Reviewer's report

Title: Tobramycin exposure from active calcium sulfate bone graft substitute

Version: 3 Date: 23 January 2014

Reviewer: Cornelia Landersdorfer

Reviewer's report:

Regarding original major comment no. 2: There still seems to be only one visual predictive check (VPC, Figure 1) provided, instead of one for each of the two doses as confirmed by the reviewers (“As requested, we provided a figure with 262 mg dose (10 g Osteoset® T) and 524 mg dose (20 g Osteoset® T). Dose difference is almost fully compensated by different bioavailability, thus giving similar predictions.”). Apologies in case of overlooking something, however the VPCs should be presented stratified by dose for the manuscript to be published.

Regarding the authors' reply to original minor comment no. 3: This reviewer disagrees with the authors that the method they chose "is usually applied in population analysis and supposed to mostly prevent this bias". The 'gold standard' approach for taking into account values below the quantification limit would be the so-called Beal M3 method (Beal SL. J Pharmacokinet Pharmacodyn. 2001; 28:481-504 is a comparison of different approaches) which can be also implemented in NONMEM FOCE.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

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.