Cosmetics Europe
the personal care association

Comments on JRC proposals for REACH Standard Information Requirements

Cosmetics Europe represents the cosmetics and personal care industry in Europe. Ranging from antiperspirants, fragrances, make-up and shampoos, to soaps, sunscreens and toothpastes, cosmetics and personal care products play an essential role in in all stages of our life. European citizens use cosmetic products as part of their daily lives, serving their essential needs and expectations. These needs and expectations drive our industry as well as delivering innovative products that enhance consumers' well-being and quality of life and boost their self- esteem.

Cosmetics Europe fully supports the ban on animal testing for cosmetics under the Cosmetic Products Regulation. The cosmetics and personal care industry has been at the forefront of developing alternatives to animal testing for regulatory safety assessment for more than 30 years and believes the only way forward for the EU is to focus on the development and regulatory acceptance of non-animal testing methods. Cosmetics Europe is a member the European Partnership for Alternative Approaches to Animal Testing (EPAA) and actively invests and engages on the topic of alternatives to animal testing.

Cosmetics Europe welcomes the opportunity to comment on the draft options developed by the JRC for the extension of REACH Standard Information Requirements (SIRs) and the increased use of New Approach Methods (NAMs).

The proposed options open the door for innovation by involving state-of-the art science into existing regulatory system. The current REACH legislative framework requires many animal tests, is time- and resource- consuming and it is mostly based on outdated assumptions (Ball et al., 2022).

By shifting the REACH paradigm toward a risk- based approach using real exposure data and human-relevant NAMs we envisage the achievement of a higher protection level while avoiding unnecessary animal testing.

Safety assessments should not simply rely on covering the classical endpoints within conventional toxicology; these should rather focus on providing the relevant information to establish whether chemicals can be used safely. It is not solely the quantity but especially the quality of produced data which will significantly improve human and environmental protection.

NAMs should be combined in a flexible way (e.g. using Defined Approaches (DA) and Integrated Approaches to Testing and Assessment (IATA)) to ensure decisions on the use of chemicals are fit-for-purpose and based on the best available science.

Further confidence building into NAMs is required to support their adoption for legal purposes and to move from animal-based approaches to 21st Century safety assessments based on NAMs.

NAMs are building blocks to be assembled for a full, robust evaluation of a given endpoint. In contrast to animal- based approaches, NAMs are not stand-alone methods and they require substantial amounts of background information and a more sophisticated interpretation.

Questions for discussion and written feedback

1) Should a Chemical Safety Assessment (CSA) be required for all REACH registered substances, or should there be derogations for substances of low concern (derogation criteria to be defined)?

   Cosmetics Europe recommends to clearly define what is considered as a substance of low concern, and the number/types of data that would be required. An option could be to determine low/medium/high concern levels based on exposure associated with known uses of the chemical and hazard reflections and to generate data accordingly. A basic CSA taking into account all available information could be the starting point and the tool to identify other relevant data that need to be generated.

2) In relation to the protection and innovation goals of the CSS, are there any gaps or redundancies in the proposed Standard Information Requirements (SIRs)?

   In general, Cosmetics Europe highlights the importance of exposure estimations when performing safety assessment (which are missing in the current proposals). Exposure estimates will define the degree of hazard data needs and guide further generation (Dent et al., 2018). In the context of REACH, particularly for low tonnage substances, the implementation of *in vitro* test batteries as part of SIR would end up being extremely costly if exposure considerations are not taken into account. Potentially, this may lead to a loss of many small volume ingredients from the market.

   Specific contradictions/gaps identified by Cosmetics Europe are listed below:

   - NAMs should not be considered as replacement of existing *in vivo* assays endpoint per endpoint; instead, NAMs should be used in an exposure-led framework designed to enable robust safety decision making (Ball et al., 2022)
   - The JRC documents states that "*NAMs should NOT be used to automatically trigger higher tier in vivo testing*". Test batteries, applicability and performance of NAMs criteria should be clearly defined to understand when *in vivo* follow up are required. The addition of some of the proposed assays as described now, could trigger additional *in vivo* studies to further confirm or contradict the results. Positive results *in vitro* should be verified with additional mechanistic investigations to exclude the possibility of an irrelevant positive result. Moreover, the scientific rationale behind the inclusion of specific assays is unclear. For example, why *in vitro* Developmental Neurotoxicity and Developmental Immunotoxicity tests are now required, on top of reprotoxicity studies? What would be the relevance of a reprotoxicity screening then?
   - Specific mentions should be added in the annexes in order to consider alternative methods under development, which is the case for long term fish toxicity tests, assessment of bioaccumulation, assessment of environmental EDCs and organ target toxicity.
   - The JRC documents states that "*Higher uncertainty for certain endpoints, compensated by safety measures in order not to lower current protection levels".* This appears to contradict the increasing body of evidence that NAMs can lead to more protective safety decisions than do traditional animal data (Paul-Friedman et al., 2019).
   - NAMs provide results that are protective enough but are not designed to reproduce *in vivo* tests endpoint per endpoint. Meaningful integration of NAMs therefore requires a different approach and a greater emphasis on exposure.
   - Weight of Evidence approaches should be used in the evaluation of NAMs data, especially when a guidance is not yet available. For example, many newly emerging NAMs are based

on human- derived systems that do not require interspecies extrapolation. A transparent characterization of the uncertainties of these methods to underpin mechanistic and human relevance is more scientifically robust than just relying on conservative default factors (Dent et al., 2018)

3) To what extent are trade-offs in the SIRs acceptable, given that it is not feasible to require a full set of information for all registered substances?

Cosmetics Europe believes that by using appropriate NAMs in an integrated manner and in combination with exposure consideration, trade-offs can be minimised.

4) In the short term, what mechanism could be put into place to ensure the efficient recognition of acceptable NAMs? Possibilities may include an Agency List, Commission List, Test Methods Regulation.

- Amend REACH (and CLP) to be 'test agnostic', it should not be linked to specific limited test protocols. A flexible, science-driven approach to addressing information requirements should be supported.
- One of the most critical components is a mechanism to allow meaningful scientific dialogue between registrants and ECHA, to ensure NAMs are applied in a robust and fit-for-purpose way.
- Recognition that NAMs require a new approach to validation. This is important because i) most of the NAMs are human- based, not developed for mimicking animal data ii) most of the NAMs don`t substitute traditional endpoints 1:1 and iii) mechanistic understanding, rather than animal tests, should be considered the gold standard. Consequently, we should focus validation efforts on evaluating NAM-based testing strategies (i.e. Define Approaches (DAs) and IATA) rather than individual NAMs.
- Clarify uncertainties associated with NAMs and define range of applicability. It should be recognised that there is significant uncertainty associated with *in vivo* tests, but we are still able to use them to make protective safety decisions.
- Collaborative efforts between regulatory authorities and industry to develop an approach to translate NAMs outcomes into a regulatory context -classification and labelling as well as risk assessment.

5) On a long term perspective, should the level of information required continue to be based largely on tonnage, or should transition to a system based on levels of concern (generic measures of hazard and exposure)?

Cosmetics Europe welcomes the proposal of a transition toward a "concerned- based approach", where NAMs are used to predict level of concern and trigger information requirements. Chemicals are currently evaluated by considering their intrinsic properties and the overall tonnage produced, where the latter is used as a surrogate for exposure (the more the production, the more the exposure). For each tonnage level, there is a mandatory list of studies to be performed. Instead, we consider more appropriate to characterise the exposure associated with known uses of the chemical and apply a battery of *in vitro* tests to identify the level of concern associated with those exposures. The many millions of Euros spent in research in recent years mean that NAMs are now mature enough to be used as part of such an integrated approach. Health Canada is already paving the way in the use of NAMs for priority setting and screening (Health Canada, 2021), and there is no reason that a similar approach cannot work in the EU.
A more intelligent, exposure-led approach to data generation would allow us to abandon the classical "ticking box" approach. Indeed, it is only after using these types of approaches that registrants can

demonstrate animal testing having been performed as a last resort and the ambition of the CSS can be achieved whilst respecting the need for minimizing animal tests. However, scientific and regulatory consensus is needed on how NAMs are going to be used and interpreted in an integrated manner. Registrants and regulators need to embrace the opportunities for greater protection and fewer animal tests that NAMs can provide.

References

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