DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

Memorandum

Date: October 19, 2001

From: Director, Division of Standards and Labeling Regulations, Office of Nutritional Products, Labeling and Dietary Supplements, HFS-820

Subject: 75-Day Premarket Notification for New Dietary Ingredients

To: Dockets Management Branch, HFA-305

New Dietary Ingredient:	Hirudo powder
Firm:	Wealth Express Industrial Ltd.
Date Received by FDA:	July 11, 2001
90-Day Date:	October 9, 2001

In accordance with the requirements of section 413(a) of the Federal Food, Drug, and Cosmetic Act, the attached 75-day premarket notification for the aforementioned new dietary ingredient should be placed on pubic display in docket number 95S-0316.

Felicia B. Satchell

Felicia B. Satchell

95S-0316

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Washington DC 20204

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Mr. Shiming Han
Vice President
Wealth Express Industrial Ltd.
Block B1, 19/F Kailey Industrial Center
12 Fung Yip St. Chai Wan
Hong Kong

Dear Mr. Han:

This letter is in response to your completed notification, dated July 9, 2001 you submitted to the Food and Drug Administration (FDA), making a submission for a new dietary ingredient pursuant to 21 U.S.C. 350b(a)(2) (section 413(a)(2) of the Federal Food, Drug, and Cosmetic Act). Your letter notified FDA of your intent to market a product containing a new dietary ingredient named "Hirudo powder." FDA received your complete submission on July 11, 2000.

21 U.S.C. 350b(a)(2) requires that a manufacturer or distributor of a dietary supplement that contains a new dietary ingredient 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 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 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 deemed 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 evaluated the information in your submission. Your submission contains evidence of history of use and other information that you assert is an adequate basis to conclude that a dietary supplement product containing Hirudo powder will reasonably be expected to be safe. However, the agency has significant concerns about the evidence on which you rely to support your conclusion.

You state that Hirudo powder has been used in traditional Chinese medicine for thousands of years. As a medicine in China, hirudo is the desiccated body of *Thitmania pigra* Whitman, *Hirudo nipponica* Whitman or *Whimania acranulata* Whitman belonging to the Hirudo family. You provided information on the historical use of Hirudo in traditional Chinese medicine as well as in modern medicine (for venous insufficiency). However, your

submission does not include information on the post-marketing history of these products in China, including adverse effect monitoring, that could contribute to demonstrating a basis to support that its use in the United States as a dietary supplement will be expected to be safe.

The Chinese literature (Exhibits A-C) referenced in your submission state that the dosage for internal use of Hirudo powder varies from 1.5 to 9 g a day used alone or in combination with other medicines. Treatment duration when mentioned is usually 4 to 6 weeks. The proposed label recommends a daily use of 900 mg Hirudo powder which is lower than those recorded levels used in traditional Chinese medicine (Exhibits A-C). However, you did not provide information on the safety of its long-term use, which is relevant to the typical use of dietary supplements by consumers.

In addition, you did not provide any information on the source of the material(s) from which this new dietary ingredient will be derived nor the procedure for its preparation in order to ensure its purity. Information that accompanied your submission did not provide an adequate basis to judge the quality of the new dietary ingredient.

The saliva of medicinal leeches contains many compounds (hirudin and other protein inhibitors, enzymes, etc.) that have anticoagulation, clot dissolving, and antiplatelet aggregation properties (Exhibits C-D). Therefore, the potential health risks from the use of this product in persons who are already taking drugs or other products which may adversely interact with Hirudin powder needs to be addressed. The agency also has significant concerns about the potential risk of serious adverse effects with use of Hirudo powder for consumers who have certain diseases or conditions. For example, Hirudo has abortive properties and can be used for abortion. Use during pregnancy and in patients with "blood vacuity but no blood stasis" are not recommended in traditional Chinese medicine (Exhibits A-C). However, no restriction of use of the dietary supplement with respect to physiological conditions or age of the consumer is noted in your submission.

Finally, please be advised that any representation that a product is intended for the diagnosis, cure, mitigation, treatment or prevention of disease in man or animals suggests that it is a drug, as defined in 21 U.S.C. § 321(g)(1)(B), and would be subject to regulation under the drug provisions of the Federal Food, Drug and Cosmetic Act. All drugs must be approved by FDA before they can be marketed in the U.S.

For the reasons discussed above, the information in your submission does not provide an adequate basis to conclude that Hirudo powder, 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 the new dietary ingredient Hirudo powder 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 products into interstate commerce is prohibited under 21 U.S.C. 331(a) and (v).

Your submission will be kept confidential for 90 days from the date of receipt, and after November 14, 2000, your submission will be placed on public display at Dockets Management Branch (Docket No. 95S-0316). Commercial and confidential information in the notification will not be made available to the public.

Should you have any questions concerning this matter, please contact me at (202) 205-4168.

Sincerely yours,

Felicia B. Satchell

Felicia B. Satchell
Director
Division of Standards
and Labeling Regulations
Office of Nutritional Products, Labeling
and Dietary Supplements

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Washington DC 20204

AUG 13 2001

Mr. Shiming Han
Vice President
Wealth Express Industrial Ltd.
Block B1, 19/F Kailey Industrial Center
12 Fung Yip St. Chai Wan
Hong Kong

Dear Mr. Han:

This is to inform you that the completed notification, dated July 9, 2001, you submitted pursuant to 21 U.S.C. 350b(a)(2) was received and filed by the Food and Drug Administration (FDA) on July 11, 2001. Your notification concerns the substance called "Hirudo Powder" that you assert is a new dietary ingredient.

In accordance with 21 C.F.R § 190.6(c), FDA must acknowledge its receipt of a notification for a new dietary ingredient. For 75 days after the filing date (i.e., September 24, 2001), you must not introduce or deliver for introduction into interstate commerce any dietary supplement that contains "Hirudo Powder."

Please note that acceptance of this notification for filing is a procedural matter and, thus, does not constitute a finding by FDA that the new dietary ingredient or supplement that contains the new dietary ingredient is safe or is not adulterated under 21 U.S.C. 342. As another procedural matter, your notification will be kept confidential for 90 days after the filing date. After October 9, 2001, the notification will be placed on public display at FDA's Docket Management Branch under docket number 95S-0316. However, any trade secret or otherwise confidential commercial information in the notification will not be disclosed to the public.

Please contact us at (202) 205-4168, if you have any questions concerning this matter.

Sincerely yours,

Felicia B. Satchell

Felicia B. Satchell
Director
Division of Standards
and Labeling Regulations
Office of Nutritional Products, Labeling
and Dietary Supplements
Center for Food Safety
and Applied Nutrition

Wealth Express Industrial Ltd

June 18, 2001

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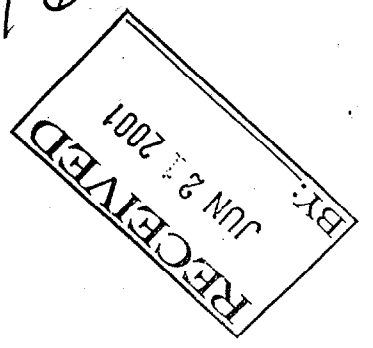

Office of Special Nutritional
(HFS-450)
Center for Food Safety and Applied Nutrition
Food and Drug Administration
200 c St. SW
Washington, DC 20204

Subject: New Dietary Ingredient Notification For "Hirudo powder"

Dear FDA officers:

As per the requirements stated within TITLE 21 Sec. 190.6, we provide with the below stated information:

1) Complete name of distributor for the new dietary ingredient:
Wealth Express Industrial Ltd.
Block B1, 19/F Kailey Industrial Center, 12 Fung Yip St. Chai Wan
HongKong.

2) Complete name of the dietary ingredient:
Hirudo powder

3) A description of the dietary supplement expected to contain the subject material is best described according to proposed conditions suggested in the labeling of the dietary supplement.
The level of the dietary ingredient is 0.9g per day. Dietary ingredient of Hirudo powder in dietary supplement is 20%, i.e. 100mg Hirudo powder per 500mg capsule. Suggested dosage in the label is three capsules after each meal, i.e. 9 capsules per day, or 900mg Hirudo powder per day.

4) Hirudo has been used in traditional Chinese medicine for thousands of years. Dosage of Hirudo is found in medical literature early originated in the 1st Century, *Synopsis of the Golden Chamber* records a dosage of 30 Hirudos per day, taken in soup with other ingredients. *Pen-ts'ao Kan-mu* published around the year of 390 also describes the dosage of Hirudo. Also extensively seen is Hirudo's dosage in current Chinese medicinal literatures, e.g. the *Pharmacopoeia of the People's Republic of China* (Edition 1995) (Exhibit A) records *a Hirudo dosage of 1.5~3g per day*; *Traditional Chinese Medicinal Science* (Exhibit B) carries the same record; the *Clinical Traditional Chinese Medicinal Science* (Exhibit C) makes more detailed explanation on Hirudo dosage: *[Dosage for Reference] for internal taking, 3~5g each day. For drenched taking, 0.3~0.5g each time,* in addition, it also illustrates 9 cases of Hirudo use and their dosages.
In this scenario, we can conclude the recommended dosage in the label of the dietary supplement is lower than those recorded in above-mentioned literatures, which shall be deemed safety to health.

Continued . . .

Block B1, 19/F Kailey Industrial Center, 12 Fung Yip St. Chai Wan, HongKong.
Phone 852-2234 6628 FAX 852-2516 7803

Wealth Express Industrial Ltd

June 18, 2001
Dear FDA officers: Food and Drug Administration

For evidence of safety, we make reference to three (a, b,c) exhibit documents and a four (d) exhibit which is a compilation of published articles pertinent to the issue. All exhibits are enclosed herein and presented in no order of significance. In the case of exhibits originally composed in the Chinese language, we also enclose the original copy in Chinese for your inspection.

Exhibit A: A translation from Chinese.
Pharmacopoeia of the People's Republic of China Edition 1995 Part I Compiled by Pharmacopeial Committee of the Ministry of Health, the People's Republic of China. Page:67

Exhibit B: A translation from Chinese.
Traditional Chinese Medicinal Science Compiled by *Yan Zhenghua, Wong Weijian, Gao Xuemin, Pang Junzhong, Shen Liansheng, Gong Shusheng* and *Yao Kuanlu* Beijing College of Traditional Chinese Medicine October 1979 page:389

Exhibit C: A translation from Chinese.
Clinical Traditional Chinese Medicinal Science, Chief Compilers: *Wong Weiliang, Fang Shuting* Henan Sci-tech Publishing House. Page:936--940

Exhibit D: a publication on the Internet.
Medicinal Leeching --Past and Present ThromboSite Newsletter Volume 1, Issue 3 (January, 1999) http://www.thrombosite.com/tsnews/tsnews1_3.html

5) The signature of the person designated by the distributor of the dietary ingredient.

Shiming Han

Shiming Han Vice President
Wealth Express Industrial Ltd.

This letter and its attachments are respectfully submitted and intended to be a premarket notification to the FDA. In due course, we request a receipt acknowledgement.

Continued . . .

Block B1, 19/F Kailey Industrial Center, 12 Fung Yip St. Chai Wan, HongKong.
Phone 852-2234-6628 FAX 852-2516-7803

Wealth Express Industrial Ltd

June 18, 2001

Dear FDA officers: Food and Drug Administration

Of course, if there are questions or clarifications needed for your review and consideration of these documents please immediately contact the undersigned and I will endeavor to address your questions and/or additional requirements.

Sincerely

Shiming Han

Shiming Han
Vice President

Enclosures

Block B1, 19/F Kailey Industrial Center, 12 Fung Yip St. Chai Wan, HongKong.
Phone 852-2234 6628 FAX 852-2516 7803