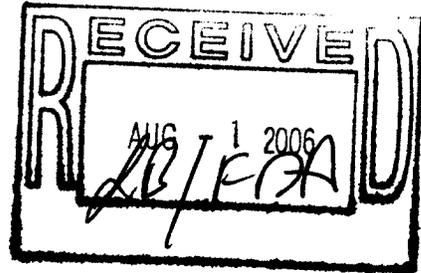


July 25, 2006

DSHEA SUBMISSION/ Additional Info ENCLOSED

Sender: Michael G. Jeffers
JLM Marketing, Inc
700 North Walnut Street
Bloomington, IN 47404

Company: JLM Marketing, Inc.
700 North Walnut Street
Bloomington, IND 47408
Phn#: (h) 812-336-6385
(o) 812-330-1526, (fx) 812-330-1524



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: Bulk, New Dietary Ingredient filing for EstroG-100 ™

Dear Sir/ Madame:

Pursuant to 21 CFR & 190.60 please be advised that JLM Marketing, Inc. of Tampa, FL, is hereby providing you with the notification of its intent to market a New, Bulk, Dietary Ingredient, called EstroG-100 ™ which is extracted from the root of the plant known as *Angelica gigas* Nakai, extracted from the stem and leaf of a plant known as *Phlomis Umbrosa*, and extracted from the leaves and stems of a third plant called *Cynanchum Wilfordii*. Enclosed with this original document are two additional copies of JLM Marketing, Inc.'s submission and the attachments thereto.

Based on the following, JLM Marketing, Inc. respectfully submits that there are no safety issues relating to its intended marketing of EstroG-100 ™ as a Bulk, New Dietary Ingredient, and derived in extract form from the root of the *Angelica gigas* Nakai plant, and the root extract of the 2 plants called *Phlomis Umbrosa* and *Cynanchum Wilfordii*.

A) Name of the New Dietary Bulk Ingredient

1st Component - *Angelica gigas* Nakai Korean

- 1) Genus Name; *Angelica*
- 2) Author; Nakai
- 3) Family; Umbelliferae
- 4) Synonyms: *Angelica cryptotaeniifolia*-Kitag
- 5) Range; East Asia, portion used; root

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2nd Component - Phlomis Umbrosa

- 1) Genus Name: Phlomis
- 2) Author: Turcz
- 3) Family: Labiate
- 4) Synonyms; None Known
- 5) Range: East Asia, portion used; root

3rd Component – Cynanchum Wilfordii

- 1) Genus Name: Cynanch
- 2) Author: (Maxim.) Hemsl
- 3) Family: Asclepiadaceae
- 4) Synonyms: Cynoctonum Eilfordii- Maxim.
- 5) Range: East Asia, portion used; root

Description of the Bulk Dietary Ingredient Called EstroG-100™

Source- EstroG-100™ is derived from the three plants noted above. The extraction process is Confidential and Proprietary and the extraction process is outlined as **Exhibit MP-A**. The KFDA has approved the key components as defined in **Exhibit KF-E** (and included the leaves portion of the Phlomis Umbrosa and Cynanchum Wilfordii), and the Manufacturing sight location in **Exhibit KF-IN**.

- 1) The key phytochemical components of EstroG-100™ are Decursin, Cinnamic Acid, and Shanzhiside Methyl Ester. The quantitative analyses of these three ingredients are performed in all commercial lots against their respective standards as outlined in the specification in **Exhibit ES**.
- 2) The chemical composition is defined with CAS information in **Exhibit CCE**.
- 3) Composition of Matter- as defined by the following specification for EstroG-100™ as Exhibit ES.
- 4) The MSDS is defined in **Exhibit MSE**
- 6) The manufacturing Process of EstroG-100™ as a Bulk Ingredient Extract is developed from extract of roots from Angelica gigas Nakai for the 1st component. The plant is grown in South Korea, and harvested after minimum of 2 years of growth. A detailed manufacturing process can be found in Exhibit MP-A.
- 7) The Manufacturing Process for the 2nd component called Phlomis Umbrosa Extract, and the 3rd component called Cynanchum Wilfordii Extract is detailed in Exhibit MP-A, and defines the extract methodology using the roots (the leaves are not included).

- 8) Each component is extracted with water, tested, and combined via blending.

B) Conditions of Use as an Bulk Dietary Ingredient

Dosage Rates from Human Clinical Studies: To achieve 98% effectiveness suggested "ingredient" dosage rates to the recipient would be 125 mgs three times per day.

Response time to intake is projected at 45-90 minutes per the inventor, Naturalendo, LTD of South Korea. This projection is based on the testimonials of users as well as the human Clinical Evaluation outlined in **Exhibit HCS**.

- 1) Human clinical evaluations were conducted on a double blind study of 48 people with no negative results during consumption (RE: toxicity, etc.)
- 2) EstroG-100 as an "ingredient" has been used in COMMERCIAL form in South Korea for over 2 years with no reports of side effects or toxicity issues in any of the reported genders and ages (per KFDA in their subsequent approval of Estromon which is the name of the COMMERCIAL product in South Korea using the Ingredient called EstroG-100 in their finished formula)
- 3) EstroG-100 showed no signs of Toxicity during animal studies as explained in **Exhibit ASE**.

D) Comparison of EstroG-100™ as a Bulk Ingredient to the Commercial Form known as Estromon which is manufactured in South Korea and distributed in Asia.

- 1) The Bulk Ingredient called EstroG-100™ is suggested in dosage rates of 125 mg, three times per day, per human clinical evaluations (Exhibit HCS).
- 2) During the human clinical evaluations of EstroG-100 the name "Estromon" was used inter-changeably as the clinical trial code name during the research phase of EstroG-100.
- 3) The finished COMMERCIAL form (capsules) includes the two stated plant root extracts and the root extract Decursinol™ combined with miscellaneous excipients. The commercial form is manufactured in South Korea. NaturalEndo, LTD is the inventor of the EstroG-100 and sponsored the human clinical trials. Enclosed is the Manufacturer, Inventor, and Distributor of the Estromon which is the commercial form are defined in **Exhibit MSL**.

- 4) The Commercial finished formula manufactured by Naturalendo is a two piece capsule and includes 125 mg of EstroG-100 along with additional excipients such as - Dicalcium Phosphate and various flow agents and binders. The formula is listed in **Exhibit FF**.
- 5) This COMMERCIAL form used in South Korea is called Estromon and established market share upon approval by KFDA (Exhibit KF-E). After full review by KFDA Estromon has been selling and thriving in the South Korea commercial sector for over two years. Consumption includes all age groups and gender. The inventor and marketer have stayed consistent to suggested market segments relative to the human clinical studies.
- 6) The phytochemical content of EstroG-100™ being submitted here as a Bulk-manufactured INGREDIENT is quantitatively and qualitatively equivalent. The inventor of the ingredient is also the distributor of the finished commercial form, Estromon™, which is being marketed in Asia as a nutritional supplement and approved for Food Use as well by KFDA.
- 7) Commercial Form and Use of EstroG-100 is defined in the Human Clinicals as a support mechanism for women past child bearing years, and with no reports of side effects.

E) The Safety of the Bulk Ingredient called EstroG-100™

Pre-clinical animal toxicology studies have found that EstroG-100 has a good safety profile up to 2 gram/Kg (of body weight) dose level. The toxicology study report is shown in **Exhibit ASE**.

- 1) The Human Clinical evaluations did not show any indications of problems arising from consumption with other ingredients, foods, etc
- 2) No Negative results were found on Acute Toxicity, Genetic Toxicity, and Subacute Toxicity evaluations as identified in Exhibit ASE.
- 3) Stability Data is defined in **Exhibit SD-E** showing the long-term stability and effectiveness of EstroG-100 under evaluation of degradation under specific time points up to 36 months.
- 4) KFDA evaluated EstroG-100 (Estromon) and found the use and human consumption acceptable for South Korea as outlined in Exhibit KF-E.

- 5) The Specification of Decursinol™ is included as **Exhibit ES**, and the MSDS Sheet for Decursinol TM is included as **Exhibit MSE**.
- 6) The manufacturer of Estromon in COMMERCIAL Form and using EstroG-100 has been inspected and certified by KFDA as noted in Exhibit KF-IN.
- 7) **Historical Data concerning use of the EstroG-100 3 primary Root Extract components is noted in Exhibit HD-AG.**

F) Literature as Points of Reference are posted in the human clinical evaluations

G) Summary

1) Based on the foregoing we believe that FDA should accept this filing on behalf of JLM Marketing, Inc. as providing sufficient evidence that EstroG-100™, as a Bulk Ingredient, extracted from the root of the Angelica gigas Nakai plant, and root extract of the 2 plants called Phlomis Umbrosa and Cynanchum Wilfordii, and when used as suggested in the dosage rates defined in the Human Clinical Evaluations (as Exhibit HCS), can reasonably be expected to be safe for human consumption.

2) Lastly, with a positive track record of Commercial Usage and Consumption of EstroG-100 as an Ingredient in the Finished Commercial Product called Estromon (Mfg: South Korea) over the past 24 months safety is traceable and verifiable via results and the approval by KFDA.

3) In support of this we have included all appropriate Exhibits defining the purity, safety, stability data, toxicity results, manufacturing protocols and specifications, animal studies, and human studies, of EstroG-100™.

If you have any further requirements for additional data please direct all correspondence to the undersigned.

Signed:.....

Michael G. Jeffers
JLM Marketing, Inc.