RA-RM for TSC35 Guidelines - Final; 23 November 2021 – Best practices

Introduction:

In many cases for the so-called "non-harmonised FCMs" substances, EU approvals are unavailable. In these cases, national legislation, where it exists, is used. For many potential migrants such as polymer production aids and/or aids to polymerisation, non-intentionally added substances (NIAS), etc… there are no harmonised legal provisions for coatings other than a provision in (EU) No 10/2011 (which doesn't apply to coated metal packaging) that it is the responsibility of industry to ensure the safety of the products they place on the market. Industry Risk Assessment can be used in some defined cases to assess and manage risk related to migrants from food contact packaging.

The guidelines are to be applied in cases where specifically permitted by regulation and in order to demonstrate compliance with Art. 3 of the Framework Regulation (EC) No. 1935/2004.

Scope: these guidelines are to support industry Risk Assessment, for food contact light metal packaging. N.B.: Further guidelines from the FCM coating value chain are available, e.g. the guidelines developed by the producers of food contact additives.[1]

The over-arching principles of the Cross-Sector Group[2] guidelines[3], (provided in Annex 1), are followed with the following sections being specific to the FCM metal packaging coating value chain.

1. Risk Assessment (RA) and Risk Management (RM) processes should take into consideration substances in the Food Contact Material/Article (FCM/FCA) including any substances anticipated to be present.

2. Risk Assessment of substances requires a reliable identification. Risk Management are the measures taken at the conclusion of Risk Assessment.

3. Substances which can only be tentatively identified by analysis, and therefore unknown to the risk assessor, are subject to a worst-case consideration regarding their potential risk, using internationally recognized scientific principles. TSC 33 guidelines[4] illustrate how they can be applied.

[1] https://fca.cefic.org/wp-content/uploads/2021/02/FCA_Risk_Assessment_Guidelines_v30-1.pdf
[2] Group formed with all voluntary European associations and industry members in the field of food contact packaging and articles. Membership of the Cross-sector group are given in Annex 3 of TSC35 Coating Guidelines.
[3] Over-arching Principles for Risk Assessment and Risk Management principles for substances
[4] TSC33 https://www.cepe.org/wp-content/uploads//2020/05/TSC33-NIAS-GUIDELINES-May-2019-v1.7.5-1.pdf

4. The ability of these substances to migrate into food under intended and foreseeable conditions of use of the FCM/FCA needs to be assessed. This means that identification of substances and estimation of their likely migration/exposure levels is necessary. This would normally involve NIAS screening analysis using scientifically sound conditions (e.g. TSC33, ILSI guidelines[5] and publications[6]).

5. If needed, 3rd Party laboratories can assist by getting access to complete product information and then carry out an evaluation and subsequent Risk Assessment independently. Final conclusion remains the responsibility of the business operator who carries out the Risk Assessment.

   3rd Parties are usually accredited by a quality system which guarantee transparency in case of control by Authorities.

6. Toxicological hazard to human health of these migrating substances shall be assessed and this can be achieved by referring to:

   - EU or Member State food contact positive lists.
   - Any available information from ECHA (REACh)[7] or EFSA.

   In the event of a migrating substance not being listed, the following strategies should be considered, as described in the decision tree of the NIAS guidelines [3, 4]:

   - Read across to similar substances for which the toxicity is known.
   - *In-silico* assessments including QSAR (Quantitative Structure-Activity Relationships)[8].
   - TTC[9] (Threshold of Toxicological Concern). This approach can be used for known substances as well as determining a threshold of migration for unknowns (Risk Management - see later).
   - Toxicological testing undertaken by one of the business operators (coating supplier or another actor upstream).

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[5] ILSI guidelines "Guidance on Best Practices on the Risk Assessment of Non Intentionally Added Substances (NIAS) in Food Contact Materials and Articles", 16/07/2015, Koster et Al.,

[6] Forthcoming ILSI publications "Critical review of analytical techniques for identification and quantification of NIAS" and "Best practices for identifying and quantifying unknown migrants from food contact materials".

[7] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment

[8] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/qsar-models#:~:text=Structure%2Dactivity%20relationship%20(SAR),knowledge%20of%20their%20chemical%20structure.

[9] Guidance on the use of the Threshold of Toxicological Concern approach in food safety assessment: 06 June 2019: https://doi.org/10.2903/j.efsa.2019.5708

- Bioassays. Note that these are an emerging science, with the applicability to FCM/FCA migrates still under evaluation[10].

7. If the migrating substance is listed and has a restriction (eg SML, QMA…), the restriction has to be applied.

8. In the event of a migrating substance not being listed: based on the hazard assessment, calculate limits considered safe for human exposure to the substance. For instance, depending on the source of information, they can be: Acceptable Daily Intake (ADI) or Tolerable Daily Intake (TDI), TWI, DNEL, thresholds derived from a TTC[11] approach etc., including those derived from industry assessment.

9. Known allocation factors have to be applied. [12]

10. Setting limits (e.g. limit of migration, concentration of the migrant in the food) which would reflect the maximum tolerable exposure.

11. In case where information is available that an actor has already undertaken the Risk Assessment for an ingredient or a finished coating, the coating supplier doesn't need to undertake a new Risk Assessment. In this case, the coating manufacturer should comply with any restrictions and ensure that relevant information is transmitted to their customers.

12. Where it is not possible to undertake a full Risk Assessment (e.g. incomplete identity), the use of TTC[11] can assist Risk Assessment and Risk Management. The following decision tree can be used:

    - Substances are grouped according to the Cramer classification. The TTC values for Cramer Classes I, II and III are 30, 9 and 1.5 µg/kg bw per day (1800, 540 and 90 µg/person/day, respectively).
    - For organophosphates or carbamates, the relevant TTC value is 0.3 µg/kg bw per day (18 µg/person/day).
    - Presence of substances that have the potential to be DNA-reactive mutagens and/or carcinogens needs to be ruled out based on the weight of evidence or other

[10] https://ilsi.eu/publication/value-and-limitation-of-in-vitro-bioassays-to-support-the-application-of-the-threshold-of-toxicological-concern-to-prioritise-unidentified-chemicals-in-food-contact-materials/.

[11] Barlow S. (2005), Threshold of Toxicological Concern (TTC), ILSI Europe Monograph.

[12] In some but not all cases additional sources of exposure may be known and these need to be considered.

tests. Otherwise the relevant TTC value is 0.0025 µg/kg body weight (bw) per day (0.15 µg/person/day).

- Similarly, for some substances the TTC concept cannot be applied[13]. Presence of those substances needs to be ruled out for TTC to be applicable.

The objective is to check if Cramer Class III can be used safely. This would give an exposure limit of 1.5 µg/kg body weight/day. If it is demonstrated that substances where Cramer Classification cannot be used [13] are absent, then a Cramer Class III approach[10] can be used.

13. Perform a compliance assessment and document using worst case calculations, analytical testing, etc., which show that, under defined conditions of use (time, temperature, foodstuffs, etc), any exposure/migration limits are not exceeded.
14. Define conditions and limitations of use for the customer based on the compliance assessment carried out. If relevant, communicate restrictions on foodstuffs (e.g. not for fatty foodstuffs or acidic foodstuffs).
15. Ensure that the conditions of processing and usage conform to those defined in the Risk Assessment and risk management and are transferred down the supply chain. This whole process needs to be documented and used in any supporting documentation.

The information transferred from the coating supplier to the can maker relies on information received from the coating manufacturer's suppliers and customers. The amount and value of this information can vary widely. In the case where it is technically not feasible to generate desired data, the coating supplier uses worst-case assumption or expert judgement.

[13] Substances which are not represented in the database or are outside the domain of applicability include:

- Inorganic substances
- Proteins
- Nanomaterials
- Radioactive substances
- Organosilicon substances
- Metals in elemental, ionic or organic form. However, in the case of organic salts, where the counter ion is an essential metal (e.g. sodium), the Scientific Committee recommends that the TTC approach could be applied to the organic ion.
- Substances with special properties:
- High potency carcinogens: aflatoxin-like, azoxy- or *N*-nitroso substances and benzidines
- Steroids
- Substances with a potential for bioaccumulation (see EFSA Scientific Committee 2012b, Section 4.4.2.4) This includes substances like polyhalogenated-dibenzodioxins, -dibenzofurans and -biphenyls.
- substances not eligible for application of Cramer class III bear structural features triggering specific biological mechanisms and/or activities and warrant more severe restrictions. These substances include dioxins, organophosphorus and direct DNA reactive mutagenic carcinogens, which are associated respectively with activation of steroid nuclear receptors, activation of arylhydrocarbon receptor, acetylcholinesterase inhibition and mutagenicity.

Conclusion:

The ideal situation is to get full set of data including an independent assessment by an authority for every chemical substance. In the absence of a full EU FCM harmonization with specific provisions for all FCMs, pragmatic scientific-based principles and approaches are required in the interim to comply with the EU FCM Framework Regulation.

Industry Risk Assessment using internationally recognized approaches consists of using all information available.

If new data become available, then it is necessary to review existing Risk Assessments and update accordingly if necessary. It is the responsibility of the business operator who carries out the Risk Assessment to keep it updated.

Annex 1 - CSG RA/RM over-arching principles

CROSS-SECTOR GROUP FOOD CONTACT MATERIALS AND ARTICLES, INCLUDING FOOD AND DRINK INDUSTRY (in short Cross-Sector Group FCMs)

September 2020

Over-arching Principles for Risk Assessment and Risk Management principles for substances

This document lays down the over-arching principles for risk assessment and risk management regarding food contact material and article safety.

It is key to keep in mind that within the complexity of the supply chain, risk assessment/risk management requirements may vary strongly on both content and level of detail. They are dependent on the sector, the position within the value chain and the type of businesses. It is incumbent on each sector/supply chain to develop their own detailed guidelines on how to risk assess and risk manage their materials.

Over-arching principles:

- All known substances potentially migrating from food contact materials (FCM) and articles (FCA), including NIAS, must be risk assessed and risk managed.
- Knowledge of hazard and exposure is required to perform risk assessments.
- Risk = Exposure x Hazard

  The hazard evaluation of substances should normally be undertaken by the first operator in the supply chain that introduces those substances.
- All risk assessors should use internationally recognised scientific principles in their assessment.
- In most cases, the higher up the supply chain, the greater the knowledge of hazard and the lower down the supply chain, the greater the knowledge of exposure. There is an absolute need for the communication of information to be transmitted up and down the supply chain. Individual sectors will detail the information required to be transferred for their purposes and:
  - Should make clear to the next business operator in the supply chain that a risk assessment has been undertaken.
  - Provide sufficient detail to the receiving operator, for the receiving operator to be able to assess if a new risk assessment should be performed.
- The risk assessment and risk management processes used must be documented and form part of the supporting documentation, which must be auditable and available to Competent Authorities on request. Supporting documentation should state which approaches have been used and why.