Injectables and Fillers: Legal and Regulatory Risk Management Issues

American Society of Plastic Surgeons
American Society for Aesthetic Plastic Surgery

With the many injectables and fillers on the market the American Society of Plastic Surgeons® (ASPS®) and the American Society for Aesthetic Plastic Surgery (ASAPS) receive frequent requests for clarification of the legal, regulatory and ethical issues raised by the topic. To address these issues this advisory will cover: 1) general information on drugs and devices; 2) the use of drugs not approved by the Food and Drug Administration (FDA); 3) reimportation of FDA approved drugs from foreign sources; 4) compounding pharmacies and counterfeit drugs; 5) provider qualifications; and 6) ethical considerations.

1. GENERAL INFORMATION

- **What is the difference between a drug and a device?**

A drug is any health care product that achieves its primary intended purpose by chemical action or being metabolized in the body; a medical device does not achieve its primary intended purpose by chemical action or being metabolized. For example, Botulinum toxin type A is a drug, while artificial skin and injectable fillers such as collagen and hyaluronic acid are classified as devices.

- **How does FDA approval or non-approval relate to the clinical use of drugs and devices?**

1. Approved for a specific use, i.e. labeled and approved by the FDA for marketing; which also allows for off-label use, i.e. legal use of a FDA-approved product outside of the clinical indications of the product labeling; and
2. Non-approved, i.e. not approved by the FDA for any purpose, and thus ineligible for off-label use.

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Two Web sites summarizing the FDA approval status of frequently used injectables and/or fillers are available at the following sites:

- ASPS Injectables-at-a-Glance: *http://www.plasticsurgery.org/news_room/press_releases/Injectables- at-a-Glance.cfm* or
- ASAPS Injectable Quick Facts: *http://www.surgery.org/press/news-release.php?iid=320&section=news- botox*

2. USE OF DRUGS THAT ARE NOT APPROVED BY THE FDA

- **Is it legal for a physician to obtain and use a product from outside of the United States that is not approved by the FDA?**

Drugs and devices not approved by the FDA for any use in the U.S. are available for use only by clinical investigators working under FDA-approved clinical study protocols. They may not be legally marketed or sold in this country. If, however, a physician injects a non-approved product that a patient brings personally to the doctor's office, the physician will not be in violation of the federal Food, Drug & Cosmetic (FD&C) Act because his or her conduct did not relate to the interstate delivery of a non-approved drug or device in the practice of medicine. The physician does risk significant liability exposure, invalidation of professional liability insurance coverage, criminal penalties and action by regulatory agencies.

- **If a patient brings a non-approved drug or device to a physician, is it legal to treat the patient using this drug or device?**

Although it may be possible to obtain non-FDA approved products from foreign sources or to have patients bring these products to the U.S. from foreign travel, members should be aware that federal law prohibits such conduct. For example, an individual who enters the country with a non-approved injectable filler in his/her luggage could be sanctioned by the FDA. Similarly, a physician who orders a non-approved injectable filler through a Canadian mail-order pharmacy could

be sanctioned by the FDA when the device arrives in the mail. Other regulatory agencies, including state medical licensing boards, would become involved if there was a patient complaint regarding the use of a non-approved drug or device.

- **What circumstances permit access to non-approved drugs and devices?**

The FDA recognizes only two circumstances in which a non-approved drug or device may be legally imported into and transported through the United States:

1. for use in approved clinical studies; or
2. for use in serious/life-threatening emergencies, if the product is under clinical investigation.

The latter exception is sometimes referred to as the "compassionate care" exception because of the humanitarian need to make available a non-approved product to a patient whose life is in jeopardy but who is not a clinical trial participant. In both instances informed consent and, to the extent possible without jeopardizing the patient's health and safety, Institutional Review Board approval must be obtained.

- **How important is it for clinical investigators to adhere to FDA-approved study protocols?**

When gaining legal access to non-approved drugs and devices through participation in approved clinical studies, it is essential to adhere to all IRB and FDA-approved study protocols. These requirements include informed consent, appropriate documentation of outcomes, and selection criteria for study subjects. Non-adherence to the protocols agreed to by the FDA and the manufacturer could potentially jeopardize the credibility and validity of the manufacturer's study data when it is reviewed by the FDA.

- **What is the risk exposure of using non-approved drugs and devices?**

Members are urged to exercise prudence and caution when dealing with non-approved drugs and devices so as to avoid enforcement actions by the FDA, licensing actions by state medical boards, and professional liability actions by dissatisfied patients.

- **What is the risk exposure of off-label use of approved drugs and devices?**

Off-label use of FDA approved drugs and devices by physicians does not carry the risks cited above, provided patient acceptance and understanding, and the treatment rationale, are well documented. For example, Botulinum toxin type A is a FDA-approved product for use in the glabellar area. Use of the product in other areas is legal and a clinical decision.

- **Can a physician advertise non-approved or off-label use?**

Members are reminded that it is illegal to commercially advertise any non-approved or off-label use; only FDA-approved uses may be commercially advertised. Moreover, members who participate as investigators in clinical trials cannot advertise their participation in the trial, nor the drug or device that is the focus of the trial, until such time as the FDA has approved it for commercial distribution.

3. REIMPORTATION OF FDA APPROVED DRUGS/PRODUCTS

Is it legal for a physician to purchase and use an FDA approved drug/product that is reimported from foreign sources?

The act of importing drugs manufactured or approved in the U.S. and approved by the FDA is called "reimportation." Despite recent support in Congress and by some state governors, the FDA and the U.S. Department of Health and Human Services ("HHS") maintain that such reimportation remains illegal and dangerous. Currently, only manufacturers are allowed to reimport their own drugs. While HHS recently created a task force to investigate the safety and efficacy of promulgating regulations that would allow for pharmacists and wholesalers to reimport FDA-approved drugs, such practices by pharmacists and wholesalers are not yet legal and any new regulations would not include physicians.

While FDA enforcement actions are concentrated against operators of foreign Internet pharmacies, both the FDA and HHS warn physicians and consumers that drugs purchased from foreign sources may be counterfeit versions of FDA-approved drugs, contaminated, outdated or improperly packaged and labeled. Physicians who directly obtain or assist their patients in obtaining prescription drugs from foreign sources may risk increased professional liability exposure. It is impossible to verify that drugs and devices obtained from out of country sources have been stored in a way to prevent degradation prior to or during shipping.

4. COMPOUNDING PHARMACIES AND COUNTERFEIT DRUGS

- **How does the FDA regulate compounding pharmacies?**

Pharmacies are permitted to compound reasonable quantities of drugs upon receipt of a valid prescription for an individually identified patient from a licensed practitioner. Compounding is recognized as appropriate where there is no commercially available drug for a particular patient. Members may, in their professional judgment, prescribe a compounded drug for individual patients in need of a customized drug. Pharmacies which mass produce compounded drugs in anticipation of receiving prescriptions, offer compounded drugs at wholesale prices to persons or entities for resale, or copy commercially available FDA-approved products risk FDA-initiated enforcement action, including warning letters, seizure, injunction, and/or prosecution for "manufacturing" drugs in violation of the FD&C Act.

- **Is it legal for a physician to purchase generic copies of brand name drugs for injection in patients?**

Members should not purchase generic copies of brand name drugs from compounding pharmacies. The FDA defines "counterfeit" drugs as drugs that are misbranded, diluted, contaminated, adulterated or expired, or "generic copies of brand name drugs." Members who purchase and inject counterfeit drugs risk enforcement actions by the FDA and state licensing authorities and, more importantly, place patients at risk due to the potential for misbranding, dilution, contamination, expiration or adulteration of the drug. For example, hyaluronic acid that was produced for topical use could potentially be repackaged as an injectable soft tissue filler by an illicit compounding pharmacy without any testing to ensure the terminal sterility of the product or its safety and efficacy. Unless you know the source of the product and have purchased it through an approved distribution channel, there in no way to verify the integrity of what is being offered by a compounding pharmacy.

5. PROVIDER QUALIFICATIONS

- **What level of training or licensure is required to administer injectables or fillers?**

The administration of injectables and fillers is a medical procedure and is subject to the same precautions of any medical procedure. Patients are advised to receive these treatments from a qualified physician. Under certain circumstances determined by the physician and applicable local and state professional practice regulations, injections may be administered by a licensed professional nurse or physician assistant. It is the physician's responsibility to ensure that the non-physician administering the injectables or fillers possess the proper education and training.

- **What are the legal requirements for physician supervision of non-physician personnel who administer injectables and fillers?**

Local and state professional practice regulations determining the supervisory involvement required vary from state to state. However, it is the individual physician of record who is ultimately responsible for both understanding and abiding by applicable local and state professional practice regulations.

- **What is the societies' position on the administration of injectables and/or fillers outside of a clinical setting such as a physician office?**

Of concern are reports of varied non-clinical settings where injectables and/or fillers are being offered. These include shopping malls, private homes, office parties, and group social gatherings. These non-clinical settings are inappropriate for several reasons:

1. inadequate patient selection
2. possible peer pressure for an individual to consent to treatment
3. providers who are not trained to administer the injectable or filler or qualified to assess or treat complications
4. lack of control over dosage and inadequate post-treatment supervision
5. the possibility of mixing alcohol and/or street drugs with injectable or medication used to control post-treatment pain and other side effects

The decision to have a medical procedure should be made without the influence of alcohol or peer pressure. The use of alcohol or other substances in conjunction with the treatment may potentially impair the individual's ability to consent to the treatment, may cause an adverse reaction, influence the provider's ability to administer the appropriate dose, or judge post-infection reactions. "Non-clinical" settings are of particular concern should an adverse incident, including an accidental overdose, occur.

6. ETHICAL CONSIDERATIONS

The ASPS and ASAPS leadership recognize that advertising from off-shore vendors supplying non-approved FDA drugs and devices, reimportation of FDA drugs and devices and requests from patients who bring these items to the physician's office for treatments can be enticing. Nevertheless, ASPS and ASAPS adhere to a joint Code of Ethics that places safety and efficacy before marketing advantage and, in all instances, seeks to minimize patient risk.

In addition, the ASPS and ASAPS joint Code of Ethics states that a member may be subject to disciplinary action, including expulsion, if the member participates in a charity raffle, fund-raising event, contest or other promotion in which the prize is any procedure. The administration of injectable or filler is considered a medical procedure.