

Exposure to mixture (“cocktails”) of chemical substances: are the health and environmental risks adequately evaluated?

Introduction

There is increasing concern in the general public about the potential toxic effects of chemical substance mixtures (in the media often referred to as “cocktail-effects”).

Humans and ecosystems are indeed continually exposed to a very complex mixture of chemical substances, the composition of which is always changing. However, in the great majority of risk assessments, only a single chemical is considered and there are no generally applicable guidelines as to when and how assessment of combinations of chemical substances should be carried out.

Are there combined effects of exposure to chemical mixtures?

Two cases should be considered :

1.1. Substances that have a similar mode of action

When substances have a similar mode of action – which means that their adverse effects are caused by similar chain of events –, their concentration can be added together to predict their combined effect. The additivity of doses is assumed over the entire range of concentrations, including those below the level at which each substance has no observed effect. In some rare specific cases, antagonistic (lower than the sum of the parts) or synergistic (greater than the sum of the parts) effects have been observed, but in general, dose addition is a reasonable conservative (protective) default approach.

1.2. Substances that have different modes of action

With mixtures composed of chemical substances with various modes of action, there is good evidence that the effects are higher than those of the individual components. At present, the safety margins that are used in risk assessment of single chemical substances could be insufficient to allow room for the effects for all possible realistic mixtures.

However, the Opinion of the Scientific Committees is that, for chemical substances that act independently, no robust evidence is available and it is very unlikely that exposure to a mixture of such substances is of health concern if the individual chemical substances are present at or below their no effect levels.

If the mode of action is not known, as is the case for many substances, the dose/concentration addition method should be preferred over the independent action approach.

Should there be more specific assessment of risks for chemical mixtures?

Specific mixture risk assessment is indeed necessary, in order to avoid underestimations of risks that might occur under the classical current approach that takes each chemical substance separately.

Except for mixtures composed of chemical substances with a similar mode of action, current evidence does not show

significant mixture toxicity at exposures at or below zero-effect levels of the individual components.

Endocrine disrupting chemical substances (specifically those that are affecting sex hormones) are often mentioned in the context of chemical mixtures, since they have effects at relatively low concentrations, although larger than the concentration of the hormones that they are affecting. Since concentrations that are found in people are very low, it is unlikely that there is an effect of chemical mixtures on these hormones.

What are the effects of chemical substances mixtures on the environment?

The general principles of the risk assessment of chemical substances mixtures is also applicable in the context of environmental toxicology, for predicting effects at population level, although the concepts of “independent action”, “dose additions” and “synergistic action” still need to be understood at the population level. At the level of communities, an additional concept of “synergism” is also possible. It requires an approach based on the understanding of ecology, of interactions between species and their environment, and of indirect effects. Consequently there is a need for improving the current knowledge and methodologies for the ecological risk assessment of chemical substances under realistic conditions.

What are the major knowledge gaps?

One major gap is the lack of knowledge on where, how often and to what extent humans and the environment are exposed to certain chemical mixtures and how exposure may change over a person’s lifetime.

For many chemical substances, there is no good information on mode of action. Interactions of chemical substances in mixtures are also difficult to foresee, particularly for long-term effects. Research is needed to define criteria that could predict potentiation or synergy.

In ecotoxicology, the problem is even more complex. A knowledge of all possible modes of action in complex biological communities is difficult (if not impossible) to be attained and ecologically relevant endpoints are generally broader and not so specific (e.g. toxicity on specific organs, etc.) as in human toxicology.

You can find this summary, along with a more detailed one on the GreenFacts website at:

<http://www.greenfacts.org/en/chemical-mixtures/index.htm>

The source document for this summary can be found on the Europa website:

http://ec.europa.eu/health/scientific_committees/all_opinions/index_en.htm