Reviewer's report

Title: Intake of Fucus vesiculosus, an Edible Brown Seaweed, Affects the Menstrual Cycle and Hormonal Status of Pre-menopausal Women

Version: 2 **Date:** 18 March 2004

Reviewer: Alison M Duncan

Reviewer's report:

General
This study explores the hormonal effects of seaweed consumption in 3 premenopausal women. This type of investigation is well warranted and the results of this study are impressive given the extremely small sample size. Specific comments are outlined below.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

1. Sample Size: The issue of sample size needs to be addressed in this study. A sample size of 3 is insufficient to draw statistically valid conclusions. This report is likely more appropriate as a case-study report rather than a full study.

2. Subject Characteristics: There needs to be more information provided about the subjects (age, body weight, use of medications, etc). In addition, it is of concern that these subjects have such irregular menstrual cycles as such variation does not contribute to a well-controlled research study.

3. Description of Data Collection: There needs to be more detail regarding when the samples were collected. It is described that blood was collected on day 21 (baseline) and then bladderwrack was consumed for 2 cycles of which blood was collected on day 21 of the second cycle. It is then unclear when samples were collected in the following cycles during the higher dose.

4. Ovulation: There is no mention of ovulation testing. How can circulating hormones be adequately assessed if there is no confirmation of ovulation? For example, if the subject did not ovulate in cycle 1 and did ovulate in cycle 2, it would appear that progesterone, collected on day 21, had increased. But this would be due to ovulation, not the intervention.

5. Lack of Washout Period: The fact that the 1400mg was consumed directly after the 700mg means that an effect of time, rather than dose, cannot be ruled out. The author should address this in the discussion.

6. Lack of Control Group: This methodological limitation should be stated more clearly in the discussion section (it is mentioned in the conclusions but only briefly).

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

1. Background, page 4, line 2: is endometriosis lower in Asian women? Do references 1 and 2 support this statement?

2. Background, page 4, line 6: use of reference 3 does not seem appropriate

3. Background, page 4, line 12: need to provide a reference for this statement (after “hyperplasia”).

4. Methods, page 6, source of kelp paragraph: it would be good to have a reference to support the statement that the doses used in this study are similar to Japanese intakes.

5. Study subjects, page 6: more detail needed; see item#2 in Compulsory Revisions.

6. Experimental Protocols, page 7: need more detail; item#3 in Compulsory Revisions.

7. Hormone Assays, page 8: need more detail here. Specify the hormones measured and the assay variability.

8. Statistics and Results: the statistics should be done on all 3 subjects combined rather than just within each subject individually.

9. Tables and Figures: there needs to be more detail provided in the footnotes of the tables and figures as to how these averages were generated (i.e. from 2 menstrual cycles before the study, etc) If this were more clearly indicated in the methods, it may then not be necessary in the tables and figures.

10. Tables and Figures: It is unclear how the 700mg/day has more than one measurement per subject as the methods indicate that blood was collected on day 21 of the second cycle of consuming 700mg/day. That is only one measurement, which would not have any variability associated with it if presented within one subject.

Discretionary Revisions (which the author can choose to ignore)
None

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

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

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:

None