DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

Food and Drug Administration
Washington, DC

3770 '01 MAY 10 P3:14

MAR 16 2001

Keith Chan, Ph.D.
GloboAsia LLC
7250 Parkway Drive, Suite 340
Hanover, Maryland 21076

Dear Dr. Chan:

This letter is in response to your submission on behalf of your client Sky BioHealth Solutions, Inc. to the Food and Drug Administration (FDA), dated December 29, 2000, for a new dietary ingredient made pursuant to 21 U.S.C. 350b(a)(2). Your letter notified FDA of Sky BioHealth's intent to market two products called "Vitalaxin" and "Biolaxin" containing 20 mcg and 10 mcg of porcine relaxin per tablet, respectively.

The term "dietary supplement" is defined in the Federal Food, Drug, and Cosmetic Act (the Act), as amended by the Dietary Supplement Health and Education Act of 1994, as a product (other than tobacco) intended to supplement the diet that bears or contains a vitamin, a mineral, an herb or other botanical, an amino acid, a dietary substance for use by man to supplement the diet by increasing the total dietary intake, or a concentrate, metabolite, constituent, extract, or combination of any of the above ingredients (21 U.S.C. 321(ff)(1)). Moreover, to be a dietary supplement, a product must be intended for ingestion in a form described in 21 U.S.C. 350(c)(1)(B)(i) or comply with 21 U.S.C. 350(c)(1)(B)(ii), must not be represented as conventional food or as a sole item of a meal or the diet, and must be labeled as a dietary supplement (21 U.S.C. 321(ff)(2)). The definition excludes an article that is authorized for investigation as a new drug, antibiotic, or biological for which substantial clinical investigations have been instituted and for which the existence of such investigations has been made public, which was not before such authorization, marketed as a dietary supplement or as a food (21 U.S.C. 321(ff)(3)(B)).

Vitalaxin and Biolaxin are not dietary supplements as defined in 21 U.S.C. 321(ff)

FDA has carefully considered the information in your submission, and the agency has concluded that Vitalaxin and Biolaxin are not dietary supplements because they do not meet the statutory definition of a dietary supplement. First, porcine relaxin is not a "dietary ingredient" as defined in 21 U.S.C. 321(ff)(1). Second, Vitalaxin and Biolaxin are excluded from the definition of a "dietary supplement" under 21 U.S.C. 321(ff)(3)(B).

955-0316

RPT94

Your new dietary ingredient notification is for porcine relaxin. Porcine relaxin is not a vitamin, mineral, herb or other botanical, amino acid, dietary substance for use by man to supplement the diet by increasing the total dietary intake, or a concentrate, metabolite, constituent, extract or combination of any ingredient described above. Porcine relaxin is also not a "dietary substance" because it cannot reasonably be viewed as a substance "for use by man to supplement the diet by increasing the total dietary intake." Relaxin is a hormone that is not food, nor is it used for food. Therefore, porcine relaxin is not a dietary ingredient.

Furthermore, your products are excluded from the definition of "dietary supplement" under 21 U.S.C. 321(ff)(3)(B). Relaxin is an article authorized for investigation as a biological for which substantial clinical investigations have been instituted in the United States, and the investigations have been made public.[1] We note that the purpose of these studies is to determine if relaxin can be used to treat systemic sclerosis with diffuse scleroderma and peripheral arterial disease.

Vitalaxin and Biolaxin appear to be drugs under 21 U.S.C. 321(g)(1)(B).

Your submission states that your products, Vitalaxin and Biolaxin, will bear directions for use instructing the consumer to take daily quantities of such products to "maintain healthy circulation and healthy collagen and elastins of the muscles, ligaments and skin." Inasmuch as your products are clearly not dietary supplements, as discussed above, or conventional foods, these products are "drugs" under 21 U.S.C. 321(g)(1)(C) if they are intended to affect the structure or function of the body. We also note that, if your products are intended for use in the diagnosis, cure, mitigation, treatment, or prevention of a disease, they would also be subject to regulation as a drug under 21 U.S.C. 321(g)(1)(B). Moreover, your products also appear to be "new drugs," as defined in 21 U.S.C. 321(p), which requires FDA approval under 21 U.S.C. 355(a) prior to marketing.

In sum, the ingredient for which you have submitted a new dietary ingredient notification is not a dietary ingredient under the Federal Food, Drug, and Cosmetic Act. Moreover, the products to which you refer in your submission appear to be drugs under the Act and thus subject to the regulatory requirements of drugs.

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[1] Connetics Corportation press release, "Connectics Names New Senior Vice President Clinical Research," February 20, 2001.

January [redacted], Your submission will be kept confidential for 90 days from the date of receipt, ~~December 2~~, 2001, and, after ~~April 2,~~ April [redacted] 2001, your submission will be placed on public display at Dockets Management Branch (Docket No. 95S-0316). Confidential commercial information in the notification will not be made available to the public.

Should you have any questions concerning this matter, please contact us 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
Center for Food Safety and Applied Nutrition

GloboAsia LLC
環亞藥業有限公司
7250 Parkway Drive, Suite 340, Hanover, MD 21076, USA
Phone: 410-712-0609, Fax: 410-712-9547

December 29, 2000

Robert J. Moore, Ph.D.
Division of Programs and Enforcement Policy
Office of Special Nutritional (HFS-456)
Center for Food Safety and Applied Nutrition
U.S. Food and Drug Administration
200 C. Street, S.W.
Washington, DC 20204

Re: 75-Day Premarket Notification for New Dietary Ingredient

Dear Dr. Moore,

As the authorized U.S. representative and on behalf of our client Sky BioHealth Solutions, Inc. (Sky BioHealth), notice is hereby given pursuant to the requirements of Section 413 (a)(2) of the Federal Food, Drug and Cosmetic Act (21 U.S.C. 350B) of the intent of Sky BioHealth to market a new dietary ingredient, porcine relaxin, in the U.S. The brand names of the products are Vitalaxin™ and Biolaxin™ oral tablets, containing 20 mcg and 10 mcg of porcine relaxin respectively.

The new dietary ingredient will be sold either as a 20 mcg (Vitalaxin™) oral tablet or a 10 mcg (Biolaxin™) oral tablet. The recommended dose is taken orally 1-2 tablets each time, once or twice daily (not to exceed maximum dosage of 80 mcg per day).

The new dietary supplement, porcine relaxin, is part of the naturally occurring polypeptide substance found in many mammalian species including humans. In humans, the relaxin is primarily synthesized by the corpus luteum in the females and in the prostate in the males. Relaxin is well known and well studied for many years in scientific literatures. Generally, a low level of relaxin is considered important in maintaining the healthy and complex normal physiological function in humans.

Since the 1950s, porcine relaxin has been studied and reported extensively in human subjects using systemic intravenous, intramuscular, subcutaneous, and intravaginal administrations. Such data are not relevant to oral administration since the doses used in those studies ranged from 20 mg to 1000 mg, which are 250 to 12,500 times higher than the maximal recommended daily dose of the new dietary ingredient, 80 mcg. However, the non-oral administration did demonstrate the safety margin of the oral porcine relaxin. Two published studies using oral porcine relaxin involving a total of 473 females, received 4-60 mg of oral porcine relaxin for the treatment of dysmenorrhea, reported no adverse effects in both studies. The dosage studied is 50 to 750 times

higher than the recommended daily intake of the new dietary supplement in this submission. In a recent study, 81 male and female subjects receiving oral intake of porcine relaxin tablets up to a maximum of 80 mcg per day for a period of 4 weeks to 15 months demonstrated minimal side effects. The new dietary ingredient is administered in oral tablet form. All excipients in the oral tablet are commonly used pharmacetuical excipients. Analytical tests were performed in the final product included protein, fat, moisture, ash, soidum, coliform, S. aureus, Salmonella, yeast, mold, aerobic plate count, arsenic, barium, cadmium, chromium, lead, mercury, selenium and sliver. Based on the above information submitted, we have concluded that this dietary ingredient, oral porcine relaxin, will reasonably be expected to be safe under the recommended Direction For Use.

Please direct all correspondence to me and feel free to call me at (410) 782-2203 (direct line) if you have any question regarding this matter.

Sincerely yours,

Keith Chan, Ph.D.
GloboAsia LLC

Enclosures: One (1) original and two (2) copies of the 75-Day Premarket Notification for New Dietary Ingredient

cc: Sky BioHealth Solutions, Inc.

New Dietary Ingredient – Oral Porcine Relaxin

75-Day Premarket Notification

Submitted by

GloboAsia LLC
(Offical Regulatory Representative)
7250 Parkway Drive, Suite 340, Hanover, MD 21076

on behalf of

Sky BioHealth Solution Inc.
10300 Valley View Road, Suite 107B
Eden Prairie, MN 55344

December 29, 2000

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1. INTRODUCTION

The new dietary ingredient, porcine relaxin, is a naturally occurring polypeptide hormone presented in the body in many mammalian species.[1] In humans, relaxin is produced primarily by the corpus luteum in both pregnant and nonpregnant females.[1] It attains the highest plasma levels during pregnancy.[1] Relaxin is also produced by the human decidua and placenta.[1] In males, relaxin is synthesized in the prostate and released in the seminal fluid.[1] An additional source of relaxin has recently been identified in the heart atria.[1] Relaxin has several well known physiological functions such as induction of collagen remodeling, softening of the tissue of the birth cannel, inhibition of uterine contractile activity, stimulation growth and differentiation of mammary gland, etc.[1] Generally, relaxin demonstrated two distinct biological activities in animals, one to cause the rapid inhibition of myometrial activity and a second to cause a slower change in the structure of connective tissue at its target sites.[2] Therefore, a low level of relaxin in the body is important in maintaining the healthy and complex normal physiological function in human.

Relaxin is a well known substance, first postulated in 1926 by Hisaw that relaxation of the symphysis pubis of the guinea pig during pregnancy is under hormonal control.[1] Since then, an extensive literature has been accumulated about the active substance, relaxin. Its role in humans has been extensively studied.[1,2] This new dietary ingredient, oral porcine relaxin, is being used to supplement the healthy relaxin levels in human by the oral administration route.

Relaxin is water-soluble and has a molecular weight of approximately 6000 Da. It consists of two chains, termed the A and B chains. Both chains are of the similar sizes, and

are covalently linked by two interchain disulfide bonds with one intrachain disulfide bond in the A chain. Species differences in amino acid sequences of relaxins vary from 30 to 60%. However, the similarity in the locations of the disulfide linkage suggests all relaxins have similar tertiary structure.[1,3] Relaxin is synthesized from its precursor, preprorelaxin, by sequential proteolytic digestion of a signal peptide and a connecting peptide between the two chains.[1,4]

Studies among several mammalian species showed that relaxin is produced in highest levels (900 pg/mL) during pregnancy by female reproductive organs, primarily corpus luteum, decidua and placenta. In non-pregnant women, relaxin is mainly produced by corpus luteum, which is responsible for the small but consistent rise (30 – 100 pg/mL) in plasma relaxin observed 9 –10 days after the LH surge.[1] Relaxin is also produced in the male. In men, the primary source is the prostate,[1,5] from which relaxin is secreted mainly in the seminal plasma.[1,6] Another source of relaxin has been recently identified in atrial cardiocytes.[1,]

Recent experimental evidence suggests that relaxin is a pleiotropic hormone, with a broad range of biologic activities on various organs and apparatuses in pregnant and non-pregnant females and in males. Biological effects of relaxin on connective tissue components, uterine motility, mammary gland, cardiovascular system, hemostasis, respiratory system, male reproductive system, brain, pituitary gland, fluid balance, and as a growth factor, have been extensively investigated.[1]

The new dietary ingredient, porcine relaxin, as contained in Vitalaxin™ 20 (20 mcg/tablet) and Biolaxin™ (10 mcg/tablet) is isolated from the ovaries of pregnant sows and is intended as a dietary supplement source for this naturally occurring polypeptide. These

dietary supplements provide the source of low level relaxin to maintain healthy circulation and healthy collagen and elastins of the muscles, ligaments and skin. This new dietary ingredient, oral porcine relaxin. given as Vitalaxin™ 20 (20 mcg/tablet) and Biolaxin™ (10 mcg/tablet) one to two tablets once or twice a day (maximum total daily dose of 80 mcg), is considered safe based upon information on human exposure to porcine relaxin as presented in Section 6. The manufacturing process is briefly described in Section 5. The modified Bullesbach and Schwabe method (1985)[7] is used to obtain porcine relaxin. The final products are enteric-coated tablets, Vitalaxin™ 20 and Biolaxin™. Each contains 20 and 10 mcg of porcine relaxin, respectively.

2. PRODUCT RELATED INFORMATION

2.1. Sponsor

SKY BioHealth Solutions, Inc.

10300 Valley View Road, Suite 107B

Eden Prairie, MN 55344

Contact Person: Frank Au

Phone: 952-946-1550, Fax: 952-996-0054

2.2. New Dietary Ingredient

Oral porcine relaxin.

2.3. Final Products

Vitalaxin™ 20 and Biolaxin™ enteric-coated tablets, containing 20 and 10 mcg of porcine relaxin, respectively.

2.4. Quantitative Compositions

2.5. Safety Evaluation of the Excipients

Safety evaluation of the new dietary ingredient, oral porcine relaxin, in human is provided separately in Section 6.2. of this submission. This section provided safety information on the excipients used in the final products.

2.5.1. Chicken egg white ovomucoid trypsin inhibitor

Ovomucoid, a trypsin inhibitor naturally occurred in the chicken egg white,[8] is included in the formulation as a protection against proteolytic enzymes for porcine relaxin, a polypeptide. Ovomucoid makes up 11% of the total proteins in the egg white and 0.8% of the total egg.[9] A 250-g chicken egg contains approximately 2 grams of ovomucoid, which is more than 10,000 fold higher than the maximum amount (80 mcg) contained in 4 Vitalaxin™ 20 tablets. The doses of chicken egg white ovomucoid trypsin inhibitor used in Vitalaxin™ 20 (20 mcg/tablet) and Biolaxin™ (10 mcg/tablet) are considered safe.

2.5.2. Bovine colostrum (milk)

The milk obtained from post parturient cows during the first 48 hours after birth. It has been used as food and is considered as safe.

2.5.3. Methocel E4M

Methocel (methylcellulose) is commonly used excipient in oral and topical pharmaceutical formulations. It is a GRAS (Generally Regard as Safe) substance.[10]

2.5.4. Microcrystalline cellulose (MCC)

MCC is a commonly used excipient in pharmaceuticals formulation primarily as a diluent in oral tablet and capsule formulations. It is a GRAS substance.[11]

2.5.5. Dicalcium phosphate (DCP)

DCP is one of the most widely used excipient in tableting in the US. It is a GRAS substance.[12]

2.5.6. Colloidal silica

Colloidal silica is commonly used excipient in pharmaceuticals, cosmetics and food products to enhancing the flow property of dry powder in a number of processes. It is a GRAS substance.[13]

2.5.7. Magnesium stearate

Magnesium stearate is commonly used excipient in cosmetics, foods and pharmaceutical formulations. It is primarily used as a lubricant in capsule and tablet

manufacture at concentration between 0.25-5.0%.[ref] Vitalaxin™ 20 and Biolaxin™ contain approximately 0.5% of magnesium stearate. It is a GRAS substance.[14]

2.5.8. Eudragit™

Eudragit™ (methacrylic acid copolymer, ammoniomethacrylate copolymer) is commonly used excipient in oral capsule and tablet formulations as film and enteric-coating coating agent. A daily intake of 2 mg/kg body weight of Eudragit™ (equivalent to approximately 150 mg for an average adult) may be regarded as essentially safe in humans.[15] The maximal daily doses (4 tablets) of Eudragit™ contained in Vitalaxin™ 20 and Biolaxin™ are 42.8 mg, it is well within the safety range.

2.5.9. Triethyl citrate

Triethyl citrate is commonly used excipient as a pasticizer for aqueous based coatings in oral sustained release or enteric-coasted capsule and tablet formulations. It is included in the FDA Inactive Ingredient Guide, 1996. It is acceptable as a food additive in Europe. Oral LD_{50} in rats is 5.9 g/kg.[16] Estimate of an acceptable daily intake in man is 0 – 20 mg/kg,[17] which is equivalent to approximately 1500 mg for an average adult). The maximal daily doses (4 tablets) of triethyl citrate contained in Vitalaxin™ 20 and Biolaxin™ are 8.56 mg, it is well within the safety range.

2.6. Contracted Manufacturer

Vesta Pharmaceuticals, Inc.

8768 E. 33rd Street

Indianapolis, IN 46226

2.7. Final Product Safety Specifications

Heavy Metals:	Arsenic	<0.5 ppm
	Barium	<0.7 ppm
	Cadmium	<0.2 ppm
	Chromium	<2.0 ppm
	Lead	<2.0 ppm
	Mercury	<0.05 ppm
	Selenium	<0.2 ppm
	Silver	<0.7 ppm
Microorganisms:	Total plate count	<20/g
	E. coli	<5/g
	Pathogenic bacteria	none found

2.8. Packaging

60 enteric-coated tablets/bottle

3. DIRECTIONS FOR USE

Take 1-2 tablets each time, up to twice daily to maintain healthy circulatory function and healthy structure of collagen and elastins of the muscles, ligaments and skin. The total maximum daily dose is 80 mcg.

4. DIEATRY SUPPLEMENT ANALYTICAL METHODS AND RESULTS

The analysis report is attached in Appendix A.

Test Facility: Analytical Chemical Services of Columbia, Inc.
9110 Red Branch Road, Suite K
Columbia, Maryland 21045

Tests conducted by: Dr. Allan Brause

Test procedures: Standard procedures as described in "AOAC Official Manuals of Analysis" 16th edition (1990), AOAC International, Arlington, Virginia, U.S.A. (Copies of the methods, except the pathogen screen, are attached in Appendix A.)

Protein:	AOAC 992.15
Fat:	AOAC 15, 920.39B
Moisture:	AOAC 15, 950.46
Ash:	AOAC 15, 923.03
Sodium:	AOAC 986.15D
Coliform, MPW:	CMEF 25:52
S. aureus:	FDA BAM7
Salmonella 55.p:	FDA BAM7 ch. 7
Yeast and Mold:	FDA BAM7 ch. 16
Aerobic Plate Count:	FDA BAM7 ch. 3
Arsenic, Cadmium, Selenium:	AOAC 986.15

Baruium, Lead:	AOAC 986.15D
Chromium:	AOAC 988.15D
Mercury:	USDA 5.002
Silver	EPA 200.7

Batch results:

The analysis results of one batch of Vitalaxin™ 20 are listed in the following table.

Lot No.: 00728B Expiration date: August, 2002

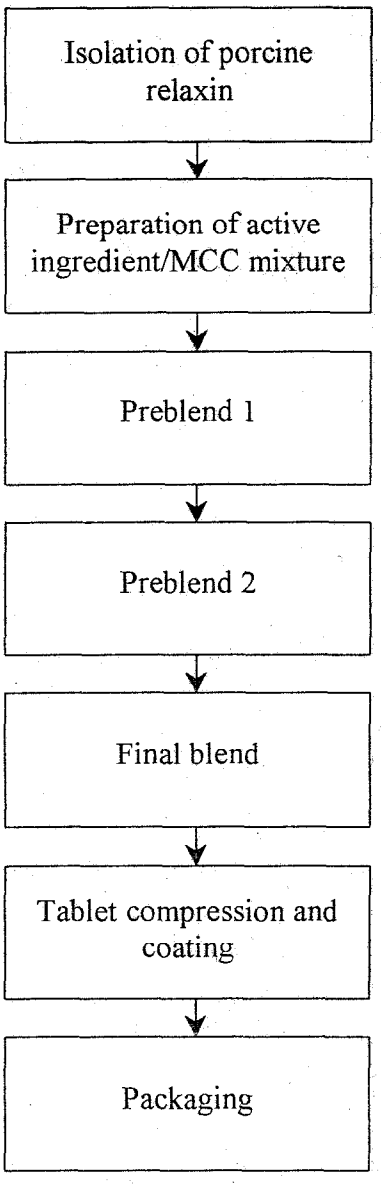
Test date: August 29, 2000 Test report date: October 16, 2000

Test	Concentration	Nutritional Value*
Protein	5.02%	0
Fat	0.53%	0
Sodium	660 ppm	0.47 mg
Heavy Metals		
Arsenic	<0.38 ppm	
Barium	< 0.65 ppm	
Cadmium	< 0.10 ppm	
Chromium	< 1.50 ppm	
Lead	< 1.70 ppm	
Mercury	< 0.03 ppm	
Selenium	< 0.15 ppm	
Silver	< 0.60 ppm	
Pathogen Screen		
Coliform	< 3/g	
Salmonella	none found	
Staphylococcus	< 3/g	
Yeast & Mold	< 1/g	
Total Plate Count	< 10/g	

*. Based on serving size: one tablet (0.78g)

5. MANUFACTURING PROCESS

The manufacturing process of the new dietary ingredient, porcine relaxin, and its final products, Vitalaxin™ 20 and Biolaxin™, are outlined in the following flow chart and briefly described in the following sections.



All manufacturing steps are performed according to approved written instructions. Each step is performed by authorized technician and witnessed and signed-off by second technician.

Isolation of Porcine Relaxin

Porcine relaxin is isolated from ovaries of pregnant sows according to the method described by Bullesbach and Schwabe with slight modification.[7] Briefly, the ovaries are collected from USDA certified slaughter houses, then ground and homogenized in aqueous hydrochloride solution. The homogenate is extracted with acetone and centrifuged. The resultant supernatant is collected and mixed with an addition amount of acetone, then centrifuged. The resultant precipitant is collected and dissolved in water. The pH value of the aqueous mixture is adjusted. The resultant supernatant is collected, dialyzed, and lyophilized to yield the final porcine relaxin powder.

Preparation of Vitalaxin™ 20 and Biolaxin™

Porcine relaxin is mixed with microcrystalline cellulose (MCC) and blended. The egg white ovomucoid trypsin inhibitor and an additional MCC are added to the mixture and blended (Preblend 1). The remaining quantity of MCC is added to the Preblend 1 mixture and blended (Preblend 2). Bovine colostrum, Methocel E4M, dicalcium phosphate, colloidal silica, and magnesium stearate are added to the Preblend 2 mitxure and blended (Final Blend). The resultant mixture is compressed into tablets which are enteric-coated with coatings of Eudragit™ and triethyl citrate, then packaged to the final products.

6. SAFETY SUMMARY OF PORCINE RELAXIN

6.1. Historical Human Use of Porcine Relaxin Other than Oral Route

Systemic intravenous, intramuscular, subcutaneous, and intravaginal administrations of high doses porcine relaxin in human have been documented since 1950s. Numerous subjects have been studied in those reports but the data from those studies are not relevant to the oral Porcine Relaxin. These doses generally ranged from 20 mg to 1000 mg, which are 250 to 12,500 times higher than the maximal recommended daily dose of the new dietary ingredient, 80 mcg. However, the non-oral adminstration did demonstrate teh safety margin of the oral porcine relaxin administration.

6.2 Historical Human Use of Oral Porcine Relaxin

6.2.1 Primary Dysmenorrhea – Treatment with oral porcine relaxin (n= 449)

In this study[18], 449 female workers at John Hancock Mutual Life Insurance Company took oral porcine relaxin under the medical supervisions of physicians, D. Abramson and D.E. Reid, as treatment for primary dysmenorrhea. Patients were assigned to 5 treatment groups, and instructed to take the medications every hour up to 6 doses. Patients were given sufficient quantities of oral porcine relaxin (Releasin) tablets to cover the 6 hourly doses. The 5 treatment groups were 4 mg (n = 121), 6 mg (n = 45), 8 mg (n = 108), 10 mg (n = 109) and 15 mg (n = 66). Since many patients were relieved after 1, 2, or 3 doses. Maximum oral dose taken was 45 mg. No adverse events were mentioned in the article.

6.2.2 Oral porcine relaxin (Releasin) in Dysmenorrhea, (n = 24)

In a Letter to Editor,[19] four physicians at the Department of Gynecology & Obstetrics and Medicine, University of Wisconsin Medical School, A.P. Crosley, Jr, M.J. Thornton, R.E. Campbell, and B. Peckham, reported the results of oral porcine relaxin as a treatment for dysmenorrhea in 24 young women. This study adapted a double-blinded, randomized and cross-over design, the patients were given placebo, 2 mg Releasin or 5 mg Releasin tablets. At the onset of menstrual pain, patients took either one tablet of placebo, or 2 mg Releasin or 3 tablets of 5 mg Releasin every hour for 4 doses, based on the treatment schedule. Maximum dose was 60 mg. No adverse events were mentioned in the article.

6.2.3 Summary

A total of 473 females, stated in the two articles, received 4 – 60 mg of oral porcine relaxin for treatment of dysmenorrhea. The doses were 50 to 750 times of the maximal daily dose of currently new dietary ingredient (80 mcg). No adverse events were reported in both articles.

6.3 Safety Evaluation of Oral Porcine Relaxin Tablets in Human Subjects

A human safety study has been investigated in the

The medical charts of 81 human subjects who visited

during the time period from April 13, 1998 to July 9, 1999 were retrospectively evaluated for the safety of taking oral porcine relaxin tablets. These subjects received oral porcine relaxin

tablets under the medical supervisions of

Both Drs. are board certified physicians in the state of Minnesota.

Among these 81 human subjects evaluated, 68 were female (17 to 70+ years of age) and 13 were male (17 to 69 years of age). Subjects received oral porcine relaxin as 10 or 20 mcg/tablet, 1 to 2 tablets each time, up to twice daily (maximum daily dose not to exceed 80 mcg/day) for 4 weeks up to 15 months. Side effects were reported voluntarily by the subjects or rquested by the physicains over the period of taking the tablets. Among all 81 subjects, 10 subjects (9F, 1M) have had at least one (1) reported side effects. The reported side effects are mild in nature (1 reported menstrual flow increase, 5 reported morning sickness like sypptoms, 2 reported breast tenderness, 3 reported headache, 2 reported acne, and 1 reported nervourness). There are a total of fourteen (14) side effects reported. The number of side effects reported in relative to the long duration of dosing make it highly unlikely that the side effects are related to the oral procine relaxin. Due to the lack of severe side effects and the mild and transient adverse events during the prolonged dosing period, we concluded that the oral porcine relaxin is reasonably safe at the recommended maximal daily dosage of 80 mcg.

7 CONCLUSION

Based upon the previous human exposure results described in Section 6, we conclude that the new dietary ingredient, oral porcine relaxin presented in Vitalaxin™ 20 and Biolaxin™, is considered safe to use at the recommended maximum oral daily dose of 80 mcg (20 mcg/tablet in Vitalaxin™ 20, 2 tablets each time, twice daily).

Based upon the safety evaluation on the excipients, the oral porcine relaxin product Vitalaxin™ 20 and Biolaxin™, is considered safe to use at the recommended maximum oral daily dose of 80 mcg (20 mcg/tablet in Vitalaxin™ 20, 2 tablets each time, twice daily).

8 REFERENCES

A copy of all articles listed in this section are attached as Appendix B of this submission.

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