Session 5: Clinical development

Human Safety Phase I Studies

Priv.-Doz. Dr. Joachim Fluhr and Betsy Hughes-Formella, PhD
bioskin GmbH, Seydelstr. 18, D-10117 Berlin
and bioskin Gmbh, Burchardstr. 17, D-20095 Hamburg

The safety battery for topically applied products typically includes evaluation of the final to-be-marketed formulation for cutaneous toxicity, most notably dermal irritation, potential for inducing contact sensitization, phototoxic potential and photoallergic contact sensitization. Even though these phase 1 safety studies are an integral part of almost every topical development program and help lay the groundwork for responsible and safe clinical development in later phases, there are no current FDA or EMEA guidelines available specific to these studies. Unfortunately, in the absence of guidelines setting down the requirements and designs for these studies, sponsors are often at a loss for rational designs and how to manage agency expectations. This presentation is intended to give an overview of the basic study designs for irritation, sensitization, phototoxicity and photosensitization as standard dermal safety tests in humans.

Studies for dermal irritation and phototoxic potential are normally conducted early in the clinical program. However, it must be kept in mind that the safety studies for the licensing application should be conducted with the to-be-marketed formulation, and that this may not be available at the earliest stages of clinical development. It may be necessary to provide human safety date before proceeding with Phase IIa studies with concept formulations, particularly in the case of NCEs. For this purpose, abbreviated designs with shorter treatment duration and fewer subjects are generally acceptable. Testing of sensitization and photosensitization is often delayed and conducted in parallel with Phase IIb or III.

The exaggerated conditions (such as occlusion) used in Phase 1 cutaneous safety testing serve to ensure that potential safety problems are not missed and can be appropriately addressed in later phase clinical trials. In order lo have confidence that tolerability issues will indeed be recognized, it is important to optimize the design used for these safety studies. After all, early recognition of safety problems may save considerable development time and costs.