

Cefic Position Paper on Combination Effects of Chemicals

Today, EU chemicals policy and risk management schemes predominantly focus on the safety of individual chemical substances. They protect public health and the environment by ensuring that no chemical substance is present in the environment at levels that might cause harm.

Recent reports have suggested that when chemical substances, both natural and man-made, are combined together (termed the combination effect) they might cause adverse effects to human health and the environment, even if the individual chemical substances (i.e., natural and man-made) are harmless. Although there is currently no evidence of such a “combination effect” from typical environmental substance levels, it is critical that we consider the possibility of harm.

Therefore, the chemical industry is engaged with European and international bodies and agencies to address this concern. Their collaborative efforts have revealed that, while it is always true that further research could provide additional insights into such a complex issue, there are now procedures and tools which can be applied to address the potential combination effects of chemical substances. These are described below.

Screening

Current research from industry, academic (including the European Commission Scientific Committees) and government sources indicate that the observed effects of combined chemical substances (i.e., at high concentration levels) in the laboratory are extremely unlikely to occur at ambient concentrations in the environment. In the rare instance when they do occur, it is unlikely to be toxicologically significant¹. Furthermore, current scientific evidence shows that when combined chemical exposures pose a risk, the risk is typically driven by one or just a few of the chemicals within the combination. As a result, **controlling individual chemicals through the current regulatory schemes will also control the overall risk from such combination exposure.**

Despite these findings the industry continues to conduct research and develop tools to identify and assess potential risks. Every day, we are typically exposed to numerous natural and man-made chemical substances. For example, our engagement in basic everyday activities such as breathing and eating exposes us to chemical substances. It is impossible to even predict all the combinations of natural and man-made substances in all possible concentrations which could arise in an environment: let alone to assess them all. **It is therefore essential to develop screening criteria and tools to prioritise the chemical combinations to be assessed and identify so-called “combinations of concern”.**

The screening criteria proposed by industry are consistent with those proposed by the EU Commission Scientific Committees. These criteria, and the newly-developed **Maximum Cumulative Ratio (MCR)**² tool, can be used to identify combinations of chemicals which are of concern, rather than attempting to evaluate many harmless combinations.

Practical tools

As part of our commitment to ensure the safety of our products, the chemical industry is working with academia and Governments to develop and share tools to assist in the risk assessment of individual substances as well as in identifying and assessing combinations of chemicals. In particular, **Cefic has developed a “decision tree, incorporating the MCR tool, for the evaluation of human and**

¹ SCHER, SCCS, SCENIHR, Opinion on the Toxicity and Assessment of Chemical Mixtures, 2012

² Paul S. Price and Xianglu Han, Int. J. Environ. Res. Public Health 2011, 8: 2212-2225; doi:10.3390/ijerph8062212

ecological effects from exposures to multiple chemicals from a single or multiple sources”³, which builds on the risk assessment framework of the WHO and the European Scientific Committees.

The proposed two-stage approach works as follows:

Stage 1: Screening Tool:

In the first stage a Screening Tool is used to identify those cases where effects from combinations of chemicals might be of potential concern and need further risk management measures:

- Step 1: identify those substances that are present at relevant concentrations in a given environment;
- Step 2: establish all the available toxicological data in relation to those substances;
- On the basis of this evidence:
 - Where all the substances present are of no, or low concern and there is nothing to suggest a possible combination effect, then the existing individual chemical assessments suffice.
 - Where a combination contains one or more substances at potentially unsafe levels, and there is nothing to suggest a possible combination effect, an additional risk assessment of the individual components is undertaken and, if necessary, additional risk management measures are implemented for the individual substances of concern.
 - Where cumulative or combination effects are a potential concern, a full cumulative risk assessment is undertaken.

Stage 2: Tiered Risk Management

Where the Screening Tool suggests that there are grounds for concern and that further risk management of combination effects is called for, the decision tree proposes a “Tiered Risk Assessment”, combining the most effective approaches (e.g. the dose/concentration addition approach relating to chemicals with a common mode of action, the independent action approach for those with different modes of action). This approach contains an increasing refinement of hazard and exposure assessment through the different tiers, which provides a structured approach for risk assessment of combination effects.

Cefic has successfully conducted proof-of-concept studies (of US⁴ and European⁵ surface water data and, of residential Indoor Air monitoring data from European studies), demonstrating the effectiveness of the decision tree tool.

Concluding remarks

The risk assessment and management approaches, under existing regulatory schemes, are effective to protect humans and the environment from exposure to environmentally relevant levels of individual substances. Managing the risks from these substances individually will in the majority of cases also ensure that combinations of chemicals do not present a risk to human health or the environment.

Our ‘combination effects’ approach offers a pragmatic and scientific way forward for effective screening of the numerous substances in a given environment, identifying the drivers of risk from combinations of chemicals, and prioritising those rare cases where there is potential for a cumulative or combination effect that requires a specific risk assessment.

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³ Price P et al., Environmental Sciences Europe 2012, 24:26

⁴ Xianglu Han and Paul S. Price, Int. J. Environ. Res. Public Health 2011, 8, 4729-4745; doi:10.3390/ijerph8124729

⁵ Price P et al., Environmental Sciences Europe 2012, 24:34