

Memorandum

JUL 5 2006

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Date:

From: Consumer Safety Officer, Division of Dietary Supplement Programs, Office of Nutritional Products, Labeling and Dietary Supplements, HFS-810

Subject: 75-Day Premarket Notification of New Dietary Ingredients

To: Dockets Management Branch, HFA-305

Subject of the Notification: **“EstroG-100™”**

Firm: JLM Marketing, Inc.

Date Received by FDA: April 10, 2006

90-Day Date: July 9, 2006

In accordance with the requirements of section 413(a) of the Federal Food, Drug, and Cosmetic Act, the attached 75-day premarket notification and related correspondence for the aforementioned substance should be placed on public display in docket number 95S-0316 as soon possible since it is past the 90-day date. Thank you for your assistance.

Victoria Lutwak

19955-0316

RPT345



JUN 14 2006

Mr. Michael G. Jeffers
JML Marketing, Inc.
700 North Walnut Street
Bloomington, Indiana 47408

Dear Mr. Jeffers:

This is to inform you that the notification, dated March 31, 2006, that you submitted 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 April 10, 2006. Additional information was received on April 18. Your notification concerned the substance that you called "EstroG-100™" that you identify as a new dietary ingredient. According to your notification, "EstroG-100™" is a combination of three botanical extracts derived, respectively, from the roots of *Angelica gigas* Nakai, *Cynanchum wilfordii* (Maximowicz) J. D. Hooker, and *Phlomis umbrosa* Turez

According to your notification, "EstroG-100™" will be marketed in pill form. The "Dosage rates of EstroG-100™" will be "96mg total of three herbals 4 times per day for a total of 384mg/ day...." "The % of each of the three herbals per pill equals 33% or 32mg per pill (of 96mg). The "[s]tated conditions of use range from reduction of peri, pre, and post menopausal symptoms."

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 21 U.S.C. 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 "EstroG-100™" will reasonably be expected to be safe.

Based on the information in your notification, FDA was unable to determine the identity of "EstroG-100™". Your notification contains no information that describes how the roots of *Angelica gigas* are processed or extracted during the preparation of your ingredient. Furthermore, your notification does not describe which parts of either *Cynanchum wilfordii* or *Phlomis umbrosa* are used or how those plant parts are processed or extracted to produce "EstroG-100™".

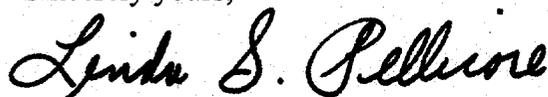
In addition, your notification contains safety information about a product you call "Estromon". Information in your notification indicates that the composition of "Estromon" contains ingredients not present in "EstroG-100™". It is unclear how "Estromon" is qualitatively or quantitatively related to "EstroG-100™" or how this information is relevant to evaluating the safe use of "EstroG-100™".

For the reasons discussed above, the information in your submission does not provide an adequate basis to conclude that "EstroG-100™", 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 April 10, 2006. 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) 436-1775.

Sincerely yours,



Linda S. Pellicore, Ph.D.
Supervisory Team Leader, Senior Toxicologist
Division of Dietary Supplement Programs
Office of Nutritional Products, Labeling
and Dietary Supplements
Center for Food Safety and Applied Nutrition

March 31, 2006

DSHEA SUBMISSION/ NOTIFICATION

Sender: Michael G. Jeffers

Company: JLM Marketing, Inc.
700 North Walnut Street
Bloomington, IND 47408
Phn#: (h) 812-336-6385
(o) 812-330-1526

APR 10 2006

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2006-3133

Name of the New Dietary Ingredient:

EstroG-100 which is combination mfg. as the following:

PRODUCT

FORM

- a) 33.3% *Phlomis Umbrosa Extract*.....herbal ex.
b) 33.3% *Cynanchum Wilfordii Extract*.....herbal ex.
c) 33.3% *Angelica gigas Nakai (Korean) Extract*.....root ex.

Description of New Dietary Ingredient:

- a) Level of the Ingredients are 100% since they are in an extract form. The EstroG-100 is a combination of two herbal extracts and one root extract. Human studies were done on the three extracts and combined with several excipients. The main components of the EstroG-100 are the three extracts stated above. Specification Enclosed (as Exhibit ES).
- b) Market scenario for the stated sector EstroG-100 is targeted for the Peri, Pre, and Post Menopausal sector for Women (as Exhibit EMS).

- c) Stated conditions of use range from reduction of peri, pre, and post menopausal symptoms. These were defined and achieved under human clinical evaluations. The end use company putting the extract as EstroG-100 into finished form will define the actual use in their marketing efforts. Enclosed is the human clinical data as analyzed by the manufacturer (**under exhibit ECD**). This data will provide a clear picture of the safety and lack of any toxicity issues under double blind conditions.
- d) Concerning Historical Data, Korean culture traces the consumption within the "Koreas" dating back to the early 1500's. We have interpreted the traditional uses from Korean to English as posted in (**Exhibit HD**). This will summarize the older uses of each component.
- e) Safety of the product has been tested within animal human clinical evaluations, double blind. The Studies of course are enclosed. We have sent a summary of the human studies to several companies for evaluation to get their opinion on potential application ideas. Enclosed is the Power Point Summary which also includes several points and show several graphs outlining toxicity, safety, and the non-addictive qualities of the Angelica gigas Nakai (Korean) extract (**note exhibit PP**).
- f) Summary of Key Points of Human Studies (Enclosed within exhibit PP)
- 1) Toxicity-none reported
 - 2) Non-Addictive
 - 3) Non-Gastro effects
 - 4) Improvement of climacteric symptoms including hot flush, and exocrine secretion
 - 5) Slight increase in Bone Density evaluations
 - 6) Reduction in Serum ALP
 - 7) Decrease in Serum Osteocalcin

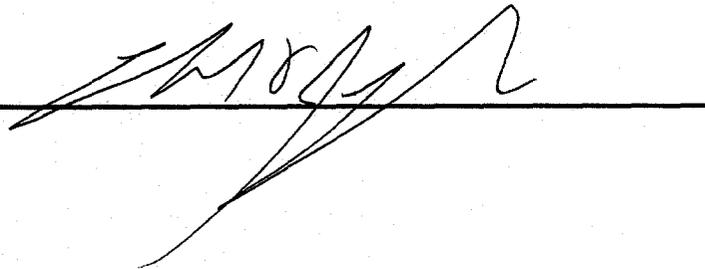
Page 3 of 3

g) The inventor of the EstroG-100 is the following:

Naturalendo Tech Co., LTD
3F, Samyeong Bldg. 1486-2, Seocho-dong
Seocho-gu, Seoul 137-869
South Korea

Signed by:

Michael G. Jeffers:

A handwritten signature in black ink is written over a solid horizontal line. The signature is stylized and appears to read 'M. G. Jeffers'.

March 25, 2006

APR 18 2006

**DSHEA SUBMISSION/ Additional Info ENCLOSED
FOR ESTRO G-100TM**

Sender: Michael G. Jeffers

Company: JLM Marketing, Inc.
700 North Walnut Street
Bloomington, IND 47408
Phn#: (h) 812-336-6385
(o) 812-330-1526

To: Division of Standards and Labeling Regulations
Office of Nutritional Products, Labeling, and Dietary
Supplements, Center for Safety and Applied Nutrition
Food and Drug Administration

RE; New Dietary Ingredient filing for *ESTRO G-100TM*. Additional categories noted in A-C as requested, and relative to the evaluation of this potential Dietary Supplement.

A) CONDITIONS OF USE, ESTO G-100TM

Dosage Rates from the HUMAN CLINICAL STUDIES Conducted by the Inventor:

- 1) To achieve Human effectiveness suggested dosage rates per the "inventor" the recipients in the Human Clinical Studies would take 128.55 mgs of the three herbals (40.81% of the total pill) combined with excipients equaling 186.45mg (59.19% of total pill) for a total pill of 315mg three times per day.
- 2) The remaining excipients in the Finished Formula were a variety of ingredients including Seaweed Calcium, Amino Acids, Vitamins, Soybean Extract, and Magnesium Stearate for the total of 59.19% of the total formula.

- 3) Response time to intake is projected at 7-10 days per the inventor, Naturalendo Tech Co., LTD.
- 4) Human clinical evaluations were conducted on a double blind study of 47 people and dosage rates for the human tests were conducted with a blended version of multiple items or the three herbals + the excipients.
- 5) The finished formula used in the Human Clinical Studies and discussed above is also used in commercial form in South Korea. The product is called "Estromon".

SUMMARY OF ESTROG-100™

- 1) The position of the inventor and manufacturer is that the active components of formula used in the human clinical evaluations that achieved the results intended are the three herbal extracts.
- 2) Thus Endo Tech hopes to market their science to the USA as EstroG-100 or the 3 active components noted as Phlomis Umbrosa, Cynanchum Wilfordii, and Angelica gigas Nakai.

DOSEAGE RATES OF ESTROG-100™

- 1) 96mg total of three herbals 4 times per day for a total of 384mg/ day to achieve results comparable to the human studies
- 2) Each of the three herbals represents a third of the dosage rate.
- 3) The % of each of the three herbals per pill equals 33% or 32mg per pill (of 96mg) which is recommended to be taken 4 times per day

MARKETING INTENT OF ESTROG-100™

- 1) Provide dosage rates of the three primary components making up EstroG-100 comparable to the Human Clinical Studies, and provided directly to Nutra Manufacturers.
- 2) Provide EstroG-100 as a component that the Nutra Manufacturer can take and then create their own finished formula. This could be with EstroG-100 as the lead product or combined with something else.
- 3) We only hope to sell EstroG-100 as an Ingredient that consists of the three herbals which represents (per Natural Endotech Co., Ltd.) the key components in their own finished formula they use in South Korea.

B) Genus Name, species (EstroG-100...3 extract components)

- | | |
|--|--|
| 1) Phlomis Umbrosa
Author: Turcz | Genus: Phlomis Family: Labiate |
| 2) Cynanchum Wilfordii
Author: (Maxim.) Hemsl | Genus: Cynanch Family: Asclepiadaceae |
| 3) Agelica gigas Nakai
Author: Nakai | Genus: Angelica Family: Umbelliferae |

C) COMMERCIAL USES EstroG-100™ in South Korea and it is called “Estromon” as a Finished Formula.

- 1) Product has been sold commercially in South Korea for the past 20 months. The Commercial form is in a 2-piece capsule and is called Estromon. The actual formula is provided in the human clinical studies included as Exhibit ECD, page #2.
- 2) Estromon includes the 3 herbal extracts plus various excipients noted above, and in page 2 of Exhibit ECD.
- 3) Estromon is sold in South Korea on the Internet and in stores, by the inventor and manufacturer called Naturalendo Tech Co., Ltd. ([www. Naturalendo.co.kr](http://www.Naturalendo.co.kr)). Each bottle includes 60 capsules.

Signed: _____

Michael G. Jeffers

EXHIBIT ES

1 PAGE TOTAL

REDACTED IN ITS

ENTIRETY

CONTAINS

TRADE SECRET

CONFIDENTIAL

COMMERICAL

INFORMATION

EXHIBIT EMS

3 PAGES TOTAL

REDACTED IN ITS

ENTIRETY

CONTAINS

TRADE SECRET

CONFIDENTIAL

COMMERICAL

INFORMATION

EXHIBIT ECD

16 PAGES TOTAL

REDACTED IN ITS

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CONFIDENTIAL

COMMERICAL

INFORMATION

Historical Records of two traditional herbal medicines, *Cynanchum wilfordii* and *Phlomis umbrosa*

I. *Cybanchi Wilfordii Radix (Cynanchum wilfordii Hemsley)*

This traditional herbal medicine was recorded in Gae-Bo-Bon-Cho published in 1108. Chinese origin of *C. auriculatum* and *C. bungei* are different from Korean traditional medicine, *C. wilfordii* Hemsley. This Korean herbal medicine was also recorded in Dong-Eui-Bo-Gam (Heo, 1610) as Eunjorong and its applications included anemia, weakness after disease as a recovery agent, weak muscle and bones and white hair. According to the Korean most famous and reliable traditional medical handbook, it is toxicologically safe. There is a tale that a man taking the dried roots of *C. wilfordii* gained libido after 7 days and had been recovered from various diseases since 100 days of taking. It has ever since been prescribed widely in Korea by oriental medicine doctors. Now, it is one of most frequently prescribed herbal medicines in Korean oriental hospitals.

• 何首烏 ○ 江原道名은오릉, 黃海道名새막불취, 性平溫味苦澁 一云甘 無毒, 主癰癤, 消癰腫, 五痔, 治積年勞瘦, 癩病, 風虛敗劣, 婦人產後諸疾, 帶下赤白, 益血氣, 壯筋骨, 填精髓, 黑毛髮, 悅顏色, 駐顏延年, ○ 本名夜交藤, 因何首烏, 服而得名, 此人, 生而閹弱, 年老無妻子, 一日醉臥田中, 見一藤, 兩本共生, 苗蔓相交, 釋合三四, 心異之, 遂採根暴乾, 搗末酒服七日, 而思人還, 百日久疾皆愈, 十年生數男, 壽至一百三十歲, ○ 蔓紫, 花黃白, 葉如薯蕷而不光, 生必相對, 根大如拳, 有赤白二種, 赤者雄白者雌, 根形如鳥獸山岳之狀者, 珍也, ○ 春末夏中初秋, 候清明日, 兼雄雌採之, 以竹刀或銅刀, 去皮薄切, 蒸暴, 一名交藤, 一名夜合, 一名九棘藤, 終始勿犯鐵, 忌食蔥蒜, 蘿蔔, 豬羊血, 無鱗魚, 凡修合藥, 須雌雄相合喫, 有驗, 『本草』 ○ 米泔浸一宿, 切片曬乾搗碎, 如作丸則黑豆汁拌蒸, 曬乾用, 『入門』

하수오(何首烏) ○ 강원도에서는 '은조물'이라고 하고, 황해도에서는 '새막뿌리'라 한다. 성질은 평(平)하고 따뜻하며 [溫] 맛은 쓰고 짠고 [苦澁] 단대(甜苦)도 한다. 독이 없다. 나력·용종과 5가지 치질을 없애며, 여러 해 될 허로로 여윈 것, 담벽·풍허(風虛)로 몸이 몹시 상한 것을 치료한다. 부인이 몸뚱이 뒤에 생긴 여러 가지 병과 적맥대하를 치료한다. 혈기를 보하며 힘줄과 뼈를 튼튼하게 하고, 정수(精髓)를 보충하며 머리털을 길게 한다. 또 얼굴빛을 좋게 하고 늙지 않게 하며 오래 살게 한다. ○ 원래 이름은 야교동(夜交藤)인데, 하수오(何首烏)라는 사람이 먹고 큰 효과를 본 때서 하수오라는 이름을 붙이게 되었다. 이 사람은 본래 몸이 약하였고 늙어서는 아내도 자식들도 없었다. 하루는 취해서 밭에 누워 있었는데, 한 덩굴에 2줄기가 따로 난 풀의 싹과 덩굴이 서니면 서로 감겼다 풀뚝다 하는 것이 보였다. 마음에 이상하게 생각되어 마침내 그 뿌리를 캐어 햇볕에 말려 짓찧은 다음 가루내어 술에 타서 7일 동안 먹었다니 성욕이 생기고 백일이 지나서는 오랜 병들이 다 나았다. 10년 후에는 여러 명의 아들을 낳았고 130살이나 살았다. ○ 덩굴은 자줏빛이고 꽃은 황백색이며, 잎은 마와 비슷한데 광택은 없으며, 반드시 맞대서 난다. 뿌리가 주먹만하고, 붉은 빛·흰빛의 2가지 종류가 있는데, 붉은 것은 수컷이고 흰 것은 암컷이다. 뿌리의 생김새가 조수나 신약처럼 생긴 것이 진품이다. ○ 낮은 봄·한여름·초가을에 날씨가 맑은 날에 암컷·수컷을 다 캐어 참대칼이나 구리칼로 겉껍질을 긁어 버리고 얇게 썰어 찌서 햇볕에 말린다. 일명 교동(交藤)·야합(夜合)·구간동(九間藤)이라고 하는데, 이 약을 다룰 때는 처음부터 마지막까지 쇠를 대지 말아야 한다. 파·마늘·무·돼지피·양의 피·비늘 없는 생선을 먹지 말아야 한다. 법제하여 약으로 쓸 때는 반드시 붉은 빛이 나는 수컷과 흰 빛이 나는 암컷을 합하여 먹어야 효과가 있다. 『향초』 ○ 삼프물에 하루밤 담갔다가 조각나게 썰어서 햇볕에 말려 짓찧어 부스르뜨린다. 알약을 만들려면 짐정콩(黑豆) 달인 물에 버무려 쪄 다음 햇볕에 말려서 쓴다. 『입문』

II. *Phlomis Radix (Plomis umbrosa Turcz)*

This traditional herbal medicine is also recorded in Dong-Eui-Bo-Gam (Heo, 1610) the medical bible for Korean oriental medicine doctors. According to the Korean most reliable handbook, it helps stop pains, skin recovery, and putting together of muscles and bones as its name stands for (in Korean the name Sok-dan meaning "connecting of cut"). It also has the effects on diseases after child delivery. It is included in various oriental prescriptions.

*續斷 ○ 性微溫味苦辛無毒。能通經脈，續筋骨，調氣，調血脈。婦人產後一切病。○ 生山野。三月後，生苗莖，四枝似
 芋麻，葉亦類，兩兩相對而生，四月開花紅白色，根如大薊赤黃色，七月八月採根陰乾，以節節斷，皮黃嫩者為真。『本草』
 ○ 能止痛生肌，續筋骨，故名為續斷。婦人崩漏帶下，尿血為最，節節斷，有烟塵起者佳，酒浸焙乾用，與桑寄生同功。『入門』

속단(續斷) ○ 성질은 약간 따뜻하며[微溫] 맛이 쓰고[苦] 매우며[辛] 독이 없다. 경맥을 잘 통하게 하고 힘줄과 뼈를
 이어주며, 기를 도와주고 혈액을 고르게 하며, 해산 후의 일체 병(一切病)에 쓴다. ○ 산이나 들에서 자란다. 음력
 3월 후에 싹이 돋아서 화살대 같은데, 네모져 있어 모시와 같으며, 잎 또한 모시와 같은데 2개씩 맞붙어서 난다. 음력
 4월에 홍백색의 꽃이 피고, 뿌리는 대개(大薊)와 같은데 적황색이다. 음력 7월, 8월에 뿌리를 캐어 그늘에서 말린다.
 마디마디가 끊어지고 퓌질이 누르고 주름진 것이 좋은 품종이다. 『본초』 ○ 아픈 것을 잘 멎게 하고 산이 살아나오게
 하며, 힘줄과 뼈를 이어주므로 속단이라고 한다. 풍우·대하·피오증을 누는 것 등 부인병에 매우 좋다. 마디마디가
 끊어지면서 연기 같은 연지가 나는 것이 좋은 것이다. 술에 담갔다가 약한 불기운에 말려 쓴다. 뽕나무겨우살이[桑寄生]와
 효과가 같다. 『입문』

<Dong-Eui-Bo-Gam (Heo, 1610)>

(Reference : Translated Dong-Eui-Bo-Gam, Bupin Publishes Co. 1999 Korea)

Dong-Eui-Bo-Gam was accomplished in 1610 by Heo Joon (1546-1615) and published in 1613. Heo referred more than 70 medical books of China and Korea, and wrote easier medical textbook to find remedies and prescription for various diseases. With its substantiality and practicability, this textbook has been recognized as one of the most important medical textbooks in East Asia, especially in Korea and published 7 times in China and Japan.

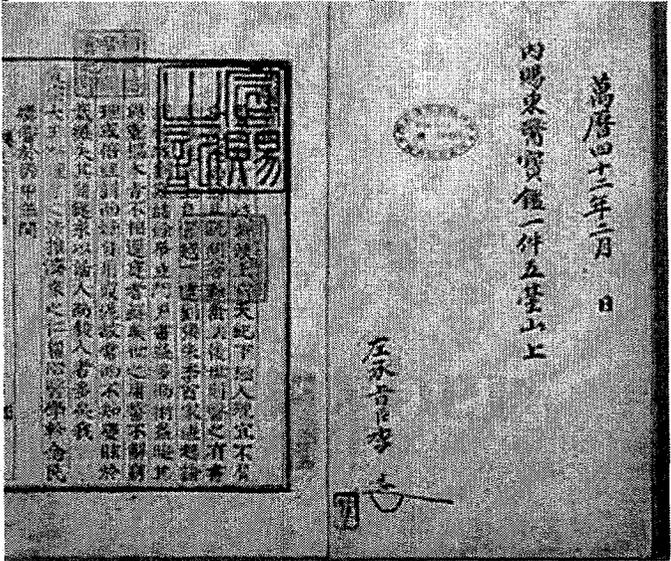


Photo of original Dong-Eui-Bo-Gam

EXHIBIT PP

6 PAGES TOTAL

REDACTED IN ITS

ENTIRETY

CONTAINS

TRADE SECRET

CONFIDENTIAL

COMMERICAL

INFORMATION