DEPARTMENT OF HEALTH AND HUMAN SERVICES Public Health Service

Food and Drug Administration
5100 Paint Branch Parkway
College Park, MD 20740

MAR - 2 2004

Richard Conant
Vice President, Technical and Regulatory Affairs
Life Sciences Division
American Institute for Biosocial and Medical Research (AIBMR), Inc.
4117 S. Meridian
Puyallup, WA 98373

Dear Mr. Conant:

This is to inform you that the notification you submitted, dated December 18, 2003, on behalf of your client, Smith Naturals Co., Ltd, pursuant to 21 U.S.C. 350b(a)(2)(section 413(a)(2) of the Federal Food, Drug, and Cosmetic Act (the Act)) was filed by the Food and Drug Administration (FDA) on December 19, 2003. Subsequently, on January 14, 2004, we received copies of the "PM Validation Package" section of your notification clarifying the numbering sequence. Your notification concerns the substance called *Pueraria mirifica* extract that you describe as an extract of *Pueraria candollei* var. *mirifica* Airy Shaw & Suvatabandhu root powder that you intend to market as a new dietary ingredient.

According to the notification the suggested daily intake on the product label is 80 milligrams (mg) a day, in two servings of 40 mg. The serving size is one capsule or tablet containing 40 mg of *Pueraria mirifica* extract. The suggested use is "Take one capsule/tablet two times a day with food." You state that the product will be marketed to post-menopausal women as a dietary supplement for maintenance of normal body function.

Under 21 U.S.C. 350b(a), the manufacturer or distributor of a dietary supplement containing a new dietary ingredient that has not been present in the food supply as an article used for food in a form in which the food has not been chemically altered must submit to FDA, at least 75 days before the dietary ingredient is introduced or delivered for introduction into interstate commerce, information that is the basis on which the manufacturer or distributor has concluded that a dietary supplement containing such new dietary ingredient will reasonably be expected to be safe. FDA reviews this information to determine whether it provides an adequate basis for such a conclusion. Under section 350b(a)(2), there must be a history of use or other evidence of safety establishing that the new dietary ingredient, when used under the conditions recommended or suggested in the labeling of the dietary supplement, will reasonably be expected to be safe. If this requirement is not met, the dietary supplement is considered to be adulterated under 21 U.S.C. 342(f)(1)(B) because there is inadequate information to provide reasonable assurance that the new dietary ingredient does not present a significant or unreasonable risk of illness or injury.

FDA has carefully considered the information in your submission, and the agency has concerns about the evidence on which you rely to support your conclusion that a dietary supplement containing *Pueraria mirifica* extract will reasonably be expected to be safe.

It is unclear to us how the history of use information you submitted in your notification relates to the *Pueraria mirifica* extract that you intend to market as a new dietary ingredient. The history of use evidence primarily relates to traditional use of the roots of *Pueraria mirifica* rather than an extract of *Pueraria mirifica* root powder. Further, it generally lacks details on the amount, frequency and duration of use and whether the plant part and preparation used are the same as what you intend to market as a dietary supplement. These details would have helped FDA to determine how this information relates to your product.

The relationship between the composition of the materials used in the various test reports and the composition of the substance you call Pueraria mirifica extract is unclear. For example, the information in an article provided in Section V, Tab 20 stated that the Smith Naturals Co., Ltd is the only company in Thailand "to achieve standardizing *Pueraria mirifica* extract by controlling the quantity of miroestrol in both the powdered and liquid extracts." The nature of this standardization is not stated. In addition, miroestrol is not quantified in the "Validation Package" included in Section V, Tab 22. However, miroestrol is clearly present as a major component in the submitted chromatograms of your product, *Pueraria mirifica* extract. A description and specifications of the method or process of obtaining your product, *Pueraria mirifica* extract, may have helped FDA clarify the identity of your product.

The animal and clinical studies submitted were insufficient to support the safety of the daily consumption of your product *Pueraria mirifica* extract. For example, in the clinical studies submitted, it is unclear if the test substances used were the same qualitatively or quantitatively as the substance that is the subject of the notification. The relationship between the dietary supplement containing *Pueraria mirifica* extract and the materials tested in the studies mentioned in the notification is not clear. Although an unpublished clinical study was mentioned, there was insufficient information to evaluate safety.

For the reasons discussed above, the information in your submission does not provide an adequate basis to conclude that your product containing *Pueraria mirifica* extract, when used under the conditions recommended or suggested in the labeling of your product, will reasonably be expected to be safe. Therefore, your product may be adulterated under 21 U.S.C. 342(f)(1)(B) as a dietary supplement that contains a new dietary ingredient for which there is inadequate information to provide reasonable assurance that such ingredient does not present a significant or unreasonable risk of illness or injury. Introduction of such a product into interstate commerce is prohibited under 21 U.S.C. 331(a) and (v).

Your notification will be kept confidential for 90 days after the filing date of December 19, 2003. After the 90-day date, the notification will be placed on public display at FDA's Docket Management Branch in docket number 95S-0316. Prior to that date, you may wish to identify in writing specifically what information you believe is proprietary, trade secret or otherwise confidential for FDA's consideration.

If you have any questions concerning this matter, please contact Victoria Lutwak at (301) 436-2375.

Sincerely yours,

Susan J. Walker, M.D.
Director
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