Author's response to reviews

Title: The development of Response Surface Pathway Design to reduce animal numbers in toxicity studies

Authors:

Sagita Dewi (gitaewi@yahoo.com)
Tore Aune (toreaun@broadpark.no)
John A.B. Aasen (John.Aasen@nvh.no)
Adrian J. Smith (adrian.smith@vetinst.no)
Stig Larsen (Stig.Larsen@nvh.no)

Version: 2 Date: 28 August 2013

Author's response to reviews: see over
Oslo, 28 August 2013

Editorial Board BMC Pharmacology and Toxicology
c/o BioMed Central, 236 Gray's Inn Road London
WC1X 8HB, United Kingdom

Dear Editor,

Enclosed please find our manuscript entitled:

The development of Response Surface Pathway Design to reduce animal numbers in toxicity studies

This manuscript describes original work and introduces a new approach in toxicity studies particularly in laboratory animal field. The manuscript has not been previously published and is not under consideration by any other journals.

The manuscript was previously submitted to BMC Medical Research Methodology and was suggested to transfer to BMC Pharmacology and Toxicology.

The concept of RSP design has been refined and developed by simulation procedures, used in vivo data from Yessotoxin study. One of the in vivo studies was conducted in 2006 and authorized by the Norwegian Animal Research Authority (FDU), in accordance with the Norwegian Regulation on Animal Experimentation. This study does not have a licence number (FOTS ID number) because it was applied for before the Authority's FOTS database was started. The other in vivo study was conducted in 2011 with the authorization of the Norwegian Animal Research Authority (FDU), application number FOTS ID: 1132, in accordance with the Norwegian Regulation on Animal Experimentation.
We have inserted some relevant information in the methods section regarding the animal experiments including approval of the in vivo study. The information related to funding and technical assistant are also added in the acknowledgments section.

**Author’s Contributions:** All the authors participated in development of the manuscript. The Response Surface Pathway design has mainly been developed by SD and SL who also performed the statistical analyses and wrote the initial draft of the manuscript. The laboratory work was performed by AS, TA and JAAB. All the authors have participated in literature review, finalizing and read the manuscript and approved the final version.

**Competing interest:** The authors have no competing interest.

**Acknowledgements:** The authors wish to thank Meabco AS for financial support, Prof. Steen Lindkaer-Jensen for scientific advice and Brit Heidenreich for technical assistance with the animal experiments. The in vivo part of the project was financed by the Norwegian Research Council (NFR), project nr 172561/S40 and support was also obtained from the ASTOX2-project (Grant-Aid Agreement No PBA/AF/08/001(01)) under the Sea Change strategy with the support of the Irish Marine Institute and the Marine Research Sub-Programme of the National Development Plan 2007–2013, co-financed under the European Regional Development Fund.

The appropriate reviewers for this manuscript are:

1. Georgia Salanti, Department of Hygiene and Epidemiology University of Ioannina
   School of Medicine University Campus Ioannina 45110 Ioannina, Greece Tel:
   +302651007807, email: gsalanti@cc.uoi.gr
2. Aurelia Tubaro, Ph.D., University of Trieste, Department of Life Science, Building B, University of Trieste, Via Valerio 6, 34127 Trieste, Italy, Tel: +39-040-558-7910, email: tubaro@units.it

We hope that the manuscript is suitable for your journal and we are looking forward for a positive response.

On behalf of authors

With best regards

Sagita Dewi, MD
Centre for Epidemiology and Biostatistics
Norwegian School of Veterinary Science
P.O. Box 8146 Dep. N-0033 Oslo, Norway
Email: gitaewi@yahoo.com