8 May 2020

Comments on CA/MS/34/2020 ´Towards a pragmatic procedure to regulate the risks of exposure to unintended combinations of chemicals in the EU´

We would like to thank the Dutch and Swedish Competent Authorities for this initiative. It has been long overdue for the EU to agree a regulatory way forward to address and manage the risks from combined exposures to chemicals in order to increase the protection of human health and the environment.

EU decision makers have neglected this topic for many years and a Commission report on the way forward agreed on in 2012[1] and originally promised for 2015 has still not seen the light of day. In 2019 the Council conclusions were a stark reminder of this total neglect.[2] Now it is high time to take these decisions in the context of the upcoming Chemical Strategy for Sustainability and the European Green Deal.

The undersigned NGOs strongly support the implementation of the proposed Mixture Assessment Factor concept as a pragmatic, effective and feasible way forward to control the risks for human health and the environment from the combined exposure to mixtures of chemicals. However, this can only be a first step.

While we agree to move ahead with the proposed focus on REACH, we would like to emphasize that there is a need for an overall approach to address combined exposures across EU legislations. Based on many contributions written on the topic over the years[3-7] we see the need for the following points to be developed:

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[1] https://ec.europa.eu/transparency/regdoc/rep/1/2012/EN/1-2012-252-EN-F1-1.Pdf
[2] http://data.consilium.europa.eu/doc/document/ST-10713-2019-INIT/en/pdf
[3] https://ec.europa.eu/environment/chemicals/effects/pdf/report_mixture_toxicity.pdf
[4] https://science.sciencemag.org/content/361/6399/224
[5] https://www.sciencedirect.com/science/article/pii/S0048969715309785
[6] https://www.government.se/4adb1a/contentassets/ee36b3e49c354bb8967f3a33a2d5ca50/future-chemical-risk-management---accounting-for-combination-effects-and-assessing-chemicals-in-groups-sou-201945

a. Establishment of a cross-cutting approach to address mixture toxicity to be integrated in and applied under all relevant EU laws

b. Systematically taking into account combination effects in risk assessment , including by using an additional mixture assessment factor by default in prospective risk assessment

c. Speeding up the replacement/substitution of harmful substances/SVHCs to minimize exposure of the general population, especially vulnerable groups, workers and the environment

Our comments on the discussion points raised in the CARACAL paper

1) On the outcome of the workshop and the proposal for a pragmatic approach to address risks from combined exposure to chemicals

We generally support the outcome of the workshop that a pragmatic approach to be implemented in EU laws is urgently needed, as we presented at the event.[8] The scientific evidence for mixture toxicity has grown over the last years and has found that chemicals contribute to mixture effects even when they occur at levels below their own individual effect concentrations. In 2019, a conference organised by the EU research projects EDCMixRisk and EuroMix highlighted again the urgent need to integrate these findings into policy and law by adopting regulatory approaches as well as employ better assessment tools for tackling mixture effects.[9] The overarching conclusion from these projects was that current regulation of man-made chemicals systematically underestimates the health risks associated with combined exposures to EDCs or potential EDCs.[10]

2) Application of a Mixture Assessment Factor (MAF) under REACH

We have advocated for the use of MAFs for many years. We support the introduction of a MAF under the REACH Annex I for the following reasons:

- The current risk assessments undertaken under REACH are likely to underestimate the risk as they are usually based on a single substance approach. Thus, safe use is

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[7] https://www.rivm.nl/en/news/proposal-to-calculate-combined-effects-of-chemicals-in-environment-at-eu-level

[8] https://www.chemischestoffengoedgeregeld.nl/sites/default/files/Final%20CHEM%20Trust%20NGO_Ninja%20Reineke.pdf

[9] https://chemtrust.org/chemical-cocktail-mixture-effects/

[10] https://edcmixrisk.ki.se/wp-content/uploads/sites/34/2019/03/Policy-Brief-EDC-MixRisk-PRINTED-190322.pdf

not guaranteed as the effects from exposure to unintended mixtures are not covered.

- The alternative to using a MAF would be a detailed risk assessment approach in each case. This would require high quality data on hazards and exposures and a specific knowledge of all potential mixture exposure scenarios. Even if the current data gaps on single substances in REACH registration dossiers will be partly closed over time, (e.g. through ECHA`s increased compliance checks), it is impossible to expect assessments for all unintended mixture situations a given chemical may end up in during its whole life-cycle. The only way forward for mixture risk assessment is the proposed generic approach.
- A deadline will have to be established to oblige registrants to update the registration dossiers to consider mixture effects. A preliminary survey by ECHA presented at the workshop showed that for some substances additional risk management measures will be needed, while this is not the case for others. [11]

Also, a 2019 joint statement from JRC and researchers from EDCMixRisk, EuroMix, EUToxRisk, HBM4EU and SOLUTIONS recommended an application of a MAF as a way to decrease the total burden of exposure to chemical mixtures.[12]

Limitations of the proposal

However, it is also important to point out the limitations of the proposed approach: as the Chemical Safety Assessment (CSA) is only required for chemicals produced above 10 tpa, the new requirement will not apply to the thousands of chemicals produced in lower volumes. A review of the impact and a follow-up to this important limitation should take place after a specified period of time.

Moreover, as the CARACAL paper states, a crucial task will be to come up with an additional approach to deal with non-threshold substances. One idea for a priority setting would be to agree on provisions requiring substitution of all the known harmful chemicals found in Human Biomonitoring studies and which are currently still allowed on the market. Similarly, actions will be needed to increase substitution of PBT and vPvB substances and other substances of equivalent level of concern found in the environment. The aim of tackling real life mixtures needs to focus on minimising exposures to SVHCs.

Under REACH this means for example that the authorisation of single/individual SVHCs should not be allowed under the ´adequate control route´ in cases of known co-exposures to similarly acting substances or substances of that same group. Applications for authorisation should also apply a MAF in the risk assessments, that means if it has not been included at

[11] https://www.chemischestoffengoedgeregeld.nl/sites/default/files/ECHA_Jack%20De%20Bruijn.pdf
[12] https://www.sciencedirect.com/science/article/pii/S0160412019331538

the registration stage (e.g. if the dossier has not been updated, yet), it should be introduced at the authorisation application stage. The systematic implementation of a MAF should also be considered for restrictions under REACH. Undertaking risk management for groups of substances rather than individual ones would make a great difference and help reduce harmful mixture effects.

3) Procedure for approach to introduce the MAF

We support introducing the MAF in the context of derivation of the DNEL and PNEC under all REACH processes for the following reasons:

- It will be more consistent and easy to manage if the additional assessment factor is already included when deriving the DNEL and the PNEC. For transparency, it may be appropriate to signal the MAF inclusion e.g. by indicating $DNEL_{M.}$
- It provides an added value in the communication to downstream users: they get a final value which already includes the consideration of unintentional mixtures.
- PNEC and DNEL derived under REACH are increasingly used in other legislation, and hence application of MAF in the context of PNEC and DNEL derivation will be more effective e.g. if a PNEC is used under the WFD or if a DNEL is used to inform OEL setting).
- Applying a MAF at the stage of the RCR is less transparent and less effective for the control of risks.

4) Procedure to be followed for determining magnitude of MAF

It is very important that the MAF is established in a transparent way, based on the scientific evidence.

It is also important to keep the purpose for the MAF in mind:

- There is a need to decrease the burden of hazardous substances and to oblige registrants to ensure safe use - which is currently not the case. It is not feasible to test all different unintentional mixture combinations.
- Mixture effects are not covered by current uncertainty factors as was well demonstrated by Martin et al. [13]
- The MAF needs to include many uncertainties and it should be protective for vulnerable populations, including during critical windows of exposure such as early-life development.
- Further, the MAF should clearly cover both the risk of mixture effects due to exposure to other chemicals and the risk of aggregated exposure to both the same chemical and other chemicals from different sources.

[13] https://ehjournal.biomedcentral.com/articles/10.1186/1476-069X-12-53

Our proposal therefore is to establish a MAF of 100 which would cover:

a. a factor 10 addressing chemicals contributing to a mixture (several hundred chemicals present are usually present in real life samples, however, it seems that often around 10 chemicals contribute to the majority of toxicity);[14]
b. a factor 10 addressing exposures from different sources (ranging from biocides, cosmetics, pesticides, detergents to uses in food contact materials, toys and other consumer products).

Conclusion

In conclusion, we support the introduction of a MAF of 100 in the derivation of the DNEL/PNEC.

The MAF can be introduced through a change in Annex I of REACH via an implementing act. In the authorisation processes, it can be implemented by authorisation applicants through a change in the guidance. In the restriction processes, it can already be used by dossier submitters and by RAC when assessing restrictions.[15]

Finally, as much as a MAF is indispensable to adjust chemical regulations to the reality of chemical exposure, it is not sufficient to fully address it. We therefore see the need to develop an overarching approach for addressing unintentional mixtures in the upcoming EU Chemicals Strategy for Sustainability. A focus on minimising exposures to harmful substances/SVHCs (in particular non-threshold SVHCs) will be crucial to develop ways forward for a clean Circular Economy. Here, the increased use of group restrictions can play an important role. In addition, improved authorisations that would only be granted with conditions taking mixture toxicity into account should be explored further.

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[14] See scoping paper from Workshop: https://www.chemischestoffengoedgeregeld.nl/content/scoping-paper-workshop-pragmatic-approach-regulatory-measures-addressing-risk-combined

[15] RAC already used a MAF to take into account mixture effects of reprotoxicants used in tatoo mixtures. Committee for Risk Assessment (RAC)Committee for Socio-economic Analysis (SEAC), see Opinion on on Annex XV dossier proposing restrictions on substances used in tattoo inks and permanent make-up ECHA/RAC/RES-O-0000001412-86-240/FECHA/SEAC/ ECHA/SEAC/RES-O-0000001412-86-265/F. https://echa.europa.eu/documents/10162/dc3d6ea4-df3f-f53d-eff0-540ff3a5b1a0