Committee for Risk Assessment **Agreed at RAC-43**

Risk-related considerations in applications for authorisation for endocrine disrupting substances for the environment, specifically OPnEO and NPnEO

This Question and Answer paper is intended to provide general advice to companies intending to apply for Authorisation of uses of OPnEO and NPnEO with regard to environmental risk assessment. It is not intended to define any 'preferred approach', nor does it give reference values.

Background

Two Substances of Very High Concern (SVHC) with endocrine disrupting properties for the environment were recently added to Annex XIV of REACH (OPnEO[1] and NPnEO[2]). These are the first two substances added to Annex XIV on the basis of such properties.

On 22 August, ECHA hosted a workshop in Brussels on 'Applications for Authorisation for Environmental Endocrine Disrupters'.

The purpose of the workshop was to have an open exchange of views between interested stakeholders on the available scientific evidence relating to the hazard and risk assessment of NPnEO and OPnEO. In particular, the workshop focussed on:

- The potential to derive thresholds or dose-response relationships for these specific substances (and the information that needs to be available to do this)
- Raise awareness of other relevant key issues when applying for authorisation (i.e. minimisation of emissions)

The workshop was attended by ca. 75 participants from across industry (35), consultancy organisations (22), Member States (13), RAC members (4), NGOs (3) and ECHA/Commission staff (7) and comprised plenary presentations from expert speakers from across regulatory, scientific and industry backgrounds. The plenary session was followed by a series of breakout discussion groups addressing key issues relevant to applications for these substances.

The outcome of the workshop was discussed during RAC-42 in September 2017, where it was agreed that the ECHA Secretariat would develop, with the assistance of interested RAC members, a 'Q&A document' addressing key technical issues for these substances.

This document was first consulted with the Committee and then agreed during RAC-43 in November/December 2017.

[1] Entry 42: 4-(1,1,3,3-tetramethylbutyl)phenol, ethoxylated [4-tert-octylphenol, ethoxylated; 4-tert-OPnEO]
[2] Entry 43: 4-nonylphenol, branched and linear, ethoxylated [4-NPnEO]

Key technical considerations[3]

Starting point

The applicant's primary goal should be to convince RAC that for their use(s) of OPnEO and NPnEO, the operational conditions and risk management measures in place are appropriate and effective in limiting the risks to the environment. This obligation remains regardless of whether the applicant decides to consider these substances as threshold or non-threshold. A clear description of the specific RMMs in place and a justification of their effectiveness is key (See also question 8).

1. Which substances and/or degradation products should be addressed in the chemical safety assessment in an application for authorisation for OPnEO and NPnEO?

Chemical safety assessment in an application for authorisation should focus on the endpoint or endpoints listed on Annex XIV (Q&A 0574). OPnEO and NPnEO were identified as endocrine disrupting substances for the environment solely on the basis of the properties of their respective alkylphenol (e.g. OP[4] and NP[5]). Therefore, the chemical safety assessment in an application for authorisation for OPnEO and NPnEO can focus solely on OP or NP, respectively.

As the degradation behaviour of OPnEO and NPnEO in the environment is complex, particularly if the identity of the starting ethoxylated substance is unknown or variable, and there are limited analytical methods available to characterise intermediate ethoxylated breakdown products in practice, it is likely to be most straightforward in an application to:

(i) Use datasets of measured concentrations of OP or NP in relevant environmental compartments (e.g. undertaken by Member States to fulfil their obligations under Article 16 of the Water Framework Directive – 2000/60/EC), but only where the reliability and representativeness of the data for the applicant can be assured.

and/or;

(ii) As a worst-case, assume that all OPnEO or NPnEO released to the environment will eventually be present as OP or NP, respectively. Alternatively, the assumptions on the degradation of NPnEO in the aquatic compartment after anaerobic wastewater treatment outlined in Annex I of the existing substances regulation (ESR) risk assessment report (RAR) for NP and NPnEO[6] could be considered, but only if applicants can provide a justification that they remain reliable and relevant in the light of any new information.

[3] NB: Process-related issues (such as derogations from the authorisation requirement for scientific research and development) are not discussed here.
[4] 4-tert-octylphenol
[5] 4-nonylphenol
[6] https://echa.europa.eu/documents/10162/efae6363-2c55-47ee-bc85-0c8d265803cf

2. Are the endocrine disrupting properties of OPnEO and NPnEO restricted to effects in fish or the aquatic compartment?

No. Although RAC acknowledges that the endocrine disrupting properties of OPnEO and NPnEO were identified primarily on the basis of effects noted in fish species, data on other taxonomic groups or compartments that could be sensitive to the endocrine disrupting properties of OPnEO and NPnEO are also relevant and should be considered carefully.

A chemical safety assessment for OPnEO and NPnEO should be undertaken according to Annex I of REACH and consider potential effects on the environment, comprising (1) aquatic (including sediments), (2) terrestrial and (3) atmospheric compartments, including the potential effects that may occur (4) via food-chain accumulation.

Exposure, hazard and risk characterisation should consider the environmental compartments for which the endocrine disrupting properties of OPnEO and NPnEO (see question 1) are known or reasonably foreseeable e.g. the terrestrial compartment may be relevant if sewage sludge from wastewater treatment is known or potentially disposed to agricultural land. Applicants should provide a justification based on an assessment of the available data, for excluding potentially relevant taxa or compartments from their chemical safety assessment. Please also see question 7.

3. Should risks to human health be assessed in an application for authorisation for OPnEO and NPnEO?

Risks to human health do not need to be assessed in the CSR included in an application for authorisation for OPnEO and NPnEO as they were listed on Annex XIV only on the basis of their endocrine disrupting properties for the environment (Article 62(4)).

However, information on other endpoints (e.g. human health, environmental or physico-chemical) might be necessary in an application when comparing the risks of continued use of the Annex XIV substance with alternatives. A suitable alternative should result in an overall reduction in risks to human health and the environment.

4. Are OPnEO and NPnEO threshold or non-threshold substances?

The scientific background to the threshold vs non-threshold discussion for endocrine disrupting substances in Authorisation was summarised in 2016 in a report by the European Commission to the European Parliament, the Council and the European Economic and Social Committee[7]. The paper concludes that the existence, or not, of a threshold for an endocrine disrupting substance will need to be justified on a case-by-case basis and that this is the responsibility of the applicant. Importantly, it is feasible that a substance has a threshold, but that it is not possible to derive this with sufficient certainty for regulatory purposes. In these circumstances a substance can be assumed by an applicant to be non-threshold.

RAC recently evaluated the available ecotoxicity dataset for NPnEO in the context of a restriction proposal. In its opinion on the proposed restriction[8], RAC used a 'conventional' PNEC (a PNEC underpinned with ecotoxicity data that was not necessarily applicable to the endocrine disrupting properties of NP) to demonstrate that the use of NPnEO in textiles posed an unacceptable risk on an EU-wide basis (i.e.

[7] https://ec.europa.eu/transparency/regdoc/rep/1/2016/EN/COM-2016-814-F1-EN-MAIN-PART-1.PDF

[8] https://www.echa.europa.eu/web/guest/previous-consultations-on-restriction-proposals/-/substance-rev/1898/term

PEC/PNEC ratio >1). However, RAC did not consider that exposure values below this PNEC were consistent with a 'safe level', specifically noting the uncertainties associated with the endocrine disrupting properties of NPnEO. Equally, RAC did not conclude on the threshold / non-threshold nature of the endocrine disrupting properties of NPnEO.

An applicant may choose to assume that OPnEO and NPnEO are non-threshold substances for the purposes of an application for authorisation. Please also see question 6.

5. Will RAC develop reference PNEC values or dose-response relationships for OPnEO and NPnEO?

No. Industry are responsible for attempting to derive threshold values or dose-response relationships for endocrine disrupting substances. RAC will evaluate any reference values proposed in an application for authorisation on a case-by-case basis.

However, potential applicants are reminded that demonstrating adequate control using a threshold is not always necessary for an authorisation to be granted. If it is not possible to determine a threshold for endocrine disrupting substances, an authorisation may be granted for the use of a substance if the socio-economic benefits outweigh the risk arising from the use and there are no suitable alternatives (Article 60(4)).

Given that, under the current understanding, there are significant uncertainties surrounding the appropriate derivation of thresholds and dose-response relationships for endocrine disrupting substances (see question 4), an applicant may choose to assume that OPnEO and NPnEO are non-threshold substances for the purposes of an application for authorisation. Please also see question 6.

6. If my application for authorisation assumes that OPnEO or NPnEO are non-threshold substances (i.e. application does not report a risk characterisation based on a PNEC value), how will my application be evaluated by RAC?

In this scenario an application for authorisation for the use of an Annex XIV substance may be granted if the socio-economic benefits outweigh the risk to the environment arising from the use and there are no suitable alternatives (Article 60(4)).

Where no dose-response is proposed, or is not supported by RAC after evaluation, RAC will evaluate the application on the same basis as an application for a PBT/vPvB substance, specifically:

(i) An evaluation of the reliability and representativeness of the description of releases to the different environmental compartments;

(ii) An evaluation of the appropriateness and effectiveness of the operational conditions and risk management measures implemented (or recommended to DUs) to prevent or minimise releases to environmental compartments as far as technically and practically possible (with the view to minimising the likelihood of adverse effects).

Where a dose-response relationship is proposed by an applicant this will be evaluated by RAC (See question 7). Should RAC support a dose-response relationship the subsequent evaluation would proceed as described above, but would also include an evaluation of the reliability and representativeness of information relevant to exposure (e.g. appropriateness and quality of analytical methods or exposure models) and risk.

The checklist for preparing an application for authorisation or a review report and ECHA's publication on 'how to apply for authorisation' provides further information on the preparation of the chemical safety report in an application for authorisation.

7. How will RAC evaluate a proposed PNEC or dose-response relationship for OPnEO and NPnEO? For example, has RAC established 'minimum information requirements' that should be satisfied?

Should an applicant choose to derive a threshold or dose-response relationship RAC will evaluate it on a case-by-case basis. RAC will base its evaluation on the requirements of Annex I of REACH and the principles outlined in ECHA Guidance (e.g. R.10). In addition, recognising the particular challenges surrounding the risk assessment of endocrine disrupting substances for the environment, RAC will pay particular attention to how applicants address the following, based on Matthiessen et al. (2016)[9]:

(i) Are reliable data available for appropriate taxa (for relevant endpoints) in appropriate compartments and have effects on all potentially relevant taxa been considered, for example the potential for effects on taxa such as molluscs, amphibians, reptiles and echinoderms; should be discussed in addition to taxa that are more typically represented in ecotoxicity datasets such as fish and rodents;

(ii) Are reliable data available for sensitive life stages, or the entire life cycle;

(iii) Have delayed and multi-generational (i.e. latent) effects been considered;

(iv) Have non-monotonic dose-response or other unusual temporal patterns of toxicity been considered?

Applicants should ensure that they adequately describe and justify the point of departure, species coverage and any assessment factor used (noting that a margin of safety approach as well as an assessment factor approach for these substances can be used). Where RAC does not support a threshold proposed by an applicant it will conclude that adequate control has not been demonstrated and undertake the remainder of its evaluation assuming that the substance is non-threshold. Where RAC does not support a dose-response relationship proposed by an applicant, or where no dose response is proposed for risk characterisation, RAC will evaluate an application on the same basis as an application for a PBT/vPvB substance (see question 6 above).

8. How will RAC assess if an applicant has minimised releases to the environment?

Where an application for authorisation is made for OPnEO or NPnEO assuming that there is no threshold, RAC will evaluate if releases to the environment have been minimised on the same basis as applications for PBT/vPvB substances.

Therefore, applicants should justify how the operational conditions and risk management measures applied, or recommended to downstream users, prevent or minimise releases to environmental compartments as far as technically and practically possible (with the view to minimising the likelihood of adverse effects).

RAC notes that certain operational conditions and risk management measures clearly result in zero releases to a particular compartment e.g. where aqueous wastes are

[9] http://onlinelibrary.wiley.com/doi/10.1002/ieam.1885/abstract

incinerated or recycled there are no releases to the aquatic compartment. However, other operational conditions and risk management measures may be consistent with minimisation despite them resulting in releases to environmental compartments where those releases are reduced to as low a level as is technically and practically possible.

In these circumstances applicants could refer to the efficiency of the risk management measures used in relation to Best Available Techniques or the relative efficiency of alternative OCs and RMMs.