

LAW OFFICES OF RUNAN ZHANG

July 19, 2004

Division of Standard & Labeling Regulations
Office of Nutritional Products, Labeling & Dietary Supplements
Center for Food Safety & Applied Nutrition
Food & Drug Administration
5100 Paint Branch Parkway
Room 4D043
College Park, MD 20740-3835

AUG 8 2004
OAB/FDA

**RE: Premarket Notification for "Shuanghuanglian – Healthy Respiration",
English description: Extract of Honeysuckle, Forsythia & Root of Skullcap**

Dear Sir or Madam:

This letter is to notify you that American Research Institute of World Traditional Medicine will function as the distributor for a Chinese herbal dietary supplement product "Shuanghuanlian – Healthy Respiration", English description: Extract of Honeysuckle, Forsythia & Root of Skullcap, in the United States.

The name and address of the distributor is American Research Institute of World Traditional Medicine at 5001 Russett Road, Rockville, MD 20853-2966.

The name of the product is "Shuanghuanglian – Healthy Respiration". The product contains three new ingredients of extracts of Chinese herbs -- honeysuckle, forsythia & root of skullcap. Shuanghuanglian – Healthy Respiration is named after the Chinese names of three new ingredient herbs: *Shuang Hua* (Honeysuckle), *Huang Qin* (Root of Skullcap), and *Lian Qiao* (Forsythia). These three ingredients have been used to produce a series of Shuanghuanglian products in China since 1993 in the forms of refined powder for injection, oral liquid, spray, and powder/grains in small bags for drinks. The ratio of the mixture of three ingredients and the manufacture procedures are the same for all different forms of products. The only difference in the production is the final step in the formation procedure, which will form final products in different shapes. The first product of Shuanghuanglian series products to be marketed in the United States will be in the form of power/grains in small bags for drink.

The Latin binomial names for each element are:

Lonicera Japonica Thunb for Honey-Suckle,

Forsythia Suspensa (thunb) Vahl for Forsythia,

Scutellaria Baicalensis Georgi for Root of skullcap.

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The recorded history of using these three new ingredient herbs in Shuanghuanglian products for their medical functions can be traced back to thousand years ago in the Chinese history. The author for the first book that listing functions of these herbs is Shizhen Li, who wrote "Bencao Gangmu" (guideline of herbs) in Ming dynasty about 800 years ago. Xingyan Sun, who wrote "Shennong Bencao Jing" (collection of herbs), collected these three herbs in Qing dynasty about 500 years ago. These herbs are also listed in the *Chinese Herbs*, edited by National Chinese Medicine Administration, published by Shanghai Science and Technology Publisher in 2000. These three herbs are also included into the English book, *Herbs*, by Lesley Bremness, published by Dorling Kindersley in London, New York and Stuttgart in the Western world in the recent years.

The Shuanghuanglian – Healthy Respiration may strengthen the immunity of human's respiratory system. No side effect has been reported so far for using the product. The health claim on the label will be "may strengthen immunity for healthy respiratory system". Since 1992, there were professional conferences and seminars discussing the medical functions and safety of the Shuanghuanglian extract in the Chinese medical field. A great number of articles on the applications of Shuanghuanglian products and results of applications were published in many medical journals in China. All articles reported positive results of applications of these products.

The name of Shuanghuanglian is used in China referring to Shuanghuanglian series products with three new ingredients made into different forms, such as Shuanghuanglian powder (the product will be marketed here), Shuanghuanglian powder injection and Shuanghuanglian spray. However, regardless of different forms, the ratio between three different ingredients in all Shuanghuanglian products remain the same in each different forms. The production procedure is the same except for the last process of formation for each final product.

Shuanghuanglian – Healthy Respiration, the first product, to be marketed in the US will be packed into small bags with a mixture of 5g of three ingredients. The content of ingredients in each bag is the mixture of 1.5g Honeysuckle, 2g Forsythia and 1.5g root of skullcap. The condition of use recommended in the label will be chewing or making drinks with hot/cold water. Adult takes 1-2 bags a time, three times a day. Children under 2 should not take more than one-half bag a day.

Ministry of Health of China approved the Shuanghuanglian Powder (product to be marketed here) on April 28, 1993 as a non-prescription herbal medicine. Shuanghuanglian products have been sold on the Chinese market in the past ten years. The name has been so well known for cold and upper respiratory system problems. There are many articles published on the application of Shuanghuanglian to treat infant pneumonia successfully. The product is even used for AIDS treatment. Toxicity test on the Shuanghuanglian Oral Liquid (for internal use) conducted by the manufacturer showed that this product is toxicity free and safe to use. The studies on the applications of Shuanghuanglian products demonstrated that this product is effective for strengthening the immune system and preventive for infection on respiration system caused by virus. There has been no report on

any safety problems caused by using Shuanghuanglian products either for internal use of injection in the past ten years.

All approved medicines have to be listed in the *Chinese Medicine Dictionary*. The Shuanghuanglian Powder is in the Chinese medicine dictionary as a proven safe Chinese herbal medicine. The Dictionary also included the method of making Shuanghuanglian Powder. In the United States, there were 74 patents approved by the US Patent Office concerning the use of Honeysuckle, 43 patents approved by the US Patent Office concerning the use of Forsythia, and 41 patents approved by the US Patent Office for the use of skullcap during 1996 to 2002. From the list of the approved patents, it shows that many of the patents concerning these three herbs are dealing with medical functions and use. Although, I have not found any dietary supplement using these herbs, these herbs are not completely new or foreign to the US market and consumers.

The person who is designated by the manufacturer to be in charge of the distribution is Mr. Changshan Liu, Director of American Research Institute of World Traditional Medicine, Inc., a nonprofit organization incorporated in Maryland. The manufacturer is Harbin Pharmaceutical Group Co., Ltd. Second Chinese Medicine Factory, which passed the GMP inspection and holds a valid certificate of GMP issued by China State Drug Administration.

Enclosed with this letter are translated materials on the Shuanghuanglian Powder (same product to be marked with the name of Shuanghuanglian – Healthy Respiration in the US) and the approval of the Ministry of Health of China for the production of the Shuanghuanglian products in different shapes and related information. As mentioned above that the ratio of three new ingredients contents in all different shapes of Shuanghuanglian products are the same. All Shuanghuanglian products in China are used for internal use or injection. These information include the following:

1. Translated Certificate of New Herbal Medicine and Approval for Manufacture of Shuanghuanglian Powder by China Health Ministry, 1993, attached with Chinese document;
2. Translated Certificate of New Herbal Medicine and Approval for Manufacture of Shuanghuanglian Powder Injection by China Health Ministry, 1993, attached with Chinese document;
3. Translation of Chinese medicine dictionary on Shuanghuanglian Powder, the product will be marketed here with the name of Shuanghuanglian -- Healthy Respiration, attached with Chinese document;
4. Introduction of Shuanghuanglian Powder;
5. Copy of translated Bencao Gangmu (Guideline of Herbs) on three new ingredient herbs, attached with the copy of Chinese book published about 800 year ago;

6. Copy of translated Shennong Beibao Jing (Collection of Herbs) on three new ingredient herbs, attached with the copy of Chinese book published about 500 years ago;
7. Translation of Chinese Herbs 2000 edition on three new ingredient herbs, attached with the copy of Chinese book;
8. Translation of Modern Study of the Medical Formulae of Traditional Chinese Medicine on Shuanghuanglian Injection Liquid attached with the copy of Chinese book;
9. Data of Experiment on Acute Toxicity of Shuanghuanglian Oral Liquid;
10. The Brief Introduction of Research Institute which conducted the experiment;
11. Study on the Shuanghuanglian Powder [injection] prepared by the manufacturer on the related data and information concerning its use and medical function;
12. Article entitled Study on Antivirus Effect of Shuanghuanglian Injection published in Chinese Traditional and Herbal Drugs in 2002;
13. Article entitled Effects of Shuanghuanglian Treatment of Child Pneumonia published in Chinese Journal of Integrated Traditional and Western Medicine in 1994;
14. Article entitled Clinical Observation of Shuanghuanglian in Treating Late Term Malignant Cancer with Complication of Lung Infection published in the Practical Journal of Integrating Chinese with Modern Medicine in 1998;
15. Article entitled Clinical Observation on Treatment of Child Pneumonia by Shuanghuanglian published in Shanghai Journal of Traditional Chinese Medicine in 1994;
16. Article entitled Clinical Observation of Treatment by Shuanghuanglian of 125 Cases of Child Upper Respiratory Tract Infection in Lishizhen Medicines and Materia Medica Research in 1999;
17. Article entitled CASE STUDY: Clinical Observations of Treating 140 Child Infectious Disease with Shuanghuanglian published in Chinese Journal of Hospital Pharmacy in 1998;
18. Article entitled 80 CASES OF MINISTERING SHUANGHUANGLIAN INJECTION IN TREATMENT OF

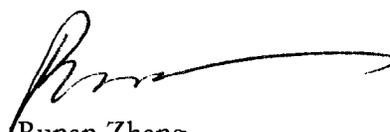
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PEDIATRIC RESPIRATORY TRACT INFECTION published in Shanxi Journal of Chinese Traditional Medicine in 1993;

19. Certificate of Good Manufacturing Practices (GMP) for Human Drugs People's Republic of China for the manufacturer of the proposed dietary supplement;
20. List of US patents concerning the three new ingredient herbs used for different functions; and
21. Copy of the English book on the three herbs.

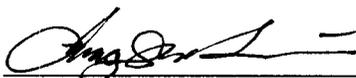
Should you have any question concerning the product, please contact me at (202) 965-4348.

Sincerely,



Runan Zhang
Council for Petitioner

Acknowledgment signature of the designated person:



Changshan Liu

Enclosure