

Format for ANSWERING REVIEWERS



March 19, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 2453-edited.doc).

Title: Word of caution before implementing ketotifen for gastrointestinal transit improvement

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Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 2453

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 We thank the reviewer for his/her constructive comments. Revision has been made according to the suggestions of the reviewer

(1) *which kind of anesthesia has been used to operate the rats*

The rats were anaesthetized using buprenorphine 0.1 mg/kg s.c. and anaesthesia was maintained using 2.5% isoflurane. The information has been added to the manuscript.

(2) *describe how rats have been sacrificed*

The rats were anaesthetized using 4% isoflurane and sacrificed by cervical dislocation. The information has been added to the manuscript.

(3) *why was been used such a small number of rats*

The study was powered for showing a difference in geometric means between the vehicle group and the high-dose ketotifen group. A 30% difference of geometric means, i.e. geometric means of 0.06 (SD 0.01) and 0.04 (SD 0.01), respectively, were expected. With $\alpha=0.05$ and $1-\beta=0.80$, a group size of 6 was sufficient to show such a difference. Unexpectedly, 4 out of 6 rats in the high-dose ketotifen died before the study endpoint, leading to a substantial group size reduction. As the main conclusion of the study (caution should be taken when administering ketotifen after abdominal surgery) would not be affected, it was considered unethical to include more rats in the experiment. With the same dropout rate, 12 additional rats should have been included to achieve a $n=6$ group size, with 8 more deaths.

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

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