported, allowing for their translation back to natural environments (OECD, 2000). In case a metal-specific BLM is available covering an appropriate pH range, a comparison of aquatic toxicity data can be made using the entire effects database for different reference pH values, relevant to the T/D data.

A9.7.2.2   *Interpretation of solubility data*

A9.7.2.2.1   When considering the available data on solubility, their validity and applicability to the identification of the hazard of metal compounds should be assessed. In particular, a knowledge of the pH at which the data were generated should be known.

A9.7.2.2.2   Assessment of existing data

Existing data will be in one of three forms. For some well-studied metals, there will be solubility products and/or solubility data for the various inorganic metal compounds. It is also possible that the pH relationship of the solubility will be known. However, for many metals or metal compounds, it is probable that the available information will be descriptive only, e.g. poorly soluble. Unfortunately~~,~~ there appears to be very little (consistent) guidance about the solubility ranges for such descriptive terms. Where these are the only information available and the solubility data cannot provide a clear answer on the solubility rate and equilibrium, it is ~~probable~~ highly recommended that solubility data ~~will need to~~ be generated using the Transformation/Dissolution (T/D) ~~P~~protocol (Annex 10).

A9.7.2.2.3   Screening test for assessing solubility of metal compounds

In the absence of solubility data for metal compounds, a ~~simple "Screening Test"~~ screening test for assessing solubility~~, based on the high rate of loading for 24 h, can~~ should be ~~used for metal compounds~~ performed as described in the Transformation/Dissolution ~~P~~protocol (Annex 10). The screening test is conducted at the high loading rate (100 mg/L) and under rapid and vigorous agitation for 24 h. The function of the screening test is~~ to~~:

-    ~~T~~to identify those metal compounds which undergo either dissolution or rapid transformation such that ~~they are~~ their ecotoxicity potential is indistinguishable from soluble forms in that they ~~and hence~~ may be classified based on the dissolved ion concentration.

-    To verify the pH dependency of the dissolution, in preparation of the full T/D test. Where data at different pH are available from the screening test ~~detailed in the Transformation/Dissolution Pprotocol~~, then the full test should at least be conducted at the pH which maximises the ~~maximum~~ solubility ~~obtained over the tested pH range should be used~~. Where data are not available over the full pH range, a check should be made that this maximum solubility has been achieved by reference to suitable thermodynamic speciation models or other suitable methods (see A9.7.2.1.2.3). In the absence of suitable data or models, it is highly recommended that solubility data are generated to cover the full pH range. It should be noted that this screening test is only intended to be used for metal compounds. Metals should be assessed at the level of the full test (see A9.7.2.2.4).

A9.7.2.2.4   Full test for assessing solubility of metals and metal compounds

~~The first step in this part of the study is, as with the screening full test, an assessment of the pH(s) at which the study~~ The full test should ~~at least~~ be ~~conducted. Normally, the Full Test should have been~~ carried out at the pH[1] that maximizes the concentration of dissolved metal ions in solution. ~~In such cases, t~~The pH may be chosen following the same guidance as given for the screening test.

Based on the data from the ~~F~~full ~~T~~test, it is possible to generate a concentration of the metal ions in solution after 7 days for each of the three loadings (i.e. 1 mg/l as "low", 10 mg/l as "medium" and 100 mg/l as "high") used in the test. If the purpose of the test is to assess the long-term (chronic) hazard of the substance, then the loadings[2] should be 0.01 mg/l, 0.1 mg/l or 1 mg/l depending on the transformation rate, and the duration of the test ~~at the low loading may~~ should be extended to 28 days~~, at an appropriate pH~~.

A9.7.2.3   *Comparison of aquatic toxicity data and solubility data*

A decision ~~whether or not~~ on how to classify the substance ~~be classified~~ will be made by comparing aquatic toxicity data and solubility data. ~~If the L(E)C₅₀ is exceeded, irrespective of whether the toxicity and dissolution data are at the same pH and if this is the only data available then the substance should be classified. If other solubility data are available to show that the dissolution concentration would not exceed the L(E)C₅₀ across the entire pH range then the substance should not be classified on its soluble form.~~ This may involve the use of additional data either from ecotoxicological testing or from applicable bioavailability-effect models. Depending on the available data, two approaches can be followed:

- If limited information on the T/D at different pH levels is available, or if the aquatic toxicity of the dissolved metal does not depend on pH, then the lowest ERV and the highest T/D result, each potentially derived at different pH levels, should provide the basis for classification (this should be used as the default approach).

- If evidence is available that the aquatic toxicity of the dissolved metal depends on pH, and sufficient toxicity data are available at varying pH levels, then a split of the acute and chronic ERVs can be performed according to the pH band. If in addition T/D data at different pH levels are available, then the classification may be derived by comparing T/D data with the ERV at corresponding pH levels, meaning that toxicity data and T/D data are in this case always compared at the same pH band. This split of the effects data into pH bands would apply in an equal way to the acute and the chronic effects data sets. The most stringent classification outcome across all pH bands should be used.

A9.7.3   *Assessment of environmental transformation*

A9.7.3.1   Environmental transformation of one species of a metal to another species of the same does not constitute degradation as applied to organic compounds and may increase or decrease the availability and bioavailability of the toxic species. However, as a result of naturally occurring geochemical processes metal ions can partition from the water column. Data on water column residence time, the processes involved at the water – sediment interface (i.e. deposition and re-mobilization) are fairly extensive but have not been integrated into a meaningful database. Nevertheless, using the principles and assumptions discussed above in A9.7.1, it may be possible to incorporate this approach into classification.

A9.7.3.2   Such assessments are very difficult to give guidance for and will normally be addressed on a case by case approach. However, the following may be taken into account:

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[1] The GHS Transformation/Dissolution protocol specifies a pH range of 6—8.5 for the 7 days test and 5.5—8.5 for the 28 days test. Considering the difficulty in carrying out transformation/dissolution tests at pH 5.5, the OECD only validated the test in the pH range of 6—8.5.

[2] Lower loading rates than 1 mg/l may not be practically feasible for each case. While T/D testing at lower loading rates is in principle the best way forward it is technically often not feasible. Extensive experience with the T/D protocol demonstrated that reliable predictions can be made for other loading rates. In order to make maximal use of existing T/D data, the 28 days results for the lower loading rates (0.1 and 0.01 mg/l) can therefore often be derived by extrapolation from evidence at other loading rates. This approach should be justified on a case-by-case basis and supported by reliable information on the T/D at different loading rates. It should be further noted that the relationship between loading rate and dissolved metal concentration may not be linear. Therefore, extrapolating T/D data to lower loadings should preferably be made by using the equations of section A.10.6.1 or alternatively by extrapolating in a precautionary way.

(a)   Changes in speciation if they are to non-available forms, however, the potential for the reverse change to occur must also be considered;

(b)   Changes to a metal compound which is considerably less soluble than that of the metal compound being considered.

Some caution is recommended, see A9.7.1.5 and A9.7.1.6.

A9.7.4   *Bioaccumulation*

A9.7.4.1   While log K_{ow} is a good predictor of BCF for certain types of organic compounds e.g. non-polar organic substances, it is ~~of course~~ irrelevant for inorganic substances such as inorganic metal compounds because metals, in contrast to organic substances, are not lipophilic and are generally not transported through cellular membranes by passive processes. Uptake of metal ions typically occurs through active processes.

A9.7.4.2   The mechanisms for uptake and depuration rates of metals are very complex and variable and there is at present no general model to describe this. Instead the bioaccumulation of metals according to the classification criteria should be evaluated on a case-by-case basis using expert judgement.

A9.7.4.3   While BCFs are indicative of the potential for bioaccumulation there may be a number of complications in interpreting measured BCF values for metals and inorganic metal compounds. For some metals and inorganic metal compounds the relationship between water concentration and BCF in some aquatic organisms is inverse, and bioconcentration data should be used with care. This is particularly relevant for metals that are biologically essential. Metals that are biologically essential are actively regulated in organisms in which the metal is essential (homeostasis). Removal and sequestration processes that minimise toxicity are complemented by an ability to up-regulate concentrations for essentiality. Since nutritional requirement of the organisms can be higher than the environmental concentration, this active regulation can result in high BCFs and an inverse relationship between BCFs and the concentration of the metal in water. When environmental concentrations are low, high BCFs may be expected as a natural consequence of metal uptake to meet nutritional requirements and in these instances can be viewed as a normal phenomenon. Additionally, if internal concentration is regulated by the organism, then measured BCFs may decline as external concentration increases. When external concentrations are so high that they exceed a threshold level or overwhelm the regulatory mechanism, this can cause harm to the organism. Also, while a metal may be essential in a particular organism, it may not be essential in other organisms. Therefore, where the metal is not essential or when the bioconcentration of an essential metal is above nutritional levels, special consideration should be given to the potential for bioconcentration and environmental concern.

For essential elements, measured BCFs decline as external concentrations increase because the internal concentrations are regulated by the organism. Non-essential metals are also actively regulated to some extent and therefore also for nonessential metals, an inverse relationship between the metal concentration and the external concentration may be observed (McGeer et al., 2003). When external concentrations are so high that they exceed a threshold level, or overwhelm the regulatory mechanism, this can cause harm to the organism. BCF and BAF may be used to estimate metal accumulation by:

(a)   Considering information on essentiality and homeostasis of metals/metal compounds. As a result of such regulation, the "bioaccumulative" criterion is not applicable to metals.

(b)   Assessing bioconcentration factors for non-essential metals, should preferably be done from BCF studies using environmental relevant concentrations in the test media.

A9.7.5   *Application of classification criteria to metals and metal compounds*

A9.7.5.1   *Introduction to the classification strategy for metals and metal compounds*

A9.7.5.1.1   Short-term (acute) and long-term (chronic) hazards are assessed individually for metals and metal compounds. For long-term hazards preference should be given in applying the approach based on chronic toxicity data. Such evidence is often available for the readily soluble metal salts. The schemes for the ~~classification~~ determination of short-term and long-term aquatic hazards of metals and metal compounds are described below and summarized ~~diagrammatically in Figure~~ in the figures:

(a)   A9.7.1 (short-term hazard classification of metals);

(b)   A9.7.2 and A9.7.3 (long-term hazard classification of metals);

    (c)   A9.7.4 (short-term hazard classification of metal compounds);

    (d)   A9.7.5 (long-term hazard classification of metal compounds).

There are several stages in these schemes where data are used for decision purposes. It is not the intention of the classification schemes to generate new data. In the absence of valid data, it will be necessary to use all available data and expert judgement.

In the following sections, the reference to the ~~L(E)C$_{50}$~~ acute and chronic ERVs ~~refers~~ to the data point(s) that will be used to select the ~~class~~ hazard categories for the metal or metal compound.

A9.7.5.1.2   When considering acute and chronic ERVs for metal compounds (ERV$_{compound}$), it is important to ensure that the data point to be used as the justification for the classification is expressed in the weight of the molecule of the metal compound to be classified. This is known as correcting for molecular weight. Thus while most metal data ~~is~~ are expressed in, for example, mg/l of the dissolved metal ion (abbreviated ERV$_{ion}$), this value will need to be adjusted to the corresponding weight of the metal compound. Thus:

~~L(E)C$_{50}$ metal compounds = L(E)C$_{50}$ of metal × (Molecular weight of metal compound/Atomic weight of metal)~~

~~NOEC data may also need to be adjusted to the corresponding weight of the metal compounds.~~

$$ERV_{compound} =$$

$$ERV_{ion} \text{ x}$$

(Molecular weight of metal compound / Σ atomic weight of the atom(s) of the metal in the compound)

where:

ERV$_{compound}$ = ERV of the metal compound

ERV$_{ion}$ = ERV of the dissolved metal ion

A9.7.5.2   *Classification strategy for metals*

A9.7.5.2.1   *Short-term (acute) aquatic hazard of metals*

The scheme for determining the short-term (acute) aquatic hazard of metals is described in this section and summarized in Figure A9.7.1.

Where the ~~L(E)C$_{50}$ for~~ acute ERV of the dissolved metal ~~ions of concern~~ is greater than 100 mg/l, the metals need not be considered further in the classification scheme.

~~A9.7.5.2.2~~   Where the ~~L(E)C$_{50}$ for~~ acute ERV of the dissolved metal ions ~~of concern~~ is ≤100 mg/l, consideration must be given to the data available on the rate and extent to which these ions can be generated from the metal. Such data~~,~~ ~~to be valid and useable~~ should ~~have been~~ be generated using the Transformation/Dissolution ~~P~~protocol (Annex 10).

~~A9.7.5.2.3~~   ~~Where such data are unavailable, i.e. there is no clear data of sufficient validity to show that the transformation to metal ions will not occur, the safety net classification (Chronic 4) should be applied since the known classifiable toxicity of these soluble forms is considered to produce sufficient concern.~~

~~A9.7.5.2.4~~   Where 7-day data from the Transformation/D~~d~~issolution protocol are available, then, the results should be used to aid classification according to the following rules~~.~~: Classify the metal as:

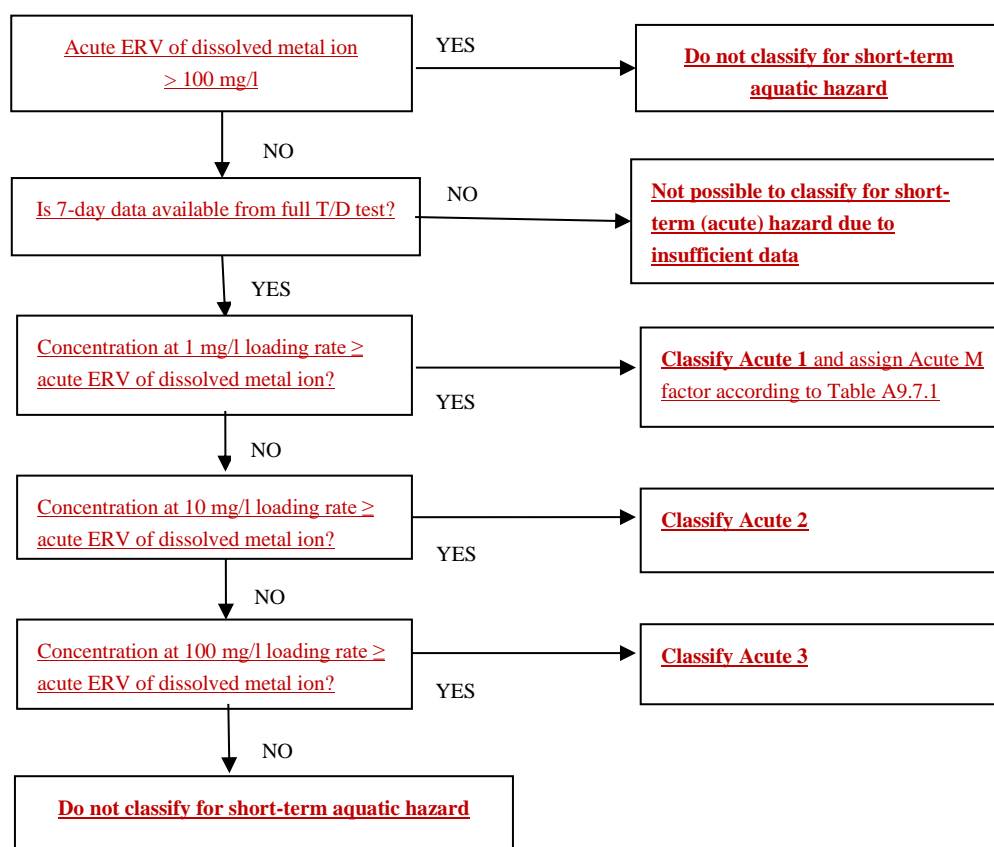~~A9.7.5.2.4.1~~   ~~7 day Transformation test~~

~~If the dissolved metal ion after a period of 7 days (or earlier) exceeds that of the L(E)C$_{50}$, then the default classification for the metals is replaced by the following classification:~~

a) Category Acute 1 if If the dissolved metal ion concentration at the low loading rate is ≥ acute ERV. L(E)C~50~, then classify as Acute 1. Classify also as Chronic 1, unless there is evidence of both rapid partitioning from the water column and no bioaccumulation Assign an Acute M factor according to Table A9.7.1;

b) Category Acute 2 if If the dissolved metal ion concentration at the low loading rate is < acute ERV, but at the medium loading rate it is ≥ acute ERV; L(E)C~50~, then classify as Acute 2. Classify also as Chronic 2 unless there is evidence of both rapid partitioning from the water column and no bioaccumulation

c) Category Acute 3 if If the dissolved metal ion concentration at the low and the medium loading rates is < acute ERV, but at the high loading rate it is ≥ acute ERV. L(E)C~50~, then classify as Acute 3. Classify also as Chronic 3 unless there is evidence of both rapid partitioning from the water column and no bioaccumulation

Do not classify the metal for short-term aquatic hazard if the dissolved metal concentration at all loading rates is below the acute ERV.

Figure A9.7.1 Classification strategy for determining the short-term (acute) aquatic hazard of metals

A9.7.5.2.2   *Long-term (chronic) aquatic hazard of metals*

A9.7.5.2.4.2   28-day transformation test

If the process described in A9.7.5.2.4.1 results in classification as Chronic 1, no further assessment is required, as the metal will be classified irrespective of any further information.

In all other cases, further data may have been generated through the dissolution/transformation test in order to show that the classification may be amended. If for substances classified as Chronic 2, 3 or 4, the dissolved metal ion concentration at the low loading rate after a total period of 28 days is ≤ long-term NOECs, then the classification is removed.

The scheme for determining the long-term (chronic) aquatic hazard of metals is described in this section and summarised in Figures A9.7.2 and A9.7.3. Metals can be classified for long-term aquatic hazard using chronic toxicity data when available, or using the surrogate approach in absence of appropriate chronic toxicity data.

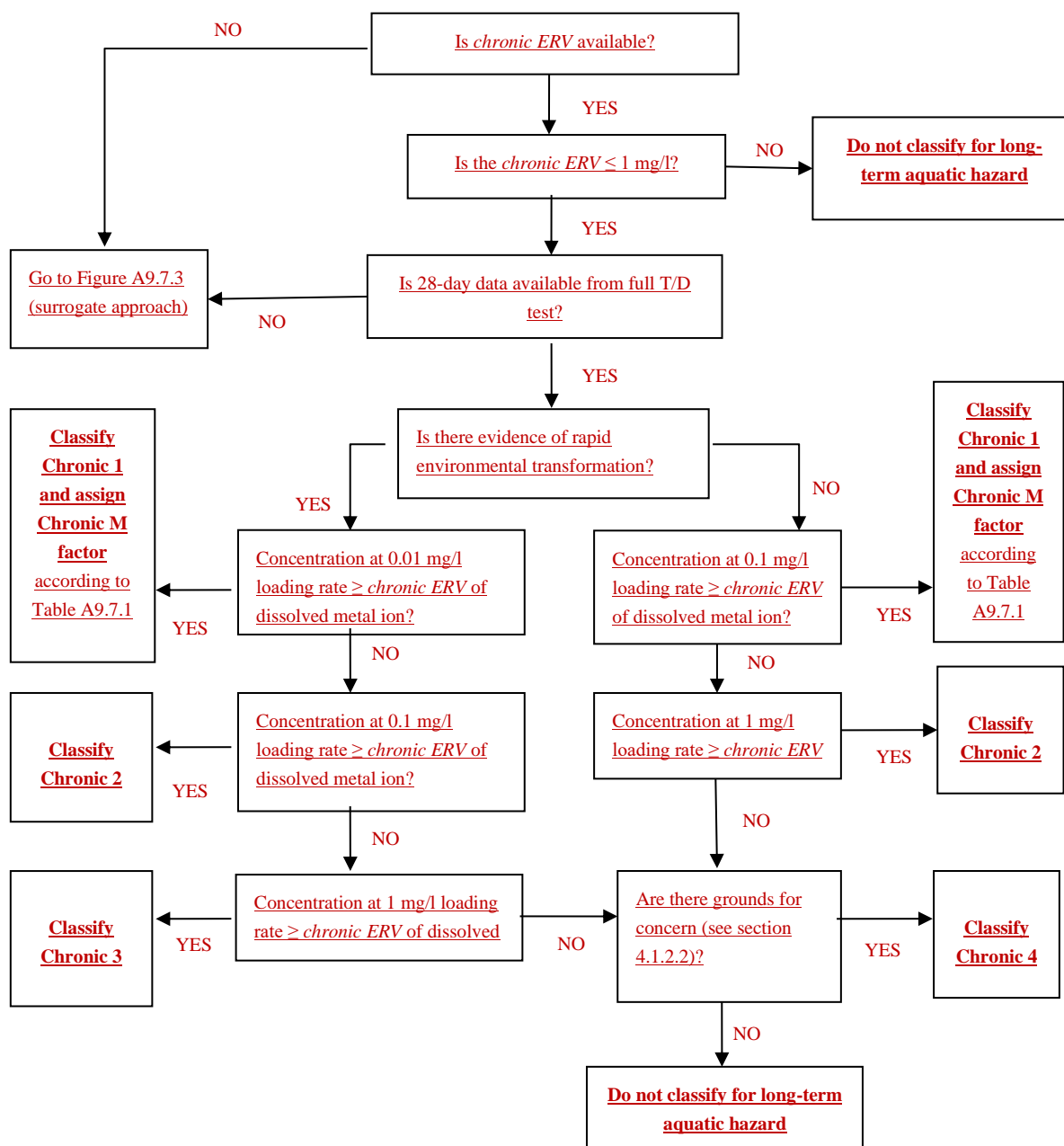A9.7.5.2.2.1   Approach based on available chronic toxicity data

Where the chronic ERV of the dissolved metal ion is greater than 1 mg/l, the metal need not be considered further in the classification scheme.

Where the chronic ERV of the dissolved metal ion is less than or equal to 1 mg/l, consideration must be given to the available data on the rate and extent to which these ions can be generated from the metal. Such data should be generated or calculated using the Transformation/Dissolution protocol (Annex 10) for 28 days (see section A9.7.2.2.4). If such data are unavailable, the surrogate approach should be used (see section A9.7.5.2.2.2). Where 28-day T/D data are available, then classify the metal as:

(a)   Category Chronic 1 if the dissolved metal ion concentration obtained at a loading rate of 0.1 mg/l (0.01 mg/l if there is evidence of rapid environmental transformation) is greater than or equal to the chronic ERV. Assign a Chronic M factor according to Table A9.7.1;

(b)   Category Chronic 2 if the dissolved metal ion concentration obtained at a loading rate of 1 mg/l (0.1 mg/l if there is evidence of rapid environmental transformation) is greater than or equal to the chronic ERV;

(c)   Category Chronic 3 if the dissolved metal ion concentration obtained at a loading rate of 1 mg/l is greater than the chronic ERV and there is evidence of rapid environmental transformation.

(d)   Category Chronic 4 if the data available do not allow classification under the formal criteria but there are nevertheless some grounds for concern (see section 4.1.2.2).

Do not classify the metal for long-term aquatic hazard if the dissolved metal ion concentration obtained from the 28-day Transformation/Dissolution test at a loading rate of 1 mg/l is less than the chronic ERV of the dissolved metal ion.

Figure A9.7.2: Classification strategy for determining long-term aquatic hazard of metals on the basis of chronic data

NO

Is *chronic ERV* available?

YES

Is the *chronic ERV* ≤ 1 mg/l? → NO → **Do not classify for long-term aquatic hazard**

YES

Go to Figure A9.7.3 (surrogate approach) ← NO ← Is 28-day data available from full T/D test?

YES

Is there evidence of rapid environmental transformation?

Classify Chronic 1 and assign Chronic M factor according to Table A9.7.1

YES

Classify Chronic 1 and assign Chronic M factor according to Table A9.7.1

Concentration at 0.01 mg/l loading rate ≥ *chronic ERV* of dissolved metal ion?

NO

Concentration at 0.1 mg/l loading rate ≥ *chronic ERV* of dissolved metal ion?

YES

Classify Chronic 2

NO

Concentration at 0.1 mg/l loading rate ≥ *chronic ERV* of dissolved metal ion?

YES

Classify Chronic 2

NO

Concentration at 1 mg/l loading rate ≥ *chronic ERV* of dissolved

YES

Classify Chronic 3

Concentration at 1 mg/l loading rate ≥ *chronic ERV*

YES

Classify Chronic 2

NO

Are there grounds for concern (see section 4.1.2.2)?

NO → **Classify Chronic 3**

YES → **Classify Chronic 4**

NO

Do not classify for long-term aquatic hazard

A9.7.5.2.2.2   The surrogate approach

Where appropriate chronic toxicity data and/or T/D data are not available, but the metal is classified for short-term (acute) aquatic hazard, then classify the metal as (unless there is evidence of rapid environmental transformation and no bioaccumulation):

(a)   Category Chronic 1 if the metal is classified for short-term (acute) aquatic hazard as category Acute 1. Assign the same M factor as for category Acute 1.

(b)   Category Chronic 2 if the metal is classified for short-term (acute) aquatic hazard as category Acute 2.

(c)   Category Chronic 3 if the metal is classified for short-term (acute) aquatic hazard as category Acute 3.

(d)   Category Chronic 4 if the data available do not allow classification under the formal criteria but there are nevertheless some grounds for concern (see section 4.1.2.2).

Do not classify the metal for long-term aquatic hazard if the metal is not classified for short-term aquatic hazard and if there are no grounds for concern.

Figure A9.7.3 Classification strategy for determining long-term aquatic hazard of metals in absence of appropriate chronic toxicity reference data and/or 28-day Transformation/Dissolution data
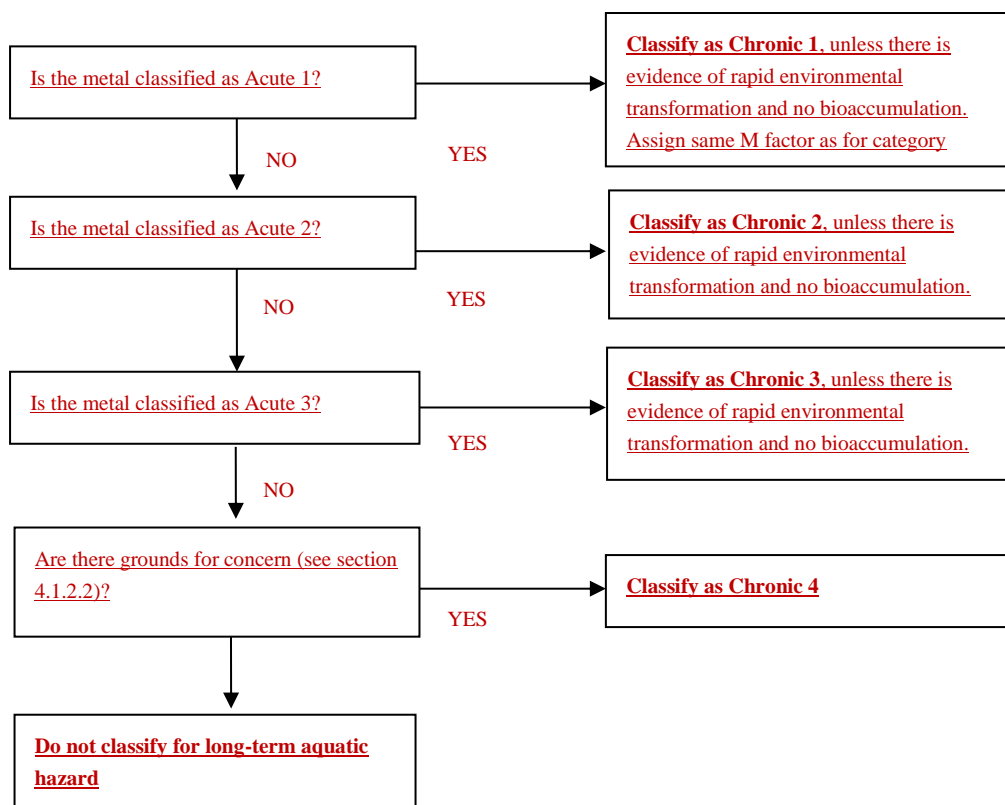
A9.7.5.3   *Classification strategy for metal compounds*

~~A9.7.5.3.1   Where the L(E)C$_{50}$ for the metal ions of concern is > 100 mg/l, the metal compounds need not be considered further in the classification scheme.~~

~~A9.7.5.3.2   If solubility ≥ L(E)C$_{50}$, classify on the basis of soluble ion.~~

~~A9.7.5.3.2.1   All metal compounds with a water solubility (either measured e.g. through 24 hour Dissolution Screening test or estimated e.g. from the solubility product) ≥ L(E)C$_{50}$ of the dissolved metal ion concentration are considered as readily soluble metal compounds.~~

Metal compounds will be considered as readily soluble if the water solubility (measured e.g. through a screening test according to the T/D protocol, or estimated e.g. from the solubility product), expressed as the concentration of dissolved metal ion, is greater than or equal to the acute ERV$_{ion}$. In the context of the classification criteria, metal compounds will also be considered as readily soluble if such data are unavailable, i.e. there are no clear data of sufficient validity to show that the transformation to metal ions will not occur. Care should be exercised for compounds whose solubility is close to the acute ERV ~~toxicity value~~ as the conditions under which solubility is measured could differ significantly from those of the acute toxicity test. In these cases the results of the ~~Dissolution~~ screening ~~T~~test are preferred. Metal compounds will be considered as poorly soluble if the water solubility (measured e.g. through a screening test, or

estimated e.g. from the solubility product), expressed as the concentration of dissolved metal ion, is less than the acute ERV~~ion~~.

A9.7.5.3.1   Short-term (acute) aquatic hazard of metal compounds

A9.7.5.3.~~1.1~~2.2   Readily soluble metal compounds are classified on the basis of the ~~L(E)C$_{50}$ (corrected where necessary for molecular weight)~~ acute ERV$_{compound}$. Classify the readily soluble metal compound as:

(a)   Category Acute 1 if ~~If~~ the ~~L(E)C$_{50}$ of the dissolved metal ion~~ acute ERV$_{compound}$ is ≤ ~~equal to or less than~~ 1 mg/l ~~then classify as Category Acute 1. Classify also as Chronic 1 unless there is evidence of both rapid partitioning from the water~~ column ~~and no bioaccumulation~~ Assign an Acute M factor according to Table A9.7.1;

(b)   Category Acute 2 if ~~If~~ the ~~L(E)C$_{50}$ of the dissolved metal ion is >~~ acute ERV$_{compound}$ is greater than 1 mg/1 but ≤ less than or equal to 10 mg/l ~~then classify as Acute 2. Classify also as Chronic 2 unless there is evidence of both rapid partitioning from the water column and no bioaccumulation~~;

(c)   Category Acute 3 if ~~If~~ the ~~L(E)C$_{50}$ of the dissolved metal ion is >~~ acute ERV$_{compound}$ is greater than 10 mg/1 ~~and ≤~~ but less than or equal to 100 mg/l ~~then classify as Acute 3;~~. ~~Classify also as Chronic 3 unless there is evidence of both rapid partitioning from the water column and no bioaccumulation~~.

Do not classify the readily soluble metal compound for short-term aquatic hazard if the acute ERV$_{compound}$ is larger than 100 mg/l.

~~*A9.7.5.3.3   If solubility < L(E)C$_{50}$, classify default Chronic 4*~~

~~A9.7.5.3.3.1   In the context of the classification criteria, poorly soluble compounds of metals are defined as those with a known solubility (either measured e.g. through 24 hour Dissolution Screening test or estimated e.g. from the solubility product) less than the L(E)C$_{50}$ of the soluble metal ion. In those cases when the soluble forms of the metal of poorly soluble metal compounds have a L(E)C$_{50}$ ≤ 100 mg/l an acute ERV$_{ion}$ equal or smaller than 100 mg/l and the substance can be considered as poorly soluble the default safety net classification (Chronic 4) should be applied.~~

~~A9.7.5.3.3.2   7 day transformation test~~

~~For poorly soluble metal compounds classified with the default safety net classification further information that may be available from the 7 day transformation/dissolution test can also be used. Such data should include transformation levels at low, medium and high loading levels.z~~

~~If the dissolved metal ion concentration after a period of 7 days (or earlier for a significant period of time) exceeds that of the L(E)C$_{50}$, then the default classification for the metals is replaced by the following classification:~~

A9.7.5.3.1.2   Poorly soluble metal compounds are classified on the basis of the acute ERV of the dissolved metal ion and 7-day Transformation/Dissolution data. Classify the poorly soluble metal compound as:

(a)   Category Acute 1 if ~~If~~ the dissolved metal ion concentration at the low loading rate is ~~≥L(E)C$_{50}$~~ equal to or greater than the acute ERV$_{ion}$, ~~then classify as Acute 1~~ and assign Acute M factor according to Table A9.7.1. ~~Classify also as Chronic 1, unless there is evidence of both rapid partitioning from the water column and no bioaccumulation~~;

(b)   Category Acute 2 if ~~If~~ the dissolved metal ion concentration at the medium loading rate is equal to or greater than the acute ERV$_{ion}$, ~~then classify as Acute Category 2. Classify also as Chronic 2 unless there is evidence of both rapid partitioning from the water column and no bioaccumulation~~;

(c)   Category Acute 3 if ~~If~~ the dissolved metal ion concentration at the high loading rate is ~~≥ L(E)C$_{50}$~~ equal to or greater than the acute ERV$_{ion}$, ~~then classify as Acute Category 3. Classify also as Chronic 3 unless there is evidence of both rapid partitioning from the water column and no bioaccumulation~~.

Do not classify the poorly soluble metal compound for short-term (acute) aquatic hazard if the dissolved metal ion concentration is below the acute ERV of the dissolved metal ion at all loading rates.

Figure A9.7.4:
Classification strategy for determining the short-term (acute) aquatic hazard of metal compounds
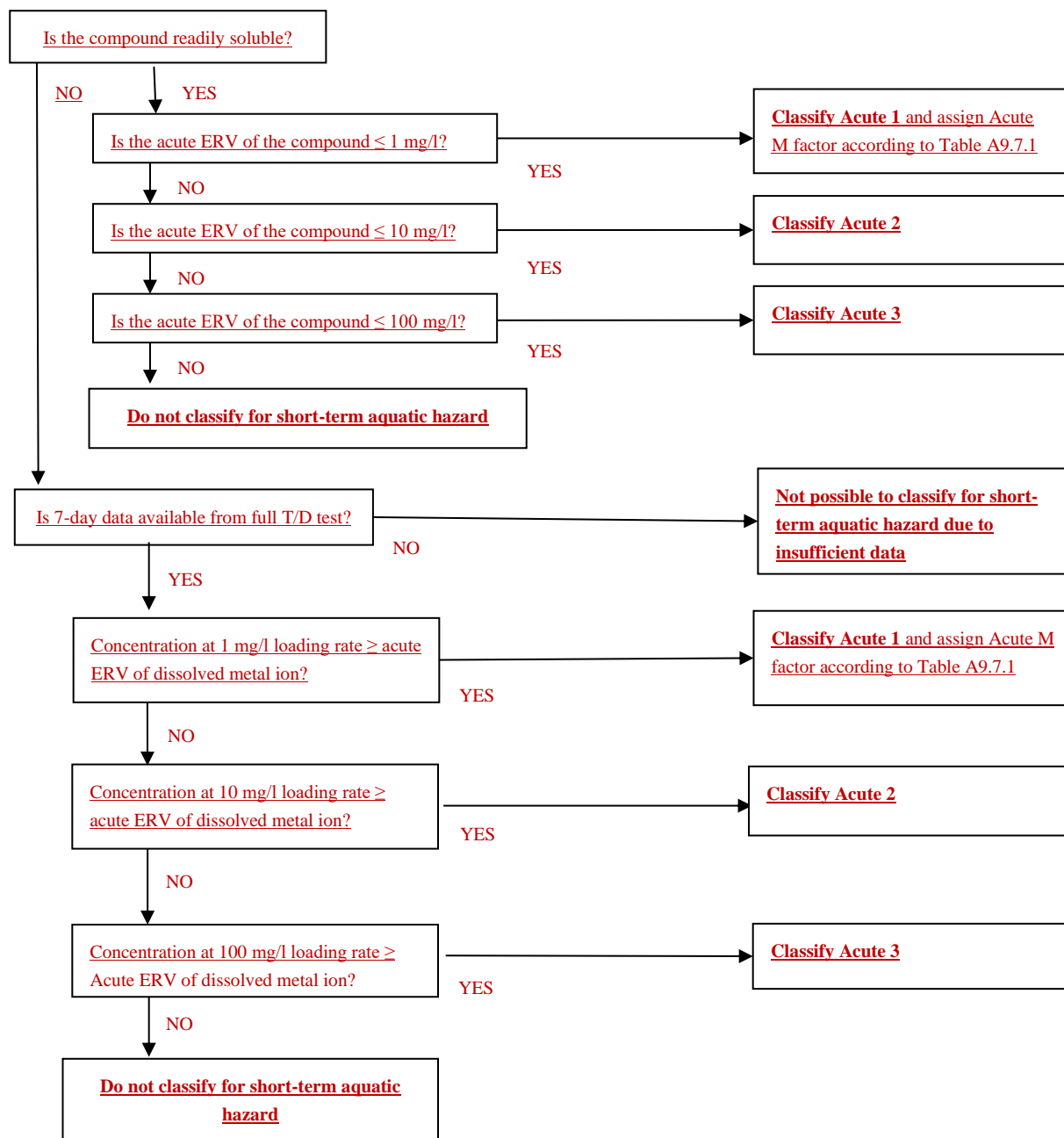
A9.7.5.3.2 Long-term (chronic) aquatic hazard of metal compounds

~~A9.7.5.3.3.3 28-day transformation test~~

~~If the process described in A9.7.5.3.3.2 results in classification as Chronic 1, no further assessment is required as the metal compound will be classified irrespective of any further information.~~

In all other cases, further data may have been generated through the dissolution/transformation test for 28 days in order to show that the classification may be amended. If for poorly soluble metal compounds classified as Chronic 2, 3 or 4, the dissolved metal ion concentration at the low loading rate after a total period of 28 days is less than or equal to the long-term NOECs, then classification is removed.

The scheme for determining the long-term (chronic) aquatic hazard of metal compounds is described in this section and summarised in Figure A9.7.5. Metal compounds can be classified for long-term aquatic hazard using chronic toxicity data when available, or using the surrogate approach in absence of appropriate chronic toxicity data.

A9.7.5.3.2.1   Approach based on available chronic toxicity data

Where the chronic ERV$_{compound}$ is greater than 1 mg/l, the metal compound need not to be considered further in the classification scheme for long-term hazard.

Readily soluble metal compounds are classified on the basis of the chronic ERV$_{compound}$. If there is no evidence of rapid environmental transformation, then classify the readily soluble metal compound as:
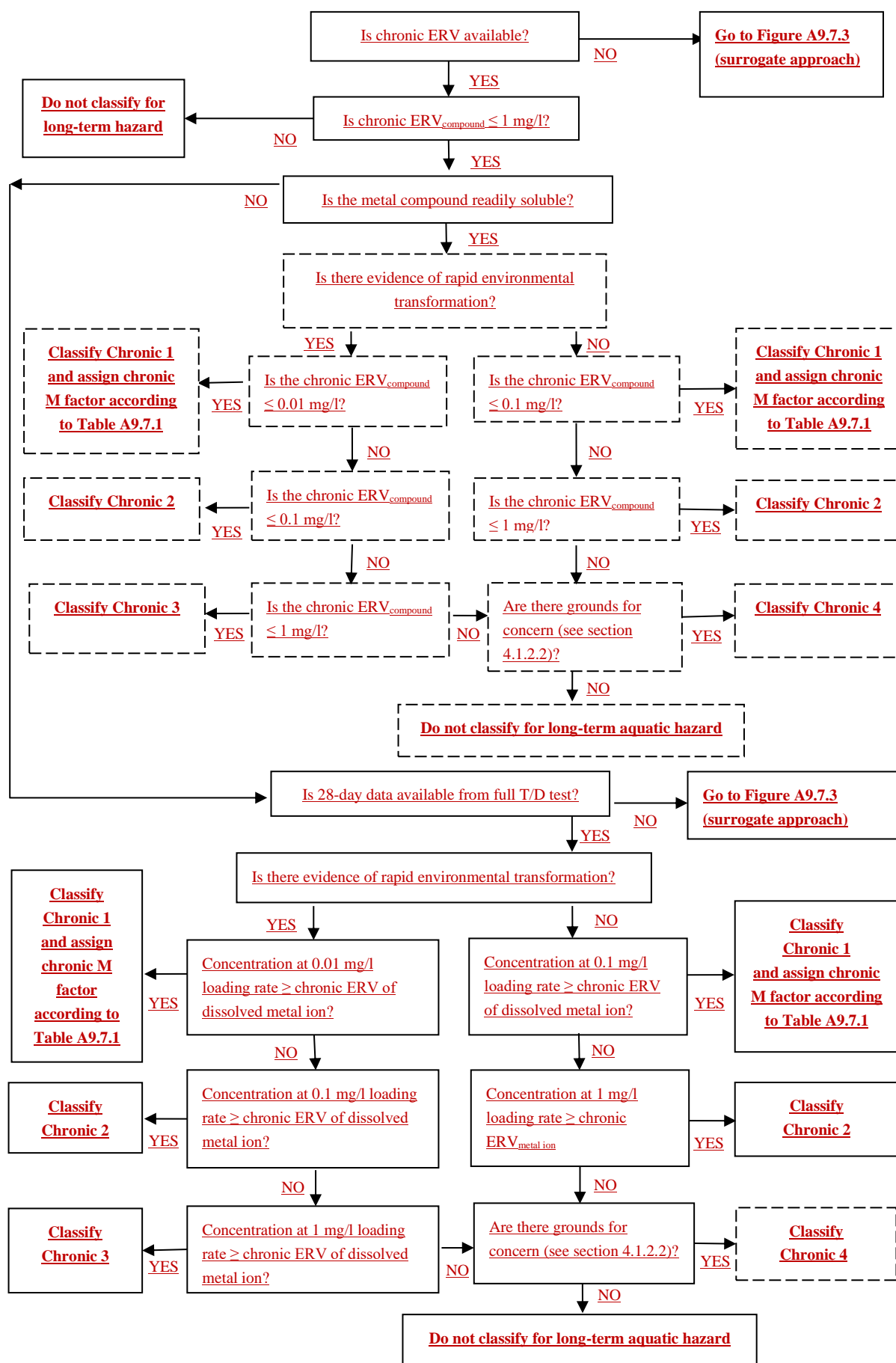
(a)   Category Chronic 1 if the chronic ERV$_{compound}$ is equal to or less than 0.1 mg/l (0.01 mg/l if there is evidence of rapid environmental transformation). Assign a chronic M factor according to Table A9.7.1;

(b)   Category Chronic 2 if the chronic ERV$_{compound}$ is equal to or less than 1 mg/l (0.1 mg/l if there is evidence of rapid environmental transformation);

(c)   Category Chronic 3 if the chronic ERV$_{compound}$ is equal to or less than 1 mg/L and there is evidence of rapid environmental transformation;

(d)   Category Chronic 4 if the data available do not allow classification under the formal criteria but there are nevertheless some grounds for concern (see section 4.1.2.2)

Poorly soluble metal compounds: Consideration must be given to the data available on the rate and extent to which these ions can be generated from the metal compound. For such rate and extent data, to be valid and useable, they should have been generated using the Transformation/Dissolution Protocol for a 28-day period. Where such 28-day T/D p data are unavailable, the surrogate approach should be used (see section A9.7.5.3.2.2). Where 28-day T/D data are available, then classify the poorly soluble metal compound as:

(a)   Category Chronic 1 if the dissolved metal ion concentration obtained at a loading rate of 0.1 mg/l (0.01 mg/l if there is evidence of rapid environmental transformation) is greater than or equal to the chronic ERV of the dissolved metal ion. Assign a chronic M factor according to Table A9.7.1;

(b)   Category Chronic 2 if the dissolved metal ion concentration obtained at a loading rate of 1 mg/l (0.1 mg/l if there is evidence of rapid environmental transformation) is greater than or equal to the chronic ERV of the dissolved metal ion.;

(c)   Category Chronic 3 if the dissolved metal ion concentration obtained at a loading rate of 1 mg/l is greater than or equal to the chronic ERV of the dissolved metal ion and there is evidence of rapid environmental transformation;

(d)   Category Chronic 4 if the data available do not allow classification under the formal criteria but there are nevertheless some grounds for concern (see section 4.1.2.2)

Do not classify the poorly soluble metal compound for long-term (chronic) aquatic hazard if the dissolved metal ion concentration obtained from the 28-day Transformation/Dissolution test at a loading rate of 1 mg/l is less than the chronic ERV of the dissolved metal ion.

Figure A9.7.5: Classification strategy for determining long-term aquatic hazard of metal compounds on the basis of chronic data

Is chronic ERV available?

NO → **Go to Figure A9.7.3 (surrogate approach)**

YES ↓

Is chronic ERV$_{compound}$ ≤ 1 mg/l?

NO → **Do not classify for long-term hazard**

YES ↓

Is the metal compound readily soluble?

NO →

YES ↓

Is there evidence of rapid environmental transformation?

YES ↓ | NO ↓

Is the chronic ERV$_{compound}$ ≤ 0.01 mg/l?

YES → **Classify Chronic 1 and assign chronic M factor according to Table A9.7.1**

NO ↓

Is the chronic ERV$_{compound}$ ≤ 0.1 mg/l?

YES → **Classify Chronic 2**

NO ↓

Is the chronic ERV$_{compound}$ ≤ 1 mg/l?

YES → **Classify Chronic 3**

Is the chronic ERV$_{compound}$ ≤ 0.1 mg/l?

YES → **Classify Chronic 1 and assign chronic M factor according to Table A9.7.1**

NO ↓

Is the chronic ERV$_{compound}$ ≤ 1 mg/l?

YES → **Classify Chronic 2**

NO ↓

Are there grounds for concern (see section 4.1.2.2)?

NO → [Is the chronic ERV$_{compound}$ ≤ 1 mg/l?]

YES → **Classify Chronic 4**

NO ↓

Do not classify for long-term aquatic hazard

Is 28-day data available from full T/D test?

NO → **Go to Figure A9.7.3 (surrogate approach)**

YES ↓

Is there evidence of rapid environmental transformation?

YES ↓ | NO ↓

Concentration at 0.01 mg/l loading rate ≥ chronic ERV of dissolved metal ion?

YES → **Classify Chronic 1 and assign chronic M factor according to Table A9.7.1**

NO ↓

Concentration at 0.1 mg/l loading rate ≥ chronic ERV of dissolved metal ion?

YES → **Classify Chronic 2**

NO ↓

Concentration at 1 mg/l loading rate ≥ chronic ERV of dissolved metal ion?

YES → **Classify Chronic 3**

Concentration at 0.1 mg/l loading rate ≥ chronic ERV of dissolved metal ion?

YES → **Classify Chronic 1 and assign chronic M factor according to Table A9.7.1**

NO ↓

Concentration at 1 mg/l loading rate ≥ chronic ERV$_{metal\ ion}$

YES → **Classify Chronic 2**

NO ↓

Are there grounds for concern (see section 4.1.2.2)?

NO →

YES → **Classify Chronic 4**

NO ↓

Do not classify for long-term aquatic hazard

A9.7.5.3.3.2   The surrogate approach

Where appropriate chronic toxicity data and/or T/D data are not available, but the metal compound is classified for short-term (acute) aquatic hazard, then the metal compound is classified according to the surrogate approach. The surrogate approach for metal compounds is identical to that for metals (see section A9.7.5.2.2.2).

A9.7.5.4   *Particle size and surface area*

A9.7.5.4.1   Particle size, or moreover surface area, is a crucial parameter in that any variation in the size or surface area tested may cause a significant change in the levels of metals ions released in a given time-window. Thus, this particle size or surface area is fixed for the purposes of the transformation test, allowing the comparative classifications to be based solely on the loading level. Normally, the classification data generated would have used the smallest particle size marketed to determine the extent of transformation. There may be cases where data generated for a particular metal powder is not considered as suitable for classification of the massive forms. For example, where it can be shown that the tested powder is structurally a different material (e.g. different crystallographic structure) and/or it has been produced by a special process and cannot be generated from the massive metal, classification of the massive can be based on testing of a more representative particle size or surface area, if such data are available. The powder may be classified separately based on the data generated on the powder. However, in normal circumstances it is not anticipated that more than two classification proposals would be made for the same metal.

A9.7.5.4.2   Metals with a particle size smaller than the default diameter value of 1 mm can be tested on a case-by-case basis. One example of this is where metal powders are produced by a different production technique or where the powders give rise to a higher dissolution (or reaction) rate than the massive form leading to a more stringent classification.

A9.7.5.4.3   The particle sizes tested depend on the substance being assessed and are shown in the table below:

Type	Particle size	Comments
Metal compounds	Smallest representative size sold	Never larger than 1 mm
Metals – powders	Smallest representative size sold	May need to consider different sources if yielding different crystallographic/morphologic properties
Metals – massive	1 mm	Default value may be altered if sufficient justification

Massive forms will usually be tested as 1 mm particles. Alternatively, the T/D testing of materials with different surface areas may result in highly reliable dissolution kinetic equations that allows to define the "Critical Particle Diameter" (CPD) for appropriate loadings for the acute and long-term hazard assessment.

A9.7.5.4.4   For some forms of metals, it may be possible, using the Transformation/Dissolution Protocol (OECD 2001), to obtain a correlation between the concentration of the metal ion after a specified time interval as a function of the surface area loadings of the forms tested. Such correlations should be established for the relevant pH ranges as specified in the Transformation/Dissolution protocol. In such cases, it could then be possible to estimate the level of dissolved metal ion concentration of the metal with different particles, using the critical surface area approach (Skeaff *et. al.*, 2000) (See reference in appendix VI, part 5, Metals and metal compounds). ~~That is, f~~From this correlation and a linkage to the appropriate toxicity data at corresponding pH level, it ~~may be~~ is possible to determine a ~~critical surface area~~ "Critical Surface Area" (CSA) of the substance that delivers the L(E)C$_{50}$ to the dissolution medium and then to convert the ~~critical surface area~~ CSA to ~~the low, medium and high~~ a Critical Particle Diameter (CPD) (see example). This CPD at appropriate mass loadings ~~used in~~ for acute and long-term hazard ~~identification. While this approach is not normally used for classification it may provide useful information for labelling and downstream decisions.~~ assessment can then be used to:

-        determine the classification category of powders based on the finest representative powder on the market and

-        determine an accurate classification of the massive metal by applying a 1 mm (default) diameter.

Within the CSA Approach an equation is developed to predict metal ion release (based on previously measured metal ion release from different loadings of the metal), which is correlated to measured surface area, and a corresponding calculated equivalent particle diameter. The basis of the CSA Approach is that the release of metal ions is

dependent on the surface area of the substance, with this release being predictable once the relationship has been established. The CSA as the surface area loading (mm²/l) to a medium that delivers a selected ecotoxicity reference value to that medium. The term SA is the measured specific surface area (m²/g) of the metal sample. The measured specific critical surface area (SA$_{crit}$) (m²/g) is the measured specific surface areas for the corresponding low, medium and high loadings which are associated with the respective acute and long-term aquatic toxicity classification categories in the classification scheme for metals and metal compounds. A typical equation for this relationship for a given substance, aquatic medium, pH and retention time is:

$$log(C_{Me(aq)}, mg/l) = a + b \; log(A_{meas})$$

$C_{Me(aq)}$ = total dissolved concentration of metal ion (mg/l) at a particular length of test time (i.e. 168 hours for short-term hazard assessment) under certain conditions (i.e. pH, specified medium, etc.), as determined by Transformation/Dissolution testing of different surface area loadings

a, b = regression coefficients

A_{meas} = initial surface area loading (mm²/l) [equals (measured specific surface area, SA, in m²/g) X (substance mass loading in g/l) X 10^6], where SA was measured with the BET nitrogen adsorption-desorption technique.

A9.7.5.4.5   Setting M factors for metals and inorganic metal compounds

For the hazard class "Hazardous to the Aquatic Environment", where the application of the normal cut-off values or concentrations limits may lead to an "under-classification" of the mixture, the M factor concept is used. The M factors are used in application of the summation method for the classification of mixtures containing substances that are classified as very ecotoxic. The concept of M factors has been established to give an increased weight to very toxic substances when classifying mixtures. This ensures that the magnitude of their toxicity is not lost in the derivation of the mixtures classification. M factors are only applicable to the concentration of a substance classified as hazardous to the aquatic environment (Categories Acute 1 and Chronic 1) and are used to derive by the summation method the classification of a mixture in which the substance is present. They are, however, substance specific and it is important that they are established when classifying substances. It is important to note that separate Acute and Chronic M factors should be derived and these may not necessarily be of the same value, depending how each was determined (e.g. the basis of the separate acute and chronic ERV values).
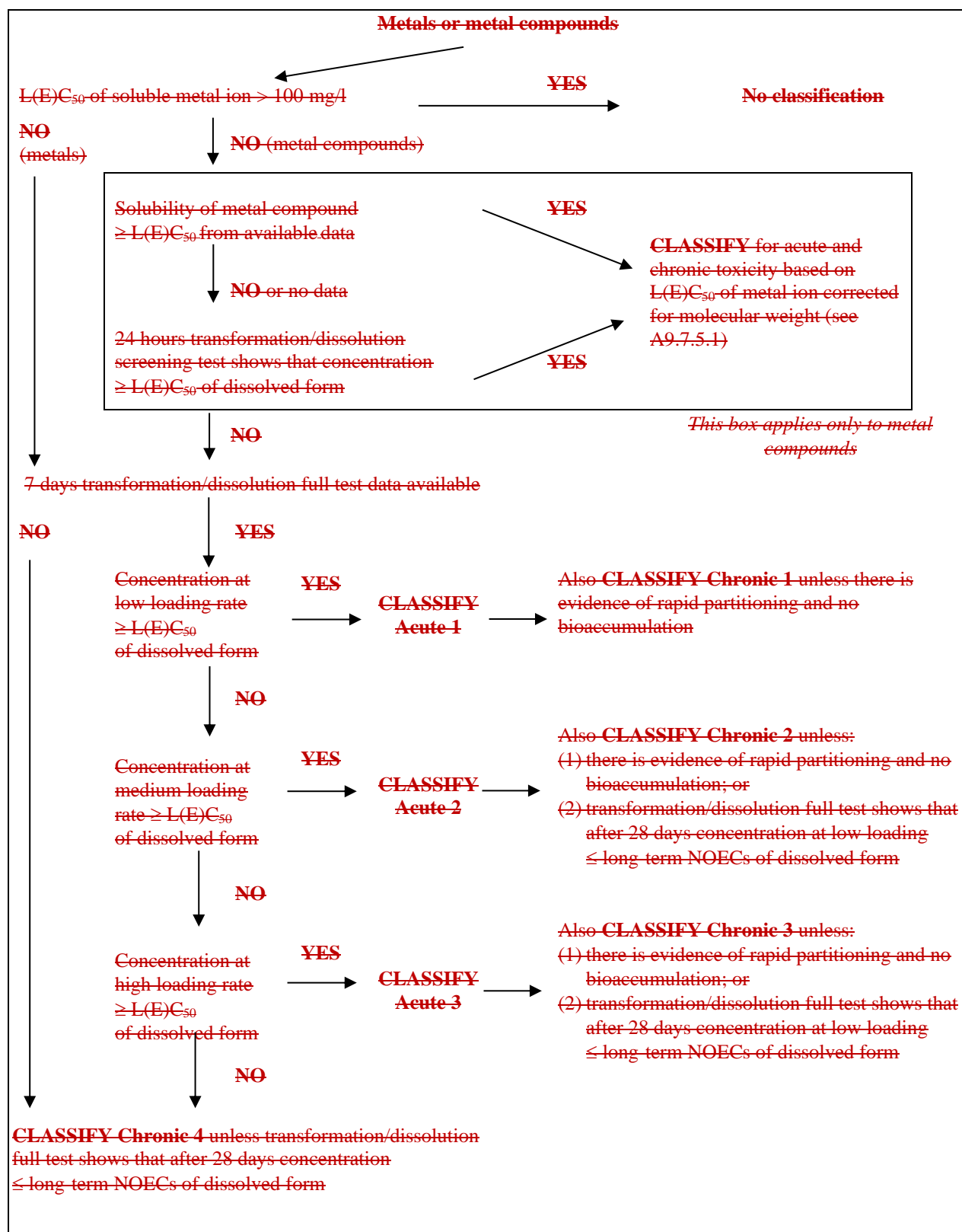
For readily soluble metal compounds M factors are applied as for organic substances (see table A9.7.1).

For poorly soluble metal compounds and metals M factors are applied based on the ratio of the dissolved metal ion concentration (obtained from T/D testing after respectively 7 and 28 days for the loading that was used to establish the classification of Category Acute 1 or Category Chronic 1) and the ERV of the dissolved metal ion. If that ratio is below 10 then an M factor of 1 is applied; if that ratio is ≥ 10 and < 100 then an M factor of 10 is applied; if that ratio is ≥ 100 and < 1000 then an M factor of 100 is applied… (continue this approach in factor 10 intervals).

Table A9.7.1 M factors for readily soluble metal compounds

Acute ERV$_{compound}$ (mg/L)	Acute Multiplication factors (M)
0.1 < Acute ERV ≤ 1	1
0.01 < Acute ERV ≤ 0.1	10
0.001 < Acute ERV ≤ 0.01	100
0.0001 < Acute ERV ≤ 0.001	1000
Continue in factor 10 intervals	

Chronic ERV$_{compound}$ (mg/L)	Chronic Multiplication factors (M)	
	No rapid environmental transformation	Rapid environmental transformation
0.01 < Chronic ERV ≤ 0.1	1	-
0.001 < Chronic ERV ≤ 0.01	10	1
0.0001 < Chronic ERV ≤ 0.001	100	10
0.00001 < Chronic ERV ≤ 0.0001	1000	100
Continue in factor 10 intervals		

Figure A9.7.1: Classification strategy for metals and metal compounds

Metals or metal compounds

L(E)C$_{50}$ of soluble metal ion > 100 mg/l → **YES** → **No classification**

NO (metals)

NO (metal compounds)

This box applies only to metal compounds

Solubility of metal compound ≥ L(E)C$_{50}$ from available data → **YES**

NO or no data

24 hours transformation/dissolution screening test shows that concentration ≥ L(E)C$_{50}$ of dissolved form → **YES**

→ **CLASSIFY** for acute and chronic toxicity based on L(E)C$_{50}$ of metal ion corrected for molecular weight (see A9.7.5.1)

NO

---

7 days transformation/dissolution full test data available

NO   **YES**

Concentration at low loading rate ≥ L(E)C$_{50}$ of dissolved form → **YES** → **CLASSIFY Acute 1** → Also **CLASSIFY Chronic 1** unless there is evidence of rapid partitioning and no bioaccumulation

NO

Concentration at medium loading rate ≥ L(E)C$_{50}$ of dissolved form → **YES** → **CLASSIFY Acute 2** → Also **CLASSIFY Chronic 2** unless:
(1) there is evidence of rapid partitioning and no bioaccumulation; or
(2) transformation/dissolution full test shows that after 28 days concentration at low loading ≤ long-term NOECs of dissolved form

NO

Concentration at high loading rate ≥ L(E)C$_{50}$ of dissolved form → **YES** → **CLASSIFY Acute 3** → Also **CLASSIFY Chronic 3** unless:
(1) there is evidence of rapid partitioning and no bioaccumulation; or
(2) transformation/dissolution full test shows that after 28 days concentration at low loading ≤ long-term NOECs of dissolved form

NO

CLASSIFY Chronic 4 unless transformation/dissolution full test shows that after 28 days concentration ≤ long-term NOECs of dissolved form

Annex 9, APPENDICES I to V *[Unchanged]*

Annex 9, APPENDIX VI

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References

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1.   **Aquatic toxicity [*Unchanged*]**

2.   **Biotic and abiotic degradation [*Unchanged*]**

3.   **Bioaccumulation [*Unchanged*]**

.   **Reference for QSAR** [*Unchanged*]

5.   **Metals and metal compounds**

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ANNEX II

Amendments to Annex 10

"Annex 10

GUIDANCE ON TRANSFORMATION/DISSOLUTION OF METALS AND METAL COMPOUNDS IN AQUEOUS MEDIA[3]

A10.1   Introduction

A10.1.1   This test guidance is designed to determine the rate and extent to which metals and sparingly soluble metal compounds can produce soluble available ionic and other metal-bearing species in aqueous media under a set of standard laboratory conditions representative of those generally occurring in the environment. Once determined, this information can be used to evaluate the short-term and long-term aquatic toxicity of the metal or sparingly soluble metal compound from which the soluble species came. This test guidance is the outcome of an international effort under the OECD to develop an approach for the toxicity testing and data interpretation of metals and sparingly soluble inorganic metal compounds (SSIMs) (reference 1, this annex and section A9.7 of Annex 9). As a result of recent meetings and discussions held within the OECD and EU, tThe experimental work on several metals and metal compounds upon which this Test Guidance is based has been conducted and reported (references 5 to 15, this annex). This test guidance has subsequently also been published as a guidance document by the OECD (reference 16).

A10.1.2   The evaluation of the short-term and long-term aquatic toxicity of metals and sparingly soluble metal compounds is to be accomplished by comparison of (a) the concentration of the metal ion in solution, produced during transformation or dissolution in a standard aqueous medium with (b) appropriate standard eco-toxicity data as determined with the soluble metal salt (acute and chronic values). This document gives guidance for performing the Ttransformation/Ddissolution tests. The strategy to derive an environmental hazard classification using the results of the dissolution/transformation Transformation/Dissolution protocol is not within the scope of this guidance document and-can be found in Annex 9, section A9.7.

A10.1.3   For this test guidance, the transformations of metals and sparingly soluble metal compounds are, within the context of the test, defined and characterized as follows:

(a)   metals, M^0, in their elemental state are not soluble in water but may transform to yield the available form. This means that a metal in the elemental state may react with the media to form soluble cationic or anionic products, and in the process the metal will oxidize, or transform, from the neutral or zero oxidation state to a higher one;

(b)   in a simple metal compound, such as an oxide or sulphide, the metal already exists in an oxidized state, so that further metal oxidation is unlikely to occur when the compound is introduced into an aqueous medium. However, while oxidization state may not change, interaction with the media may yield more soluble forms. A sparingly soluble metal compound can be considered as one for which a solubility product can be calculated, and which will yield small amount of the available form by dissolution. However, it should be recognized that the final solution concentration may be influenced by a number of factors, including the solubility product of some metal compounds precipitated during the transformation/dissolution test, e.g. aluminium hydroxide.

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[3]   *OECD Environment, Health and Safety Publications, Series on Testing and Assessment, No. 29, Environment Directorate, Organisation for Economic Co-operation and Development, April 2001.*

A10.1.4   This test guidance is not applicable to organometal compounds.

A10.2   Principles

A10.2.1   This test guidance is intended to be a standard laboratory Ttransformation/Ddissolution protocol based on a simple experimental procedure of agitating various quantities of the test substance in a pH buffered aqueous medium, and sampling and analysing the solutions at specific time intervals to determine the concentrations of dissolved metal ions in the water. Two different types of tests are described in the text below:

A10.2.2   *Screening Ttransformation/Ddissolution test – sparingly soluble metal compounds*

A10.2.2.1   For sparingly soluble metal compounds, the maximum concentration of total dissolved metal can be determined by the solubility limit of the metal compound or from a screening Ttransformation/Ddissolution test. The intent of the screening test, performed at a single loading, is: to identify those compounds which undergo either dissolution or rapid transformation such that their ecotoxicity potential is indistinguishable from soluble forms, and to verify the pH dependency of the dissolution, in preparation of the full T/D test (See A9.7.2.3).

A10.2.2.2   Sparingly soluble metal compounds, having the smallest representative particle size on the market are introduced into the aqueous medium at a single loading of 100 mg/l. Such dissolution as will occur is achieved by agitation during a 24 hours period. After 24 hours agitation, the dissolved metal ion concentration is measured.

A10.2.3   *Full Ttransformation/Ddissolution test - metals and sparingly soluble metal compounds*

A10.2.3.1   The full Ttransformation/Ddissolution test is intended to determine level of the dissolution or transformation of metals and metal compounds after a certain time period at different loadings of the aqueous phase. Normally massive forms and/or powders are introduced into the aqueous medium at three different loadings: 1, 10 and 100 mg/l. A single loading of 100 mg/l may be used if a significant release of dissolved metal species is not anticipated. Transformation/Ddissolution is accomplished by standardized agitation, without causing abrasion of the particles. The short-term Ttransformation/Ddissolution endpoints are based on the dissolved metal ion concentrations obtained after a 7 days Ttransformation/Ddissolution period. The long-term Ttransformation/Ddissolution endpoint is obtained during a 28 days Ttransformation/Ddissolution test, using a single loading of 1 mg/l, 0.1 mg/l, or 0.01 mg/l depending on the transformation rate.

A10.2.3.2   As pH has a significant influence on Ttransformation/Ddissolution both the screening test and the full test should in principle be carried out at a pH that maximizes the concentration of the dissolved metal ions in solution. With reference to the conditions generally found in the environment a pH range of 6 to 8.5 must be used, except for the 28 day full test where the pH range of 5.5 to 8.5 should be used in order is recommended if technically feasible to take into consideration possible long-term effects on acidic lakes.

A10.2.3.3   As in addition the surface area of the particles in the test sample has an important influence on the rate and extent of transformation/dissolution, powders are tested at the smallest representative particle size as placed on the market, while massives forms are tested at a particle size representative of normal handling and use. A default diameter value of 1 mm should be used in absence of this information. For massive metals, this default may only be exceeded when sufficiently justified. The specific surface area should be determined in order to characterize and compare similar samples. The tested material should also be free from oxidation/corrosion layers due to storage, given the latter may disturb the transformation rate. Appropriate pre-treatment of the samples is recommended.

A10.3   Applicability of the test

This test applies to all metals and sparingly soluble inorganic metal compounds. Exceptions, such as certain water reactive metals, should be justified.

A10.4   Information on the test substance

Substances as placed on the market should be used in the transformation/dissolution tests. In order to allow for correct interpretation of the test results, it is important to obtain the following information on the test substance(s):

(a)   substance name, formula and use on the market;

(b)   physical-chemical method of preparation;

(c)   identification of the batch used for testing;

(d)   chemical characterization: overall purity (%) and specific impurities (% or ppm);

(e)   density (g/cm^3) or specific gravity;

(f)   measured specific surface area (m^2/g)- measured by BET N$_2$ adsorption desorption or equivalent technique, and particle size distribution;

(g)   storage, expiration date;

(h)   known solubility data and solubility products;

(i)   hazard identification and safe handling precautions;

(j)   Safety Data Sheets (SDS) or equivalent.

A10.5   **Description of the test method**

A10.5.1   *Apparatus and reagents*

A10.5.1.1   The following apparatus and reagents are necessary for performing tests:

(a)   pre-cleaned and acid rinsed closed glass sample bottles (A10.5.1.2);

(b)   transformation /dissolution medium (ISO 6341) (A10.5.1.3);

(c)   test solution buffering facilities (A10.5.1.4);

(d)   agitation equipment: orbital shaker, ~~radial impeller,~~ laboratory shaker or equivalent (A10.5.1.5);

(e)   appropriate filters (e.g. 0.2 μm Acrodisc) or centrifuge for solids-liquid separation (A10.5.1.10~~.7~~) ~~acrodisc~~ filter should be flushed at least three times with fresh medium to avoid ~~elevetaed~~ elevated trace metals in the sample at time 0;

(f)   means to control the temperature of the reaction vessels to ± 1.5°C in the range 20-23 °C, such as a temperature-controlled cabinet or a water bath;

(g)   syringes and/or automatic pipettes;

(h)   pH meter showing acceptable results within + 0.2 pH units;

(i)   dissolved oxygen meter, with temperature reading capability;

(j)   thermometer or thermocouple; and

(k)   analytical equipment for metal analysis (e.g. atomic adsorption spectrometry, inductively coupled ~~axial~~ plasma mass spectrometry) of acceptable accuracy, preferably with a limit of quantification (LOQ) five times lower than the lowest chronic ecotoxicity reference value or the lowest acute ecotoxicity reference value if only a 7-day test is conducted;

A10.5.1.2   All glass test vessels must be carefully cleaned by standard laboratory practices, acid-cleaned (e.g. HCl or aqua regia) and subsequently rinsed with de-ionized water. Specific attention to the type of glassware is required for metals that can be released from the glass. The test vessel volume and configuration (e.g. one- or

two-litre reaction kettles) should be sufficient to hold 1 or 2 l of aqueous medium without overflow during the agitation specified. If air buffering is used (tests carried out at pH 8), it is advised to increase the air buffering capacity of the medium by increasing the headspace/liquid ratio (e.g. 1 l medium in 2.8 l flasks).

A10.5.1.3   A reconstituted standard water based on ISO 6341 should be used [4], as the standard Ttransformation/Ddissolution medium. The medium should be sterilized by filtration (0.2 μm) before use in the tests. The chemical composition of the standard Ttransformation/Ddissolution medium (for tests carried out at pH 8) is as follows:

$NaHCO_3$	:	65.7 mg/l
KCl	:	5.75 mg/l
$CaCl_2.2H_2O$	:	294 mg/l
$MgSO_4.7H_2O$	:	123 mg/l

For tests carried out at lower or higher pH values, adjusted chemical compositions are given in A10.5.1.7.

A10.5.1.4   The concentration of total organic carbon in the medium before adding the substance, should not exceed 2.0 mg/l.

A10.5.1.5   In addition to the fresh water medium, the use of a standardized marine test medium may also be considered when the solubility or transformation of the metal or metal compound is expected to be significantly affected by the high chloride content or other unique chemical characteristics of marine waters and when toxicity test data are available on marine species. When marine waters are considered, the chemical composition of the standard marine medium is as follows:

NaF	:	3mg/l
$SrCl_2.6H_2O$	:	20 mg/l
H_3BO_3	:	30 mg/l
KBr	:	100 mg/l
KCl	:	700 mg/l
$CaCl_2.2H2O$	:	1.47g/l
Na_2SO_4	:	4.0 g/l
$MgCl_2.6H2O$	:	10.78 g/l
NaCl	:	23.5 g/l
$Na_2SiO_3.9H2O$	:	20 mg/l
$NaHCO_3$	:	200 mg/l

The salinity should be 34 ± 0.5 g/kg and the pH should be 8.0 ± 0.2. The reconstituted salt water should also be stripped of trace metals (from ASTM E 729-96).

A10.5.1.6   The transformation/dissolution tests are to be carried out at a pH that maximizes the concentration of the dissolved metal ions in solution within the prescribed pH range. A pH-range of 6 to 8.5 must be used for the screening test and the 7-day full test, and a range of 5.5 to 8.5 for the 28 day full test (A10.2.3.2).

A10.5.1.7   Buffering at pH 8 may be established by equilibrium with air, in which the concentration of CO_2 provides a natural buffering capacity sufficient to maintain the pH within an average of $\pm$ 0.2 pH units over a period of one week (reference 7, Annex 10). An increase in the headspace/liquid ratio can be used to improve the air buffering capacity of the medium.

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[4]   *For hazard classification purposes the results of the dissolution/transformation Transformation/Dissolution protocol are compared with existing ecotoxicity data for metals and metal compounds. However, for purposes such as data validation, there might be cases where it may be appropriate to use the aqueous medium from a completed transformation test directly in an OECD 202 and 203 daphnia and fish ecotoxicity test. If the $CaCl_2.2H_2O$ and $MgSO_4.7H_2O$ concentrations of the transformation medium are reduced to one-fifth of the ISO 6341 medium, the completed transformation medium can also be used (upon the addition of micronutrients) in an OECD 201 algae ecotoxicity test.*

For pH adjustment and buffering down to pH 7 and 6 and up to pH 8 and 8.5, Table A10.1 shows the recommended chemical compositions of the media, as well as the CO_2 concentrations in air to be passed through the headspace, and the calculated pH values under these conditions.

Table A10.1: Recommended chemical composition of testing medium

Chemical composition of medium	$NaHCO_3$	6.5 mg/l	12.6 mg/l	64.75 mg/l	194.25 mg/l
	KCl	0.58 mg/l	2.32 mg/l	5.75 mg/l	5.74 mg/l
	$CaCl_2.2H_2O$	29.4 mg/l	117.6 mg/l	294 mg/l	29.4 mg/l
	$MgSO_4.7H_2O$	12.3 mg/l	49.2 mg/l	123.25 mg/l	123.25 mg/l
CO_2 concentration (balance is air) in test vessel		0.50 %	0.10 %	0.038 % (air)	0.038 %(air)
Calculated pH		6.09	7.07	7.98	8.5
the $CaCl_2.2H_2O$ and $MgSO_4.7H_2O$ concentrations of the transformation medium are reduced to one-fifth of the ISO 6341 medium, the completed transformation medium can also be used (upon the addition of micronutrients) in an OECD 201 algae ecotoxicity test.					

NOTE 1: *The pH values were calculated using the FACT (Facility for the Analysis of Chemical Thermodynamics) System (http://www.crct.polymtl.ca/fact/fact.htm).*

NOTE 2: *While the protocol was only validated for the pH range 6.0-8.0, this table does not prevent attaining pH 5.5. Composition for pH 8.5 has not been verified experimentally in presence of metal.*

NOTE 3: *Equilibration via headspace is recommended given CO2 gas bubbling does not guarantee equal distribution between different test vessels.*

A10.5.1.8 Alternative equivalent buffering methods may be used if the influence of the applied buffer on the chemical speciation and transformation rate of the dissolved metal fraction would be minimal. pH should not be adjusted during the test using an acid or alkali.

A10.5.1.9 During the full Transformation/Dissolution test, agitation should be used which is sufficient to maintain the flow of aqueous medium over the test substance while maintaining the integrity of the surface of the test substance and of any solid reaction product coatings formed during the test. For 1 *l* of aqueous medium, this may be accomplished by the use of:

(a) a radial impeller set at 200 r.p.m., with blades deployed 5 cm from the bottom of a 1 *l* reaction kettle. The radial impellers consist of two fixed polypropylene blades of dimensions 40 mm width by 15 mm height on a PVC coated steel rod 8 mm diameter and 350 mm long; or

(b) a 1.0 to 3.0 *l* flask capped with a rubber stopper and placed on an orbital or laboratory shaker set at 100 r.p.m.

Other methods of gentle agitation may be used provided they meet the criteria of surface integrity and homogeneous solution.

A10.5.1.10 The choice of solids-liquid separation method depends on whether adsorption of soluble metal ions on filters occurs and whether or not a suspension is generated by the agitation prescribed in A10.5.1.9, which will in turn depend on particle size distributions, the shape of the particles and particle density. For solids of density greater than approximately 6 g/cm^3 and particle size ranges as low as 50 % < 8 µm, experience has shown that the gentle agitation methods prescribed in A10.5.1.9 are unlikely to result in suspensions. Hence, filtration of a sample through e.g. a 25 mm diameter 0.2 µm hydrophilic polyethersulphone membrane syringe filter (as an option, overlain by a 0.8 µm prefilter) will result in a solution essentially free of solids. Alternative techniques may be considered in case of finer particles. If there is concern that particles will remain in suspension, then filtration efficiency should be checked prior to any testing. Options that could be considered to increase filtration

efficiency include centrifugation followed by filtration, or waiting for about 5 minutes for the suspension to settle. However, in the event that suspensions occur, stopping the agitation to allow the suspension to settle for about 5 minutes prior to taking a solution sample may be useful.

A10.5.2 *Prerequisites*

A10.5.2.1 *Analytical method*

A suitable validated analytical method for the total dissolved metal analysis is essential to the study. The analytical detection limit should preferably be 5 times lower than the appropriate chronic or long term ecotoxicity reference value, orfrom the acute exotoxicity tests reference value in case a 7-day test is conducted.

The following analytical validation aspects are at a minimum to be reported:

(a)   detection and quantification limit of the analytical method;

(b)   analytical linearity range within the applicable analytical range;

(c)   a blank run consisting of transformation medium (this can be done during the tests);

(d)   matrix effect of the transformation medium on the measurement of the dissolved metal ion;

(e)   mass balance (%) after completion of the transformation test;

(f)   reproducibility of the analysis;

(g)   adsorptive properties of the soluble metal ions on the filters (if filtration is used for the separation of the soluble from the solid metal ion).

A10.5.2.2 *Determination of the appropriate pH of the dissolution medium*

If no relevant literature data exist, a preliminary screening test may need to be carried out in order to ensure that the test is performed at a pH maximizing Ttransformation/Ddissolution within the pH range described in A10.2.3.2 and A10.5.1.6.

A10.5.2.3 *Reproducibility of transformation data*

A10.5.2.3.1   For a standard set-up of three replicate test vessels and two replicate samples per test vessel at each sampling time, it is reasonable to anticipate that for a constant loading of a substance, tested in a narrow particle size (e.g. 37 - 44 µm) and total surface area range, the within-vessel variation in transformation data should be < 10 % and the between-vessel variation should be < 20 % (reference 5, this annex). This variability may be higher at the lower loadings.

A10.5.2.3.2   To estimate the reproducibility of the transformation test, some Guidance is given in the following. The results can be used to eventually improve on reproducibility by adjusting the final test set-up through varying the number of replica test vessels and/or replica samples or further screening of the particles. The preliminary tests also allow for a first evaluation of the transformation rate of the tested substance and can be used to establish the sampling frequency.

A10.5.2.3.3   In preparing the transformation/dissolution medium, the pH of the medium should be adjusted to the desired pH (air buffering or CO_2 buffering) by agitation for about half an hour to bring the aqueous medium into equilibrium with the buffering atmosphere. At least three samples (e.g. 10 - 15 ml) are drawn from the test medium prior to addition of the substance, and the dissolved metal concentrations are measured as controls and background.

At least five test vessels, containing the metal or metal compound (e.g.100 mg solid/l medium), are agitated as described in A10.5.1.9 at a temperature ± 1.5°C in the range 20 - 23 °C, and triplicate samples are taken by syringe from each test vessel after 24 hours. The solid and solution are separated by membrane filter as

described in A10.5.1.10, the solution is acidified with one or two drops of trace metal grade HNO_3 with the target pH 1 and analyzed for total dissolved metal concentration.

A10.5.2.3.4 The within-test vessel and between-test vessel means and coefficients of variation of the measured dissolved metal concentrations are calculated.

A10.5.2.3.5 To ensure reproducibility of transformation data, it is recommended that:

(a) new laboratories use a training set;

(b) one metal powder with specified surface conditions be used as standard control; and

(c) one or two laboratories be responsible for reference chemicals.

It may be necessary is a requirement to check the specific surface areas of the powder samples.

A10.5.3 *Test performance*

A10.5.3.1 *Screening Transformation/Dissolution screening test – sparingly soluble metal compounds*

A10.5.3.1.1 After dissolution medium is prepared, add the medium into at least three test vessels (number of test vessels depend on the reproducibility obtained during the preliminary test). After a half-hour of agitation to bring the aqueous medium into equilibrium with the atmosphere or buffering system (paras. A10.5.1.6 to A10.5.1.8), the pH, temperature and dissolved O_2 concentrations of the medium are measured. Then at least two 10 - 15 ml samples are taken from the test medium (prior to addition of the solids test material) and the dissolved metal concentration measured as controls and background.

A10.5.3.1.2 The metal compound is added to the test vessels at a loading of 100 mg/l and the test vessels are covered and agitated rapidly and vigorously (e.g. on an orbital shaker at 200 rpm, if feasible). After the 24 hours agitation, the pH, temperature and dissolved O_2 concentrations are measured in each test vessel, and two to three solution samples are drawn by syringe from each test vessel and the solution is passed through a membrane filter as described in A10.5.1.10 above, acidified (e.g. 1 % HNO_3) and analysed for total dissolved metal concentration.

A10.5.3.2 *Full Transformation/Dissolution test - metals and metal compounds*

A10.5.3.2.1 Repeat A10.5.3.1.1

A10.5.3.2.2 For 7-day test, substance loadings of 1, 10 and 100 mg/l, respectively, are added to the test vessels (number of which depends on the reproducibility as established in sub-section A10.5.2.3), containing the aqueous medium. The test vessels are closed (but allowing for equilibration with air if required) and agitated as described in A10.5.1.9. If a 28-day test is to be conducted, then the loading may be 0.01 mg/l, 0.1 mg/l or 1 mg/l depending on the transformation rate. Tthe test with 1 mg/l loading may be extended to 28 days, provided that the same pH value is to be chosen for both 7 day and 28-day tests. However, since The 7-day tests are only conducted at pH ranges of 6 and higher, separate 28-day tests are neededup to 8.5, while a somewhat broader cover the pH range of between5.5 and 6to 8.5 is recommended if technically feasible for the 28-day tests. It may also be useful to include a A concurrent control test with no substance loaded (i.e. a blank test solution) is required. At established time intervals (e.g. 2 hours, 6 hours, 1, 4 and 7 days for the short-term test and additionally at e.g. 14, 21 and 28 days for the long-term test), the temperature, pH and dissolved O_2 concentrations are measured in each test vessel, and at least two samples (e.g. 10 - 15 ml) are drawn by syringe from each test vessel. The solid and dissolved fractions are separated as per A10.5.1.10 above. The solutions are acidified (e.g. 1% HNO_3) and analysed for dissolved metal concentration. After the first 24 hours, the solution volumes should be replenished with a volume of fresh dissolution medium equal to that already drawn. Repeat after subsequent samplings. The maximum total volume taken from the test solutions should not exceed 20 % of the initial test solution volume. The test can be stopped when three subsequent total dissolved metal concentration data points vary no more than 15 %. The maximum duration for the loadings of 10 and 100 mg/l is seven days (the short-term test) and 28 days for the loading of 1 mg/l test medium (the long-term test).

A10.5.4   *Test conditions*

A10.5.4.1   The Transformation/Dissolution tests should be done at a controlled ambient temperature ± 1.5°C in the range 20 – 23 °C.

A10.5.4.2   The Transformation/Dissolution tests are to be carried out within the pH range described in A10.2.3.2 and A10.5.1.6. The test solution pH should be recorded at each solution sampling interval. The pH can be expected to remain constant (± 0.2 units) during most tests, although some short-term pH variations have been encountered at 100 mg/l loadings of reactive fine powders (reference 7, this annex), due to the inherent properties of the substance in the finely divided state.

A10.5.4.3   Above the aqueous medium, the head space provided by the reaction vessel should be adequate in most instances to maintain the dissolved oxygen concentration above about 6.0 mg/l, which is 70 % of the saturation level of 8.5 mg/l. However, in certain instances, reaction kinetics may be limited not by the availability of molecular oxygen in the head space above the solution but by the transfer of dissolved oxygen to, and removal of reaction product away from, the solid-solution interface. In this case, little can be done, other than await the restoration of equilibrium.

A10.5.4.4   To reduce chemical and biological contamination as well as evaporation, the Transformation/Dissolution kinetics must be performed in closed vessels and in the dark, whenever possible.

A10.6   **Treatment of the results**

A10.6.1   *Screening test*

The mean dissolved metal concentrations at 24 hours are calculated (with confidence intervals).

A10.6.2   *Full test: Determination of the extent of Transformation/Dissolution*

A10.6.2.1   *Short-term test*

The dissolved metal concentrations, measured during the different short-term (7 days) tests, are plotted versus time, and the Transformation/Dissolution kinetics may be determined, if possible. The following kinetic models could be used to describe the Transformation/Dissolution curves:

(a)   Linear model:

C_t = $C_0 + kt$, mg/l

where:

C_0 =   initial total dissolved metal concentration (mg/l) at time t = 0;
C_t =   total dissolved metal concentration (mg/l) at time t;
k   =   linear rate constant, mg/l-days.

(b)   First order model:

C_t = $A (1-e^{(-kt)})$, mg/l

where:

A   =   limiting dissolved metal concentration (mg/l) at apparent equilibrium
        =   constant;
Ct   =   total dissolved metal concentration (mg/l) at time t;
k   =   first order rate constant, 1/days.
(c)   Second order model:
Ct   = $A (1-e^{(-at)}) + B (1-e^{(-bt)})$, mg/l

where:

Ct   =   total dissolved metal concentration (mg/l), at time t;
a   =   first order rate constant, 1/days;

$$b \quad = \quad \text{second order rate constant, 1/days;}$$
$$C \quad = \quad A + B = \text{limiting dissolved metal concentration (mg/l).}$$

(d) Reaction kinetic equation:

$$C_t \quad = \quad a\,[1-e^{-bt} - (c/n)\{1 + (b\,e^{-nt} - n\,e^{-bt})/(n-b)\}], \text{ mg/l}$$

where:

$$C_t \quad = \quad \text{total dissolved metal concentration (mg/l) at time t;}$$
$$a \quad = \quad \text{regression coefficient (mg/l);}$$
$$b,c,d \quad = \quad \text{regression coefficients (1/days);}$$
$$n \quad = \quad c+d.$$

Other reaction kinetic equations may also apply (reference 7 and 8, this annex).

For each replicate vessel in the transformation test, these model parameters are to be estimated by regression analyses. The approach avoids possible problems of correlation between successive measurements of the same replicate. The mean values of the coefficients can be compared using standard analysis of variance if at least three replicate test vessel were used. The coefficient of determination, r^2, is estimated as a measure of the "goodness of fit" of the model.

The release rate may also be expressed relative to the surface area of the test substance (e.g. $\mu g/mm^2$) to allow for a comparison of the release rates between different surface loadings or particle sizes.

A10.6.2.~~1~~2   *Long-term test*

The dissolved metal concentrations, measured from the 1 mg/l loading during the 28-day test, are plotted versus time and the transformation/dissolution kinetics determined, if possible, as described in A10.6.1.

A10.7   Test report

The test report should include (but is not limited to) the following information (see also A10.4 and A10.5.2.1):

(a)   Identification of the sponsor and testing facility;

(b)   Description of the tested substance;

(c)   Description of the reconstituted test medium and metal loadings;

(d)   Test medium buffering system used and validation of the pH used (as per paras. A10.2.3.2 and A10.5.1.6 to A10.5.1.8) description of the analytical method;

(e)   Detailed descriptions of the test apparatus and procedure;

(f)   Preparation of the standard metal solution;

(g)   Results of the method validation;

(h)   Results from the analyses of metal concentrations, pH, temperature, oxygen;

(i)   Dates of tests and analyses at the various time intervals;

(j)   Mean dissolved metal concentration at different time intervals (with confidence intervals);

(k)   Transformation curves (total dissolved metal as a function of time);

(l)   Results from transformation/dissolution kinetics, if determined;

(m)   Estimated reaction kinetic equation, if determined;

(n)   Deviations from the study plan if any and reasons;

(o)   Any circumstances that may have affected the results; and

(p)   Reference to the records and raw data.

Annex 10

APPENDIX

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