

6/1/2010

---

**Review:** NIOSH Skin Notations Review - Group A  
**Profile Number:** 01  
**Profile Title:** 1,3-Dichloropropene (1,3-D)

---

### Summary

Both reviewers generally agreed that the document clearly outlines the systemic health hazards, direct health hazards, and immune-mediated responses associated with skin exposure to 1,3-Dichloropropene. The scientific rationale behind the skin notation assignments was judged to be sufficient and adequately described.

### Recommendations

- Under the summary of the data from the predictive algorithm, instead of the confusing use of "...therefore, X is considered to be absorbed through the skin", use "indicates that X may significantly contribute to overall body burden." (Q1, Reviewer 1)
- Emphasize important (and unusual) evidence that 1,3-D is taken up through the skin from vapor. (Q1, Reviewer 1)
- Make clear that cancer designations were not based on dermal exposure but rather oral studies. (Q2, Reviewer 1)
- Emphasize that Kezic study is vapor exposure. (Q2, Reviewer 1)
- Misleading to describe results from DEREK software were, "indicating that the substance does not have structural alerts from skin irritation." Instead, leave as, "predicted... to be negative for skin irritation." (Q3, Reviewer 1)
- First sentence at the top of page 4 is not clear - could be misread as implying that 1,3-D is a tumor initiator. (Q3, Reviewer 1)
- In description of case reports, make it clearer that the observation that people were sensitized was based on patch testing. (Q5, Reviewer 1)
- The trans isomer of 1,3-D is shown but not labeled as such. Because 1,3-D has two isomers found in commercial products, it might be worthwhile to show the structural formula of both isomers. (Q10, Reviewer 2)

### Suggested additional scientific data to review:

- See... [http://www.reachcompliance.eu/english/legislation/docs/launchers/CLP/launch-Table\\_3-1.htm](http://www.reachcompliance.eu/english/legislation/docs/launchers/CLP/launch-Table_3-1.htm). (Q12, Reviewer 1)
- GHS designation in Europe is...

Acute Tox. 4 *	H312
Skin Irrit. 2	H315
Skin Sens. 1	H317 (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:

Yes. However, more generally I think it is a little confusing in each of these documents under the summary of the data from the predictive algorithm to say "... therefore, X is considered to be absorbed through the skin". These data contribute to the final decision and it might be better to just say something like "indicates that X may significantly contribute to overall body burden".

In the case of 1,3-D I think it is important (and unusual) that there is evidence it is taken up through the skin from vapour. This could be emphasized a bit more.

Reviewer 2:

This document describes studies that show the absorption of 1,3-D vapor through the skin of humans. In addition, it shows the calculation of a SI ratio that indicates 1,3-D absorption through the skin contributes to the overall body burden of this chemical. It provides a discussion of dermal LD50 studies in animals showing neurotoxic symptoms. Therefore, it does clearly outline the systemic health hazards associated with skin exposure to 1,3-D.

**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 might be clearer if the sentence on page 2 starting "Table 2 summarises..." started as a new paragraph and it was made clear that these cancer designations were not based on dermal exposure but rather oral studies.

Also, the sentence starting "However, results from use..." might read better starting "The results from ..." Emphasise that the Kezic et al study is vapour exposure.

Reviewer 2:

The rationale and logic for the SK:SYS notation given in this document are clear.

**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:

Generally yes. Although similar to the point made above about the systemic uptake I think it is misleading to describe the results from the DEREK software as "indicating that the substance does not have structural alerts for skin irritation". Better to just leave it at "predicted... to be negative for skin irritation."

The paragraph at the top of page 4 is not clear. I think the problem is the first sentence, which could be misread as implying that 1,3-D is a tumour initiator.

Reviewer 2:

This document provides a discussion of primary skin irritation tests and acute dermal toxicity studies in animals, thereby explaining the direct health hazard associated with the exposure of skin to 1,3-D.

**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

Reviewer 2:

The rationale and logic for the assignment of SK:DIR (IRR) notation to 1,3-D is sufficiently discussed in this document.

**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. On line two of this section say "... in human case reports..." Also, in the description of the case reports make it clearer that the observation that these people were sensitized was based on patch testing.

Reviewer 2:

This document provides a good description of human and animal studies showing skin sensitization following exposure of the skin to 1,3-D.

**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:

The assignment of the SK:SEN notation to this chemical is sufficiently justified by the data presented in this document.

**7. If the ID<sup>(SK)</sup> or SK were assigned, is the rationale and logic outlined within the document?**

Reviewer 1:

N/A

Reviewer 2:

These notations were not assigned in this document.

**8. Are the conclusions supported by the data?**

Reviewer 1:

Yes, although as I have indicated previously I would not put the references in the summary to make it more readable.

Reviewer 2:

The conclusions that 1,3-D can be absorbed through the skin and cause neurotoxicity, that it has the potential to cause skin irritation and skin sensitization in humans, are all supported by the data presented in this document.

**9. Are the tables clear and appropriate?**

Reviewer 1:

Yes

Reviewer 2:

The tables are clear and appropriate.

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

Reviewer 1:

Yes

Reviewer 2:

The document is well organized. In Section 1.1 [General Substance Information: 1,3-Dichloropropene (1,3-D)], the trans isomer of 1,3-D is shown but not labeled as such. Since this compound has both cis and trans isomers and they are both found in commercial products using this compound, it might be worthwhile to show the structural formula of both isomers.

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

Reviewer 1:

Generally yes. Specific comments made elsewhere.

Reviewer 2:

The language used in this manuscript is clear and concise.

**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, although the GHS designation in Europe is...

Acute Tox. 4 *	H312
Skin Irrit. 2	H315
Skin Sens. 1	H317

See... [http://www.reachcompliance.eu/english/legislation/docs/launchers/CLP/launch-Table\\_3-1.html](http://www.reachcompliance.eu/english/legislation/docs/launchers/CLP/launch-Table_3-1.html)

It might also be useful to say something about the vapour pressure of 1,3-D somewhere in the document

Reviewer 2:

I do not know of any additional scientific data on 1,3-D that should be included in this document.

**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

Reviewer 2:

I agree with the scientific rationale given for the skin notation assignments for 1,3-D. I recommend that this manuscript be accepted as a final skin notation profile.