



## Exposure and Absorption of Hazardous Materials through the Skin

none

To cite this article: none (2000) Exposure and Absorption of Hazardous Materials through the Skin, International Journal of Occupational and Environmental Health, 6:2, 148-150, DOI: [10.1179/oeh.2000.6.2.148](https://doi.org/10.1179/oeh.2000.6.2.148)

To link to this article: <https://doi.org/10.1179/oeh.2000.6.2.148>



Published online: 19 Jul 2013.



Submit your article to this journal [↗](#)



Article views: 22



View related articles [↗](#)



Citing articles: 1 View citing articles [↗](#)

## Exposure and Absorption of Hazardous Materials through the Skin

This journal issue is a testament to the important contributions made in the field of percutaneous absorption by such early research pioneers as Janusz Hanke, Tadeusz Dutkiewicz, and Jerry Piotrowski. Beginning with their landmark research on the absorption of benzene through human skin, originally published in 1961 and appearing in English for the first time in this issue, these three individuals have made significant contributions regarding the potential for percutaneous absorption of such industrial chemicals as aniline, styrene, toluene, carbon disulfide, acrylonitrile, and nitrobenzene. Their work has helped others recognize the potential importance of skin exposures and has raised an awareness of the need to protect workers and the public from these exposures.

The ramifications of exposure of the skin to toxic chemicals are still poorly understood. It is comparatively easy to obtain documentation that occupational and environmental skin exposures to chemicals are a significant cause of dermatitis. In addition, during the past century a fair number of acute poisonings have been reported for many chemicals where the primary means of exposure was to the skin. Adverse outcomes resulting from chronic, lower-level skin contacts with chemicals have been documented far less frequently. The lack of data on health effects with chronic exposures should not be interpreted as a lack of effect, however, but as evidence of the difficulty in measuring human exposures and in linking exposures to health risks. Such difficulties have forced us to rely on lab-

oratory studies and predictive equations to assess the likelihood that such exposures might adversely impact human health.

Although laboratory-based *in vitro* and *in vivo* testing has produced permeation rates for many compounds, the use of different experimental methods to obtain these rates has produced dissimilar results, sometimes differing by a few orders of magnitude.<sup>1</sup> Currently there is a need for experimental procedures that are validated against human skin, with the objective of reaching a consensus adoption of standardized protocols producing universally accepted permeation rates. Additional precise empirical data will facilitate the development of structural-activity relationship models that will make possible accurate estimation of skin permeation rates for compounds not yet tested. Once the permeation rate of a chemical is available, health risks can be predicted, based on the use of surface concentration, skin surface area exposed, and duration and frequency of exposure to estimate absorbed amounts. The absorbed dose, coupled with the kinetics of metabolism and elimination, can then be related to experimental systemic toxicologic data.

Qualitative guidance criteria, provided as "skin notations," have been adopted by workplace exposure standards organizations worldwide as footnotes to air concentration limits. Historically, the criterion for a skin notation is the recognition that skin exposure and absorption can significantly contribute to systemic effects.<sup>2</sup> That is, skin exposure when added to the dose received by

inhalation may cause increased toxicity. By definition, the notation does not specifically apply to chemicals that have direct effects on the skin, such as irritation and allergic sensitization.

In the 1980s it was estimated that over 13 million workers in the United States were potentially exposed to chemicals with the U.S. Occupational Safety and Health Administration (OSHA) skin notation, but the actual extent of exposure is unknown.<sup>3</sup> The American Conference of Governmental Industrial Hygienists (ACGIH) presently assigns skin notations to at least 170 of 650 compounds that have threshold limit values (TLVs). OSHA listed 147 skin notations in the (judicially revoked) 1989 revised Permissible Exposure Limit (PEL) table Z-1000, and the National Institute for Occupational Safety and Health (NIOSH) presently assigns 142 skin notations to its Recommended Exposure Limit (REL) list of compounds. Worldwide, at least 275 skin notations exist for chemicals identified as skin-absorption hazards. The number of compounds with skin notations, however, represents only a small fraction of the approximately 30,000 compounds in commercial use, many of which might be absorbed through the skin.

The process by which chemicals have been identified as skin-absorption hazards by these standard-setting organizations has been criticized as inconsistent and often poorly documented.<sup>4-6</sup> After reviewing the 1986 TLV Documentation, Scansetti et al.<sup>5</sup> found that only 54% of the compounds with skin notations had been assigned the notations based on animal experimental

dermal lethal dose and/or reports of human toxicity. Of the remaining 46%, 20% were unreferenced assignments, 14% were based on undocumented statements, 8% were based on skin effects, and 4% were based on chemical analogy. A lack of adequate supporting documentation to justify a skin notation, however, should not lead to the conclusion that skin exposure to that chemical is safe. As can be seen in the above assessment, the available information supporting many of the assignments is often very sparse.

Several approaches have been proposed for both improving the identification of notation-worthy chemicals and improving the consistency of the justifying documentation. For systemically acting chemicals, these approaches recommend basing the skin notation on empirical data, such as dermal LD<sub>50</sub>,<sup>7-10</sup> or use of calculated permeation data,<sup>6</sup> which are then compared with some measure of toxicity to determine the relative risk of exposure. Neither of these is without flaws. Dermal LD<sub>50</sub> data are not available for all compounds and, where available, may require extensive literature search and evaluation to assess the adequacy of the experimental protocol and to determine whether deaths were due to systemic or localized effects. Empirical permeation data are available for many industrial compounds, but some effort may be required to evaluate the validity of the protocols.

Skin notations could also be assigned using calculated permeation coefficients (Kps) that are commonly modeled from saturated aqueous solutions. The permeation coefficient is the ratio of flux over concentration. Generally, Kp is concentration-independent up to aqueous saturation, whereas above saturation, the mass transfer rate is more or less constant.<sup>11</sup> This presents a convenient modeling advantage since a maximum flux rate can be predicted. This approach to estimating risk from skin exposure has been recently proposed by the U.S.

Environmental Protection Agency (EPA) as the currently preferred method and has undergone extensive internal and external review.<sup>12</sup> A limitation of this predictive approach is that the rate of permeation of a chemical can be affected by its vehicle as well as by its presence in a chemical mixture. Presently it is not possible to predict the impacts of different vehicles and co-exposures on absorption.

Some have advocated the eventual establishment of quantitative dermal occupational exposure limits, or DOELs<sup>13</sup>; no such quantitative guidelines currently exist. The establishment of quantitative guidelines would provide some definite benefits. It can be argued that DOELs would encourage the development and implementation of corrective or preventive actions that could reduce exposures. Certainly, the advent of airborne exposure limits in the 1930s spawned major advances in monitoring and control of potential inhalation hazards. In addition, quantitative guidance criteria provide a measure of the potential of the exposures to cause adverse effects by virtue of their relative values, which is not evident in qualitative warnings. Quantitative guidance criteria could encourage the collection of objective measurements of exposure, rather than simply implementing precautions without verifying their efficacy. Quantitative surface or skin measurements would also allow comparison of the contribution of skin exposure to inhalation exposure from airborne chemicals, thus providing a better indication of total exposure potential through all routes.

It can be also argued that the paucity of available data does not currently permit establishment of any guidelines. European exposure standards groups, such as the Health and Safety Executive of the United Kingdom, are considering the use of broad occupational exposure bands for setting limits when inadequate toxicologic information exists for a chemical. Briefly, when

the lack of toxicological data prohibits setting a precise occupational exposure limit but the data suggest an exposure limit ranging within an order of magnitude, exposure may be acceptable up to the upper limit but normally should be kept as low as reasonably practicable below that limit.<sup>14</sup> Such an approach has been recently postulated for establishing DOELs.<sup>15</sup>

Another recent proposal for deriving quantitative DOELs, however, requires empirical information that is currently available for only a few compounds.<sup>16,17</sup> Some have argued, in fact, that the factors that influence the effects of percutaneous exposure are so complex as to make quantitative exposure limits meaningless.<sup>18</sup> There are still numerous unresolved issues. It must be defined whether the allowable concentrations should refer to work surfaces, skin, or clothing surfaces. Inherent variability in skin absorption rates related to skin condition, environmental conditions, and effects of co-exposures make it uncertain how protective numerical criteria would actually be in real-world settings. Other variables that influence absorption, such as temperature, frequency of exposure, and the effects of mixtures, must also be taken into consideration. Finally, exposure assessment methods and strategies are still in the early stages of development and validation.

Perhaps a more feasible semi-quantitative approach would be to limit not the concentration but the maximum time allowed for a dermal exposure to occur, as proposed by Walker et al.<sup>19</sup> Thus, rather than attempting to quantify the exposure concentration, primary effort would be focused on prevention of skin exposures by limiting the durations of situations in which people are exposed to potentially hazardous chemicals. This could entail performing an appropriate risk assessment, perhaps some limited surface sampling, and use of rational professional judgment, an approach that is similar to established ap-

proaches used for evaluation and control of potential respiratory hazards.

When developing an approach to expand the qualitative notations or develop new semiquantitative skin-exposure guidance criteria, the following points should be considered: 1) the need for criteria, including potential costs and benefits incurred; 2) the feasibility of developing criteria; and 3) the expectation of application and response by the intended audience. The approach should be technically and economically feasible so that it can be implemented fairly quickly. Also, the approach selected should be clearly stated and its limitations cited. It is reasonable to expect future improvement of the predictive models of skin absorption potential and, therefore, more plentiful data to support the establishment of exposure guidelines. Consensus on reasonable approaches to establishing skin-exposure limit guidelines, as well as preventive approaches for minimizing exposures, are certainly needed.

The 21st century will bring further advances and expand our knowledge in the fields of occupational and environmental skin exposures and direct and systemic health effects from such exposures. This journal issue is certainly a great stepping stone for such an endeavor. The ultimate goal of all progress remains the application of scientific knowledge towards preventing health effects from occupational and environmental skin exposures and assuring safety and health at work (and beyond) for all people.

MARK F. BOENIGER, MS, CIH  
BORIS D. LUSHNIAK, MD, MPH  
*National Institute for  
Occupational Safety and Health*

4676 Columbia Parkway, R-12  
Cincinnati, OH 45116  
Phone: (513) 841-4503  
Fax: (513) 841-4483  
E-mail: <bd11@cdc.gov>

Special thanks are due to Drs. Mitch Singal, Marie Haring-Sweeney, and Sid Soderholm and Ms. Wendy Wippel at NIOSH for their helpful comments during the preparation of this commentary.

### References

1. Vecchia BE. Estimating the dermally absorbed dose from chemical exposure: data analysis, parameter estimation, and sensitivity to parameter uncertainties. MS Thesis, Colorado School of Mines. Golden, CO, 1997.
2. American Conference of Governmental Industrial Hygienists (ACGIH). TLVs and BEIs: Threshold Limit Values for Chemical Substances and Physical Agents. Cincinnati, OH, 1999.
3. National Institute for Occupational Safety and Health. National Occupational Exposure Survey, 1981-1983. DHHS (NIOSH) Publication No. 88-106. Special Data Analysis, 1988.
4. Grandjean P. Preventing percutaneous absorption of industrial chemicals: the "skin" denotation. *Am J Ind Med* 1988; 14:97-107.
5. Scansetti G, Piolatto G, Rubino G. Skin notations in the context of workplace exposure standards. *Am J Ind Med*. 1988; 14:725-32.
6. Fiserova-Bergerova V, Pierce JT, Droz PO. Dermal absorption potential of industrial chemicals: criteria for skin notation. *Am J Ind Med*. 1990;17: 617-35.
7. Kennedy GL, Brock WJ, Banerjee AK. Assignment of skin notation for threshold limit values of chemicals based on acute dermal toxicity. *Appl Occup Environ Hyg*. 1993;8:26-30.
8. European Center for Ecotoxicology and Toxicology of Chemicals. Strategy for assigning a "skin notation." Report 31 (Revised). Brussels, Belgium, 1993.
9. de Cock J, Heederick D, Kromhout H, Boleij JSM. Strategy for assigning a "skin notation": a comment. *Ann Occup Hyg*. 1996;40:611-4.
10. European Center for Ecotoxicology and Toxicology of Chemicals. Special Report No. 15. Examination of a proposed skin notation strategy. Brussels, Belgium, 1998.
11. Bunge AL, Cleek RL, Vecchia BE. A new method of estimating dermal absorption from chemical exposure. 3. Compared with steady-state methods for prediction and data analysis. *Pharmaceut Res*. 1995;12:972-82.
12. U.S. Environmental Protection Agency. Risk Assessment Guidance for Superfund. Vol. 1: Human Health Evaluation Manual, Supplemental Guidance, Dermal Risk Assessment, Interim Guidance. NCEA-W-0364, May 1998, External Review Draft.
13. Fenske R, Van Hemmen JJ. Occupational skin exposure to chemical substances: setting limits. *Ann Occup Hyg*. 1994; 38:333-6.
14. Guest I. The Chemical Industries Association guidance on allocating occupational exposure bands. *Ann Occup Hyg*. 1998;42:407-11.
15. Evans P. A banding approach to controlling the risks from dermal exposure. *Skin Contacts*, newsletter of the Dermal Exposure Network, Europe, June issue, 1999.
16. Bos PMJ, Brouwer DH, Stevenson H, Boogaard PJ, de Kort WLAM, van Hemmen JJ. Proposal for the assessment of quantitative dermal exposure limits in occupational environments: Part 1. Development of a concept of derive a quantitative dermal occupational exposure limit. *Occup Environ Med*. 1998; 55:705-804.
17. Brouwer DH, Hoogendoorn L, Bos PMJ, Boogaard PJ, van Hemmen JJ. Proposal for the assessment of quantitative dermal exposure limits in occupational environments: Part 2. Feasibility of study for application in an exposure scenario for MDA by two different dermal exposure sampling methods. *Occup Environ Med*. 1988;55:805-11.
18. Packham CL. Setting limits on occupational skin exposure to chemical substances (letter to the editor). *Ann Occup Hyg*. 1995;39:125-6.
19. Walker JD, Whittaker C, McDougal JN. Role of the TSCA interagency testing committee in meeting the U.S. government data needs: designating chemicals for percutaneous absorption rate testing. In: Marzulli FN, Maibach HI (ed). *Dermatotoxicology*. 5th ed. Bristol, PA: Taylor & Francis, 1996:371-81.