6/2/2010

Review: NIOSH Skin Notations Review - Group A
Profile Number: 16
Profile Title: Glutaraldehyde

Summary

Each reviewer had varying opinions on the systemic health hazards associated with skin exposure to glutaraldehyde, but agreed on the direct hazards and immune-mediated responses. Specifically, Reviewer 1 believes the data would be more conclusive if the manuscript emphasized that the chemical is corrosive to the skin at high concentrations. Both reviewers find the manuscript acceptable; however, there are some minor reservations and several recommendations as outlined in the section below.

Recommendations

- The apparent positive result from the calculated SI ratio should be discussed and dismissed. (Q1, Reviewer 1)
- The statement on page 3 "therefore glutaraldehyde is considered to be absorbed through the skin following dermal exposure" is confusing and contradicts the main conclusions. (Q1, Reviewer 1)
- Add need for chronic exposure data in animals because of chronic use in man. (Q1, Reviewer 2)
- Add the "NOEL" for irritation in man. (Q3, Reviewer 2)
- Some assessment of the concentration related direct effects on the skin would be advantageous, i.e. its irritant at lower concentration. (Q4, Q5 Reviewer 1)
- Add the scenario in which ACD occurs in man: a) As preservative, b) Healthcare worker. (Q5, Reviewer 2)
- Does it cross react with formaldehyde? (see Cont. Derm. ~ 20 years ago) (Q5, Reviewer 2)
- Review Azadi – is this ICU (immunologic contact urticaria) potentially fatal or not? (Q5, Reviewer 2)
- Emphasize that glutaraldehyde is corrosive to the skin at high concentrations. (Q8, Reviewer 1)
- Inclusion of references in the summary is unhelpful to the reader and unnecessary. (Q8, Reviewer 1)
- Reference extensive reviews by California agencies. (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:
Generally yes, and I agree that it is not appropriate to assign a SK: SYS notation. However, the apparent

positive result from the calculated SI ratio should be discussed and dismissed. The statement on page 3 "therefore glutaraldehyde is considered to be absorbed through the skin following dermal exposure" is confusing and contradicts the main conclusions.

Minor points – consistent in use of comma in numbers, e.g. 2,970 mg/kg and 2000 mg/kg.

Might be clearer if the phrase "through the skin" was added in the final para of Section 2, i.e. "… is poorly absorbed through the skin, as reflected…"

Reviewer 2:
No. Add need for chronic exposure data in animals because of chronic use in man.

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:
N/A

Reviewer 2:
NA

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:
Yes

Reviewer 2:
Partially. Add the "NOEL" for irritation in man.

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:
Yes, I agree that in high concentrations glutaraldehyde is corrosive (SK: DIR(COR)). However, it would seem as though some way of recognizing the concentration related direct effects on the skin would be advantageous, i.e. its irritant at lower concentration.

Reviewer 2:
Yes

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:
Yes, again this is clear. However, it seems from the evidence presented that the potential for sensitization is concentration related and some assessment of the lower limit for the induction of sensitization would be helpful.

Reviewer 2:
Partially. Add the scenario in which ACD occurs in man:
a) As preservative
b) Healthcare worker

Add elicitation "NOEL" (human).

Add– does it cross react with formaldehyde (see Cont. Derm. ~ 20 years ago).

Review Azadi – is, this ICU (immunologic contact urticaria– potentially fatal) or not

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:
Yes

Reviewer 2:
Partially. See #5 (above)

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

Reviewer 1:
N/A

Reviewer 2:
NA

8. Are the conclusions supported by the data?

Reviewer 1:
Yes, although I think it would be helpful to emphasize that glutaraldehyde is corrosive to the skin at high concentrations.

Minor suggestions…

I think the inclusion of so many references in the Summary is unhelpful and makes the text less easily read. The references are all available in the body of the document so I think the focus in the summary should be to get a clear message over to the reader.

8th last line of the summary, "… on both humans and animals, is sufficient to…"

Reviewer 2:
Partially. see #5 above.

9. Are the tables clear and appropriate?

Reviewer 1:
Yes

Reviewer 2:
Yes

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

Reviewer 1:
Yes

Reviewer 2:
Yes

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

Reviewer 1:
Yes

Reviewer 2:
Yes

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:
No

Reviewer 2:
Partially. See #5 above.

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 scientific rationale and final recommendations in the report, with the minor reservations noted above.

Reviewer 2:
Acceptable. Would benefit by competing #5.

NB Reference extensive reviews by California agencies.

Add statement re data (or lack of) on:
a) Photoirritation
b) Photoallergic Contact Dermatitis
c) "Validity" of penetration algorithm