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Sentencing of Food and Drug Offenses

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Member of the Commission –

Good morning. My name is Robert Perlstein. I am a Medical Officer in the Division of Metabolic and Endocrine Products, Office of New Drugs, at the Center for Drug Evaluation and Research for the United States Food and Drug Administration ("FDA"). I have held this position for 9 1/3 years. Among my duties at FDA are the review of many of the applications filed by drug manufacturers for approval to market human growth hormone ("hGH") formulations to treat specific indications. I attended Williams College and Duke University School of Medicine. I completed my internal medicine training at the Albert Einstein affiliated hospitals in the Bronx, New York, and an endocrinology fellowship at the Brown University affiliated hospitals in Providence, Rhode Island. I retired from the United States Air Force Medical Corps as a full colonel after 20 years of service. During my active duty, I was the Chief of Medicine and Internal Medicine Residency Director at Keesler United States Air Force Medical Center in Biloxi, Mississippi. For the last six years of my active duty, I also served as an Associate Professor of Medicine at the Uniformed Services University of the Health Sciences in Bethesda, Maryland, a position I retain today. I am also an endocrinology consultant for Walter Reed Army Medical Center in Washington, DC, and I am Board Certified in Internal Medicine and Endocrinology.

hGH is a 191-amino acid polypeptide hormone secreted by the anterior pituitary gland. It has important metabolic effects, including stimulation of protein synthesis and cellular uptake of amino acids, and stimulates normal growth in children. FDA has approved hGH products manufactured by eight different manufacturers for multiple indications in children with short stature and in adults (see attached table). The approved indications in children with short stature include growth hormone deficiency, Prader Willi syndrome, Turner syndrome, and chronic renal insufficiency. The approved indications in adults include biochemically documented, severe growth hormone deficiency due to defined organic diseases, AIDS wasting, and short bowel syndrome. FDA has not approved the use of any hGH product for athletic performance enhancement or as a treatment for anti-aging. All hGH products are prescription drugs because of their

potential adverse effects and are not safe for use except under the supervision of a practitioner licensed by law to administer such a drug.

There are well known adverse effects associated with the use of hGH. The use of hGH is frequently associated with fluid retention, which can cause edema, arthralgia (joint pain), myalgia (muscle pain), and carpal tunnel syndrome. It can also exacerbate preexisting hypertension (high blood pressure) and congestive heart failure. The risk of incurring the side effects associated with fluid retention increases with age. hGH also has anti-insulin, diabetogenic effects that may contribute to the development of diabetes mellitus, especially in those predisposed to this disease.

If excessive amounts of hGH are injected over a prolonged period of time, it may lead to the development of acromegaly (typically the result of an unusual pituitary tumor which secretes hGH in an unregulated, autonomous fashion). Adults with acromegaly have enlarged hands and feet, a protruding jaw and forehead (so-called acromegalic facies, which can be quite deforming), and often develop enlarged internal organs including the heart (so-called acromegalic cardiomyopathy), hypertension, diabetes mellitus and sleep apnea. If left untreated, patients with acromegaly die prematurely, most often due to cardiovascular disease.

It is possible, but not yet proven, that the prolonged use of hGH (either directly or via its mediator/surrogate insulin-like growth factor I [IGF I]) may increase the risk of *de novo* cancer or the growth rate of preexisting cancer. In this regard, patients with naturally occurring acromegaly (see above) have an increased risk of colonic polyps and colon cancer.

According to information provided to me by FDA's Office of Criminal Investigations, people who use hGH for bodybuilding or other types of athletic performance enhancement will typically use doses ranging from 1.3 to 3.3 **milligrams** per day (equivalent to approximately 16 to 41 **micrograms** per kilogram in an 80 kilogram (176 lbs.) individual) over the course of 6 to 12 months. I understand that some of these

users may, in addition, take prescription drugs such as insulin and oral agents (actos and glucophage) to counteract the known diabetogenic effects of hGH, prescription diuretics such as lasix to counteract the known fluid retention effects of hGH, and prescription antihypertensives such as captopril, diovan, and clonidine, to counteract the known hypertensive effects of hGH. Other prescription drugs sometimes abused in conjunction with hGH include tamoxifen (an anti-estrogen drug), dostinex, cytomel/other thyroid medications, and erectile dysfunction drugs such as viagra and cialis. It is my further understanding, based on information provided to me by the FDA's Office of Criminal Investigations, that the vast majority of bodybuilders who use hGH and other prescription drugs obtain these drugs without a valid prescription from illicit sources, and use them without any medical supervision whatsoever.

In my opinion, the use of hGH at these doses and under these conditions creates significant health risks, particularly when used without the supervision of a well-trained, licensed physician. When hGH is used under proper medical supervision (i.e., in adults with biochemically documented, severe growth hormone deficiency due to defined organic diseases), the dose is carefully titrated to achieve appropriate age- and gender-dependent levels of serum IGF I. The bodybuilding dosages noted above (approximately 16 to 41 micrograms per kilogram in an 80 kilogram (176 lbs.) individual) clearly exceed the typical dose required by adults with severe growth hormone deficiency (approximately 5 to 10 micrograms per kilogram). These higher doses increase the risk of the well known adverse effects of hGH described above, and the lack of adequate monitoring by a well trained physician enhances these risks. Furthermore, the use of other prescription drugs to counteract these side effects without medical supervision may result in many additional health concerns, including hypoglycemia (insulin and oral agents), serious electrolyte disturbances and dehydration (diuretics), and hypotension (antihypertensives).

I am also aware that hGH is prescribed by some physicians and used by some people to counteract the effects of aging. There appears to be a misconception by some that hGH is both safe and effective as an anti-aging treatment. In fact, peer-reviewed

medical literature clearly and indisputably indicates that the proven benefits of hGH treatment in the elderly are small and the risks are substantial, even when hGH is prescribed under careful and appropriate medical supervision. A systematic review published in the Annals of Internal Medicine in January 2007 by endocrinologists at Stanford University reviewed the results of 31 controlled, published studies evaluating the use of hGH in elderly populations (see attached article). Although there was some evidence that hGH use in the healthy elderly may minimally improve body composition, there was an unacceptably high rate of adverse events. The authors of this systematic review therefore concluded that: (1) although hGH has been "widely publicized" in lay magazines and on the internet as a safe and effective anti-aging treatment in the healthy elderly, there was "little evidence" to support these claims; and (2) hGH **cannot** be recommended as an anti-aging treatment.

It is my further understanding, based on information provided to me by the FDA's Office of Criminal Investigations and my reading of the medical literature, that many individuals illicitly use anabolic steroids as performance enhancers, and that some individuals use both anabolic steroids and hGH. As in the case of hGH, the inappropriate, inadequately monitored use of anabolic steroids is associated with well known adverse effects (including testicular atrophy, infertility, prostatic hypertrophy, liver tumors, gynecomastia, decreased HDL cholesterol, etc). In my opinion, the unique adverse effects associated with the inappropriate, inadequately monitored use of hGH, and the unique adverse effects associated with the inappropriate, inadequately monitored use of anabolic steroids are potentially **equally** dangerous to the user.

I appreciate the opportunity to testify here today. I'm happy to answer any follow-up questions.

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