

Use of Off-Label and Non-Approved Drugs and Devices in Plastic Surgery

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Our ultimate goal as plastic surgeons is to provide the best possible result for our patients with the minimum amount of morbidity. In our rapidly expanding technological world, various drugs and devices have been developed in the hope of continual improvement of outcomes and, therefore, patient satisfaction.

According to a joint advisory issued by the American Society of Plastic Surgeons and the American Society for Aesthetic Plastic Surgery,¹ “the use of drugs and devices on humans within the United States falls into one of three categories”:

1. Approved for a specific use [i.e., labeled and approved by the U.S. Food and Drug Administration (FDA) for marketing];
2. Approved and permitted for off-label use (i.e., legal use of an FDA-approved product outside of the clinical indications of the product labeling); and
3. Non-approved (i.e., not approved by the FDA for any purpose, and thus ineligible for off-label use).

Two circumstances are recognized by the FDA for a non-approved drug or device to be legally imported into and transported within the United States. The first is in approved clinical studies; the second is in serious or life-threatening emergencies, if the product is under clinical investigation. This compassionate-care exception refers to the humanitarian need for a non-approved product to be available for a patient whose life is in jeopardy but who is not part of a clinical trial. In both instances, informed consent and institutional review board approval must be obtained.

Plastic surgeons must use discretion when dealing with non-approved devices and drugs

to avoid enforcement actions by the FDA, actions by state medical boards, sanctions by your national organization or subspecialty board of the American Board of Medical Specialties, or professional liability actions.¹

Most drugs and devices utilized daily by plastic surgeons have been meticulously designed, thoroughly tested, and subsequently approved by the FDA before their use in the United States. Plastic surgeons have independently modified the use of some of these products. These uses, when performed outside of the manufacturer’s package insert specifications, are termed “off-label” uses.

There are many examples of widespread off-label uses of products. One of the most prominent is the use of botulinum toxin type A for chemodenervation of muscles of facial expression other than glabellar rhytids. That means that its use on other regions, including the most frequently addressed areas, such as the lateral canthal rhytids (crow’s feet), upper lip rhytids, and neck/platysmal banding, is *not* FDA-approved.^{2,3} As a matter of fact, before April of 2002, the use of botulinum toxin on even glabellar rhytids was considered off-label.

Breast augmentation is a common example in which several frequently performed procedures fall outside manufacturer’s (and FDA) recommendations, including closed capsulotomy, iodophor pocket irrigation, implant overfill and underfill, and endoscopically assisted augmentation. This was discussed recently in an excellent article by Dowden et al.,⁴ who make the salient point that although off-label uses are not technically illegal, their non-approved use without express written informed consent can be a set-up for potential litigation, including damages not covered by professional

liability insurance, loss of medical license, and possible criminal action.

Leukotriene receptor antagonists [Accolate (Zeneca Pharmaceuticals, Wilmington, Del.) and Singulair (Merck & Company, Whitehouse Station, N.J.)] are used to ameliorate the effects of capsular contracture. These products have primary roles in asthma treatment. They have recently found clinical application in plastic surgery for their immunomodulation properties in the inflammatory cascade, with improvement in women with Baker III or IV breast implant capsular contractures.⁵ Some surgeons are now using these medications prophylactically in "high-risk" women (those with prior capsular contracture or periprosthetic infection and those with a history of a tendency to form hypertrophic scars) in addition to treating already established contractures.⁵ Although clearly these are off-label uses of these products, they are not illegal.

Another example of off-label use that deserves mention is the growing popularity among some antiaging physicians and surgeons of prescribing human growth hormone for certain patients to combat the effects of aging.⁶ Although there are studies documenting an improvement in lean body mass, a decrease in adipose tissue mass, an increase in skin thickness, and an increase in bone density, none of these studies are randomized, blinded, controlled studies that have been peer-reviewed. Yet this pharmacologic and endocrinologic manipulation is still increasing in popularity. The long-term effects of this are yet to be studied, as well.

The purpose of this Viewpoint is not to delve into the pros and cons of each of these drugs and devices and the merits of their off-label or non-approved uses. It is also not to reprimand the surgeons who are utilizing the products in this way. Instead, it is to bring to light the fact that there are many practices that are currently considered "routine" by many surgeons that are, in fact, not sanctioned by either the FDA or the manufacturer. Although they may not be illegal and may be "safe," they require special consideration by both the surgeon and the patient.

It is our responsibility as surgeons to read the manufacturer's label and to be familiar with the intended use and utilization of the product. It is paramount to know what is "on-label" and what is "off-label." This may sound obvious, but many surgeons do not even know that what

they are doing is non-approved.⁷ Ignorance is not defensible in patient care, nor will it stand in trial. Once you are knowledgeable about the intended use of the product, it is necessary to be familiar with the available literature on the off-label use of the product. The literature is replete with various authors' case reports, anecdotes, and clinical experiences with products and techniques. Familiarity with the current literature is mandatory when using any product intended for patient benefit.

Perhaps the most vital aspect of off-label use is the involvement of the patient in the medical decision-making process. Two main areas require specific disclosure and documentation. The first discussion should be about the product and its off-label usage. The second important discussion should specifically disclose the nonexperimental nature of the proposed treatment. Informed consent is standard practice for all surgeons, no matter how large or small the procedure. This discussion of the risks, benefits, and options must include the disclosure that the intended procedure or use of the product is not supported by either the manufacturer or the FDA. It should include the reasons why the surgeon believes that, in his or her experience, the benefits to the patient outweigh the risks. This discussion should be clearly documented in the medical record, and a separate consent form should be used in these situations. Although this kind of discussion and consent will not prevent litigation, it will serve to help protect the surgeon from claims of intent to harm. The plaintiff may assert automatic negligence by the surgeon because he or she used the product or procedure off-label. Courts have held that it is not negligence per se (automatically) as long as the treatment is not experimental and is disclosed.

Drugs and devices not yet approved by the FDA are prohibited for use except in approved clinical studies. However, medical products and medications are used off-label by physicians and surgeons for uses other than those prescribed by the manufacturer and the FDA. This practice is widespread and legal. Despite this prevalence, there is no substitute for an educated physician and an educated patient. The patient's benefit and outcome are the driving force behind the application of these products, and future well-designed studies may prove or disprove the legitimacy of their use. In the meantime, full disclosure and frank discus-

sion are critical for moral, medical, and legal purposes.

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