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Miljøstyrelsen
Kemikalier

Høringssvar fra DCE - Nationalt Center for Miljø og Energi, Aarhus Universitet vedr. høring af Kommissionens meddelelse om kombinationseffekter af kemikalier

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General comments:
It is much appreciated that the EC is addressing the difficult topic of scientific risk assessment of chemical mixtures. There are still many gaps in our knowledge, as well as many emerging proposals on approaches and technologies to close these. The main challenge is accurate assessment of mechanisms and modes of action of the compounds, as a prerequisite for science based mixture assessment. Here the chronic effects are most relevant, due to the typical environmental exposure levels, and also the most challenging. In general, we find that emerging technologies such as both computational and experimental toxicogenomic methods (e.g. High Throughput Screening tools (HTS) and the Adverse Outcome Pathway (AOP)) should be better reflected as potential methods to increase the scientific understanding of mechanisms and modes of action in the document.

Moreover, reference to the National Research Council report: Toxicity Testing in the 21st Century: A Vision and a Strategy (Washington, DC: National Academy Press, 2007), and subsequent scientific developments (e.g. AOP http://www.oecd.org/dataoecd/50/39/49963554.pdf) in the area needs to be included. We find that reference to the ongoing exposome research in the EU and globally should be mentioned also as technologies that will allow a more accurate and precise assessment of mixture risks to man and the environment.

Specific comments:
There is an important distinction and development missing with regards to modes of action (MoA) and chronic toxicity. We absolutely need to know the way a chemical expresses its effect in order to address mixtures. We mostly talk about modes of action and less of mechanisms – mainly because we so far are concerned from a regulatory point about the modes. The mode of action is the result of the mechanisms (e.g. endocrine disruption is a mode of action, but it is a function of a series of endocrine mechanisms along the HPG-axis). The mechanism of action of a chemical substance depends upon the concentration, exposure site and organism exposed. For chronic effects we need to detail the mechanisms of action to determine the potential effects. In

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other words, we need to determine the molecular initiating events (MIEs) in order to determine the adverse outcome pathways (AOP) and thus predict the mode of action and thus facilitate assessment of mixtures with the same MIEs and AOPs.

Narcotic compounds:
Please note, that for more than 60-75% of known chemicals and >95% of the total exposure tonnage there is very little or non-existing scientific knowledge of their acute AOP/MoA – let alone their chronic ditto. These are called narcotic compounds – compounds which disrupt cell membrane integrity, typically causing lethality within hours. These are indirectly mentioned on page 6 last sentence in textbox 3 under unknown MoAs. Again in textbox 5 second paragraph – within ecotoxicology the chronic MoAs are sparse for the majority of compounds and exposures, effectively making it difficult to predict mixture toxicity, making concentration addition (CA) the best solution from a regulatory perspective but the science behind is not strong. With CA there is however, the risk over-conservative assessments as well as recognizing the relatively weak science behind (in many ways comparable to extrapolation/assessment factors) - may work but the scientific reliability is not strong either way.

Paragraph 5.2 conclusion (2): *Such guidelines shall not replace existing rules where such exist nor shall they impose additional obligations or burdens on economic operators.*
We wonder how the statement matches the transformation of the EU economy? E.g. REACH and a strengthened chemicals policy could prove to be a commercial benefit to the companies in the long run and to the EU.