6/2/2010

Review: NIOSH Skin Notations Review - Group A
Profile Number: 19
Profile Title: Methyl Cellosolve

Summary

Both reviewers agreed with the rationale behind the skin notation assignments and found the conclusions to be acceptable. The reviewers generally agreed that the document provided a fairly clear outline of the systemic health hazards, direct health hazards, and immune-mediated responses associated with skin exposures to Methyl Cellosolve. However, both reviewers had several recommendations for improving readability and organization of the document. These are detailed below.

Recommendations

- In the sentence "...estimated uptake through the skin to be 55% of the total uptake of methyl cellosolve in a combined inhalation and dermal exposure..." specify the air concentration. (Q1, Reviewer 1)
- In the first paragraph, split off the animal/modeling data into a new paragraph. (Q1, Reviewer 1)
- It seems probable that any workplace exposure would have been to both dermal and inhalation routes – this is not made clear. Please provide some information about how the dermal exposure occurs, e.g., the extent and duration of exposure. (Q1, Reviewer 1)
- In the epidemiologic studies of reproductive and developmental effects, what dermal exposure occurred? (Q1, Reviewer 1)
- For Table 2, make it clear that these designations are based on an overall evaluation of the evidence for exposure by all routes. (Q1, Reviewer 1)
- Information summarized from the literature should be better quantified. (see Q1 Reviewer 2)
- The logic for assigning the SYS notation is clear; the designation of those systemic effects (Critical effects) is less clear and needs to be better supported within the document. (Q2, Reviewer 2)
- Page 6 under 3.0 – "Busy Run Research Center" should be Bushy Run... (Q3, Reviewer 2)
- Unclear why Table 2 is included in the document. (Q9, Reviewer 2)
- For Table 1, using the phrases "reproductive system" and "developmental system" is unusual (Q9, Reviewer 2)
- Page 4 - the paragraph beginning "Dermal studies in animals showed that methyl cellosolve is a reproductive and developmental toxicant" proceeds to only cover reproductive toxicity; should remove "developmental." (Q10, Reviewer 2)
- Document would benefit from some editorial review to clarify some text. (Q11, Reviewer 2)

- It is perhaps worth highlighting that dermal uptake can occur from vapor in addition to direct contact with the liquid. (Q13, Reviewer 1)

Suggested additional scientific data to review:

- GHS classification in Europe…

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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, although I have some specific comments below.

In the sentence "…estimated uptake through the skin to be 55% of the total uptake of methyl cellosolve in a combined inhalation and dermal exposure…" specify the air concentration.

In first paragraph split off the animal/modeling data into a new paragraph, i.e. at "In rats, Sabourin et al. .."

As noted in other reviews, I think it is generally inappropriate to say "therefore, X is considered to be absorbed through the skin following dermal exposure" based on the modeled data alone (although in this case it is probably reliable).

Here "2 g/kg" is quoted where in other documents it is 2,000 mg/kg.

I haven't checked the references in the paragraph starting "Several studies have shown the effects of repeated dermal exposures in humans." However, it seems probable that any workplace exposure would have been to both dermal and inhalation routes – this is not made clear. Please provide some information about how the dermal exposure occurred, e.g. the extent and duration of exposure.

In the epidemiologic studies of reproductive and developmental effects, what dermal exposure occurred?

"Table 2 provides a summary of carcinogenic designations from multiple governmental and nongovernmental organizations for methyl cellosolve." – make it clear that these designations are based on an overall evaluation of the evidence for exposure by all routes.

Reviewer 2:
The document provides a fairly solid summary of the data available to outline the systemic health effects of methyl cellosolve, however in several cases, information summarized from the literature should be better quantified. For example, it would be helpful to provide concentration information for exposures, not just "liquid methyl cellosolve". Also, the author describes human dermal exposure studies in which subjective central nervous system effects occurred, and then starts the next paragraph (page 3) with "The central nervous system effects and hematological changes seen in humnas have been observed in animals as well". Then NO supporting evidence for central nervous system effects in animals is

provided.

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, this is clear.

Reviewer 2:
The logic for assigning the SYS notation is clear; the designation of those systemic effects (Critical effects) is less clear and needs to be better supported within the document - I believe this is mostly an organizational issue - see response to #10.

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, clear.

Reviewer 2:
The direct health hazards appear to be outlined well. (Busy Run Research Center should be Bushy Run... - Page 6 under 3.0 heading).

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:
N/A

Reviewer 2:
The compound is not assigned DIR notation and this is justified.

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

Reviewer 2:
Limited information is available regarding the senstitization potential of methyl cellosolve and this is clear 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:
N/A

Reviewer 2:
The compound is not assigned SEN notation and this is justified

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.

9. Are the tables clear and appropriate?

Reviewer 1:
Yes

Reviewer 2:
It's not clear why Table 2 is included in this document - why is only carcinogenic potential afforded a separate table? Also, table 1 should identify the critical effects as central nervous system, reproductive toxicity, developmental toxicity, hematological effects, and immunotoxicity. Using the phrase "reproductive system" or "developmental system" is unusual.

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

Reviewer 1:
Yes

Reviewer 2:
Page 4 - the paragraph beginning "Dermal studies in animals showed that methyl cellosolve is a reproductive and developmental toxicant" proceeds to only cover reproductive toxicity; thus the first sentence should remove "developmental".

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

Reviewer 1:
Yes

Reviewer 2:
I think the document needs some editorial review to clarify some text (for example instead of "clipped backs" should be "clipper-shaved backs".

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:
GHS classification in Europe…

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Reviewer 2:
No, a cursory literature search did not identify additional data that should be included.

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 rationale and conclusions.

It is perhaps worth highlighting that dermal uptake can occur from vapour in addition to direct contact with the liquid.

Reviewer 2:
I agree with the rationale for the notation assignments.