White Paper Guidance for Physicians on Hormone Replacement Therapy

(HRT)

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Endorsing Organizations

Academy of Anti-Aging Medicine - China
Academy of Anti-Aging Medicine - Iberia
Academy of Healthy Aging
Academy of Optimal Aging
Academy of Successful Aging
American Academy of Age Management
American Academy of Anti-Aging Medicine (A4M)
American Academy of Longevity Medicine
American College of Longevity Medicine
American Society of Longevity Medicine
Anti-Aging Medicine Specialisation
Asia-Oceania Federation of Anti-Aging Medicine (AOFAAM)
AustralAsian Academy of Anti-Aging Medicine (A5M)
Belgian Society of Anti-Aging Medicine (BELSAAM)
European Academy of Quality of Life and Longevity Medicine (EAQUALL)
European Organization of Scientific Anti-aging Medicine
European Society of Anti-Aging Medicine (ESAAM)
German Society of Anti-Aging Medicine (GSAAM)
German Society of Hemotoxicology
Hellenic Academy of Antiaging Medicine
Indonesian Society of Anti-Aging Medicine
International Academy of Anti-Aging Medicine
International Academy of Longevity Medicine
International Hormone Society (IHS)
Japan Anti-Aging Medical Spa Association (JAMSA)
Japanese Society of Clinical Anti-Aging Medicine (JSCAM)
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Sociedad de Medicine Antievejenimiento y Longevidad de Gran Canaria
Society for Anti-Aging & Aesthetic Medicine Malaysia (SAAAMM)
South African Academy of Anti-Aging & Aesthetic Medicine (SA5M)
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Thai Academy of Anti-Aging Medicine
Thai Association of Anti-Aging Medicine
Anti Aging Research and Education Society, Turkey
Center for Study of Anti-Aging Medicine - UDAYANA University, Indonesia.
World Academy of Anti-Aging Medicine (WAAAM)
World Academy of Longevity Medicine
World Society of Anti-Aging Medicine (WOSAAM)

It is the position of the American Academy of Anti-Aging Medicine (A4M), its numerous worldwide affiliated scientific and medical societies, and befriended organizations, that the use of banned drugs or hormones for athletic enhancement constitutes inappropriate misuse. The A4M, its affiliates, and its befriended organizations (hereinafter referred to as "AM"), do not endorse orcondone the use of any illicit substances for the purpose of athletic enhancement or sports cheating.

However, AM is resolute in defending the rights of the patient working in conjunction with their physician in choosing any and all justifiable therapies, drugs and interventions which can be shown to improve either the quality or duration of the human lifespan or the form and function of the individual's physiology in order to achieve greater vitality and health at every age. It is in fact the physician's duty to act as an advocate for the patient's right to obtain the full lawful measure of scientific medical therapeutics necessary for optimum health and personal freedom of choice in healthcare.

Introduction

The American Academy of Anti-Aging Medicine (A4M), its affiliates, and its befriended organizations (hereinafter refered to as "AM), promotes the appropriate application of modern and advanced medical technologies to address the changes in chemical, hormonal, physical, and nutritional needs that occurs with aging. The scientific literature supports the benefits claimed by returning hormones to their physiological state when determined to be deficient.

Experienced anti-aging physicians have been prescribing bio-identical hormone replacement therapy (BHRT) for more than 20 years. For women, benefits may include:

- reduced osteoporosis and restoration of bone strength
- reduced hot flashes and vaginal dryness
- better maintenance of muscle mass and strength
- improved cholesterol levels

- reduced risk of endometrial and breast cancer
- reduced risk of depression
- improved sleep
- better mood, concentration and memory
- improved libido
- fewer side effects than with synthetic hormones

[Reed KD. Natural hormone replacement therapy: what it is and what consumers really want. International Journal of Pharmaceutical Compounding. 2001;5(5):332-335; Drusko J. Natural isomolecular hormone replacement: an evidence-based medicine approach. International Journal of Pharmaceutical Compounding. 2000;4(6):414-442; Boothby L, et al. Bioidentical hormone therapy: a review. Menopause. 2004;11(3):356-367.]

An extensive list of peer-reviewed references documenting the beneficial effects of HRT in adults is presented as Appendix A. Recent legal actions taken against some compounding pharmacies and physicians continue to be played out in the news. Regardless of the merits or lack of merits to these allegations, these accusations should alert us to the responsibilities that each physician faces with the decision to practice hormone replacement therapy. Attempts are being made to criminalize the practice of medicine where variations to State Board-favored traditional care is undertaken. Thus we are now seeing situations where there are no injured patients and no victims being made the basis of criminal proceedings against health professionals. This is an affront to our profession and the very notion of optimal healthcare. Errors or debate in prescribing guidelines are administrative issues: for officials to abuse their authority in recasting minor issues as criminal acts is in itself unjust and may be considered as criminal abise of their publicly elected positions.

Unfortunately, media confusion and outright deception have muddled the reality of what has occurred in the practice of hormone replacement therapy, where doctors' legal and ethical physiological use of hormones and supplements has been misrepresented as being the inappropriate use of hormones for sports enhancement. Every time that a physician breaches the practice of good medicine by prescribing medications inappropriately under the guise of hormone replacement therapy and/or anti-aging medicine, that physician jeopardizes not only the future of our profession, but the life expectancy of us all.

Using the combined knowledge and skills of a significant and elite group of consultants regarding the medical and legal applications of hormone replacement therapy, The American Academy of Anti-Aging Medicine (A4M), its numerous worldwide affiliated scientific and medical societies, and befriended organizations, offers the following policy positions which may help to offer general recommendations and guidelines to practitioners. However, anything offered herein should *not* be construed as legal or medical advice, and applicable state laws and regulations vary widely and should be strictly adhered to. It is recommended that any practitioner seeking specific advice of this type should contact a duly licensed and knowledgeable attorney in the state of practice and/or the medical licensing board of that state. There is no guarantee that these recommendations will fully protect a practitioner from actions taken by various state medical boards, but it is our hope that they will minimize the extent to which false accusations will be actualized.

Furthermore, the ultimate burdens for both the medical and legal issues rest with the treating physician. Therefore, it is imperative that all practitioners consult with their own State Board, the boards of any other states in which they may be deemed to practice, and legal counsel in all applicable jurisdictions regarding the content of this position paper.

Hormone Replacement Therapy

Introduction

Hormone replacement therapies with controlled substances such as testosterone and growth hormone have been used since many years. The first testosterone treatment of testosterone deficiency in adult men started around 1940 started ands since more than 40 years growth hormone is given to treat short stature children and since 1985 with the safer, not contaminated recombinant growth hormone, product of biotechnology. End of the 1980's, the first trial of adults with growth hormone deficiency were published, and since the beginning 1990s, growth treatment of adult patients started in private medical practice.

Testosterone and growth hormone are natural compounds made by the human body. Both hormones are controlled substances in the USA. They have been and are used in adults to correct testosterone and growth hormone deficiencies, often caused by the natural aging of the endocrine glands. Natural does not mean healthy as many studies have shown the association of various agerelated diseases and possibly psychiatric disorders with low levels of these hormones, and their improvement or possibly cure with replacement therapy at small physiological doses.

Most traditional endocrinologists have had no intense training in treatment of testosterone and growth hormone deficiencies. They generally have excellent training in the treatment of diabetes, but lack of interest and expertise in how to treat testosterone and adult growth hormone deficiencies and some other hormone deficiencies that may accelerate aging.

Because of this lack of knowledge, many of them have rejected these treatments and confused them with the improper use at excessive doses by 4 sports athletes searching to improve their performance. The American Academy of Anti-Aging

Medicine (A4M), its numerous worldwide affiliated scientific and medical societies, and befriended organizations, do not approve the improper use of these substance in sports, but do point to the right of every patient who is suffering from one of these deficiencies to get relief from their complaints by the adequate hormone treatment.

A. Selection of Patients

Historically, patients who were considered for Hormone Replacement Therapy, other than those with classical hormone deficiency syndromes (i.e., Diabetes, Hypothyroidism, Addison's disease, and Menopause, to name a few) were typically over the age of 45. This age criterion no longer applies when we take into consideration the thousands of individuals who have developed Traumatic Brain Injury-Hormone Deficiency Syndrome, which studies suggest can be treated by the use of Hormone Replacement Therapy.

Therefore, age as the single criterion for patient selection has become a moot point leaving documentation of laboratory defined hormonal deficiencies as the gold standard for any replacement strategy.

Recommendations for the Selection of Patients

The same concerns that exist in any other area of medicine, including screenings for contraindications, for example, apply in the field of Hormone Replacement Therapy. Additional considerations include, but are not limited to:

1. Treatment should be based upon having documented hormone deficiencies;
3. Screening should be done for participation in professional sports;
4. Screening should be done for prior hormone use and the following practice should be undertaken:

Copies of medical records should be requested from prior physician(s) to document any previous hormone deficiencies. Because individuals who have recently used "steroids"" can transiently depress their hormone levels creating the perception that they are deficient and need hormone replacement therapy.

B. Medical Records

Proper documentation of medical treatment is important and a requirement in all areas of medicine. Illegible or incomplete medical records may subject practitioners to regulatory actions and potential misinterpretation of actual sound medical practice. Many prudent practitioners use a computer based reporting system in which the patient's visit records are recorded and transcribed. The use of a computerized menu-driven EMR (Electronic Medical Records system) can help avoid the lack of appropriate and illegible documentation.

AM does not endorse or condone the prescription or dispensation of controlled substances or any prescription drugs outside the scope of a bona fide physician-patient relationship. It is incumbent upon every practitioner to comply with the obligations imposed by federal and state laws and regulations in this area. The following subsections present examples of some of the most crucial components to practitioners' medical records that will be evaluated in determining whether a proper patient-physician relationship exists.

C. Patient History

A comprehensive medical history is essential to document rational support for ordering laboratory tests and for any subsequent treatment which may be required.

Additionally, the documentation of conditions such as Orchitis in a male to account for Hypogoadism, birth control use for prolonged periods of time, Polycystic Ovarian Disease, and a variety of medications and toxic reactions, are important to support the medical need for hormone therapy.

Recommendations for the Patient's History

AM recommends that a comprehensive Patient Medical History should be conducted as part of the intake procedure during a patient's initial visit. This history should include a comprehensive system review and comprehensive or interval past, family, and social history as well as a comprehensive assessment/history of prior hormone therapies and pertinent risk factors. The elements of the above history should include all those suggested by the AMA's current procedural terminology codebook.

A review of medical events in the patient's family that includes significant information about: the health status or cause of death of parents, siblings, and children; specific diseases related to problems identified in the chief complaint or history of the present illness, and/or system review; and diseases of family members that may be hereditary or place the patient at risk.

The patient's history should include a chronological description of the development of the patient's present illness

from the first sign and/or symptom to the present. This includes a description of location, quality, severity, timing, context, modifying factors, and associated signs and symptoms significantly related to the presenting problem(s).

D. Laboratory Testing

Accusations of insurance fraud may occur when insurance companies believe that physicians are ordering unnecessary laboratory tests on patients. A proper medical history, as outlined above, including a review of symptoms, — which helps define the medical problem, clarify the differential diagnosis and importantly identify needed testing — allows for proper documentation that will help support any requested testing. Failure to obtain a proper medical history and review of symptoms can open up the physician to the potential of being investigated for improper ordering of laboratory tests, since states generally have a group of Business and Professional Codes (B&P) that defines and regulates professional conduct expected by businesses. These regulations are state driven and will vary from state to state and practitioners should check with local counsel to determine their state specific requirements. However, most professional conduct regulations encompass similar principles.

As an example, in the state of California one of their regulations concerning physician prescribing is as follows:

Repeated acts of clearly excessive prescribing or administering of drugs or treatment, repeated acts of clearly excessive use of diagnostic procedures, or repeated acts of clearly excessive use of diagnostic or treatment facilities as determined by the standard of the community of licensees is unprofessional conduct for a physician and surgeon, dentist, podiatrist, psychologist, physical therapist, chiropractor, or optometrist. Any person who engages in repeated acts of clearly excessive prescribing or administering of drugs or treatment is guilty of a misdemeanor and shall be punished by a fine of not less than one hundred dollars ($100) nor more than six hundred dollars ($600), or by imprisonment for a term of not less than 60 days nor more than 180 days, or by both the fine and imprisonment. (California B&P section 725)

Recommendations for Laboratory Testing

1. Practitioners should always conduct a proper review of symptoms that will support any testing;
2. Never send in a diagnostic code (ICD-9) to justify the ordering of laboratory tests unless that code can be substantiated with proper chart documentation.
3. Never send in an insurance claim for office visits with CPT codes that cannot be substantiated and always ensure that proper documentation of any substantiation is in place. Practitioners should be scrupulous in avoiding Insurance Fraud, or even the appearance of Insurance Fraud.
4. Never prescribe a medication that the patient will receive and the pharmacy will bill toan insurance company unless the rationale for the treatment can be substantiated and proper documentation of that substantiation is in place.

E. Interpretation of Laboratory Results

If there is an area in which the practice of hormone replacement therapy is most unique, and also the most open to a Medical Board's scrutiny, it is the manner in which hormone level results are interpreted. The practice of medicine is being replaced by a financially calculating industry that decides treatment based upon numerical results. These results do not take into consideration the clinical acumen of the practice of medicine that a physician has developed over the years of his/her practice.

Mainstream medicine deals with dichotomic treatment practices on a daily basis. What is the laboratory test for depression, anxiety, bipolar disorder, and other medical conditions that fail to be quantified by a numerical test? In such cases, it becomes the medical judgment of the physician to treat a patient with medication in the absence of a measurable basis.

The use of "natural" thyroid in patients whose TSH levels for example are not yet over 5.5 has stimulated controversial cases where the treating physician has been dragged into court to explain why a thyroid supplement was administered to a patient who is not yet sick? Several, often recent, studies have now been published that show that levels of TSH within the reference range, between 2 – and 5.5, in certain categories of patients have been reported to be associated with pathological abnormalities and even diseases. It is therefore to no surprise that the American Association of Clinical Endocrinologists has therefore narrowed in 2002 the serum TSH reference range to 0.3-3.0 mIU/L, lowering the upper reference end to 3. The National Academy of Clinical Biochemistry, the world's most respectful organisation for editing guidelines on laboratory test interpretation, reduced the upper end of the reference range from 5.5 to 4.1 mIU per liter in 2003. The latter group also stated that "more than 95% of healthy, euthyroid subjects have a serum TSH between 0.4 - 2.5 mIU per liter" and that "patients with a serum TSH above 2.5 mIU per liter, when confirmed by repeat TSH measurement made after three to four weeks, may be in the early stages of thyroid failure, especially if thyroid peroxidase antibodies are detected." In 2003, the consensus panel (Endocrine Society, American Association of Clinical Endocrinologists, and American Thyroid Association) recommended a target TSH range of 1.0 to 1.5 mIU per liter in patients already receiving thyroxine therapy. The concept of Interventional Endocrinology acknowledges the fact that not everyone experiences symptoms of deficiency

– relative or absolute - at the same levels. Therefore, taking a comprehensive medical history and physical can act to substantiate the application of replacement/supplementation protocols, in accordance with accepted standards of care. Clear documentation in this regard helps support the physician's approach in treating the patient.

F. Physical Examination

A "good faith" physical examination is one of the requirements of having personal knowledge of the medical status of an individual patient. Normally, this includes the standard – hands-on, examination of all systems: HEENT, Cardiovascular, Pulmonary, Gastric, Genitalia, Musculoskeletal and Neurological. This also should include the Vital Signs; Weight, Height, Blood Pressure, Pulse and Respirations. Additional testing, where appropriate, based upon history and the initial "standard" physical examination might include but are not limited to the following: EKG, Chest x-ray, Ultra-fast CT, Bone Density, and referral for GI assessment.

Recommendation for the Physical Examination

1. Before dispensing any prescription medication, a complete Physical Examination should be performed in accord with applicable laws. If indicated perform additional tests to address any suspicious physical findings.

G. Treatment protocols

Treatment protocols should be based upon credible scientific literature and currently accepted practice. The hormone therapy consensuses of the International Hormone Society that are heavily referenced may serve as a model (visit www.intlhormonesociety.org for details).

H. Prescriptions

To dispense controlled substances, a professional must know the requirements for a valid prescription. A prescription is an order for medication that is dispensed to or for an ultimate user. A prescription for a controlled substance must be dated and signed on the date when issued. The practitioner is responsible for making sure that the prescription conforms in all essential respects to both federal and state laws and regulations. A prescription order for a controlled substance may be issued only by a physician, dentist, podiatrist, veterinarian, mid-level practitioner or other registered practitioner who is: (1) authorized to prescribe controlled substances by the jurisdiction in which he/she is licensed to practice; and (2) Registered with DEA or exempted from registration (i.e., Public Health Service and Bureau of Prison physicians). Federal regulations (21 CFR 1306.04(a)) related to prescribing contain two key operational phrases, italicized below: (a) A prescription for a controlled substance to be effective must be issued for a *legitimate medical purpose* by an individual practitioner acting in the *usual course of his professional practice*. The responsibility for the proper prescribing and dispensing of controlled substances is upon the prescribing practitioner, but a corresponding responsibility rests with the pharmacist who fills the prescription. An order purporting to be a prescription issued not in the usual course of professional treatment or in legitimate and authorized research is not a prescription within the meaning and intent of section 309 of the Act and the person knowingly filling such a purported prescription, as well as the person issuing it, shall be subject to the penalties provided for violations of the provisions of law relating to controlled substances.

Recommendation for Writing Prescriptions

Generally, a prescription must include the patient's full name and address, and the practitioner's name, address, and registration number. The prescription must also include the drug name, strength, dosage form, quantity prescribed, directions for use, and number of refills. Where an oral prescription is not permitted, a prescription must be written in ink or indelible pencil or typewritten and must be manually signed by the practitioner. The practitioner is responsible for making sure that the prescription conforms to federal and all applicable state laws and regulations.

The Office Sale and Dispensing of Medications

Although there are general guidelines set forth by the Federal government [21 CFR 1306.04(b): "A prescription may not be issued in order for an individual practitioner to obtain controlled substances for supplying the individual practitioner for the purpose of general dispensing to patients."], the ability of physicians to distribute medications of all classifications from their offices is regulated by each state. Therefore, it is imperative that physicians review their own state's regulatory laws and guidelines. While state regulations will vary, record keeping and proper labeling of dispensed medications are central to most states' regulatory scheme. As an example, California mandates the following requiring physician dispensing:

A legally licensed Medical practitioner is in breach of this section of code if they: Fail to keep complete and accurate records of purchases and disposals of substances listed in the California Uniform Controlled Substances Act (Division 10 (commencing with Section 11000) of the Health and Safety Code) or controlled substances scheduled in the federal Comprehensive Drug Abuse Prevention and Control Act of 1970 (21 U.S.C. Sec. 801 et seq.), or pursuant to the federal Comprehensive Drug Abuse Prevention and Control Act of 1970. A

physician and surgeon shall keep records of his or her purchases and disposals of these controlled substances or dangerous drugs, including the date of purchase, the date and records of the sale or disposal of the drugs by the physician and surgeon, the name and address of the person receiving the drugs, and the reason for the disposal or the dispensing of the drugs to the person, and shall otherwise comply with all state recordkeeping requirements for controlled substances. In the government's attempt to prevent the illegal sale and distribution of medications classified as Schedule III, laws have been enacted to make it mandatory to provide additional information about the prescriber (physician) and recipient (patient). This information is computerized and can be used to monitor both physicians and patients in terms of the number and quantity of medication that is prescribed over time.

Schedule III is added to the CURES requirement: As of January 1, 2005, all pharmacies have begun submitting Schedule III prescription information to the Controlled Utilization Review and Evaluation System (CURES) program. The CURES program compiles prescription data in a statewide database to assist state law enforcement and regulatory agencies in their efforts to reduce prescription drug diversion. This was apparently precipitated by the highly publicized prosecutions related to BALCO and allegations of athletic Steroid Abuse. This obviously impacts the sale and distribution of

Testosterone and related hormones of treatment.

Prior to this change, pharmacies were required to electronically transmit only Schedule II prescription information to the CURES program. New legislation, Senate Bill 151 (Burton, Chapter 406, Statutes of 2003), requires the same information be transmitted for Schedule III prescriptions. In addition to requiring submission of Schedule III prescription information, the bill required prescribers **dispensing** these drugs to submit prescription information to the CURES program beginning on July 1, 2004. Physicians "dispensing" from the office must comply with the mandated regulatory filings at the same level as a pharmacy. In order to comply with the reporting regulations, pharmacies and dispensing prescribers must submit the following information for each scheduled II and III prescription filled:

- Full name, address, gender, and date of birth of the patient;
- Prescriber's category of licensure, license number, and federal controlled substance registration number;
- Pharmacy prescription number, license number, and federal controlled substance registration number;
- NDC (National Drug Code) number of the controlled substance dispensed;
- Quantity of the controlled substance dispensed;
- ICD-9 (diagnosis code), if available;
- Date of issue of the prescription; and
- Date of dispensing of the prescription.

Recommendation for the Office Sale and Dispensing of Medication:

1. All states have specific requirements for the dispensing of medication. Practitioners are urged to learn about their own states requirements for dispensing all medications from the applicable state board(s).

2. In accordance with federal law, prescriptions for a controlled substance must affix to the container a label showing the pharmacy name and address, the serial number of the prescription, date of initial dispensing, the name of the patient, the name of the prescribing practitioner, and directions for use and cautionary statements, if any, contained on the prescription as required by law. FDA regulations require that the label of any drug listed as a "controlled substance" in Schedule II, III, or IV of the Controlled Substances Act must, when dispensed to or for a patient, contain the following warning: ***CAUTION: Federal law*** prohibits the transfer of this drug to any person other than the patient for whom it was prescribed.

3. In many cases state law is more stringent than federal law, and must be complied with in addition to federal law. Professionals dispensing controlled substances should make sure they understand their state and federal controlled substance regulations.

J. Self-Prescribing by Physicians

Although there isn't a legal statute that specifically states that a physician cannot write a prescription for personal use, there are a number of Medical Board actions against physicians for the self-dispensing of narcotics and medication of abuse where the stated physician(s) lost their license to practice medicine.

K. Internet Pharmacies The DEA has provided the following information on its Web Site (http://www.deadiversion.usdoj.gov/faq/internetpurch.htm):

"Federal law requires that a prescription for a controlled substance to be effective must be issued for a legitimate medical purpose by an individual practitioner acting in the usual course of his professional practice' (21 CFR 1306.04(a)). Every state separately imposes the same requirement under its laws. Under Federal and state law, for a doctor to be acting in the usual course of professional practice, there must be a bona fide doctor/ patient relationship.

For purposes of state law, many state authorities, with the endorsement of medical societies, consider the existence of the following four elements as an indication that a legitimate doctor/patient relationship has been established:

- A patient has a medical complaint;
- A medical history has been taken;
- A physical examination has been performed; and
- Some logical connection exists between the medical complaint, the medical history, the physical examination and the drug prescribed. "A patient completing a questionnaire that is then reviewed by a physician hired by or working on behalf of an Internet pharmacy does not establish a doctor/patient relationship. A consumer can more easily provide false information in a questionnaire than in a face-to-face meeting with the physician. It is illegal to receive a prescription for a controlled substance without the establishment of a legitimate doctor/patient relationship, and it is unlikely for such a relationship to be formed through Internet correspondence alone. However, this is not intended to limit the ability of practitioners to engage in telemedicine. For purposes of this guidance document, telemedicine refers to the provision of health care using telecommunication networks to transmit and receive information including voice communications, images and patient records. "Some Internet sites recommend to the patient that they not take a new drug before they have a complete physical performed by a doctor. These sites then ask the patient to waive the requirement for a physical and to agree to have a physical examination before taking the drug they purchase via the Internet. The physical examination does not take the place of establishing a doctor/patient relationship. The physical exam should take place before the prescription is written. These types of activities by Internet pharmacies can subject the operators of the Internet site and any pharmacies or doctors who participate in the activity to criminal, civil, or administrative actions. For DEA registrants, administrative action may include the loss of their DEA registration. Additionally, providing false material information to obtain controlled substances could be considered obtaining acontrolled substance by fraud and deceit, which is subject to Federal and State penalties."

L. Delivery of a Controlled Substance or Drug Product Containing Listed Chemicalsto Persons in Another Country

Controlled substances that are dispensed pursuant to a legitimate prescription may not be delivered or shipped to individuals in another country without proper authorization. Any such delivery or shipment is an export under the CSA, and cannot be conducted unless the person sending the controlled substances:

1. Has registered with DEA as an "exporter" (see 21 CFR 1301); and

2. Has obtained the necessary permits(s), or submitted the necessary declaration(s) for export as outlined in 21 CFR 1312.

M. Compounding Pharmacy

Compounding by pharmacists has been a foundational aspect of the practice of pharmacy.

While today the majority of prescription medication is mass-produced by pharmaceutical companies, many patients require custom-made preparations that are prescribed by their physician and compounded by a trained pharmacist. These custom-prepared prescription medications must originate from a physician's order and be specifically written to meet that individual patients need. Federal and state laws prohibit the compounding of medication that is not pursuant to a doctor's order. Compounding pharmacies are strictly regulated by regulations from state boards of pharmacy. However, there have been many efforts recently to allow federal oversight of this practice. Recent legislation has been drafted that would usurp long-established state practices, concerning compounding, and turn the oversight over to the FDA. Despite this pending legislation, courts have repeatedly upheld pharmacists' rights to compound despite repeated attempts by the FDA to challenge the activity. In May 2006, a U.S. District court judge ruled that the compounding of ingredients to create a customized medication in accordance with a valid prescription does not create a new drug subject to the FDA's approval process (see Medical Center Pharmacy et al. v. Gonzales et al.). Additionally, the U.S. Supreme Court has held as unconstitutional FDA's repeated attempts to regulate pharmacist compounding.

Recommendation for the use of a Compounding Pharmacy

The use of customized prescription medications must originate from a physician's order and be specifically written to meet an individual patient's need (i.e., a commercially available product would not meet the patient's need) and be compounded by a trained licensed pharmacist.

N. Appropriate Patient Monitoring

Although there are generally no state or federal guidelines for mandatory monitoring of patients receiving Testosterone or Growth Hormone, there is an implied responsibility that would follow the "Standards of treatment" for your specific medical community.

O. Off-Label Prescription Drug Prescribing

It is important for all practitioners to understand the legal basis and ability to prescribe drugs for "offlabel" uses, and to adhere to all applicable limitations. An "off-label" use of a drug or a device is simply a use for a condition or in a manner

not appearing on the FDA approved label.

1 The American Medical Association reported in 1995 that approximately half of all prescriptions were written for "off-label" uses. Moreover, the General Accounting Office (GAO) has testified that 90 percent of cancer drug use, 80 percent of pediatric use, and 80-90 percent of drugs used to treat rare diseases are prescribed "off-label."

2 Perhaps the best known example is aspirin. For years, physicians prescribed aspirin to reduce the risk of heart attacks. However, the FDA did not approve such usage until 1998. While some "off-label" therapies are widely accepted, and 1 James M. Beck & Elizabeth D. Azari, *FDA, Off-Label Use, and Informed Consent: Debunking Myths and* Misconceptions, 53 FOOD & DRUG L.J. 71, 71 n.2, (1998). A recent FDA presentation defined off-label drugs as medicines "use[d] for indication[s], dosage form[s], population[s] or other use parameter[s] not mentioned inthe approved labeling." Janet Woodcock, *Lecture to Drug Information Association, A Shift in the Regulatory Approach*, (June 23, 1997), at www.fda.gov/cder/present/diamontreal/regappr/sld001.htm.

2 *Final Report on the Activities of the House Comm. on Government and Oversight,* 104th Cong. 2d Sess. 104 H. REP. 874 (Section 2), (January 2, 1997) at 114.

The FDA and various court decisions have recognized that "off-label" prescribing is a legitimate part of the practice of medicine. The FDA's policy on "off-label" prescribing states that "a physician may, as part of the practice of medicine lawfully prescribe a different dosage for his patient, or may otherwise vary the conditions of use from those approved in the package insert." This policy was affirmed by the FDA's Policy office by William B. Schultz, Deputy Commissioner for Policy in the FDA in 1996.4 "Off-label" Prescribing of Human Growth Hormone The federal hGH statute criminalizes whoever knowingly distributes, or possesses with intent to distribute, human growth hormone 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, and pursuant to the order of a physician [21 U.S.C. § 333(e)]. Growth hormone cannot be prescribed or dispensed for non-medical purposes. Since the natural aging process is neither a disease nor any other recognized medical condition, "anti-aging therapy" or "reversing the aging clock" is absolutely not a valid basis upon which to distribute hGH. Of course, "bodybuilding" is not a valid basis nor is improving athletic performance.

The Secretary of Health and Human Services (i.e., the Food and Drug Administration) authorizes the uses for which prescription drugs may be marketed. Pharmaceutical companies can be – and have been – sanctioned by the FDA for marketing products for "unapproved" uses. As previously described, in the case of most pharmaceuticals, the uses for which practitioners may prescribe or dispense FDA-approved drugs include "off label" uses.

The FDA has taken the language of the federal hGH statute to mean that all prescribing of hGH must be "on label" (i.e., for an "authorized use"). Although the treatment of adult growth hormone deficiency is an authorized use of hGH and it is therefore clear that a legitimate prescription for hGH replacement therapy is lawful, controversy continues. There is not yet a consensus among the medical community as to what constitutes a "deficiency" of growth hormone in an adult. Further, controversy has arisen over how to diagnose such a deficiency. For example, some staunch critics of growth hormone replacement therapy have opined that an arginine stimulation test must be administered in order to properly diagnose adult growth hormone deficiency. They point to the language on the package inserts of some commercially available brands of hGH recommending arginine stimulation tests and claim that said language makes this specific test mandatory in order to comply with the statute and avoid the commission of a federal felony. Such an interpretation of the law means that the package insert dictates to a physician not only the approved uses for the product, but in the case of growth hormone deficiency, how the diagnosis should be made. The "no off-label" interpretation held by FDA means that prescribing hGH for an authorized use such as legitimate adult growth hormone deficiency would be lawful, but prescribing for anything other than authorized uses –even to treat serious diseases where research indicates that hGH would be beneficial – would not.

While a literal reading of the statute may support this interpretation, it is improbable that Congress ever intended to suppress the development and application of medical uses of HGH to treat disease. The FDA's interpretation of the law places greater limitations on HGH prescribing than exist for controlled substances such as morphine and opiates, which may be prescribed for any legitimate medical purpose. Nothing in the legislative history proves that Congress ever intended that. In fact, Steven R. Salbu, *Off-Label Use, Prescription, and Marketing of FDA-Approved Drugs: An Assessment of Legislative and Regulatory Policy*, 51 FLA. L. REV. 181, 202 n.130.

4 William B. Schultz, Deputy Commissioner for Policy Food and Drug Administration, Department of Health and Human Services, Before the Committee on Labor and Human Resources, United States Senate, February 22, 1996.

This interpretation of the law seems completely at odds with the intent of Congress to treat anabolic steroids more harshly than HGH, not the other way around. Ultimately, legislative or judicial clarification of these issues may be required.

Meanwhile, practitioners are urged to adhere to the strictest standards of the law.

The therapeutic value of HGH was validated by a study conducted in Stockholm, Sweden. Data concerning visits to the doctor, number of days in hospital, and amount of sick leave were obtained from patients included in KIMS (Pharmacia International Metabolic Database), a large pharmacoepidemiological survey of hypopituitary adults with GHD, for 6 months before GH treatment and for 6-12 months after the start of treatment. Assistance required with normal daily activities was recorded at baseline and after 12 months of GH therapy. Quality of life (QoL) (assessed using a disease-specific questionnaire, QoL-Assessment of GHD in Adults) and satisfaction with physical activity during leisure time were also assessed. For the total group (n = 304), visits to the doctor, number of days in hospital, and amount of sick leave decreased significantly ($P < 0.05$) after 12 months of GH therapy. Patients also needed less assistance with daily activities, although this was significant ($P < 0.01$) only for the men. QoL improved after 12 months of GH treatment ($P < 0.001$), and both the amount of physical activity and the patients' satisfaction with their level of physical activity improved after 12 months ($P < 0.001$). In conclusion, GH replacement therapy, in previously untreated adults with GHD, produces significant decreases in the use of healthcare resources, which are correlated with improvements in QoL. [Hernberg-Stahl E, Luger A, Abs R, Bengtsson BA, Feldt- Rasmussen U, Wilton P, Westberg B, Monson JP; KIMS International Board., KIMS Study Group. Pharmacia International Metabolic Database, "Healthcare consumption decreases in parallel with improvements in quality of life during GH replacement in hypopituitary adults with GH deficiency," *J Clin Endocrinol Metab*. 2001 Nov;86(11):5277-81]

P. Insurance

Medical liability insurance carriers have recently formed a new medical specialty division for the antiaging healthcare practitioner. Their position on underwriting coverage for hormones focuses on these specific areas: hands on training combined with your level of experience, FDA approval, and HRT must be performed by a licensed physician, NP, PA or RN. Underwriting makes a decision on whether or not to cover your specific situation. You are covered unless the procedure is specifically excluded. Several new carriers have entered this market. Their names and contact information are available online at www.worldhealth.net.

Q. Conclusion

In addition to allowing doctors to prescribe approved drugs (other than human growth hormone) for "off-label" uses, the FDA has never sought to restrict the ability of third-parties to publish and disseminate scientific information about "off-label" uses. The FDA has repeatedly recognized the importance of "open dissemination of scientific and medical information regarding these treatments."5

The FDA has, however, traditionally viewed manufacturer dissemination of such materials as promotion that constitutes advertising and thus violates the FD&C Act.6 FDA regulation in this area has focused on "determining whether an industry-supported activity is independent and not generally subject to regulation," as opposed to manufacturer-supported and therefore regulated.7 It is in providing guidance on this issue that the FDA's policies have changed most dramatically in recent years, particularly in response to First Amendment criticisms.

5 WLF v. Friedman, 13 F. Supp. 2d at 56.

6 Final Guidance on Industry-Supported Scientific and Educational Activities , 62 Fed. Reg. at 64,076.

7 *Id.*