

Miller, Diane M. (CDC/NIOSH/EID)

From: Dotson, G. Scott (CDC/NIOSH/EID)
Sent: Monday, December 01, 2008 4:22 PM
To: Miller, Diane M. (CDC/NIOSH/EID)
Subject: FW: Review of NIOSH document: Skin notation strategy (Docket 153)
Attachments: Responses to Reviewer Q.doc; ATT641781.htm

FYI

G. Scott Dotson, Ph.D., M.Sc.

Senior Service Fellow-Industrial Hygienist
Centers for Disease Control and Prevention
National Institute for Occupational Safety and Health
Education and Information Division
4676 Columbia Parkway, MS C-32
Cincinnati, Ohio 45226-1998
Phone: (513) 533-8540
Fax: (513) 533-8230

From:
Sent: Monday, December 01, 2008 3:07 PM
To: Dotson, G. Scott (CDC/NIOSH/EID)
Subject: Re: Review of NIOSH document: Skin notation strategy

Very sorry for delay. Are you around ?
Comments attached. I had also made some edits in doc, but wanted to discuss.

Responses to Peer Reviewer Questions

1. Are proposed classes of skin notations appropriate? Yes. But would revise definition of Sen.
2. Are proposed criteria for skin notation appropriate? Yes. For Sen would clarify that sensitization can be documented by antigen specific immune responses other than patch testing. This is already implied /stated in some places, would just make more explicit. Ex - page 19 - line 7. (e.g. patch testing or antigen-specific immune responses such as antibody responses or lymphocyte proliferation.)
3. Is the proposed assignment of multiple skin notations useful? Yes.
4. Should the SEN notation apply strictly to ACD or is it appropriate to assign the SEN notation for other immune-mediated responses, such as respiratory sensitization, airway hyperactivity and mucosal inflammation, associated with dermal exposure to compound?

Yes appropriate to use for other immune-mediated responses. However terminology needs editing. Skin exposure or any exposure causes systemic sensitization. Sensitization is systemic condition (immune cells circulate). The immune / allergic response can occur at local sites (eg airways, lung, skin) following re-exposure (elicitation) at that site. Would avoid "respiratory sensitization" or wording that suggests that skin exposure causes asthma or diseases at distant sites. Skin exposure causes systemic sensitization that can contribute to subsequent development asthma following airway exposure. Skin or respiratory in front of sensitization usually refers to route of sensitization - via skin or respiratory track. To avoid confusion I try to separate the "site" from word "sensitization" since sensitization is systemic. This has major implications as industry goes nuts at the suggestion that skin exposure causes lung or airways disease.

5. Propose harmonization scheme OK ? Yes.

6. Additional information ? (or less information)

a. would minimize mechanistic discussion - eg Type I, Type IV. Current terminology is primarily IgE-mediated or cell mediated immune response. Since immunology quickly gets complicated, easy be "out-of-date" - less said probably the better.

b. Table EI - page 68 - would add terms such as allergen, atopy, rhinitis, sinusitis, lung diseases (asthma, hypersensitivity pneumonitis, chronic beryllium disease etc), IgE, IgG, T cells, sensitization, etc. List is very complete for skin - less so for lung / allergy / asthma / immune responses terms.

c. P 85 Table D2 - missing some key chemicals would rank in top 30 - but OK. Suspect that's because started with prior list 142 chemicals - and as noted list is only first 30 - NIOSH will get to others. E.g. Several key diisocyanates missing - MDI, HDI. Also anhydrides.

d. Terminology - as above some terms / definitions "sensitization" "sensitizing effects" "respiratory sensitization" need some edits to be more accurate immunologically.

"Dermal" refers to one layer of the skin - the dermis, which is below the epidermis. More accurate would be use of "skin" or "cutaneous" as in "skin exposure" or "cutaneous exposure".

6. Additional info - quite complete.

7. Yes data cited OK.

8. Conclusions appropriate - yes.

Document overall very well done - and important contribution.

See also edits in document.