

6/2/2010

Review: NIOSH Skin Notations Review - Group A

Profile Number: 20

Profile Title: 2-Butoxyethanol (BE)

Summary

Both reviewers agreed with the scientific rationale and the skin notation assignments or the logic behind not assigning certain notations for this compound. Reviewer 2 found the systemic health hazards, direct health hazards, and immune-mediated responses associated with skin exposure to be clearly outlined. However, Reviewer 1 had several problems with the readability of the document (see Recommendations and the Question 1 comments). Also, both reviewers found a significant typo in the final conclusion for the SK:SYS notation, which is detailed in the recommendations section.

Recommendations

- Improve readability of certain sections. (Q1, Reviewer 1)
- Preserve the order that the experimental permeation coefficients/absorption rate results with different concentrations – i.e., stick with low to high or high to low. (Q1, Reviewer 1)
- Express Wilkinson and Williams data in terms of mass of BE for easy comparison. Stick to mg/kg rather than $\mu\text{mol/kg}$ for applied dose. (Q1, Reviewer 1)
- Make it clear that the evaluations in Table 3 consider all evidence, not just dermal exposures. (Q1, Reviewer 1)
- Page 5, final conclusion states, "Therefore, on the basis of the data for this assessment, BE is not assigned the SK:SYS notation." This is incorrect. The notation is assigned and should be assigned. (Q2, Reviewers 1 and 2)
- Table 2 is not necessary. (Q9, Reviewer 2)
- Remove the references from the final summary to improve readability. (Q13, Reviewer 1)

Suggested additional scientific data to review:

- The relevant European GHS classifications are:

Acute Tox. 4 * H302

Skin Irrit. 2 H315 (Q12, Reviewer 1)

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:

No, some of the text is particularly difficult to read, e.g. "Although no dermal lethal concentration (LDLo) for humans has been identified, the reported values for dermal LD50 (the dose resulting in 50% mortality in the exposed population) of undiluted BE ranged from 0.11 to 0.56 mL/kg (corresponding to 99–505 mg/kg) [Carpenter et al. 1956; Duprat and Gradiski 1979] under occlusive conditions and 2.0 mL/kg (1,804 mg/kg) under nonocclusive conditions [Carpenter et al. 1956] for rabbits." The text should be improved to make it a little more readable.

I is a little confusing changing the order that the experimental permeation coefficients/absorption rate results with different concentrations – i.e. stick to low to high or high to low.

Express the Wilkinson and Williams data expressed as "nanomoles per square centimeter per hour" also in terms of mass of BE for easy comparison. Also, stick to mg/kg rather than $\mu\text{mol/kg}$ for applied dose.

In the sentence containing "compared with 11.2% (after 6 hours) in pig skin under semioclusive conditions and only 5.6% (after 1 hour)..." switch the order of the data so the 1 hr comes before the 6 hr.

"exposures (25% of the surface area, such as parts of both arms and head exposed)"

Delete "therefore, BE is considered to be absorbed through the skin following dermal exposure."

Make it clear that the evaluations in Table 3 consider all evidence not just dermal exposures.

Reviewer 2:

This document was well prepared and clearly outlines the systemic health hazards

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:

Yes, it is clear although there is an error in the final conclusion... "Therefore, on the basis of the data for this assessment, BE is not assigned the SK: SYS notation."

Reviewer 2:

SYS notation is assigned and the rationale and logic behind the assignment is clearly described. However, on page 5 the author states that BE is NOT assigned the SK:SYS notation - which is in error since it is assigned the notation and should be assigned the notation.

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:

The author does a nice job outlining the justification for assigning the DIR notation.

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:

I agree that DIR (IRR) is appropriate.

Reviewer 2:

BE is assigned SK:DIR (IRR) notation and this is logical based on the information

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

The sentence "DEREK predicted BE to be negative for skin sensitization." Is a shorter form than has been used in other documents.

Reviewer 2:

No case reports are available and very limited number of studies in humans and animals regarding skin sensitization and this is clearly stated.

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:

N/A

Reviewer 2:

The SEN notation is not assigned and the reasoning is clear.

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

Reviewer 1:

N/A

Reviewer 2:
Not applicable

8. Are the conclusions supported by the data?

Reviewer 1:
Yes

Reviewer 2:
Overall the conclusions are supported by the data and clearly described.

9. Are the tables clear and appropriate?

Reviewer 1:
Yes

Reviewer 2:
Tables 1 and 3 are clear and appropriate; Table 2 is not necessary.

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

Reviewer 1:
Yes

Reviewer 2:
Yes, the document is organized appropriately and consistently 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:
As noted above the text is in places difficult to read.

Reviewer 2:
Yes. This was clearly written (best of the 3 I reviewed).

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:
The relevant European GHS classifications are:

Acute Tox. 4 * H302
Skin Irrit. 2 H315

Reviewer 2:
I am not aware of additional missing information and a quick literature search did not reveal missing information.

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:

Yes

Removing the references from the final summary will make it easier to read.

Reviewer 2:

I agree with the scientific rationale and skin notation assignments for this compound.