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To whom it may concern

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Laundry detergent residues on textiles - Critical review of the value of cytotoxicity tests for the prediction of adverse skin reactions

Occasionally, case reports on adverse skin reactions are brought to our attention. They are related to wearing textiles treated with Ecolab laundry detergents in a washing process. The reports indicate that chemical residues due to the washing process are the suspected root cause.

A washing process specifically implemented on site by Ecolab aims to make sure that the application of Ecolab products provides both an excellent washing result and the absence of critical chemical residual traces on the fabric. To confirm that the concentration of residues is in a tolerable range, textiles treated with Ecolab products have to fulfil the specification as established by generally accepted standards[1].

Provided that the textiles were processed as prescribed by Ecolab and proved to be within the specification the notion of skin compatibility can be further confirmed dermatologically.

So, the assessment strategy follows a tiered approach – determination that residues levels are within the specification and confirmation in dermatological trials. The approach provides a robust basis for the assumption that treatment of textiles with Ecolab products does not adversely affect skin tolerance in humans wearing those textiles.

Our test and assessment policy follows established rules. Whenever we conduct tests for product safety reasons they must fulfil the criteria of validity and relevance. The higher tier human patchtests are the definitive test to decide whether potential residues on the textile could be relevant for detrimental skin effects such as irritation. Ecolab selects dermatological institutes for

[1] A well-known standard in this respect is the "OekoTex® 100" standard, which defines maximum residue levels for organic incrustations, inorganic incrustations, anionic surfactants and non-ionic surfactants. Moreover, OekoTex ® 100 contains specifications for formaldehyde and pH. When the specification is met, this supports the notion of no health concern as related to residues.

these tests which are qualified to conduct such studies according to internationally applicable standards, in a state-of-the-art manner and in compliance with the ethical principles for clinical trials.They investigate effects on human beings, who we aim to protect with our safety strategy. As confirmatory tests human patch tests are not intended for the identification of hazardous effects. Instead, they are conducted to confirm an initial assumption of safety.

Patch tests with textiles treated with laundry detergents realistically mimic the human exposure. For the question of health concern related to residues they can be regarded as a 'gold standard'. For that purpose they are ranked highest in the test hierarchy.

As alternatives to investigations on human beings other test models may be used. Test models are methods, which do not use the object of protection (Humans). Instead, they use surrogates. Such surrogates may be e.g. cell cultures or artificial skin. Those models also have to demonstrate their relevance and reliability. This is generally conducted in so-called ring-tests, which are internationally coordinated and supervised by competent authorities[2]. At the end of the day the models have to deliver comparable results to the 'gold standards'.

If a method has been validated and accepted Ecolab also uses such test methods. We especially apply them in tiered test programs. Previous validation proving reliability and relevance is what we also demand of models which are suggested to us from third parties. In this context we are occasionally facing suggestions to conduct cytotoxicity tests to investigate skin compatibility.

We do not consider this a valid approach.

Cytotoxicity tests are well suited to investigate mucous membrane compatibility. Consequently, and for good reasons, they have been introduced e.g. into the respective ISO norm for medical devices. However, they are NOT validated for the identification of skin effects: In ring trials they proved not to be predictive.

The final conclusion of an EU workshop on this topic is still valid[3]: Cytotoxicity tests are not suitable for the hazard identification regarding local skin effects.

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[2] In the European Union this is the European Center for the Validation of Alternative Methods (ECVAM).

[3] 'Early *in vitro* studies looked for basic cytotoxicity in cell cultures and skin explants (for example, 76). The endpoints studied were related to cell viability, i.e. dye exclusion, vital dye uptake, enzyme release, amino acid or glucose utilization, or lactate production. Later, MTT came into routine use as a quantitative measure of cell viability (for example, 77). Two main conclusions can be drawn from these cytotoxicity-based studies. Firstly, they indicated that cell culture tests, without a stratum corneum barrier, had limited predictive power (overprediction was common, because not all compounds can penetrate the stratum corneum). Secondly, they showed that, although there is a correlation between irritant potential and reduced cell viability, there are other important confounding factors, and that general cytotoxicity is not an adequate predictive tool when used alone. Therefore, much effort is currently being dedicated to the identification of more-specific endpoints for skin irritancy (morphology, expression and release of cytokines, and skin physiology), based on present knowledge of the progression of skin irritation *in vivo*.' Van de Sandt et al, ECVAM workshop report 1999.

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The safety for human and environmental health is an inherent feature of Ecolab products and processes. State-of-the-art methods and procedures are used for conducting these tasks. In our work we follow internationally adopted standards and guidelines to make sure a broad acceptance with customers, authorities and other stakeholders. As an outcome of this strategy we conclude that treatment of textiles as prescribed by Ecolab does not give rise to a residue and a human health concern.

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