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March 6, 2008

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Dear Mr. Brown,

Please find enclosed my observations regarding human growth hormone distribution and suggestions regarding sentencing guidelines for growth hormone distribution related offenses.

Thank you very much for your and the Commission's willingness to consider my comments.

Most Sincerely,

Thomas Perls MD, MPH
Associate Professor of Medicine
Boston University School of Medicine

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[101]

Thomas Perls, MD, MPH
Associate Professor of Medicine
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Sentencing of human growth hormone offenses
Submitted to the United States Sentencing Commission

March 6, 2008

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Introduction

My name is Thomas Perls MD, MPH. I am board certified in Internal Medicine with added qualifications in Geriatrics and I am a Fellow of the American College of Physicians. I am an Associate Professor of Medicine at the Boston University School of Medicine and I am clinical staff at Boston Medical Center. I also direct the New England Centenarian Study (www.bumc.bu.edu/centenarian) and I receive funding from the National Institute on Aging for my research activities. Over the past 10 or so years I have become increasingly aware of the marked growth in the anti-aging industry and its promotion of scientifically unfounded claims while anti-aging clinics and websites sell drugs such as testosterone and growth hormone to gullible clients. In 2005, I was lead author of a paper published in the Journal of the American Medical Association (JAMA), titled "Growth hormone for "anti-aging": Clinical and Legal issues".¹

With my continued monitoring of the industry and the germane scientific and clinical literature, I was recently asked to be a medical expert witness, appearing before the U.S. House of Representatives' Oversight Committee the day before the Roger Clemens – Brian McNamee hearing, in order to answer the committee members' questions about growth hormone. My expertise and clinical background has also led to the Drug Enforcement Agency (Arizona and New York offices) and Assistant U.S. Attorney (Denver) to seek my expertise in assisting with the evaluation of clinical practices by medical practitioners and compounding pharmacies distributing growth hormone and testosterone for anti-aging (alternatively called hormone-replacement programs, age-management or longevity medicine).

I feel it is extremely important to point out to the Commission the brazen and what I see as wide-spread and highly marketed and promoted illegal and medically dangerous distribution of growth hormone particularly by members of the anti-aging industry.

In the course of my reviewing DEA-seized medical records from several anti-aging clinics, I was aghast at what I observed as repeated and obvious ethical and professional misconduct as well as the breaking of numerous State and Federal laws. It is in part, out of my concern for the past, present and future

patients of these and many other clinics, that I am writing this summary of observations and suggestions to you.

Growth Hormone Deficiency in Adults

HGH levels gradually decline in adults with minimal or no negative health consequences for the vast majority of the population. The anti-aging industry, the primary pusher and seller of hGH in this country, advertizes that normal declines in hGH cause decreases in strength, muscle mass, sleep, and sexual performance. They go on to claim that replenishing growth hormone to levels present at younger ages stops or reverses these problems as well as aging itself.^{2, 3} This is a ruse.⁴⁻⁷

There are a few medical conditions in adults that merit the use of growth hormone.

The Medically Appropriate and Legal Indications for hGH Distribution

Recognizing the potential for growth hormone abuse, Congress amended the Food Drug and Cosmetic Act in the late 1980s and early 1990's⁸ stipulating that hGH can be distributed to adults for only three specific indications approved by the Secretary of Health and Human Services.^{9, 10}

1. AIDS Wasting Syndrome
2. Short bowel syndrome, and
3. Growth Hormone Deficiency (GHD)

GHD is very rare, occurring at a rate of about 1 adult out of 10,000¹¹ and the legal diagnosis requires documentation of disease, such as a cancer, or trauma to the pituitary gland and a failed stimulation test.¹² Often times, GHD is accompanied by deficiencies of other pituitary gland-produced hormones.

In January, 2007, the FDA released an alert reminding those that distribute growth hormone for anti-aging, body-building and athletic enhancement that they are doing so illegally.¹³

In response to government statements that hGH distribution for anti-aging is illegal, compounding pharmacies and anti-aging clinics that distribute hGH have received advice from Rick Collins JD and others to now claim that they are distributing or prescribing the drug for an FDA-approved indication, presumably adult growth hormone deficiency (GHD).^{14, 15} According to the FDA and the American Association of Clinical Endocrinologists (AACE), a legal and legitimate diagnosis of GHD **must** include (1) an evaluation of the anterior pituitary gland demonstrating an inadequate response to a stimulation test

(hGH level $<5 \mu\text{g/L}$), and (2) demonstrated clinical or pathological evidence of pituitary disease or trauma or documented GH deficiency in childhood.¹⁶

The package inserts for four of the five brands of hGH approved for GHD: Genotropin (Pfizer),¹⁷ Humatrope (Eli Lilly),¹⁸ Norditropin (Novo Nordisk),¹⁹ and Nutropin (Genentech)²⁰ all mandate diagnostic criteria consistent with the FDA and AACE positions. For reasons unknown, the package insert for Saizen (Serono)²¹ uses the word "should" instead of "must" with regard to the need for a stimulation test; an ambiguity that some in the anti-aging industry use as a loophole to avoid the stimulation test.¹⁵ Serono should correct its package insert. Even if the stimulation test is not performed, legal distribution of hGH still requires the demonstration of clinical or pathological evidence of disease, and the FDA has been clear that aging is not a disease. Making the diagnosis of GHD on the basis of IGF-1 levels without the documentation of hypothalamic or pituitary disease is inaccurate²² and I contend that it is both medically unethical and unprofessional to prescribe or administer hGH to the greater than 99 percent of the public²³ who do not meet the FDA's and AACE's diagnostic criteria for GHD.

Use of hGH Supplementation in Healthy Adults and Potential Risks

A recent Stanford University review of 31 clinical studies of hGH use among healthy, normally aging individuals found the only benefit to be a slight increase in muscle mass. The documented negative side effects included soft tissue swelling, joint pains, carpal tunnel-like syndrome, breast enlargement, and diabetes.²⁴ Other side effects include liver and heart enlargement, increased pressure around the brain (called pseudotumor cerebri) and high blood pressure. In a 2002 Johns Hopkins study published in JAMA, about 50% of subjects experienced side effects, primarily joint pains and extremity swelling. 13% developed elevated blood sugars or diabetes.²⁵

Ironically, there is no credible scientific evidence that hGH substantively increases muscle strength or aerobic exercise capacity in normal individuals.²⁵⁻²⁸ Recent experiments in laboratory mice by Bonkowski et al.,²⁹ Coschigano et al.,³⁰ and a recent study in centenarians³¹ reaffirm the observation that GH deficiency or resistance to GH action is associated with *longer* life spans, not *shorter* ones.

With regard to the most feared risk of hGH administration, cancer, Smith and colleagues cite 3 studies demonstrating strong associations between endogenous levels of insulin-like growth factor-1 (IGF-1) and prostate, colon and pre-menopausal breast cancer, and they posit potential mechanisms for how IGF-1 and hGH promote cancer.³² Sonntag et al. document evidence that hGH and artificially elevated IGF-1 levels are risk factors for lung, breast, and prostate cancers.³³ Conway-Campbell and colleagues

demonstrated that growth hormone induces tumor formation and progression in rats, and enhances metastases or spread of cancer.³⁴

In the context of these and other studies, and in the absence of long-term human studies proving the safety and efficacy of hGH in normally aging adults, the claim that "the side effect profile of (h)GH therapy is nominal..."³⁵ is not supported by empirical evidence. It is theoretically possible that declines in hGH experienced as a function of age is an adaptive response to accumulating cell damage^{36, 37} and offers protection from various age-related diseases (e.g. cancer).

Illegal and Medically Inappropriate Distribution of hGH

Since 1990, a growing network of compounding pharmacies, anti-aging clinics, and physicians have created what some within the industry estimate is a 2 billion dollar-a-year business for distributing hGH³⁸— a distribution network involving hundreds of thousands³⁹ of weight training enthusiasts, practitioners and promoters of anti-aging medicine, and those who have fallen victim to growth hormone replacement scams.

I personally have found websites of 279 anti-aging clinics that advertise hGH treatment and 26 pharmacies that distribute the drug to these clinics or sometimes directly to users. I have certainly discovered only a fraction of what exists out there (see figure 1, below).

Sample of
Compounding pharmacies n=26 &
Anti-aging, age-management, longevity, rejuvenation or wellness clinics n=276
advertising on the internet that they provide growth hormone

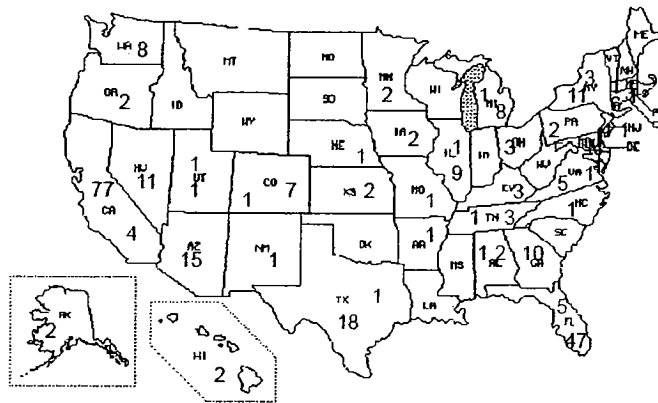


Figure 1

Researched and constructed by Thomas Perls MD, MPH for the Oversight Committee, House of Representatives. February, 2008

Of the seized anti-aging clinic records I have reviewed for the DEA, the average patient that first presents to the clinic is not a person in their 60s or 70s seeking alleviation of their age-related problems, but rather, a male in his late 20's to mid 40's, weight training nearly daily, in otherwise excellent health, clearly seeking anabolic steroids and hGH.

A Case Example of an Anti-Aging Clinic's Promotion and Sale of Human Growth Hormone:

The below is my summary of a doctor who owns and runs an anti-aging clinic, whose medical records and website I reviewed for the DEA.

Dr. M, is an Arizona based physician who runs the M anti-aging clinic, which is advertized on the internet and in brochures as an anti-aging clinic. He indicates that he is board certified in anti-aging medicine. All of the patients under Dr. M's care that were reviewed by me were placed on a "hormone replacement program" that included not only growth hormone but also hormones such as testosterone, pregnenolone, dihydroepiandrosterone (DHEA), human chorionic gonadotropin (HCG), thyroid hormone and drugs that increase testosterone levels such as arimidex. These hormone replacement programs are

invariably very expensive (about \$15,000 per year) and most patients were also sold expensive vitamin supplements (about \$1,200 per year). The average age of the 19 patients reviewed was 43 yrs old, with a range from 30 yrs to 60 yrs. Nearly all were in very good physical condition upon presentation except for a man with chronic fatigue syndrome and a few patients with medical problems that in my opinion were either ignored by or went unrecognized by Dr. M.

The hormone replacement programs that the patients were placed on are similar to anabolic steroid and growth hormone regimens used by body builders. In fact, many of Dr. M's patients that were reviewed were body builders and some were already on anabolic steroids, growth hormone and other drugs before coming to his clinic. As such, most of the patients reviewed appear to be coming for body building drug regimens and were clearly seeking more anabolic steroids, growth hormone and other drugs.

Whether one calls the therapies these patients were receiving body-building or anti-aging, in either case, the hormones and care provided by Dr. M fell far outside what would be regarded as standard medical care, even by alternative or complementary medicine standards. In my opinion, the health related risks that Dr. M exposed these patients to far outweighed any benefit. There were numerous instances of side effects or illnesses in which these drugs would worsen the patient's condition(s) including various serious ones such as cardiac arrhythmias, elevated blood sugars (pre-diabetes), and obstructive sleep apnea.

Despite most of the patients generally being in good physical condition with normal laboratory values, Dr. M provides a statement that in several variations appears in nearly all the charts of his that I reviewed: "After about a 2.5 hr discussion on anti-aging medicine, all aspects of the treatment plan, each of the hormones and particularly all the risks and benefits of them the following program was formulated." And he goes on to assert the following problems, which in nearly all the cases, again cannot be supported by the data.

- Low level deficiency of Growth Hormone
- Low level deficiency of Testosterone
- Low level deficiency Thyroid
- Low level deficiency DHEA

Even if Dr. M claims after the fact that some of the levels fall at the low end of normal limits, even in the remotest extreme of standard medical practice, provision of hormones to most of the patients I reviewed was not only unwarranted, but because of potential side effects, they were contra-indicated.

In all the cases I reviewed, Dr. M sold human growth hormone (hGH) directly to the patients, and there was not in any instance medical history or laboratory evidence supporting a diagnosis of Adult Growth Hormone Deficiency Syndrome (AGHDS) alternatively called Growth Hormone Deficiency (GHD) which would be required in order to legally prescribe, distribute/sell and administer HGH to these patients. The IGF-1 levels were almost always within normal range, but it must be noted that even IGF-1 levels are lower than normal, this would not be enough to make an accurate diagnosis of AGHDS (an extremely rare diagnosis, occurring in about 1 per 10,000 adults).⁴⁰ As detailed below, patients accurately diagnosed with this syndrome or disorder would need clinicopathological evidence of damage to their anterior pituitary gland and would have to fail a growth hormone stimulation test.

Consensus statements by the American Association of Clinical Endocrinologists (AACE)¹⁶ and the GH Research Society in association with the European Society for Pediatric Endocrinology, Lawson Wilkins Society, European Society of Endocrinology, Japan Endocrine Society, and Endocrine Society of Australia⁴¹ have been published indicating that hGH should not be used for anti-aging.

The patients were usually also provided with other hormones including testosterone, thyroid hormone and DHEA, also unwarranted, again in nearly all the cases, given the normal lab values and lack of clinical symptoms. One might argue that thyroid supplementation is warranted by anticipating a potential hypothyroidism caused by anabolic steroid administration, but firstly the patients should not be on steroids in the first place and second one should prove the diagnosis of hypothyroidism before providing thyroid supplementation.

All the billing I observed was on a cash-only business with patients providing credit card numbers that would be billed for the provision of drugs and services. Typically, growth hormone alone cost about \$3,000 to \$4,000 every 3 months.

There was also typically a \$600 professional fee, again about every 3 months. Of course there were also charges for all the other drugs eg. Testosterone, arimidex, HCG, pregnenolone, DHEA and thyroid hormone. Importantly, these drugs were directly distributed to the patient along with syringes, on the M anti-aging clinic premises. In a few cases, growth hormone was sent, interstate (therefore violating the law concerning interstate distribution of GH) from Arizona to California and Wisconsin. As you can see, patients were spending huge amounts of money from \$3,000 to \$4000 every 3 months.

Below, I indicate specific instances of what I believe to be violations of medical ethical and professional conduct, Arizona law statutes and Federal law, as well as Federal Trade Commission laws, by Dr. M.

Ethical Misconduct:

1. Conflict of Interest. Dr. M, sold growth hormone at a considerable profit to his patients without letting them know he was making money on the drug he was telling them they needed. This constitutes professional misconduct.⁴²

According to the document, "The Arizona Medical Board's Guidelines For Physicians Who Incorporate Or Use Complementary Or Alternative Medicine In Their Practice", such a sale of drugs at a profit constitutes a conflict of interest (e.g. the doctor's decision to sell hGH to the patient could be swayed by the profit he makes on the drug).⁴³ Particularly in the setting of not disclosing his financial interest in the sale of these products to the patient, this is ethical misconduct.

2. Misleading or False Claims in Advertising.

- a. In a M Anti-aging clinic advertisement brochure, the following claims appear: *"In combination with proper diet, exercise and nutritional supplements, total hormone restoration therapy has consistently shown to slow down and even reverse the aging process"*.⁴⁴ There has been no credible evidence in the scientific literature supporting these claims.
- b. The brochure and the November, 2006 version of the M Anti-aging clinic website also state the following: *"Improving the quality of life with an appropriate anti-aging program has shown these proven benefits: Reduce fat, increase lean muscle mass, increase energy level, improve exercise endurance, improve long and short term memory, improve sexual performance and libido, boost the immune system, reduce risk of osteoporosis, reduce risk of cardiovascular disease, minimize symptoms of menopause for women and andropause for men, thickens and reduce wrinkles."* These panacea-like claims are common in the antiaging industry and are misleading at best. No therapy has been demonstrated to do all of these things, particularly one specific to an "anti-aging program". A conscientious and effective program of exercise, diet and not smoking will do many of these things. There is no evidence that the addition of the hormones and supplements prescribed and in most cases distributed and sold by Dr. M will provide any additional benefit in achieving these goals. If anything, over the long term this regimen could cause substantial physical harm.

- c. On the November, 2006 version of the M Anti-aging clinic website, the following statement appears: *"Myth: Anti-aging medicine is a non-mainstream, alternative field of medicine. Fact: Anti-aging medicine is a widely accepted field of medicine. Just like internal medicine or orthopedic surgery, there is a Board..."* By indicating that there is a "Board" of anti-aging medicine, Dr. M attempts to provide a false sense of credibility. There is no American Board of Medical Specialty (ABMS)-recognized Board of anti-aging medicine. Elsewhere on the website, Dr. M states that he is an active member and diplomat of such a board and organization. In addition to the fact that providing a false credential is unethical, this might also violate Arizona law; that is, claiming board certification in a medical specialty that would not be recognized by the Arizona Medical Board.^{45, 46}

Some telling quotes from Dr. M with my comments in brackets...

- (a) M: "However, the past 10-plus years of study show that anti-aging programs have been associated with less disease, lower morbidity and better quality of life."⁴⁷

[I know of no such studies that have passed unbiased peer review]

- (b) M: "Everything I do, including the way I administer hormones and supplements, is based on hundreds of studies that support anti-aging medicine and its safety and efficacy."⁴⁷

[Again, I am unaware of unbiased peer reviewed clinical studies that support this statement which is commonly stated by members of the Anti-Aging industry]

- (c) "Years of scientific research have shown a major part of the aging process is the decline of many crucial hormone levels from their youthful peaks. In combination with proper diet, exercise and nutritional supplements, total hormone restoration therapy has consistently shown to slow down and even reverse the aging process"⁴⁴

[This is an unfounded statement. There are no unbiased peer reviewed studies demonstrating that hormone replacement therapy slows or reverses aging.]

Such misleading and/or scientifically unsubstantiated advertising is ethical misconduct. According to The Arizona Medical Board's "Guidelines For Physicians Who Incorporate Or Use Complementary Or Alternative Medicine In Their Practice": *"In advertising a practice or while*

*consulting with a patient, a physician may not make false or fraudulent claims. A physician may not claim that a particular treatment can cure, alleviate or ameliorate a disease or condition unless the claim is supported by valid, conventional science. A physician's personal experience, patient testimony and other anecdotal evidence is not sufficient evidence to support a claim of a treatment's efficacy and safety."*⁴⁸

3. Unproven Efficacy and Unsafe Treatment Plan. In all the charts I reviewed, Dr. M states some variation of the following: "After about a 2.5 hr discussion on anti-aging medicine, along with the risks and benefits of all the hormones the following program was designed for the patient."

On the November, 2006 version of the M Anti-aging clinic website, the following is also stated: "**Total Hormone Restoration** This involves measuring and restoring to youthful levels all of your important hormones. These include human growth hormone (HGH), testosterone, DHEA, melatonin, thyroid, pregnenolone, (and estrogen and progesterone in women). Determining which, and how much of each hormone is based on medical history, physical exam, age-related testing, and blood tests. Because the cost of growth hormone is significant, programs excluding HGH are available." Given the advertising and his discussion of anti-aging medicine with the patient, it is clear that Dr. M is providing multiple hormones and neutraceuticals as a part of what he calls an "anti-aging program". Particularly, in most cases, in the face of no laboratory evidence of any hormone deficiencies "Total hormone restoration" falls completely outside the realm of an alternative medicine treatment where, according to the Arizona State Medical Board, there must be a well-founded expectation of benefit to the patient. In addition, the hormone replacement regimen provided to this patient poses more than minimal risk. Specifically, testosterone replacement may increase patients' long term risks for cardiovascular and cerebrovascular disease.^{49, 50} Anastrozole (Arimidex) and HCG, also frequently given to the patients, also increase testosterone levels and therefore also increase vascular risk. Other drugs commonly provided as part of Dr. M's "hormone replacement program", Pregnenolone and DHEA, are prohormones of testosterone and can also lead to testosterone-related side effects.

Some notable quotes from Dr. M along with my comments in brackets:

(a) "There are four parts to any anti-aging regimen, says M: proper diet, proper exercise, proper supplementation and hormone restoration therapy"⁴⁷

[Endocrinologists would argue that there are not clinical studies supporting "hormone restoration therapy" particularly in the case of HGH and normal aging.]

(b) "For instance, human growth hormone has become known as a very important factor in how fast a person ages, Growth hormone levels tend to diminish as we get older. Maintaining higher levels of growth hormone result in less body fat, more muscle, improved libido, thicker skin, less wrinkles, better immune function, and much more."⁵¹

[Such panacea-like claims are common in the antiaging industry literature with no studies supporting such global benefits. Several studies have shown minor improvements in muscle mass (but not strength), decreased body fat and no improvement in the other claimed benefits. They don't mention the high rates, up to 50%, of adverse side effects (organ enlargement, carpal tunnel like syndrome, glucose intolerance, and hypertension) and 13% who can develop diabetes.^{25, 52}]

[c] "Patients in their early 60s, 70s, and 80s have been experiencing dramatic results according to M. 'Patients over 60 may feel the benefits sooner, and they may be more pronounced, but starting the program at a younger age (35-40) may provide the maximum long-term benefits,' says M"⁴⁷

[Given the increased risk with aging for many different cancers, older patients may be the most at risk to the cancer potentiating effects of GH. There are no long term studies of GH administration.]

The use of unsafe and not previously demonstrably effective treatments is experimental in nature and a physician who wishes to use such a treatment should only do so under rigidly controlled conditions that meet all State and National standards and protocols for research including submission of the proposed treatment to an Institutional Review Board for approval.⁵³ In addition to therefore being unethical, the provision of hormones classified as drugs under these conditions meets the criteria of professional misconduct.⁵⁴

Professional Misconduct (According to Arizona State law)

1. Arizona State Legislature, 32-1401 states that "Unprofessional Conduct" includes the following: (j) Prescribing, dispensing or administering any controlled substance or prescription-only drug for other than accepted therapeutic purposes.⁵⁴ For the details of how this pertains to Dr. M, see "Unproven Efficacy and Unsafe Treatment Plan", above.

Along the same lines, Dr. M's "total hormone replacement" or the provision of HGH in particular, especially in the setting of no proven deficiency either clinically or by laboratory standards, would also violate another rule of misconduct: (y) The use of experimental forms of diagnosis and treatment without adequate informed patient consent, and without conforming to generally accepted experimental criteria including protocols, detailed records, periodic analysis of results and periodic review by a medical peer review committee as approved by the FDA or its successor agency.⁵⁵

3. Arizona State Legislature, 32-1401. Definitions 27 "Unprofessional conduct" includes the following, (mm) The representation by a doctor of medicine or the doctor's staff, employer or representative that the doctor is boarded or board certified if this is not true or the standing is not current or without supplying the full name of the specific agency, organization or entity granting this standing.⁵⁶ Given that board certification in anti-aging medicine is not recognized by the American Board of Medical Specialties, the representation by Dr. M that he is board certified in Anti-Aging Medicine is false and misleading. Along the same lines, another statute may be violated (bb) Representing or holding oneself out to being a medical specialist when such is not the fact.⁴⁶

Of note, Dr. M was quoted in a Phoenix magazine article: "anti-aging medicine is a bona fide field of medicine just like internal medicine or pediatrics."⁴⁷

4. Arizona State Legislature, 32-1401. Definitions. 27. "Unprofessional conduct" includes the following, whether occurring in the State or elsewhere. (hh) Prescribing, dispensing or administering anabolic-androgenic steroids to a person for other than therapeutic purposes. Nearly all the patient records I reviewed did not demonstrate clinical histories, or physical or laboratory findings to support the prescribing of testosterone or Deca Durabolin (nandrolone).

Violating Arizona Criminal Law

1. Arizona Revised Statute, ARS 32-1996E states "A person who dispenses human growth hormone in violation of this chapter is guilty of a class 6 felony". The chapter being referenced by this statute subsection is chapter 18, title 32.

2. Arizona Revised Statute, 13-3401.6.(d).(xxii) designates testosterone as a "dangerous drug", and the Arizona criminal statute for illegal distribution of testosterone is ARS 13-3407A7. As noted above, testosterone therapy cannot be justified in the cases of most of the patient records I reviewed within the realm of a reasonable standard of medical care. In the cases of patients who may have obstructive

sleep apnea, or whose PSAs or bad cholesterol profiles increased over the course of treatment, the testosterone may truly be manifesting itself as dangerous.

Violating Federal Law

1. Dr. M prescribed, distributed and/ administered (see medication administration log) hGH without meeting any of the legally allowed adult indications for hGH (AIDS wasting syndrome, short bowel syndrome, and Adult Growth Hormone Deficiency Syndrome, AGHDS), alternatively named Growth Hormone Deficiency (GHD).^{1, 13} As further discussed below, according to Federal law, to appropriately and legally justify administration of hGH for AGHDS, one must perform an appropriate anterior pituitary stimulation test (e.g. with growth hormone stimulation hormone, arginine, and much more rarely, insulin) and measure a less than minimum response in GH production along with a clinicopathological finding to explain the relative anterior pituitary responsiveness.^{9, 10, 13}

As is the case for anabolic steroids, the legal provision and distribution of hGH is narrowly defined. In 1988 and again in 1990, Congress amended the Food, Drug, and Cosmetic Act (FDCA) to enact more stringent controls with higher penalties for offenses involving the distribution of anabolic steroids and hGH [codified at 21 USC §333(e)(1)].⁹ In 1993, the provisions outlawing the distribution of specifically growth hormone were recodified as 21 USC §333(f) (pursuant to PL No. 103-80, §3(e), 107 Stat 775). Section 303 (f)(1) of the FDCA permits distribution of hGH in connection with (1) "treatment of a disease" or (2) "other recognized medical condition" that has been authorized by the Secretary of Health and Human Services.^{9, 10}

Please note the potential confusion in the code: As noted above, the provisions outlying the distribution of specifically growth hormone were recodified as 21 USC §333(f) (pursuant to PL No. 103-80, §3(e), 107 Stat 775). Yet, the code is frequently cited as 21 USC §333(e) - even in the current proposed amendments to the sentencing guidelines.

Provision of hGH is legal for children with short stature (defined as a height 2 standard deviations below the mean for the child's age and sex) who have GHD, poor growth due to renal failure, Turner syndrome, or Prader-Willi syndrome, and for children small for gestational age (children who at birth were 2 standard deviations below the mean for weight or length or both who maintain a small body size beyond the age of 2 years)⁵⁷ and for idiopathic short stature⁵⁸ (defined as height 2.25 standard deviations below the mean for age and sex, or the shortest 1.2% of children).^{16, 59}

As stated earlier, in adults the FDA has stated that distribution of hGH is legal for only 3 conditions: wasting syndrome of AIDS (this does not include lipodystrophy⁶⁰), short bowel syndrome and AGHDS. AGHDS must meet 2 diagnostic criteria¹²: biochemical diagnosis of adult GHD by means of a subnormal response to the standard growth hormone stimulation test (peak GH, <5.0 ng/L); and the demonstration of a pathological cause of the poor response such as pituitary disease, hypothalamic disease, surgery, radiation therapy, or trauma or patients who were GH deficient during childhood. Only 1 case per 10,000 adults per year meet these criteria for the diagnosis of GHD; 3 cases per 10 000 also include adults who received GH treatment as children.¹¹

Also, as earlier stated, in January 2007, the FDA released an alert stating unambiguously that anti-aging, body-building and athletic enhancement are not approved indications for hGH, that importation of foreign and unapproved hGH for compounding or distribution in the U.S. is illegal, and that physician prescribing of hGH for an unapproved purpose is part of the distribution chain of hGH and is therefore also illegal.⁶¹

Measurement of IGF-1 levels (a claimed proxy for GH levels) in older adults, when demonstrated to be lower than that of young adults, does not constitute a scientific^{16, 62} or legally¹² accepted diagnosis of AGHDS.

Among all the Dr. M patient records I reviewed, a stimulation test was not performed, and in most cases, the patients were in good physical condition without any evidence provided of pituitary gland pathology. Clinics in general would never perform such a test because in almost all cases the test would not support the legal distribution of hGH.

2. Distribution and administration of compounded hGH (an unapproved drug). There is no documentation as to why Dr. M has chosen to administer and distribute compounded HGH (with B12) to his patients, rather than hGH alone. His pivotal role in the distribution of an unapproved drug to a patient may violate Federal law. The FDA considers distribution of compounded hGH as distribution of an unapproved drug. This is clearly stated in the case of importing hGH for the purpose of compounding in an FDA alert.¹³ Portions of that alert state the following:

Section 303(e) (1) of the FDCA, 21 U.S.C. § 333(e) (1), prohibits knowingly distributing, or possessing with the intent to distribute, HGH for any use in humans other than the treatment of a disease or other recognized medical condition, where such use has been authorized by the Secretary of Health and Human Services (HHS) under section 505 of the FDCA (21 U.S.C. § 355) and pursuant to the order of a

physician. The Secretary of HHS has not authorized, for example, any HGH use for anti-aging, bodybuilding, or athletic enhancement. Thus, distributing, or possessing with the intent to distribute, HGH for these uses or any other unapproved use violates section 303(e) (1) of the FDCA. A violation of section 303(e)(1) carries up to 5 years imprisonment and fines and, if the offense involves an individual under the age of 18 years of age, up to 10 year imprisonment and fines.

HGH products are new drugs and cannot be legally marketed in the U.S. without an approved application. The few HGH products that have been approved for sale by FDA are sold either in liquid form or as lyophilized powders that are labeled for reconstitution by the health care professionals who dispense them. Accordingly, FDA considers both imported HGH lyophilized powder products and liquid HGH products to be finished dosage form drugs, not APIs. Unless these products are the subject of approved new drug applications, they violate section 505 of the FDCA, 21 U.S.C. § 355, and may not be legally imported into the U.S.

Some HGH marketers may claim that their HGH drug products are intended for use in pharmaceutical compounding. These drugs should be evaluated on a case-by-case basis considering the factors in FDA Compliance Policy Guide, section 460.200, and the specific prohibitions set forth in section 303(e) of the FDCA, 21 U.S.C. § 333(e).

HGH intended for pharmacy compounding should be reviewed on a case-by-case basis. Consistent with its Compliance Policy Guide on human drug compounding and the prohibitions set forth in section 303(e) of the Act, 21 U.S.C. § 333(e), FDA may exercise its enforcement discretion in certain instances to allow the importation of HGH for use in traditional pharmacy compounding. In general, FDA should exercise its enforcement discretion only in those instances where (1) the compounded product is intended for a use that has been authorized by FDA for HGH under section 505 of the FDCA; and (2) the drug will be compounded to meet the individual medical needs of a specific patient who cannot be treated with an FDA-approved HGH drug product (e.g., the patient is allergic to the commercially available FDA-approved HGH product).

4. Violating Federal Trade Laws. Common marketing practices regarding GH and related products may also be illegal. In a recent case brought before the US District Court by the Federal Trade Commission (FTC) regarding a defendant selling products claimed to contain GH, the FTC stated several claims that illustrate findings that can lead to fines and disciplinary action⁶³:

1. "The dissemination of false advertisement for the purpose of inducing the purchase of a drug or device pursuant to 15 USC § 52(a) is an unfair or deceptive practice within the meaning of 15 USC § 45(a)."
2. "The defendant deceptively promotes and sells HGH products with claims that are wholly false and cannot be substantiated."
3. "The defendant's claims are false and cannot be substantiated with competent scientific

General Observations from the Two Other Anti-Aging Clinics That I Reviewed

Perhaps one of the most disturbing observations to be made regarding my review of medical records from these clinics was how little information they contained. In some instances there was only a minimal amount of laboratory data accompanying the prescriptions and demographic information. In other cases, it appears that the patient was never seen by the doctor and minimal data were collected by office staff. Making matters much worse was that this inadequate evaluation and oversight is in the context of providing growth hormone, multiple anabolic steroids, and other drugs with potential and potent adverse effects. Follow-up visit documentation was practically nonexistent and some of the patients were not seen again after receiving their drugs so it is impossible to know who sustained harm from the growth hormone and other drugs.

It was clear that the majority of patients were coming to the clinics for body building despite statements by the doctors that they were there for anti-aging. Most of the patients came to the clinics in excellent health with active exercise regimens. All the patients received prescriptions for hGH without appropriate workup or evidence for Adult Growth Hormone deficiency Syndrome. The distribution of anabolic steroids and growth hormone for the patients I reviewed fell completely outside the standard of medical care and as in the case of Dr. M, above, I found numerous and repeated instances of both professional and ethical misconduct as well as violations of both Arizona state and Federal laws particularly with regard to the distribution of growth hormone and anabolic steroids.

Human Growth Hormone Distribution in the United States Resembles a Narcotics Trafficking Ring

Recent high profile cases have revealed a network of anti-aging clinics and compounding pharmacies violating the law with regard to the distribution of hGH. In 2007, Pfizer Pharmaceuticals was fined \$34 million for promoting hGH as an anti-aging and athletic enhancing intervention;⁶⁴ Specialty Services

Distribution, Inc. was fined \$10 million for distributing hGH for athletic enhancement, cosmetic, or anti-aging uses;⁶⁵ the FDA, DEA, and FBI conducted crackdowns (Operation Phony Pharm⁶⁶ and Operation Raw Deal⁶⁷) on national and international trafficking in anabolic steroids and hGH; and Operation "Which Doctor" led to the prosecution of doctors being paid by pharmacies to write prescriptions for hGH without having ever seen the patients.⁶⁸ Despite these actions, the use of hGH remains pervasive and staunchly defended by the anti-aging industry.

As an illustration of how profitable illegal sales of hGH have become, consider the single example of Lowen's Compounding Pharmacy, recently investigated by the New York State Bureau of Narcotic Enforcement. The investigation revealed that the pharmacy would purchase 25 grams of imported hGH for \$75,000; convert each gram into 3,000 IU's of hGH; then sell the drug for \$6 to \$18 per IU, -- netting a profit of \$375,000 to \$1.34 million dollars.⁶⁹ In that raid, narcotics officials seized 90 grams of hGH powder worth \$7.2 million, including a shipment destined for The Health and Rejuvenation Center, an anti-aging clinic in Palm Beach Gardens, Florida.⁷⁰

In the case of the M anti-aging clinic that I described above, the DEA seized 75 vials (6-7 mg/vial) of human growth hormone. Among the patient records I reviewed, all the patients were prescribed and sold, on the anti-aging clinic premises, 1-3 month supplies of growth hormone along with alcohol swabs and syringes. Dosing ranged from .6u to 4 units per day, 6 to 7 days a week. Vials were sold to patients in batches, from 5-15 vials at a time at \$280 per vial. From other documents found by the DEA, it appears Dr. M purchased the growth hormone from a compounding pharmacy for about \$90 a vial, turning a profit of \$190 per vial.

An important feature of hGH distribution for anti-aging and body building is that the vast majority of users pay out-of-pocket for the drug. As a result of these cash-only transactions and the fact that hGH is often misbranded (e.g. illegally imported or made into a "new drug" by combining hGH with another compound⁷¹), the actual number of people receiving hGH as part of an anti-aging treatment regimen is likely to be much higher than a previous estimate of 30,000 users.⁷² If one compounding pharmacy has been caught with 270,000 IU of hGH, as in the case of the Lowen's Pharmacy raid, and a weekly regimen for a single patient ranges from 2-10 IU per week, then it is reasonable to assume, given the hundreds of clinics where hGH is available and hundreds of websites and pharmacies that advertise the drug, that previous estimates of the number of illicit users of hGH for anti-aging and athletic enhancement or body building, combined, is profoundly underestimated.

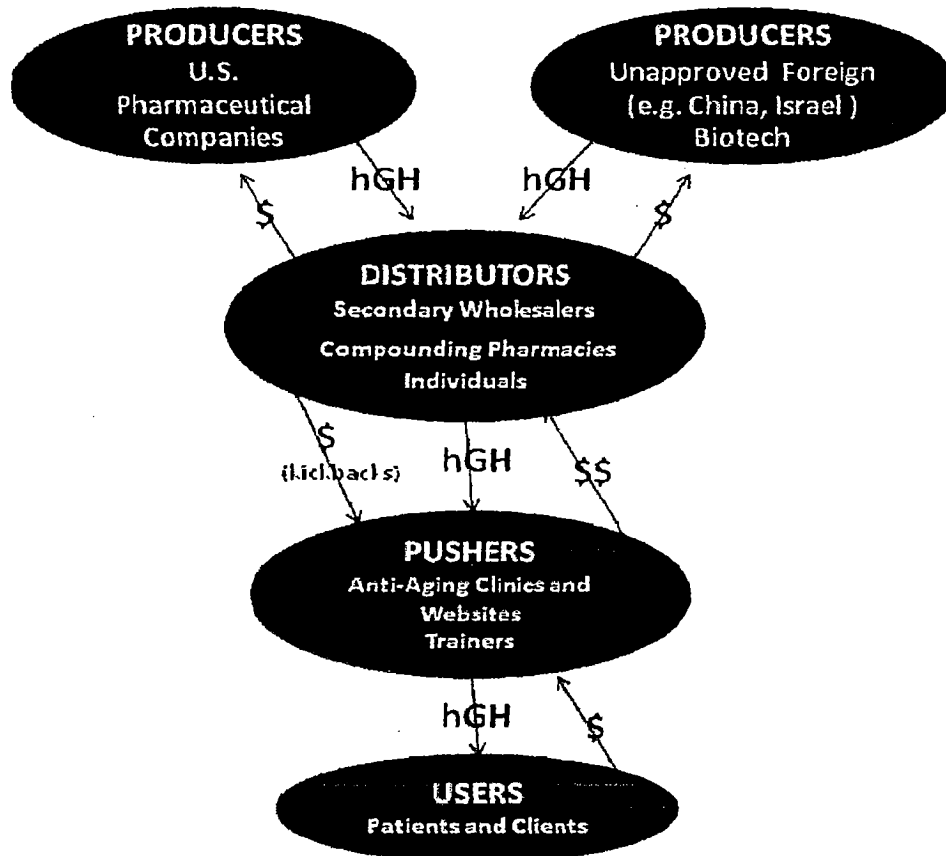


Fig. 2 The growth hormone trafficking ring: The cash-only business of websites or clinics working closely together with compounding pharmacies to turn huge profits⁷³, the national and international anti-aging and age-management organizations assisting in and facilitating the marketing of the growth hormone for anti-aging, and drug companies turning a blind eye to how and to whom their product is distributed bear similarity to what some investigative reporters have likened to a narcotics trafficking ring.^{74, 75}

Another consequence of a cash-only business is that there is no independent means to detect and monitor adverse events. People who might have experienced side effects may simply stop taking the drug and end their relationship with the website or clinic without reporting the problem, especially when the side effects are reversible. If hGH caused more severe health consequences, including cancer and death, there is little incentive for clients to pursue legal action when causation is difficult to prove, or because clients are often required to sign contracts that absolve the provider of any potential wrongdoing. Finally, there is an explicit disincentive for anti-aging practitioners to report adverse experiences with hGH.⁷⁶

In summary:

The reemergence of the health and longevity salesman has exploded on the heels of growth hormone. Just the name "growth hormone" invokes visions of the fountain of youth. Thus, with deceptive marketing and unethical physicians who wield inappropriate influence over their patients, illegal and dangerous growth hormone distribution has become pervasive. Likely somewhere in the range of currently 200,000 Americans have been misled to believe in the purported magical powers of growth hormone, whether they be anti-aging, body building or injury repairing. Profits from the sale of growth hormone, particularly at the level of secondary wholesalers and compounding pharmacies rival if not better those seen in the crack cocaine trade. With such outrageous profits, hundreds of unscrupulous doctors and businesses are willing to take the risk of illegally prescribing and distributing growth hormone. Profits are set aside for intimidating lawyers and deceptive lobbying and marketing campaigns to keep the industry alive, growing and safe for its producers, distributors, pushers and users.

Experts in the care of patients with true growth hormone-related problems clearly state that giving growth hormone for anti-aging or age-management or body building is not medically appropriate particularly when weighing the high risk to benefit ratio.^{6,7,16}

Thus, in terms of law enforcement and sentencing guidelines, the focus of attention should be on the producers and distributors. Because of sophisticatedly deceptive and widespread marketing practices and in the case of clinics, the unusual power a doctor can have over a patient, the users seem to be more the victims. Herein lies, in my opinion, the reason why sentencing guidelines for growth hormone-related offenses must be strong and intimidating: to protect the public from this highly unethical industry that bilks its victims out of tens of thousands of dollars and in many cases exposes them to unnecessary and potentially serious harm. In fact, the current laws pertaining to growth hormone really pertain to the drug's distribution, and not its possession by users.

Recommendations**Responses to Specific Issues For Comment**

1. How human growth hormone (hGH) should be quantified under §2D1.1 (Unlawful Manufacturing, Importing, Exporting, or Trafficking (Including Possession with Intent to Commit These Offenses)).

Most growth hormone appears to be distributed as a lyophilized powder and it is therefore generally measured as a weight. Supporting the use of weight (mg) is the fact that most sales of GH between producers and distributors are based on weight.

Clients or patients will often be instructed to inject themselves with a specific volume of growth hormone solution (powder reconstituted with water) of a particular concentration. However, by knowing the concentration of growth hormone in solution, these volumes can of course still be converted to mg amounts of growth hormone. Even if a quantity of growth hormone is expressed on the vial as some number of international units, one can use the conversion rate of 2.7 IU per mg growth hormone to determine the weight.

2. The existing definition of "unit" applies to trafficking in steroids, which is a Schedule III controlled substance with a penalty scheme similar to distribution offenses involving human growth hormone (hGH). The Commission requests comment regarding the harmfulness of hGH offenses relative to steroid offenses. Are hGH trafficking offenses more harmful, less harmful, or approximately equal in harm? Based on that comparison, what quantity of vials, IU, or mg of hGH should be used to determine a "unit" for purposes of calculating the base offense level (e.g., one vial, 3 IUs, 1 mg)?

In reviewing the medical records from anti-aging clinics and reading the blogs of body-building sites, I have almost never seen growth hormone given in isolation. It is almost always given in conjunction with one or more anabolic steroids (e.g. testosterone, nandrolone etc) whether the intended illegal purpose be anti-aging, body-building or athletic enhancement. From my review of Dr. M's medical records, the severity and rate of harmful side effects and the potential for harm to the patient for the typical doses of growth hormone and testosterone are approximately similar. Of significant concern is the possibility that growth hormone and testosterone may be additive in promoting certain severe and perhaps life threatening diseases such as obstructive sleep apnea and cancer. For these reasons, it would make sense for growth hormone offenses to be similar to anabolic steroids in terms of calculating the base offense level.

My understanding is that The Drug Equivalency Table under **§2D1.1** establishes one unit of a Schedule III substance to be equivalent to one gram of marijuana. A unit of anabolic steroid is 10 cc or 50 pills. In the case of the clinics I reviewed, a usual dose of testosterone cypionate was about 1 cc of about 200 mg/cc once per week. Thus, in this case, a 10 dose supply or 2 grams of testosterone would equal a gram of marijuana. If one assumes the usual starting dose of growth hormone in an anti-aging clinic to be 0.25

mg (about 0.25 cc of a 6 mg/6cc vial), then 10 doses would be 2.5 mg. Thus, in terms of equivalency to testosterone, in terms of dosing, cost and potential harm, it would make sense to me that **2.5 mg lypholyzed growth hormone would = 1 Unit.**

In the Drug Quantity Table, **§2D1.1** offenders responsible for 40,000 or more units of Schedule III substances receive a maximum base offense level of 20. Using the above reasoning, 40,000 units of growth hormone would equal 100,000 mg or 100 grams of growth hormone.

To place this amount in perspective, the amount of growth hormone seized in the Lowen's Pharmacy case was 90 grams of hGH powder (translating into level 18) worth \$7.2 million, some of which was destined for The Health and Rejuvenation Center, an anti-aging clinic in Palm Beach Gardens, Florida.⁷⁰

In Dr. M's case, 75 vials, or about 450 mg (which he bought for about \$90 and sold for \$330 per vial) worth \$24,750 450 mg, were found in his clinic and seized by the DEA. 450 mg would equal 180 units and lead to an offense level of 6.

To me, the level offense of 18 makes sense in the case of the amount of growth hormone seized in the Lowen's Pharmacy case, particularly in light of the maximum sentence (without enhancements) stipulated by Congress. Regarding the case of Dr. M, a number of enhancements (suggested below, question #5) would increase the offense level to a point that incarceration would be considered.

3. The Commission requests comment regarding whether a maximum base offense level should apply in §2D1.1 for an offense involving the distribution of human growth hormone (hGH). For certain types of controlled substances, the marijuana equivalencies in the Drug Equivalency Table in §2D1.1 are "capped" at specified amounts. For example, anabolic steroids and other Schedule III controlled substances, which also have a statutory maximum of 5 years' imprisonment, are subject to a maximum base offense level of 20. Should the Commission similarly provide a maximum base offense level for offenses involving the distribution of hGH and, if so, what maximum base offense level should apply?

My understanding of the law stipulates a maximum of 5 years and a maximum fine of \$250,000 for distribution offenses related to growth hormone and thus the maximum level, without enhancements should be consistent with this. I do feel though that additional enhancements are very important and necessary and I discuss this below.

4. Should the Commission amend the commentary to §2D1.1 in Application note 8 to cover offenses involving human growth hormone (hGH)? Specifically, the enhancement at §2D1.1 (b) (6) defines "masking agent" as "a product added to, or taken with, an anabolic steroid to prevent detection of the anabolic steroid in an individual's body." Masking agents also can be taken to prevent the detection of other controlled substances including hGH. Should the Commission expand the definition of masking agent, and thus application of the enhancement, in a manner that covers hGH?

While I am unaware of agents that can mask use of growth hormone, I don't see any reason why the Commission shouldn't expand the definition to cover hGH.

Human Growth Hormone also may be used to enhance an individual's performance. Should the Commission expand the scope of the enhancement at §2D1.1 (b) (7) pertaining to the distribution to an athlete to cover offenses involving hGH? Application Note 8 instructs the court on how to apply §3B1.3 (Abuse of Position of Trust or Use of Special Skill) in a case in which a coach used his or her position to influence an athlete to use an anabolic steroid. Similarly, a coach may use his or her position to influence an athlete to use hGH. Should the Commission modify Application Note 8 to include cases involving hGH?

Yes, I agree that given the continued desire of those who illegally distribute growth hormone to market the drug to athletes, the scope of enhancement at §2D1.1 (b) (7) pertaining to the distribution to an athlete should cover offenses involving hGH.

Along these lines though, I feel it is very important to point out that given the many anti-aging clinics that now distribute growth hormone, it is likely that athletes represent a minority of those who receive illegally distributed growth hormone. In fact, as pointed out earlier, the FDA, in its January 2007 Alert, clearly pointed out that besides athletic related use, anti-aging and body building are important illegal uses of growth hormone.¹³ Thus, if special note (and level enhancements) is to be made for coaches who use their position to influence an athlete's use of growth hormone, the cases of physicians illegally distributing growth hormone, who likewise can have disproportionate and convincing influence over their patients, should also receive specific attention for using such influence to their benefit. Mention of only the coach-athlete relationship may provide the impression that the unethical use of power by a doctor over his or her patient in order to sell and distribute growth hormone is less important, so hopefully specific mention of physicians can be made here.

I believe application of U.S.S.G. § 3B1.3 (Abuse of Position of Trust or Use of Special Skill)⁷⁷ can address a physician's abuse of power, as in the sentencing of Dr. Shortt who received a two-level enhancement for his use of the special skill as a doctor.⁷⁸

In a particularly egregious example, in my review of DEA seized anti-aging clinic medical records, I read instances of the doctor continuing growth hormone in patients (and continuing to make more money) who experienced new elevated blood sugars, elevated blood pressure or upper extremity swelling, despite concerns voiced by the patients.

5. The Commission requests comment regarding whether §2N2.1 (Violations of Statutes and Regulations Dealing with Any Food, Drug, Biological Product, Device, Cosmetic or Agricultural Product) adequately addresses numerous statutes referenced to that guideline. The statutes referenced to §2N2.1 prohibit conduct ranging from regulatory offenses with a statutory maximum of 1 year imprisonment (e.g. 21 USC §643 record keeping requirements) to violations of the Prescription Drug Marketing Act of 1987 that carry a statutory maximum penalty of 10 years imprisonment. Should the Commission provide alternative base offense levels, specific offense characteristics identifying aggravating factors warranting an enhanced sentence, or some combination of these to more adequately address these offenses? If so, what should be the offense levels associated with alternative base offense levels and/or specific offense characteristics?

The Commission is very wise to consider the changing landscape and variations of not just illegal growth hormone distribution, but also, I would argue, it needs to do the same for anabolic steroids. Growth hormone and anabolic steroids are no longer distributed and sold to users in back alleys and locker rooms. As illustrated in the above Figure 2, brazen and very wealthy narcotics-like trafficking rings are operating in broad daylight. The black market for extra doses of Serostim sold by sufferers of AIDS wasting syndrome is no longer necessary. Taj Mahal like anti-aging clinics (e.g. Cenegenics^{79, 80} in Las Vegas and Florida) and Beverly Hills doctors⁸¹ appear on television shows such as 60 minutes and Anderson Cooper 360 professing the longevity enhancing wonders of growth hormone. Thus, just about anyone can walk into any one of hundreds of anti-aging clinics across the country and purchase vials of growth hormone and testosterone, be taught how to inject the drugs and then take the lot home to inject on their own. There are also at least hundreds of websites selling growth hormone, many without ever arranging for a physician to see the patient and some which pay physicians to write prescriptions without ever seeing or even speaking with the patient. This new environment for distributing growth hormone merits a number of special considerations in sentencing:

(1) Numerous clinics and obviously websites market their services including growth hormone "replacement" on the internet and at times via other media such as newsletter advertisements, and radio and magazine features. Perhaps this can be addressed by §2D1.1(b)(5): "Distribution of a controlled substance through mass-marketing by means of an interactive computer service leads to a two-level-enhancement."⁸² Also pertaining to such advertising is 21 U.S.C. § 843(b): §2D1.6. Use of Communication Facility in Committing Drug Offense; Attempt or Conspiracy."

I agree with suggestions by the FDA:

(2) "Add 21 U.S.C. § 333(e)(2) - distribution of HGH to a person under 18 years of age - to the § 2D1.2 Guideline, which presently applies to controlled substance offenses involving protected locations (e.g., schools) or pregnant or underage persons."

(3) "Add an application note to § 2N2.1 to include substantial risk of bodily harm as a basis for upward departure."

and

(4) "for criminal offenses involving misbranded or adulterated products where "loss" is relevant to the sentence to be imposed, loss should be determined by calculating the full amount paid (by consumers and others) for the adulterated or misbranded product, without any deduction or subtraction for the value of the product." My understanding is that this could apply to doctors, compounding pharmacies or other distributors who sell illegally imported growth hormone (eg jinropin) or an adulterated version of growth hormone such as compounded cyanobalamin-B12.

(5) Given the brazen attitudes of those who openly and deceptively advertise growth hormone for anti-aging, body-building or other non-approved uses, and make it so easy for patients to obtain the drug by providing free-standing clinics, I suggest that physicians and others who illegally distribute growth hormone out of offices or clinics be regarded as managing a drug establishment for example as in **§2D1.8. Renting or Managing a Drug Establishment; Attempt or Conspiracy** (Statutory Provision: 21 U.S.C. § 856). Per the Sentencing Commission's guidelines, "*This section covers the offense of knowingly opening, maintaining, managing, or controlling any building, room, or enclosure for the purpose of manufacturing, distributing, storing, or using a controlled substance contrary to law (e.g., a "crack house").*" In the context of reasons for other level enhancements, an offense level enhancement of 2 levels appears appropriate to me. In the case of clinic chains, where an offender owns and manages

multiple clinics, one should consider the level enhancement per each establishment up to some maximum.

Additional considerations for level enhancements:

- (6) Engaging in monetary transactions over \$10,000 per patient per year
- (7) Physical or mental harm to a patient resulting from illegally distributed growth hormone
- (8) Contracting with a person to provide a testimonial, either public or private
- (9) Receiving money or gifts of any form from a distributor of what will ultimately be illegally distributed growth hormone in exchange for a patient's or client's purchase of that growth hormone
- (10) Providing money or gifts to others who refer patients or clients that ultimately receive illegally distributed growth hormone
- (11) Inadequate record keeping, including the omission of major components of a medical record such as history of present illness, physical examination, assessment and plan, laboratory results, and/or medical justification for the administration of growth hormone.
- (12) No intent by the physician to see the patient again, once they have received illegally distributed growth hormone
- (13) Never seeing the patient
- (14) interstate commerce (eg mailing illegally distributed growth hormone to out-of-state clients or patients)
- (15) Two level enhancement for creating a reckless risk of bodily injury to clients or patients. Increasingly greater levels for, respectively, actual reversible harm, permanent harm, or death.
- (16) Two level enhancement for illegally distributing growth hormone to 10-49 patients within a single year and a three level enhancement for doing so for 50-99 patients and a four level enhancement in the case of >100 patients in a single year.
- (17) Disseminating literature, books, brochures, other forms of media that claims administration of growth hormone slows or reverses or helps to slow or reverse aging and age-related diseases, syndromes and/or problems.

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[42] Arizona State Legislature, 32-1401. Definitions. 27. "Unprofessional conduct" includes the following, whether occurring in the state or elsewhere: (ff) Knowingly or failing to disclose to a patient on a form that is prescribed by the board and that is dated and signed by the patient or guardian acknowledging that the patient or guardian has read and understands that the doctor has a direct financial interest in a separate diagnostic or treatment agency or in nonroutine goods or services that the patient is being prescribed and if the prescribed treatment, goods or services are available on a competitive basis. This subdivision does not apply to a referral by one doctor of medicine to another doctor of medicine within a group of doctors of medicine practicing together.

[43] Arizona, Medical Board. The Arizona Medical Board's Guidelines For Physicians Who Incorporate Or Use Complementary Or Alternative Medicine In Their Practice. ? year URL:

<http://www.azmd.gov/Alternative%20Medicine/Alternative%20Medicine%20in%20Physician%20Practice.pdf>. , pp. Some physician practices have begun selling healthcare related products directly to patients.

The law does not directly prohibit this practice, but any fraud or misrepresentations would violate the Medical Practice Act. Due to the potential for conflicts of interests, however, physicians should not sell, rent or lease health-related products or engage in exclusive distributorships and/or personal branding. If a physician chooses to make products directly available to patients, the physician must disclose to the patient that the physician has a financial interest in the goods or services.

[44] Hammer Institute for Anti-Aging Medicine, Advertisement Brochure.

[45] Arizona State Legislature, 32-1401. (mm) The representation by a doctor of medicine or the doctor's staff, employer or representative that the doctor is boarded or board certified if this is not true or the standing is not current or without supplying the full name of the specific agency, organization or entity granting this standing. Definitions. 27. "Unprofessional conduct" includes the following, whether occurring in the state or elsewhere.

[46] Arizona State Legislature, 32-1401. . Definitions. 27. "Unprofessional conduct" includes the following, whether occurring in the state or elsewhere: (bb) Representing or holding oneself out to being a medical specialist when such is not the fact.

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<http://www.azmd.gov/Alternative%20Medicine/Alternative%20Medicine%20in%20Physician%20Practice.pdf>: In advertising a practice or while consulting with a patient, a physician may not make false or fraudulent claims. A physician may not claim that a particular treatment can cure, alleviate or

ameliorate a disease or condition unless the claim is supported by valid, conventional science. A physician's personal experience, patient testimony and other anecdotal evidence is not sufficient evidence to support a claim of a treatment's efficacy and safety. A physician may, however, inform the patients of his/her experiences with using a particular treatment. When advising patients on treatment

options, a physician must disclose to the patient the physician's basis for making claims of the efficacy and safety of a particular treatment.

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[51] Hammer Institute for Anti-Aging Medicine, Advertisement (one page).

[52] Liu H, Bravata DM, Olkin I, et al. . Systematic review: the safety and efficacy of growth hormone in the healthy elderly. *Ann Intern Med* 2007;**146**: 104-115.

[53] Arizona, Medical Board. The Arizona Medical Board's Guidelines For Physicians Who Incorporate Or Use Complementary Or Alternative Medicine In Their Practice. ? year URL: <http://www.azmd.gov/Alternative%20Medicine/Alternative%20Medicine%20in%20Physician%20Practice.pdf>. : The treatments offered should, at a minimum:

- have a favorable risk/benefit ratio compared to other treatments for the same condition;
- be based upon a well founded expectation that it will result in a favorable patient outcome, including preventive practices; and
- be based upon the expectation that a greater benefit will be achieved than can be expected with no treatment.

The physician should consider treatments that are safe and demonstrably effective first when developing a treatment plan. The use of unsafe and not demonstrably effective treatments is experimental in nature and a physician who wishes to use such a treatment should only do so under rigidly controlled conditions that meet all State and National standards and protocols for research including submission of the proposed treatment to an Institutional Review Board for approval.

[54] Arizona State Legislature, 32-1401. Definitions. 27. "Unprofessional conduct" includes the following, whether occurring in this state or elsewhere: (j) Prescribing, dispensing or administering any controlled substance or prescription-only drug for other than accepted therapeutic purposes.

[55] Arizona State Legislature, 32-1401. Definitions. 27. "Unprofessional conduct" includes the following, whether occurring in the state or elsewhere: (y) The use of experimental forms of diagnosis and treatment without adequate informed patient consent, and without conforming to generally accepted experimental criteria including protocols, detailed records, periodic analysis of results and periodic review by a medical peer review committee as approved by the FDA or its successor agency.

[56] Arizona State Legislature, 32-1401. Definitions 27 "Unprofessional conduct" includes the following: (mm) The representation by a doctor of medicine or the doctor's staff, employer or representative that the doctor is boarded or board certified if this is not true or the standing is not current or without supplying the full name of the specific agency, organization or entity granting this standing.

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- [77] §3B1.3. , Abuse of Position of Trust or Use of Special Skill. If the defendant abused a position of public or private trust, or used a special skill, in a manner that significantly facilitated the commission or concealment of the offense, increase by 2 levels. This adjustment may not be employed if an abuse of trust or skill is included in the base offense level or specific offense characteristic. If this adjustment is based upon an abuse of a position of trust, it may be employed in addition to an adjustment under

§3B1.1 (Aggravating Role) ; if this adjustment is based solely on the use of a special skill, it may not be employed in addition to an adjustment under §3B1.1 (Aggravating Role) . URL:

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[78] UNITED STATES of America, Plaintiff-Appellee, v. James M. SHORTT, Defendant-Appellant, United States Court of Appeals, Fourth Circuit. - 485 F.3d 243, Argued February 2, 2007 Decided May 10, 2007 Dr. James M. Shortt pleaded guilty to one count, of a 43-count indictment, charging him with participating in a seven-year conspiracy to distribute and dispense and to cause to be distributed and dispensed anabolic steroids and human growth hormone, in violation of 21 U.S.C. §§ 841(a)(1), 333(e), and 846. URL: <http://64.233.169.104/search?q=cache:-bxKes9FllwJ:cases.justia.com/us-court-of-appeals/F3/485/243/+level+enhancement+%C2%A72D1.1+physician&hl=en&ct=clnk&cd=11&gl=us>.

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