Lube-Tech
PUBLISHED BY LUBE: THE EUROPEAN LUBRICANTS INDUSTRY MAGAZINE
No.52

Skin compatibility of cutting fluids: in vitro / in vivo test strategy

Abstract
Three water-based cutting fluids containing different biocide concentrations and different emulsifier systems were tested for skin compatibility using *in vivo* and *in vitro* systems. Used and unused samples of one of the cutting fluids were compared using the *in vitro* system. With the *in vivo* test, a 24 h Patch Test revealed good skin compatibility for all the cutting fluids tested, with no significant differences between the three samples. In contrast the *in vitro* tests using human epidermal or human cornea skin models revealed significant differences between the samples. Differences were observed between the three unused cutting fluids, and between the used and the unused samples. To summarise, *in vitro* test systems using human skin models provide useful option for a sensitive test of the skin compatibility of cutting fluids in long term contact with the skin.

Key words
Skin compatibility, cutting fluid, skin model, *in vitro* test, contact dermatitis.

Introduction

Contact dermatitis in metal workers is considered to be the most relevant occupational illness in the metal working industry. Different studies report a 20-25% prevalence of hand eczema in metal workers (1,2). Irritant contact dermatitis is more often diagnosed than the allergic contact dermatitis (3). Several different chemicals with which metal workers have skin contact contribute to the high prevalence of contact eczema, including cleaning detergents, solvents, degreasers and metalworking fluids. Though rarely harmful on short-term exposure, metalworking fluids may evolve their harmful attributes after long term and repeated contact with the skin. Since several hours of contact on each working day is typical in many working environments, even a low irritant capacity contributes to the high incidence of contact eczema in this work group. The use of cutting fluids with good skin compatibility is therefore an important factor in preventing occupational hand dermatitis in metal workers. In recent studies, both *in vitro* and *in vivo*, the irritancy of different cutting fluids was compared. Both strategies have advantages, but also limitations.

In vivo studies on human volunteers are of the highest relevance for predicting skin irritancy. However, when looking at chronic skin irritancy induced by mild irritants, established *in vivo* studies often fail to predict the irritant potential. For example in a study by de Boer et. al. (4) different metal working fluids induced only minimal skin irritation, even after stripping of the stratum corneum and repeated application to the forearm skin over 5 days. Differentiation between the tested fluids and water was only possible for one of three cutting fluids tested. In addition, in *in vivo* tests the safety of volunteers has the highest priority. Hence, some products may not be tested. A study director should take into account the higher penetration rate of components and a higher risk of sensitisation under the conditions of a repeated patch test design. This holds especially true for all used cutting fluids for which the exact composition is not known.

For *in vitro* tests correlation to the *in vivo* situation has to be verified before they can be used as a predictive tool. On the other hand, *in vitro* test procedures can be used with any sample and at any concentration. The analysis of the irritancy potential is based on the measurement of inflammation mediators or on the quantification of cell damage. This allows a relatively sensitive analysis of the irritant potential of test substances, since the biochemical parameters increase before clinical symptoms are manifest. However, careful examination of the test results is necessary due to the model nature of *in vitro* tests. Correlation with the *in vivo* situation can only be assumed when validated test designs are used. In previous studies, the BUS model was accepted as an *in vitro* model for testing the skin compatibility of cutting fluids (5). Although it served for some time as a suitable test system, it also has some disadvantages such as the lack of standardisation and insufficient data for correlation with the *in vivo* situation.

Today, 3-dimensional cell cultures from human skin cells, so called skin models, have gained increasing importance as alternative to *in vivo* test systems (6). Due to great efforts of the cosmetic and raw material industry to find alternative methods to replace animal testing, the development of skin models has made fast improvements in the last years. The reconstituted human skin model, cultivated from human epidermal skin cells on a collagen matrix, was validated for the toxicological endpoint skin corrosion by ECVAM (European Centre for the Validation of Alternative Methods) (7). The validation study was performed in three independent laboratories and proved that this human skin model was able to correctly predict the corrosion potential of 12 OECD reference chemicals. The validation procedure led to a new OECD Guideline for the testing of chemicals for skin corrosion based on skin models (8). So far, three different skin models have been validated according to the OECD TG 431 as suitable test systems for skin corrosion: EPISKIN™, EpiDerm™ and SkinEthic™. Skin corrosion, defined as the production of irreversible tissue damage of the skin following the application of a test material, is certainly not induced by the application of metal working fluids. The damage to skin by long term contact with this product category is a mild irritation, with irritation being defined as the production of reversible tissue