

6/7/2010

Review: NIOSH Skin Notations Review - Group A
Profile Number: 10
Profile Title: Ethylene Glycol Dinitrate (EGDN)

Summary

Reviewers agree that the manuscript clearly outlines the systemic health hazards associated with EGDN dermal exposure. They also agree on the clarity outlining the absence of direct health hazards, and feel there is insufficient data to conclude immune-mediated responses. Both reviewers note a lack of information concerning the SYS (FATAL) notation, and agree on the justification for not assigning SEN and DIR notations. The review contains several recommendations listed below.

Recommendations

- The systemic effects of EGDN in animals and humans exposed through non-dermal routes should be briefly summarized. (Q1, Q2, Reviewer 1)
- Insufficient data are available to assign the FATAL notation. More description is needed on the exact circulatory system effects observed and if they are clearly associated with EGDN exposures. (Q2, Reviewer 2)
- The justification for identifying cardiovascular effects to exposures is weakly described in the document and should be better described from the primary literature (Einert et al. 1963; Hogstedt and Axelson 1977). (Q8, Reviewer 2)
- It's not clear why Table 2 is included. The summary of carcinogenic designations for EGDN by other governmental and nongovernmental agencies seems out of place since these carcinogenic designations are not specific to dermal exposures. (Q9, Reviewer 2)
- Page 3 end of last paragraph just before Table 2: the author notes that "Table 2 provides summary of carcinogenic designations for epichlorohydrin..." which must be a cut-and-paste typo from a similar document. (Q11, Reviewer 2)
- The document needs stronger justification for the identification of the toxic effect. Suggest adding several sentences to the section on epidemiological studies to note the conclusion of the authors. (Q13, Reviewer 2)

Verbatim Reviewer Comments

1. Does this document clearly outline the systemic health hazards associated with exposures of the skin to the chemical? If not, what specific information is missing from the document?

Reviewer 1:

Data is presented supporting the conclusion that EGDN is absorbed through the skin of exposed humans, and suggesting that it causes systemic health effects after dermal absorption. The systemic effects of EGDN in animals and humans exposed through non-dermal routes should be briefly summarized.

Reviewer 2:

Yes, the document clearly describes the existing literature with sufficient detail to follow the exposure information and the systemic health hazard is summarized.

2. If the SYS or SYS (FATAL) notations are assigned, is the rationale and logic behind the assignment clear? If not assigned, is the logic clear why it was not (e.g., insufficient data, no identified health hazard)?

Reviewer 1:

The rationale for the SYS notation is clear, but would be strengthened by addition of information on the known systemic effects of EGDN (from non-dermal exposure route studies), as mentioned in response to (1) above.

Reviewer 2:

The document is clear in that insufficient data are available to assign the FATAL notation. The systemic toxicity (cardiovascular) is based on epidemiological studies that indicate circulatory system effects, and this should be better described - what exact circulatory system effects were observed and are they clearly associated with EGDN exposures

3. Does this document clearly outline the direct (localized) health hazards associated with exposures of the skin to the chemical? If not, what specific information is missing from the document?

Reviewer 1:

The document clearly presents data supporting the conclusion that EGDN does not cause direct effects on the skin.

Reviewer 2:

There do not appear to be any localized health hazards associated with dermal exposures to EGDN

4. If the DIR, DIR (IRR), or DIR (COR) notations are assigned, is the rationale and logic behind the assignment clear? If not assigned, is the logic clear why it was not (e.g., insufficient data, no identified health hazard)?

Reviewer 1:

The rationale for not assigning a DIR notation is clearly and logically presented.

Reviewer 2:

The justification for not assigning DIR notation to this compound is well described.

5. Does this document clearly outline the immune-mediated responses (allergic response) health hazards associated with exposures of the skin to the chemical? If not, what specific information is missing from the document?

Reviewer 1:

The document presents data supporting the conclusion that insufficient data are available to assign the SEN notation to EDGN.

Reviewer 2:

There are very limited data for determining whether EGDN is a skin sensitizer - this is described in the document.

6. If the SEN notation is assigned, is the rationale and logic behind the assignment clear? If not assigned, is the logic clear why it was not (e.g., insufficient data, no identified health hazard)?

Reviewer 1:

The reason for not assigning the SEN notation to EDGN is clearly and logically presented.

Reviewer 2:

The justification for not assigning SEN notation to this compound is well described.

7. If the ID^(SK) or SK were assigned, is the rationale and logic outlined within the document?

Reviewer 1:

NA

Reviewer 2:

This was not assigned.

8. Are the conclusions supported by the data?

Reviewer 1:

NA

Reviewer 2:

Yes, although as noted above, the justification for identifying cardiovascular effects to exposures is weakly described in the document and should be better described from the primary literature (Einert et al. 1963; Hogstedt and Axelson 1977).

9. Are the tables clear and appropriate?

Reviewer 1:

The tables are clear and appropriate.

Reviewer 2:

It's not clear why Table 2 is included. The summary of carcinogenic designations for EGDN by other governmental and nongovernmental agencies seems out of place since these carcinogenic designations are not specific to dermal exposures.

10. Is the document organized appropriately? If not, what improvements are needed?

Reviewer 1:

The document is appropriately organized.

Reviewer 2:

The organization of the document is appropriate and consistent with the phenol example provided in the NIOSH guidance document.

11. Is the language of the manuscript acceptable as written? If not, what improvements are needed?

Reviewer 1:

The language is acceptable as written.

Reviewer 2:

Page 3 end of last paragraph just before Table 2: the author notes that "Table 2 provides summary of carcinogenic designations for epichlorohydrin..." which must be a cut-and-paste typo from a similar document.

12. Are you aware of any scientific data reported in governmental publications, databases, peer reviewed journals, or other sources that should be included within this document?

Reviewer 1:

I am not aware of any additional data which should be included.

Reviewer 2:

I am not aware of anything missing and ran a cursory literature search to check.

13. What is your final recommendation for this manuscript? (Do you agree with the scientific rationale that serves as a basis for the skin notation assignments?)

Reviewer 1:

I agree with the skin notation assignments for EGDN presented in this document.

Reviewer 2:

I agree with the rationale for the notation assignment, but would feel more comfortable if the document itself provided stronger justification for the identification of the toxic effect - adding several sentences to the section on epidemiological studies to note the conclusion of the authors should be sufficient.