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## Proceedings of the International Conference on Occupational & Environmental Exposures of Skin to Chemicals: Science & Policy

Hilton Crystal City September 8-11, 2002

### A Mathematical Approach for Evaluating Dermal Exposure and Facilitating Assignment of Skin Notations

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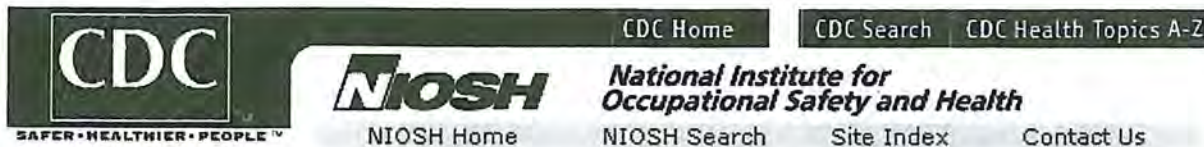
Dermal exposure to hazardous substances is of increasing concern for workers in various occupational environments. The National Institute for Occupational Safety and Health (NIOSH) currently has skin notations (SNs) as a part of the Recommended Exposure Limits (RELs) for 142 compounds and chemical groupings, serving as a mechanism to inform the workers of health risks from dermal exposure to these substances. In the present for the SNs only provide a qualitative indication of skin hazards. An explicit approach is needed that quantitatively characterizes dermal absorption potential of chemical and facilitates systematic assignment of the SN.

Here we present an evaluation scheme that can be used as a tool to assess the contribution of hazards to systemic toxicity via skin absorption when empirical data are not readily available or are of questionable quality. In this scheme, a mathematical model is used to predict the skin permeation coefficient ( $K_p$ ) of a chemical based on its octanol-water partitioning coefficient and molecular weight. The  $K_p$  is used to determine the dermal uptake of chemical from saturated aqueous solution (dermal dose) following a conservative default scenario in which the unprotected palmar skin on both hands (a surface area of 360 cm<sup>2</sup>) of a worker is continuously exposed for 8 hours. The dermal dose is compared to the dose absorbed and accumulated in the body via inhalation in 8 hours (inhalation dose), as estimated by multiplying the chemical's REL with an inhalation volume of m<sup>3</sup> and a default retention factor of 75%. A chemical is considered a dermal absorption hazard if the ratio of skin dose to inhalation dose (S-I ratio) is equal to or larger than one. The evaluation was performed for 137 REL compounds with SNs for which the parameters required for model input were properly identified.

The preliminary results show that 70 of the 137 evaluated compounds were considered by the scheme as a possible absorption hazard (a positive compound). The S-I ratio for 53 positive compounds (76%) was exceeded in 2 hours after the onset of exposure, indicating that the dermal uptake needed to reach the toxic levels of these compounds proceeded at a rate higher than that for the uptake by inhalation. To examine the applicability of the scheme and of underlying assumptions to chemicals of different toxicological and chemical properties, the negative compounds were reviewed for toxic effects reported for dermal exposure and analyzed for structural composition. The reviews established that for 28 negative compounds the skin absorption of chemical resulted in acute and chronic toxicity (including tumorigenic and reproductive effects), and for 9 compounds the absorption might result in marginal or less-than-marginal toxicity. The primary adverse effects from dermal exposure to 20 compounds were combinations of skin irritation, sensitization and/or physical damage. The structural analysis shows that 48 negative compounds (approximately 72%) have aromatic or cyclic rings in the chemical structure. Those with bicyclic heptane derivatives, heterocyclic rings with nitrogen, oxygen and/or sulfur, and organophosphates were among the substances for which the scientific information and modeling results disagreed on the significance of dermal absorption to systemic toxicity. The same informational review and structural analysis are currently underway for the compounds considered as positive absorption hazards. Limitations, alternative scenarios, and potential application in SN evaluation of the current approach will be discussed.

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## The International Conference on Occupational & Environmental Exposures of Skin to Chemicals: Science & Policy

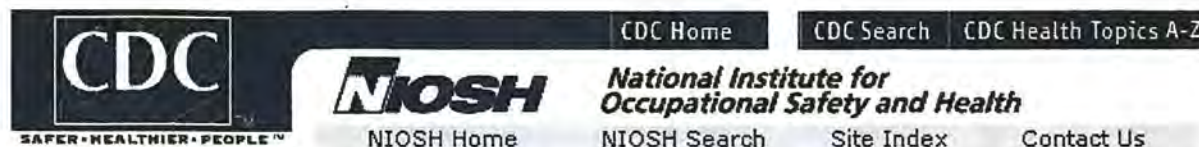
September 8, 2002 - September 11, 2002

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The National Institute for Occupational Safety and Health (NIOSH) co-sponsored this inaugural conference to bring together dermatologists, occupational hygienists, laboratory researchers, policy makers and other to focus on the science, knowledge gaps and policy opportunities related occupational and environmental exposures of the skin to chemicals.

The site was the Hilton Crystal City at Ronald Reagan National Airport hotel. The main conference was followed by a one-day workshop focusin on specific research and public health opportunities for decreasing the burden of skin exposures to chemicals in both workplaces and the gener environment.

Approximately 135 individuals attended. A second conference is expecte in 2004.

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