1 December 2020

Description of uncertainties in the evaluation of restriction proposals (Restriction Task Force[1])

1. Introduction

The REACH review action 10 ("Frame the application of the precautionary principle") asks ECHA's Risk Assessment Committee (RAC) and Socio-economic Analysis Committee (SEAC) to ensure that their opinions on restriction proposals indicate when scientific data do not permit a complete evaluation of risks. This indication should include what information would be needed to address the uncertainties identified, the timeline for generating such information (if possible, at all) and an overview of the potential consequences of inaction. This would enable the European Commission to consider if action is warranted based on the precautionary principle as underpinned in the legal text of REACH. This paper does not cover when or how to implement the precautionary principle in restriction cases.

The REACH review action 10 identified ECHA's approach to *Weight of Evidence/Uncertainty in Hazard Assessment*[2] as well as EFSA's *Guidance on Uncertainty Analysis in Scientific Assessments*[3] as sources of inspiration for increasing transparency in regulatory decision-making (especially with regard to restriction proposals).

In addition, the recommendations of the Restriction Task Force (RTF) have previously proposed:

- Dossier Submitters to highlight key issues in dossiers, including uncertainties and deficiencies and gaps that would limit the possibility to establish that the Union-wide risk is not adequately controlled. Focusing on these elements will facilitate the evaluation of RAC/SEAC. These elements should be clearly marked in the dossier, e.g. by specific subsections.
- Committees to make opinions on the Dossier Submitter's proposal; the absence of key information could be flagged under the heading of 'relevant uncertainties' in the opinion.

2. Actions already taken

As a result of the existing RTF recommendations, new sections on uncertainties were added to the Annex XV restriction dossier template and the Committees Opinion template. However, it was always recognised that supporting guidance on how to fill in those sections would be needed.

Taking into account existing guidance on uncertainty analysis[4], initial considerations on uncertainties have also been added to the Framework for RAC and SEAC in checking conformity and developing opinions on restriction proposals, see: https://echa.europa.eu/documents/10162/13641/rest_framework_of_guiding_principles_agreed_rac_seac_en.pdf.

[1] This paper was developed by the Restriction Task Force, consisting of representatives from Member State Restriction Dossier Submitters, ECHA's Risk Assessment Committee (RAC) and Socio-Economic Committee (SEAC) members and secretariat, and the Commission (DG ENV and DG GROW). It was endorsed at the CARACAL-35 meeting on 31 March 2020.
[2] https://echa.europa.eu/support/guidance-on-reach-and-clp-implementation/formats
[3] https://www.efsa.europa.eu/en/efsajournal/pub/5123
[4] https://echa.europa.eu/documents/10162/13632/information_requirements_r19_en.pdf

The RTF recommends the introduction of standardised wordings for Dossier Submitters and the Committees as a supplement to the previous RTF recommendations as a way to implement REACH review action 10. Guidance including instructions on how to use standardised wording would need to be prepared to this end. This guidance would be voluntary but the requirement to provide more clarity on uncertainties would remain even if the guidance is not used.

3. Next steps/approach

Uncertainty assessment should not be limited to forming scientific opinions but should be integral part of the preparation of a regulatory impact analysis. Hence, any approach developed for the work of the ECHA Committees should also be incorporated into the working practices of Dossier Submitters and cover both risk and other impact elements in the Annex XV restriction dossier – the new guidance would hence need to cover both elements.[5]

An assessment of the data gaps relevant for the decision and the time needed to fill them (if possible) as well as the potential consequences of inaction should be clearly reflected in the Annex XV dossier. The same box approach as used by RAC and SEAC for the analysis of relevant uncertainties should be used to provide considerations on this issue.

If the proposed approach is endorsed by CARACAL, then ECHA secretariat will develop standardised wording for Dossier Submitters and Committees, in the spirit of the EFSA guidance (see Appendix I for some examples). This framework of wording, applied on a case-by-case basis, should clearly state in a qualitative manner the uncertainties for both the hazard/risk assessment as well as for the socio-economic assessment, including the analysis of alternatives:

- What elements are uncertain (such as the hazard, the uses, the emissions, the availability of alternatives and technologies, the estimation of the socio-economic impacts of the restriction) and what is the consequence for the restriction being proposed;
- Why the elements are uncertain (in strive for efficiency only those uncertainties identified as relevant to the outcomes of the case should be further scrutinised);
- What was done by the Dossier Submitter/Committees to reduce a specific element of uncertainty;
- How long would it take and how costly would it be to generate sufficient additional information to fill the identified gap(s);
- How important any remaining uncertainty is to affect the conclusions of the opinion.

Whilst agreeing on standardised wording is likely to be a major task, there is still a merit of such an approach because it would help to streamline the evaluations of RAC and SEAC, help to ensure equal treatment of uncertainties across cases, and foster the public trust in all these working activities.

ECHA secretariat has started to consider how such guidance should look like (see Appendix II for some initial examples). It is proposed to devote some time of the RTF to discuss

[5] Guidance on some of the relevant aspects is already available, e.g. in specific sections on uncertainties in ECHA's SEA guidance https://echa.europa.eu/documents/10162/23036412/sea_restrictions_en.pdf/ and in the EC Better Regulation guidelines http://ec.europa.eu/smart-regulation/guidelines/docs/br_toolbox_en.pdf.

suggestions for standard wording and a streamlined approach for characterising relevant uncertainties found in existing restriction cases, and to test them on one to two restriction cases during 2021. EFSA experts will be invited to explain the guidance and exchange specific cases where the guidance has been applied.

Appendix I: Summary of EFSA guidance on communicating uncertainties

In 2018, EFSA published a comprehensive 'Guidance on uncertainty analysis in scientific assessments'. In addition to the guidance document, EFSA also published a separate paper[6] devoted to how uncertainties in scientific assessment work could be most effectively communicated to different audiences. The paper identifies EFSA's target audiences (largely overlapping with ECHA's target audiences): decision-makers, assessors, industry, non-governmental organisations (NGOs)/specialised media, general media, and informed/concerned citizens. It clusters these audiences "according to their scientific literacy and temporal relationship with EFSA's communications into three broad categories – 'entry', 'informed' and 'technical' levels".

According to EFSA's categorisation, political decision-makers – the "customers" of RAC and SEAC opinions – belong to the 'informed' audience. They are characterised by their thorough knowledge of institutional processes and relationships and their extensive understanding of the EU system, on one hand, and by their basic understanding of scientific assessment on the other hand. This requires presenting the complexities of scientific assessment in a simplified manner without exaggerating or downplaying uncertainties.

In light of the above, a number of guiding principles for communicating uncertainties emerge for both Dossier Submitters and ECHA's scientific Committees. These can be summarised as follows.

For Dossier Submitters:

- The Dossier Submitter should make clear whether scientific conclusions relate to real world conditions (e.g. measured exposure) and outcomes or to specific conditions and/or assumptions (i.e. reasonable worst-case). When conclusions are based on the result of a model or statistical analysis, the Dossier Submitter should remember to consider uncertainties not quantified within the model or analysis, including uncertainties about the assumptions of the model or analysis and any extrapolation from it to the real quantity or question of interest.
- For any impact assessed, the Dossier Submitter should not express more precision than is justified by the scientific assessment. When using probability to express uncertainty, always express it numerically. If the Dossier Submitter does provide a verbal expression, then they should report the numeric expression first and the verbal expression second, as this has been shown to improve the consistency of interpretation. If a numeric expression of probability cannot be provided, then it must be stated so explicitly.
- When estimating the probability, frequency or incidence of outcomes or events, the Dossier Submitter should express them as frequencies (e.g. 10 per 1 000) as this makes it easier for people to understand and use them. This is especially true if probabilities are conditional and the audience needs to infer unconditional probabilities for outcomes of interest to them (e.g. infer the probability of an endpoint from two pieces of information: the conditional probability of developing an endpoint given exposure, and

[6] EFSA (European Food Safety Authority), Hart A, Maxim L, Siegrist M, Von Goetz N, da Cruz C, Merten C, Mosbach-Schulz O, Lahaniatis M, Smith A and Hardy A, 2019. Guidance on Communication of Uncertainty in Scientific Assessments. EFSA Journal 2019; 17(1):5520, 73 pp. https://efsa.onlinelibrary.wiley.com/doi/full/10.2903/j.efsa.2019.5520

the likelihood of a specific exposure level), as it has been shown that people can do this more reliably using frequencies. Using frequencies to quantify variability also reduces the risk of confusing variability and uncertainty. It should be kept in mind that whilst the latter could be resolved at least in theory, the former cannot[7].

- When reporting a range for a quantitative estimate, always be accompanied with a (precise or approximate) probability for that range. Indicate which values within the range are more likely if this might be important for understanding and decision-making. Presenting a central estimate as well as the range will indicate whether the distribution is skewed to one side. If more detail on the shape of the distribution is needed, it should be considered including quartiles or a box plot.
- When giving an approximate probability, it should always be provided lower and upper bounds (e.g. 66–90%). When the probability refers to a range of values of a quantity of interest, give both a lower and upper bound for the range when both are available from the assessment (e.g. a confidence interval from a statistical analysis).
- Where relevant, a clear and concise summary of relevant uncertainties should be included in the Annex XV restriction dossier. This should include the overall impact of uncertainty on the conclusions and the major sources of uncertainty. A more elaborated discussion (incl. means to reduce uncertainties) could be relegated to the specific annex.

For ECHA's committees:

- Flag relevant uncertainties only, it is well understood that no scientific assessment is 100% certain but standard uncertainties that would not challenge the conclusions of the Dossier Submitter do not have to be highlighted in the same way as crucial uncertainties, especially those that might present a large downside risk.
- Communicate information about options for addressing uncertainty, especially if the uncertainty is substantial or might cause concern.
- If the Annex XV restriction dossier evaluates any risk management options for dealing with uncertainty (e.g. precautionary action), present these as options and analyse them but refrain from endorsing them as this would be outside ECHA's remit.
- If the assessment specifies any options or requirements for further data or analysis aimed at reducing uncertainty, communicate these by briefly listing the options or requirements and differentiate between data that it exists in principle (even though it might not yet been readily available) and data that does not exist but could at least in principle be produced.

[7] See https://en.wikipedia.org/wiki/Uncertainty_quantification#Aleatoric_and_epistemic_uncertainty

Appendix II: Some examples of standard phrases

Exemplary wording from EFSA's Guidance on Communication of Uncertainties (see Boxes 1-9 and in particular Boxes 2-7 in the document linked to in footnote 5):

- We recognize that ECHA's opinions on restriction proposals are targeted at a relatively broad audience including multiple stakeholders. The stakeholders vary in their technical understanding and may not follow uncertainty communication at a technical level, e.g. uncertainty expressed as probability distribution.
- Following EFSA's Guidance, it is hence proposed to tailor the communication of uncertainty to the needs of the 'informed level audiences'. Below Boxes 2-7 from the Guidance document are reproduced to give a first gasp of possible wording in different contexts.

Box 2: Guidance for communicating a description of sources of uncertainty

ENTRY LEVEL 	• State that uncertainties exist, using the wording in the scientific output. Example: *'The experts identified limitations in the data on exposure and toxic effects of ZEN and its modified forms'.* (Based on the Zearalenone (ZEN) in feed example, EFSA CONTAM Panel, 2017.)
INFORMED LEVEL 	• As for entry level, state that uncertainties exist. • Include in the message a brief description of the sources of uncertainty that have the biggest impact on the respective key messages. (If necessary, consult the assessors to identify these.) Example: *'The experts identified limitations in the data on exposure and toxic effects of ZEN and its modified forms, for example (…)'.* (Based on the Zearalenone (ZEN) in feed example, EFSA CONTAM Panel, 2017.)
TECHNICAL LEVEL 	• When documenting sources of uncertainty in the assessment report, assessors should include brief text descriptions suitable for subsequent use in communications to informed audiences without using specialist technical terms. • Assessors should try to identify which sources of uncertainty have most influence on their conclusions, either by qualitative assessment or by influence or sensitivity analysis (EFSA Scientific Committee et al., 2018a). • Where there is conflicting evidence on an issue, this is a source of uncertainty which must be documented and taken into account in uncertainty analysis, and may be assessed using a weight of evidence approach (EFSA Scientific Committee, 2017).

Box 3: Guidance for communicating qualitative descriptions of the direction and/or degree of uncertainty using words or symbols[(a)]

ENTRY LEVEL

- Avoid altering the wordings used by assessors to describe the direction and/or degree of uncertainty, or factors contributing to uncertainty (Box 2). Always check the rewording with the assessors if you do.
- State clearly what outcomes and conditions this expression of uncertainty refers to (see Box 1).
- Make clear that any uncertainty referred to in the communication has been taken into account in the assessment conclusion.

Example:

'The Panel noted that there was very high uncertainty about the exposure estimates and took this into account in its conclusion that there is no health concern'.

(Based on the Zearalenone (ZEN) in feed example, EFSA CONTAM Panel, 2017.)

INFORMED LEVEL

- As for entry level, with the following differences:
  - Before communicating the uncertainty expression, describe a few examples of the evidence/data that were considered and the uncertainties affecting the assessment.
  - Optionally, mention specific methods that were used in evaluating the uncertainty.
  - Optionally, mention factors contributing to the overall uncertainty, including the relative importance of individual sources of uncertainty and things like the relevance and reliability of evidence (e.g. in weight of evidence assessments, see EFSA Scientific Committee 2017).
  - Clearly distinguish individual sources of uncertainty from overall uncertainty about the assessment conclusions.

Example:

'The Panel noted that a high proportion of measurements of ZEN and its modified forms in feed were below the limit of detection, leading to very high uncertainty when estimating exposure'.

(Based on the Zearalenone (ZEN) in feed example, EFSA CONTAM Panel, 2017.)

TECHNICAL LEVEL

- If using '+' and '−' or other symbols to indicate the direction and magnitude of uncertainty, accompany these with quantitative definitions of their meaning, as discussed in Annex 5 of EFSA Scientific Committee et al. (2018b).

(a): The Uncertainty Analysis GD recommends that uncertainty should not be expressed qualitatively unless it is also expressed quantitatively or is a standard outcome of a standardised procedure. However, the use of qualitative expressions only will continue in some assessments until the Uncertainty Analysis GD is fully implemented. Therefore, the guidance in Box 3 applies to those cases as well as to cases in which quantitative information is also provided.

Box 4: Guidance for communicating inconclusive assessments

ENTRY LEVEL 	• Communicate clearly that EFSA is unable to give any conclusion on the quantity or question of interest to which this message refers. If the assessment is inconclusive, this implies that nothing further can be said and therefore the communication should avoid using language that might suggest otherwise. • Indicate very briefly the sources of uncertainty that contribute most to this outcome (e.g. lack of data, poor quality or limited relevance of data). Example: *'EFSA's experts could not reach a conclusion on the risk for cattle, ducks, goats, horses, rabbits, mink and cats because of a lack of data'.* (Based on the Zearalenone (ZEN) in feed example, EFSA CONTAM Panel, 2017.)
INFORMED LEVEL 	• Describe the main sources of uncertainty in more detail, but concisely, following the guidance in Box 2. • Inconclusive assessments are especially likely to include options or requirements for obtaining further data. Communicate these as instructed in Section 3.1.5 on 'Addressing the uncertainties'. Example: *'EFSA's experts could not reach a conclusion on the risk for cattle, ducks, goats, horses, rabbits, mink and cats due to limitations in available data on exposure and toxic effects of ZEN and its modified forms, for example (…)'.* (Based on the Zearalenone (ZEN) in feed example, EFSA CONTAM Panel, 2017.)
TECHNICAL LEVEL 	• When explaining why the assessment is inconclusive, include a description of the key sources of uncertainty that are responsible for this. • If the assessment is not totally uncertain, try to express what the science can say and quantify the uncertainty unless the risk manager/legislation requires that only unqualified conclusions be given.

Box 5: Guidance for communicating unqualified conclusions with no expression of uncertainty

ENTRY LEVEL 	• Report the unqualified conclusion for this message using the same wording as the assessors. Example: *'EFSA's experts concluded that the exposure to feed containing ZEN 'in farm situations' is a low health risk for sheep, dog, pig and fish, and an extremely low health risk for poultry'.* In this example, the word 'low' refers to the conclusion on the level of health risk. There is no expression of uncertainty about this – no indication that the risk might be other than 'low', i.e. an unqualified conclusion about the level of risk. (Based on the Zearalenone in feed example, EFSA CONTAM Panel, 2017.)
	• Include a link to an FAQ that explains the meaning of the unqualified conclusion and the definition used for it in the scientific assessment. In the example above, a link should be provided to the definition of 'low risk' that is used in assessments of health risk for farmed animals exposed to contaminants.
INFORMED LEVEL 	• As for the entry level. • Optionally, describe briefly how the assessment was made (i.e. what evidence and methods were used to arrive at the conclusions). • Briefly describe some examples of uncertainties affecting the assessment for this message, as identified in your completed template, consulting Box 4 for guidance on how to communicate this. • If the assessment contains any verbal or numerical expression of the impact of the uncertainties as identified in your template, follow the respective guidance in Boxes 6–9 below. • Say that the assessors took the uncertainties into account when reaching their conclusion(s) for this message. Example: *'Following the standard assessment procedure (or "Using the evaluation system agreed for contaminants in feed""), experts estimated that high exposure to feed containing ZEN is below the reference value for a health risk for sheep, dog, pig and fish, and well below the reference value for chicken and turkeys. They therefore concluded that the exposure to feed containing ZEN "in farm situations" is a low health risk for sheep, dog, pig and fish, and an extremely low health risk for poultry'.* *'In reaching this conclusion, the experts took account of limitations in the data on exposure and toxic effects of ZEN and its modified forms, for example (…)'.* (Based on the Zearalenone (ZEN) in feed example, EFSA CONTAM Panel, 2017.)
TECHNICAL LEVEL 	• Provide the information needed for the FAQ required at the entry level communications (see above). • Specify what level of certainty is associated with each unqualified conclusion. Risk managers can explain why that level of certainty is appropriate for decision-making, if considered necessary. Make this information available to interested parties in suitable ways, e.g. in an FAQ and/or in documentation or guidance on the assessment methodology.

Box 6: Guidance for communicating a precise probability

ENTRY LEVEL 	• State clearly what the probability refers to, including whether it refers to a numerical estimate or a qualitative conclusion. When the probability refers to a numerical estimate, also state the range of the quantity that the probability refers to (see example below). Example: *'The Panel estimates that, under current regulations, the total number of infested tulips in in greenhouses in the EU is 60,000. Based on what is known, the Panel is 50% certain that the number is between 10,000 and 200,000 infested plants'.* *(Based on the Nematodes example, EFSA PLH Panel, 2017.)*
INFORMED LEVEL 	• As for entry level, with the following differences: – Before giving the probability, describe a few examples of the evidence/data that were considered and the uncertainties affecting the assessment, and state that the experts took these into account when assessing their level of certainty. – Optionally, mention specific methods that were used in quantifying the uncertainty, e.g. modelling, statistical analysis, expert knowledge elicitation (EKE), or a combination of these. Example: *'The Panel performed its assessment using a mathematical model of the entry of nematodes into the EU and their establishment and spread in greenhouse tulips. Uncertainty on the factors represented in the model was quantified by expert judgement, taking into account the limitations of the available data. The Panel estimates… [continue as for entry level]'.* *(Based on the Nematodes example, EFSA PLH Panel, 2017.)*
TECHNICAL LEVEL 	• No specific guidance for assessors other than the general guidance for assessors in Section 3.2 (above).

Box 7: Guidance for communicating an approximate probability

ENTRY LEVEL

- State clearly what the probability refers to, including whether it refers to a numerical estimate or a qualitative conclusion. When the probability refers to a numerical estimate, also state the range of the quantity that the probability refers to.
- An approximate probability may comprise a range of probabilities chosen by the assessors from the approximate probability scale (Table 4), or a different range of probabilities specified by the assessors.
- Always communicate the quantitative range of probabilities because this expresses the assessors' conclusion without ambiguity. If a verbal expression is also used, present the quantitative probability first (e.g. '66–90% certain (likely)') because it has been shown that this order leads to more consistent understanding than if the verbal expression is presented first (see Section 3.1)
- To avoid inconsistency and misunderstanding, do not use the verbal terms in Table 4 to refer to any probabilities or ranges of probabilities other than those shown in this table.

Example:

'The experts considered it 66–90% certain (likely) that the increasing proportion of elderly and susceptible people has contributed to the rise in Listeria cases'.

(Based on the *Listeria* in ready-to-eat foods example, EFSA BIOHAZ Panel, 2018.)

INFORMED LEVEL

- As for entry level, with the following differences:
  - Before giving the probability, describe a few examples of the evidence/data that were considered and the uncertainties affecting the assessment, and state that the experts took these into account when assessing their level of certainty.
  - Optionally, mention specific methods that were used in quantifying the uncertainty, e.g. modelling, statistical analysis, expert knowledge elicitation (EKE), or a combination of these.

Example:

'Experts began work on the Scientific Opinion after the 2015 EU summary report on foodborne zoonotic diseases identified an increasing trend of listeriosis over the period 2009–2013. The Panel performed a statistical analysis, which confirmed the increasing trend, and developed a mathematical model of the factors influencing the incidence of infections. Considering the modelling results and the degree of support from indicator data, the experts…' [continue as for entry level].

(Based on the *Listeria* in ready-to-eat foods example, EFSA BIOHAZ Panel, 2018.)

TECHNICAL LEVEL

- Use different probabilities or ranges from those shown in Table 4 if they better express your judgement (EFSA Scientific Committee et al., 2018a). In such cases, avoid accompanying it with any verbal probability expression because a harmonised interpretation exists only for the terms in Table 4.