Reviewer’s report

Title: The peroxisome proliferator-activated receptor (PPAR) alpha agonist fenofibrate maintains bone mass, while the PPAR gamma agonist pioglitazone exaggerates bone loss, in ovariectomized rats

Version: 2 Date: 28 March 2011

Reviewer: Susan Y Y Smith

Reviewer’s report:

- Minor Essential Revisions

1. Results: Page 10, line 24: Femoral BMD should read BMC.

2. Results: Page 11, line 13: Suggest stating Feno and WY maintained femoral BMD at Sham and/or OVX levels, since WY was comparable to OVX while Feno was increased. The important finding is that PIO exacerbated the effects of OVX, as stated.

3. Results: Page 12, line 10 and Table 2: CD is flagged as significant vs OVX (bb) and FENO OVX (c), not vs Sham. Please check which is correct – statement or flagging.

4. Results: Page 12, line 11 and Table 1: SMI was not significantly higher than the Sham group for WY OVX – check accuracy of statement.

5. Results: Page 12, line 22 and Table 3: Bending moment or energy absorption was not significantly lower at the femoral neck for OVX compared to PIO: check accuracy of statement.

6. Results: Page 13, lines 1-4: It is unusual to correlate specific bone strength parameters from one site with whole body in vivo parameters. Also, the ultimate bending moment may correlate better with BMC rather than BMD at appropriate sub-regions of the excised femur, i.e. proximal femur BMC with femoral neck ultimate bending moment, and mid femur shaft BMC with femoral shaft bending moment. The correlations actually presented are not very informative as is and may be better excluded. If kept, then some clarification is needed to state if these results are for all groups combined and if so, was a test of equality performed first.

7. Discussion: Page 15, line 2: Suggest modify comment on impaired bone quality since this is difficult to define based on the results: suggest stating what the data shows: OVX control rats had significantly reduced changes in femoral BMC and BMD associated with reduced biomechanical strength parameters compared to sham controls.

8. Discussion: Page 15, line 8: Clarify: “..peak bone mass, a parameter which is considered.”.

9. Discussion: Page 16, line 1-6: The two sentences seem disconnected. The second sentence should be stated initially to indicate Feno and WY maintained
bone strength at the femoral neck comparable to Sham controls. These findings are consistent with maintenance of femoral BMC at Sham control levels (WY) or slightly higher (Feno). BMD may not correlate with these raw strength parameters as well as does BMC so probably should not be mentioned here. Note: femoral BMC was measured for the whole femur and may not correlate well with femoral neck bone strength specifically. A sub-region analysis of the femurs would provide stronger data but the point is made sufficiently with the data as presented.

10. Discussion: Page 17, line 3: Suggest clarify sentence, disjointed and poorly constructed.


- Discretionary Revisions

1. Materials and Methods: Page 6, lines 4-6: I am still uncertain what EV is. For standard nomenclature, the authors should consult: J Bone Miner Res. 2010 Jul;25(7):1468-86. Guidelines for assessment of bone microstructure in rodents using micro-computed tomography. Bouxsein ML, Boyd SK, Christiansen BA, Guldberg RE, Jepsen KJ, Müller R.

2. Results: Page 9, lines 19-24, page 18 line 19: Order of wording: “…% fat/lean mass….” (rather than “…fat/lean mass %…”).

3. Results: Page 10, line 7: Suggest:”..not within the scope..”.

4. Results: Page 11, lines 3-11: Punctuation in parentheses should be “:”, not “;”, e.g. SHAM: +3.3 etc.

5. Discussion: Page 15, line 23-24, and page 18 line 5: Change neither, nor to read either, or. Line 7: typo: trough to read through.

6. Discussion: Page 16, line 16: Suggest add: “…increased bone turnover associated with ovariectomy.”

7. Discussion: Page 18, line 22: “..is in accordance….”.

8. Figure legends: Page 28, Figure 1: Typo: “…% of body..” General comment: check flags a,aa, aaa, b, bb etc for use specific to each graph.

9. Figure 1: suggest move y axis to the left to see time 0 data points unobstructed.

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.