Dermatotoxicological and other Safety Testing Methods without Animals - State November 2013

Session 1: Dermatotoxicological risk assessment without animal testing

OECD update on local skin and eye toxicity – a never ending story?

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Upon adoption of the 7th Amendment of the Cosmetics Directive 76/768/EEC ten years ago in 2003, of the two proposed deadlines for phasing-out of safety testing in animals, it seemed realistic to achieve the goal of a complete replacement for assessments of local skin and eye toxicity by a battery of in silico and in vitro methods by 2009, while all experts agreed the deadline of 2013 for animal free testing of repeated dose toxicity, reproductive toxicity and toxicokinetics cannot realistically be met. Since also in other regulatory areas there is an international commitment to reduce and, wherever possible, replace toxicity testing with animals, many OECD projects are dealing with refining, reducing and replacing animal based methods. Several of the recent past and current OECD projects are focused on local toxicity of skin and eye. The presentation will cover an update on these activities.

In the area of skin toxicity, project leaders in collaboration with the OECD Expert Group "Skin Irritation and Corrosion" have between 2010 and 2012 revised Test Guidelines (TG) 430 and TG 431 to include Performance Standards for similar "me-too" methods, which was in particular necessary for the Reconstructed human Epidermis (RhE) Corrosion Test (TG 431). In addition TG 431 was revised to cover now the performance of various epidermis models to sub-categorize corrosive test chemicals into potency classes. Furthermore, TG 439 (RhE Skin Irritation Test) was revised to increase the understanding of common elements and differences of the protocols used with the four currently accepted RhE models (EpiSkin, EpiDerm, SkinEthic, and LabCyte). The revised Test Guidelines mentioned have been adopted in April 2013. The currently final task of the OECD Expert Group is the finalization of a German project, the "OECD Guidance Document on an Integrated Approach on Testing and Assessment (IATA) for Skin Corrosion and Irritation" which explains the available in silico, in vitro and in vivo tests and proposes an integrated strategy for their use, leaving the Draize skin test as limited a least resource.

In eye toxicity, project leaders in collaboration with the OECD Expert Group "Eye Irritation" have between 2011 and 2012 revised TG 437 (BCOP) and TG 438 (ICE) to enlarge their applicability from the limited positive identification of chemicals causing serious eye damage to the identification of chemicals not requiring the classification of eye irritation (absence of hazard potential). Both revised Test Guidelines mentioned have been adopted in April 2013, while a new Test Guideline on the "Cytosensor Microphysiometer" has not been adopted by the OECD. A new Draft Test Guideline, the "Short Term Exposure for Eye Hazard Potential" (STE Test) is currently published for national comments, and may be adopted in the future. Given the so far limited applicability of all in vitro "eye toxicity" methods adopted by the OECD, there is a strong call for

development of a Guidance Document (analogue to the Guidance Document for Skin Irritation / Corrosion mentioned above).

Thus, although expected 10 years ago, we are not “done” today with fully replacing the need of animal tests for topical toxicity testing, in particular for eye irritation / eye corrosion. The conservative position in in accepting alternative approaches in this area is due to the fact that protecting the eye from damages is regarded of higher value than protecting the skin from damages. However, new meta-analyses of Draize eye test data show for the first time that even the over-sensitive Draize eye test is producing false negative predictions.