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FDA DRAFT

RE: **Orally absorbed HGH**

I have reviewed site literature you have provided regarding what is referred to as "Orally Absorbed HGH 1", and the new product, "Orally absorbed HGH 1 Pro", along with the promotional brochure. Based on my experience dealing in food and drug issues, policies and procedures, as a consulting attorney, you requested an evaluation regarding the legalities pertaining to marketing the Orally Absorbed HGH.

Orally Absorbed HGH is stated to be a natural human growth hormone botanically derived and structured for rapid absorption. I am restricting this review to FDA concerns for marketing Orally Absorbed HGH, and I have not evaluated your formulation, or your manufacturing processes. This opinion assumes the product is a source of natural human growth hormone, not limited to recombinant HGH due to the fact it is derived from a living organism.

With the exception of some labeling recommendations contained herein, the product because of its natural occurring source could be marketed as a food supplement. As such the FDA involvement would be to the extent of the Dietary Supplement Health and Education Act of 1994 (DSHEA) THE FEDERAL FOOD, DRUG AND COSMETIC ACT

Section 3O3(e) (1) of the Food Drug and Cosmetic Act (FDCA) states that;

as provided in paragraph 2, any person who distributes or possesses

with the intern to distribute arty anabolic steroid for any use in humans

other than the treatment of disease pursuant to the order of a

physician shall be imprisoned for not more than three years..."

Section (e) (1) was further amended under public law 101-647 (IO4STAT 4853) to state;

"Except as provided in paragraph 2, whoever knowingly distributes, or possess with intent to distribute, human growth hormone for any use in humans other than the treatment of

disease or other recognized medical condition, where such use has been authorized by the secretary of health and human services under section 505 and pursuant to the order of a physician, is guilty of an offense punishable by not more than....''

It should be noted that this additional section to (e)(1) was added to the Crime Control Act of 1990 and perhaps should have been repealed from the Food Drug and Cosmetic Act. In any event, the Crime Control Act contains a separate section under Title 19, which deals with the Anabolic Steroids Control Act of 1990. Enforcement of (e)(1) is to be accomplished by the Drug Enforcement Agencies.

Anabolic steroids are synthetic derivatives of testosterone or are substances designed to mimic the anabolic properties of testosterone. The legislative history of the Anabolic Steroid Control Act points out, like the hormone testosterone itself; anabolic steroids have both anabolic and androgenic properties. The Anabolic Steroids Act was necessary, as found by the sub-committee which pointed out that, anabolic steroids were being abused for non-therapeutic purposes at an alarming rate. They were being abused primarily by, but by no means exclusively by, high school, college, and professional athletes in an effort to enhance athletic performance, or body image. It was pointed out that abuse of the drugs could have a significant adverse health consequence, both physically and psychologically. The committee further pointed out, that human growth hormone (HGH) is often mistakenly considered an anabolic steroid, which it is not, and in fact, HGH or somatotropin, is a natural human hormone secreted by the pituitary gland. Further, body organs depend on human growth hormone for proper growth and development. Synthetic replicas which were being used were known and marketed as somatrem and somatropin. This committee pointed out that HGH was to be prescribed for children who fail to grow property due to insufficient natural production of the hormone HGH. High dosage levels of HGH in normal adults was found to cause acromegaly, a disease that can cause enlargement of the face, feet, hands, and major organs and will reduce the life span of an afflicted individual. This law targeted specific suppliers beyond those of the normal ''drug pusher'' and made it a crime for a ''physical trainer or advisor'' to endeavor to persuade or induce an individual to whom he is providing athletic services to, to legally possess or use anabolic steroids. It even further describes a physical trainer/advisor as any professional or amateur coach, manager, trainer, instructor, or other such person who provides any athletic physical instruction training, advice, assistance or other such service. Clearly the intent of the law was to remove anabolic steroids and synthetically manufactured anabolic growth hormones from abuse by athletes and their trainers. The house report pointed that the purpose for the law was to amend the controlled substance act to provide criminal penalties for coaches and other physical trainers and advisors who endeavor to persuade or induce any person to illegally posses or use steroids.

However, congress recognized the need for exempting products which have no significant potential for abuse. Section 302 creates an exemption for substances that because of their concentration, preparation, mixture or delivery system, have no significant potential for abuse. It further states that these substances such as the testosterone-containing scrotum

patches used by some hypogonadal males, would otherwise be subject to the scheduling. Scheduling is not necessary, because of their method of' application, which renders them ill suited for abuse. After regulatory review, the Secretary of Health and Human Services may recommend such substances for exemption to the Attorney General.

Clearly, Orally Absorbed HGH has no significant potential for abuse based on its delivery system, potency, and natural formulation. Further, the Food Drug and Cosmetic Act, points out that human growth hormone is not an anabolic steroid. Based on the above and the House report, human growth hormone, while it may be mistaken as an anabolic steroid, it is defined as somatrem, somatropin, or an analog of either of them. Therefore, the amendment making it illegal to distribute human growth hormone would not be applicable to the product Orally Absorbed HGH since it is a naturally occurring product, derived from a living organism (e-coli), nor is it an analog of an anabolic substance, per BioPrime.

FDA DRUG DEFINTIONS

201 (g)(1) The term drug means:

(A) Articles recognized in the official USP, official HPIJS, or official NF or, or any supplement to any of them; and

(B) Articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention disease in man or other animals; and…

(C)…

(D) Articles intended for use as a component of any articles specified in clauses A, B or C. A food for which a claim subject to sections 403(r)(1)(B) or 403(r)(3) or sections 403(r)(1)(B) or 403(r)(3) Is made in accordance with the requirements of section of 403(r) is not a drug… A food, dietary ingredient, or dietary supplement for which a truthful and not misleading statement is made In accordance with section 403(r) is not a drug under clause C, solely because of the label or labeling contains such a statement.

In analysis of this definition, there are four important sections. The most important section is the fact that the act defines a drug in terms of particles'', and not in terms of ingredients or products. Thus, a drug could be a vitamin, air, , fire, mineral, herb, water, synthetic compound, or in the one specific instance, crushed rock, if it is intended for use in the diagnosis, cure, mitigation, treatment or prevention of disease or, if other than food, it is intended to effect the structure or any function of the body. Other areas of these definitions deal with intended use, disease and the exclusion for foods bearing allowable health claims. If a product is to be considered a drug, FDA approval is required prior to marketing. Those drug products that are not generally recognized among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs as safe and effective for use. These products would be considered new drugs.

OVER THE COUNTER VS PERSCRIPTION DRUGS

In 1972 the agency commenced the review of therapeutic classes of drugs in conditions under which they are amenable to self-diagnosis and treatment by consumers with safe and effective drugs. Specific ingredients were considered by expert panels and their conclusions were published in the Federal Register as proposed rules. Following a comment period, a tentative monograph is published, and after an additional period of comment and agency review, a final monograph is published. A monograph is simply a formula, or recipe, if you will,

The agency reviewed specific ingredients and categorized them under an OTC drug review process. The following OTC categories were noted:

Category l: Generally recognized as safe and effective and not misbranded for over the counter use. The ingredients would be included in a proposed monograph.

Category II: Not generally recognized as safe and effective or misbranded for OTC use, based on review of the ingredients, claims etc. and these would be excluded from a monograph.

Category lll: Not generally recognized as safe and effective for OTC use based on insufficient data to conclude that the ingredient, claims or other conditions are or are not Category l or ll. These conditions would be excluded from the monograph.

The resulting monographs really fill into two simple categories, either positive or negative. A monograph in which the agency concludes that certain ingredients are Category I under specific conditions of use would be positive. The opposite is true for the negative monograph in which the agency has concluded that no ingredient is generally recognized as safe and effective and/or the conditions are not suitable for OTC use/treatment.

There are no monographs, classifications, or ingredients for Orally Absorbed HGH, under the OTC monograph system. However, an understanding of the OTC drug section is important when making an adequate differentiation of disease versus permissible structure-function claims. This was one of the major impacts of the DSHEA.

Under the DSIJEA, a dietary supplement must bear a disclaimer specified in section 403(r)(6)(c) of the act.

The statement contains and must be prominently displayed and in boldfaced type, the following; **“This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, care, or prevent disease.”**

It should be recognized that this statement still concerns the FDA when products contain a category II or lll ingredient. As stated above, Orally Absorbed HGH does not fall within any of the OTC panel review Category l, ll or lll products. Orally Absorbed HGH is to be marketed as a food supplement, and therefore subject to the DSHEA.

AIALYSIS UNDER DSHEA

Under the definition section, the tern dietary supplement includes a vitamin, mineral, and herb or botanical, and amino acid. or a dietary supplement 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 ingredients described in the above. Further, the term dietary supplement means a product that is labeled as a dietary supplement.

Dietary supplement labeling can include any publication, including an article, chapter in a book, or an official abstract of a peer reviewed scientific publication.., and it will not be defined as labeling the dietary supplement, if

I) it is not false or misleading,

2) it does not promote a particular manufacturer or brand of a dietary supplement.

3) it is displayed or presented or is displayed or presented with other such items on the same subject matter so as to present a balanced view of the available scientific information of a dietary supplement,

4) is displayed in an establishment is physically separate from the dietary supplements and

(5) it does not have appended to it any information by sticker or other method.

This section of the DSHEA is very important in the analysis of Orally Absorbed HGH and its literature. The act further points out that a statement for dietary supplements may be made, if the statement claims a benefit related to a classical nutrient deficiency disease, and discloses the prevalence of such disease in the United States, describes the role of the nutrient or dietary ingredient intended to affect the structure or function in humans, characterizes the documented mechanism by which a nutrient Or ingredient acts to maintain such a structure or function, or describes general well being from consumption of a nutrient or dietary ingredient. This will be the controlling section used to analyze most of the literature for Orally Absorbed HGH. In order to make these statements the manufacturer of the dietary supplement must have substantiation that the statement is truthful and not misleading, and this is where the prominent display and bold-faced type for the food and drug statement must come into play. Again, this statement is,"This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent disease."

I feel this section is controlling in the development of some of the language in the informational brochure to accompany Orally Absorbed HGH.

The DSHEA places the burden of proof on the FDA to show a product does not comply with the Act, and/or is misbranded. The misbranding or labeling section of the DSHEA is fairly straightforward and will provide the basis for some of my comments and recommendations regarding the literature and labeling.

In substance, compliance with the DSHEA would serve to allow Orally Absorbed HGH to be recognized and marketed as a food supplement. The Act itself exempts dietary supplements

from pre-market review and approval and firms are not required to submit safety and efficacy data to the FDA.

NATIONAL INSTITUTE OF HEALTH

The National Institute on Aging (NIA), which is part of the National Institutes of Health, conducts research to find out how hormone supplements affect people. In most cases, the hormone supplements, as reported by NIA, "it is not known how much is too much or too little, and for some whether hormone supplements should be taken at all'.

Major concerns have been that hormones taken in the right balance, helps us stay healthy, however, in the wrong amount. it could be harmful. A recent talk paper from NIA points out that certain hormone supplements have received a lot of attention, such as DHEA, HGH, Melatonin, and even Testosterone. It points out that claims regarding these supplements, which deal with making a person feel young again, or the prevention of aging are unproven. Further, this talk paper points out that hormone supplements, are not regulated as drugs by the FDA, but they are sold as nutritional supplements. Caution to the consumer is made regarding how these products are produced, since there is no FDA oversight regarding the products labeling or manufacturing processes. However, NIA clearly agrees that levels of some hormones decrease as a normal part of aging. The body simply fails to make enough hormones for certain reasons. Further concerns seems to be raised regarding hormone supplements, because they may not have the same effect on the body as one's own naturally produced hormones, because the body may produce them differently. NIA does admit that human growth hormone levels often decrease as people age.

I would like to point out that under the findings section of the DSHEA, the government points out there is a growing need for emphasis on the dissemination of information linking nutrition and tong term good health. The NIA positions remain general and may not take into account the clinical data used to support comments regarding Orally Absorbed HGH, nor is natural compounding.

The documents reviewed from NIA to be disseminated to the public are somewhat confusing in that they speak of hormone supplements as nutritional supplements and certainly Melatonin and DHEA are widely available over the counter in most any pharmacy and health food store. While I have not been able to locate human growth hormone and testosterone, it does not mean that these products are not available in an over the counter nutritional supplement form at the same time, especially as homeopathy. In fact in another document produced by NIA, it clearly states that testosterone, estrogen, and HGH are available by prescription only. However, since Orally Absorbed HGH is technically a naturally occurring source for HGH, it may not be targeted as the focus for the NIA comments on "fountain of youth" products. However, the NIA papers raise some concern regarding dosage levels such as homeopathic formulations and necessary effectiveness issues. Moreover, clearly a distinction can be drawn between Orally Absorbed HGH and those products that are injected. BioPrime has stated that Orally Absorbed HGH contains less than one, one-thousandth, (1/1000) to one five-hundredth (1/500) the concentration of HGH found in the

injectables. The injectables are simply to supply a large source of HGH to the body and NIA's comments regarding the need for well controlled studies to determine exact amounts of HGH seem to be targeted to this injectable product line. The mode of action for Orally Absorbed HGH is stated to be 'to facilitate the body's own production of HGH as well as supplying a very low dosage of HGH''. The stimulation of the body's own production of HGH is important since questions could arise regarding the supplementation of HGH injections may further inhibit natural production from the pituitary gland. BioPrime states that it has research showing that the low dosage administration of HGH facilitates the body's own production of HGH rather than slowing the pituitary glands production by over-supplementation (homeopathy).

RECOMMENDATIONS

A. Orally Absorbed HGH 1

1. Sodium was tested at 3 mg/L concentration from a portion of one vial. 21 CFR 101.9 may require its' content to be listed as zero, because it is less than 5 milligrams per serving, however, these regulation are directed at nutritional labeling for foods. It is referenced in 21 CFR 101.36 dealing with dietary supplements of vitamins and minerals. Since there are not specific regulations pertaining to Orally Absorbed HGH, 101.36 was used as a guide. I would recommend the ingredients be listed as found on the Orally Absorbed HGH label. The Orally Absorbed HGH statement could be added as a separate descriptive explanation.

2. The quantity per serving, drop or spray should be placed on the label. Each five (5) drops contains ____ amount of naturally derived growth factor or HGH.

3. Directions for Use

Take as a dietary supplement orally 5 drops twice a day. Five (5) drops in the morning and 5 drops in the evening.

For most effective results place the drop under the tongue and allow approximately 2 minutes before swallowing.

4. Warnings

Add: Keep out of Reach of Children

Add: Do not use if you are pregnant or lactating unless on the order of a physician.

5. Manufacturer/Distributor

Under 21 CFR 101.5, state your connection with the manufacturer such as "manufactured for -or- distributed by". You can eliminate the street address in your label if your street address is in the current city directory Thus you can just add the city, state and zip code.

6. Unless there is a reason or need to ask the consumer to consult a physician, I do not see the need for this statement. In fact, it would imply the product is a prescription drug.

7. Add lot numbers and expiration dates.

B. Orally Absorbed HGH Pro

1 Same as Orally Absorbed HGH 1.

2. Remove FDA approved Facility statement. FDA does not approve facilities.

3. Add Distributed by BioPrime Inc.

4 Add zip code

5. Quantify quantity in fluid ounces also

C. STORAGE CONDITIONS

Since you are packaging in amber bottles, do you have special storage requirements? If so, you may want to add them.

D. HORMONE STATEMENT

1 You may want to add a brief description of your product - Pointing out the HGH is a hormone naturally produced by the body's pituitary gland. Point out that your formulations serves to supplement the body's declining HGH, while also acting to stimulate the body's own production of HGH which has been shown to decline with age.

E. AMINO ACID

Certain amino acid combinations are supposedly promoted to stimulate HGH. There must be supportive date to support these claims. I would be sure to compare the Orally Absorbed HGH data side by side to the ammo acid formulations to justify how the determination of stimulations were made.

F. LITERATURE

If you are claiming that Orally Absorbed HGH has all the attributes in the brochure, then you need to support them as per section 5 of the DSHEA. The data must be from Orally Absorbed HGH, not HGH in general.

If you have any questions concerning this evaluation please feel free to contact me.

Sincerely,

James E. Lenick, Esq.