Reviewer's report

Title: N-nitrosoethylurea in the mammary gland: is there a non-carcinogenic dose?

Version: 1 Date: 23 March 2009

Reviewer: Nilda de Vargas Barbosa

Reviewer's report:

Dear Editor,

This work proposed to conduct an NMU dose-response experiment for determining whether low doses of NMU are able to producing tumors or neoplastic alterations in mammary glands. The results obtained by group are a good contribution for development of experimental models of mammary carcinogenesis. The methodology used is sound, the manuscript is relatively well written and the work should be of interest to the general readership of the journal. However, I have some points that I realize that authors should consider to improve the quality of the manuscript.

Below are some issues with the current draft.

Major Revisions

1. Title: the title must be more informative and to emphasize better the specific effects found with the low doses of NMU on mammary carcinogenesis in female Wistar-Furth rats.

2. All sections in the text must be numbered

Introduction

1. It is not clearly explained in this section the significance to chemically-induced carcinogenesis studies offered by choosing of doses non-carcinogenic of NMU since this compound is firstly used to induce tumorogenesis process. The authors should incorporate this information arguing better the importance of search by the boundary between the non toxic and toxic activity of NMU. In my point of view, this information can be characterized as one of objectives of study.

2. A brief mention about the mechanism(s) of action(s) involved in the carcinogenic effect of NMU should be included in this section.

Materials and Methods

1. Animal sub-item: I suggest that the sub-item “Tumor induction and detection” be added...

2. The authors should to specify how the latency and incidence measurements were recorded...for example: tumor incidence (% of animals that develop at least
one tumor…??).

Results

1. What reasons the authors attribute to explain the differences found between thoracic and abdominal mammary glands with relation to latency and incidence parameters??
2. Incidence of palpable tumors Item: the last paragraph is confusing and needs to be rewritten
3. The description of results related to histopathology of tumors is very extensive and can be condensed.
4. Page 10, last line: Adjust the sentence ...” time dependant”..
5. Page 11, line 11: The term “dosed animals” should be substituted by groups (.. lower than in 20 and 30 NMU groups).
6. Page 14, line 9: Replace the ...“could be” by “were“

Discussion and Conclusion

1. The language style of discussion must be improved.
2. Page 17, paragraph 1: The last sentence .....”This is consistent with ......in neoplastic development”.... should be revised and rewritten
3. Please edit the English of sentences below. It is not clear in present form.
   - “A dose-response study .................increased and the latency decreased as the dose was increased from 25mg NMU/kg BW to 75mg NMU/kg BW.”
   - “Similarly, an additional dose-response study highlights the importance of the route of NMU exposure as the Sprague-Dawley rats receiving an intravenous infusion of NMU at 50 days of age seemed to develop tumors faster than those i.p. injected Wistar-Furth rats in our study; nevertheless, the overall tumor burden appeared similar’.
4. The conclusion of work should be revised and rewritten too.

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests.