Author’s response to reviews

Title: The Temporal Reliability of Serum Estrogens, Progesterone, Gonadotropins, SHBG and Urinary Estrogen and Progesterone Metabolites in Premenopausal Women

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Dear Editors,

Thank you for considering our revised manuscript. Our sincere thanks go as well to the reviewers. We found their suggestions to be both thoughtful and helpful, and the manuscript is much improved as a result, particularly by establishing more appropriate limitations on our conclusions. A point-by-point response indicating the actions we took in response to each reviewer's comments follows:

Reviewer 1: Dr. Timothy Key
1 The sections are now in proper order.
2 A sentence adding that results are relative to creatinine excretion was added to the Urine Analysis subsection.
3 Our laboratory scientists prefer grams as a unit of measurement.
4 The authors feel this paragraph is most appropriate for the results section.
5 Corresponding months were added to the x axis of the figures. The figure 4 scale was left unchanged because the authors felt that the point of the figures was to convey the amount of variation and overlap relative to the other figures. Changing the scale of one of the figures would defeat this purpose.
6 The discrepancy between the OR result for SHBG in Table 3 and the text was corrected.

Reviewer 2: Dr. Christopher Longcope
1&6 Day 19 of the menstrual cycle was chosen as the day to obtain samples because of the relative stability of some of the analytes at this phase and because it allowed us to use a minimum progesterone level to screen out anovulatory cycles. Logistical and monetary constraints make the acquisition of samples on the day best suited to each analyte unfeasible. A sentence limiting the conclusions we draw to samples obtained at mid-luteal phase has been added to the discussion section.
2 The fact that blood was not drawn over a 30-40 minute period has been mentioned as an additional limitation.
3 While it is true that OvuQuick (not OvuKit) is not 100% accurate, research does indicate that it is highly accurate (93% with respect to predicting ovulation). This is an acceptable level of accuracy and we feel that though it is an additional source of error, it does not represent a fundamental flaw in our study design. The predictive validity of the kit and the reference to the validity study have been added to the sample collection subsection.
4 Anovulatory cycles were not included in the analysis. The sentence indicating this has been rewritten to make this fact clearer to the reader.
5 We agree that variation in cycle length is an additional limitation and a sentence indicating as much has been added to the discussion section.
Yours sincerely,

Gertraud Maskarinec, MD, PhD