



*Sound Policy. Quality Care.*

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**Physician-Directed Applications (Off-Label Use)**  
**A Position Statement of the Alliance of Specialty Medicine**

The following societies within the Alliance of Specialty Medicine have approved this statement:

American Association of Neurological Surgeons  
American Association of Orthopaedic Surgeons  
American Gastroenterological Association  
American Society of Cataract & Refractive Surgery  
American Urological Association  
Coalition of State Rheumatology Organizations  
Congress of Neurological Surgeons  
National Association of Spine Specialists  
Society for Cardiovascular Angiography and Interventions

**Physician-Directed Applications**

Physician-directed applications, also known as “off-label”<sup>1</sup> uses, are an integral component of the art and science of medical practice, particularly for specialty physicians. Physicians may choose to use medical products such as prescription drugs, biologics, and devices, for uses not listed in the United States (US) Food and Drug Administration (FDA) approved or cleared labeling.

**Background**

It is not uncommon for some off-label uses of medical products to become standard of care in the practice of medicine.<sup>2</sup> In fact, off-label uses of certain medical devices and drugs can be found in standard textbooks for medical subspecialties. In certain patient populations, such as children and cancer patients, off-label use of medical products is extensive, when appropriate therapies have not been developed or evaluated for the populations or a clinical trial is not feasible (such as in the case of rare diseases). In these circumstances, physician-directed applications provide treatments that may not otherwise be available for some of the nation’s youngest and most critically-ill patients.

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<sup>1</sup> “Off-label” use for prescription drugs, biologics, and approved medical devices means any use that is not specified in the labeling approved by the FDA. For cleared medical devices, “off-label” means any use that is not included in the cleared “indications for use.” Labeling is considered as any written material which accompanies, supplements, or explains the product.

<sup>2</sup> Refer to relevant medical specialty society for specific examples.

Physicians use the best available clinical evidence, judgment, and consideration of individual patient circumstances and preferences in treating and managing disease and injury. The Alliance of Specialty Medicine (“the Alliance”) recognizes that good medical practice and the best interests of the patient require that physicians use legally-available drugs, biologics, and devices according to their best knowledge and judgment. Physicians are reporting to Alliance member societies that their patients are opting out of treatment involving off-label uses because of the patients’ perception that the procedures are experimental. This behavior is particularly common within pediatric populations. Patients and/or their representatives are often concerned about off-label use, even when there are scientifically valid data that support the safety and efficacy of the use.

### **FDA Regulatory Principles and Labeling**

The FDA regulates the marketing approval and/or clearance, labeling, and promotion of pharmaceutical, medical device, and biologic products in the United States. Products may only be labeled, promoted, and advertised for the uses that the FDA has approved or cleared. Labeling claims of a medical product are negotiated between the FDA and the manufacturer to ensure that the labeling accurately reflects the safety and effectiveness data presented in the manufacturer’s marketing application. Furthermore, a drug, device, or biologics manufacturer may choose, for economic reasons, not to pursue additional labeling for indications that may increase the cost of obtaining FDA approval or clearance. As a result, the label may not reflect changes in indications, contraindications, warnings, or dosage, supported by new data that becomes available after approval or clearance. The Alliance encourages manufacturers to submit data on the safety and effectiveness of off-label indications to the FDA and to seek the expansion of the indications for which their regulated products are approved or cleared.

### **Practice of Medicine Exception**

The Food and Drug Administration does not have the statutory authority to regulate the practice of medicine. In 1998, the US Supreme Court issued a judgment in *Buckman v. Henney* affirming physicians’ right to use any FDA- approved therapies they believe are in the best interests of their patients. In addition, section 906 of the federal Food, Drug, and Cosmetic Act addresses the issue of the practice of medicine, and states the following:

*Nothing in this Act shall be construed to limit or interfere with the authority of a health care practitioner to prescribe or administer any legally marketed device to a patient for any condition or disease within a legitimate health care practitioner-patient relationship. This section shall not limit any existing authority of the Secretary to establish and enforce restrictions on the sale or distribution, or in the labeling, of a device that are part of a determination of substantial equivalence, established as a condition of approval, or promulgated through regulations. Further, this section shall not change any existing prohibition on the promotion of unapproved uses of legally marketed devices.*

The FDA acknowledges that physicians may prescribe or administer any legally-marketed product for an off-label use within the practice of medicine.

### **Standards of Care**

Standards of care change over time, and the emergence of new literature may alter treatment patterns. Consequently, there are instances when the off-label use of medical products evolves to be recognized as a generally accepted medical standard. There are also instances in which the labeled uses of medical products are found to have contraindications and interactions that reduce their safety and efficacy. Specialty physicians are encouraged to notify the relevant agency or institution of adverse events related to the use of medical products.

### **Informed Consent**

Physicians and medical institutions have varied practices for obtaining and documenting informed consent provided to patients that may or may not address off-label use. In some instances where an off-label use has come to be considered a standard of care in the clinical community and/or raises little risk of an adverse outcome, the use may not be discussed specifically with the patient. However, physicians should use their clinical judgment in determining the need to discuss specific off-label uses with patients, and include information about such uses in informed consent materials, where the off-label use could be a significant factor in the patient's decision about whether to undergo the procedure. If a patient has questions, the physician should also personally inform the patient that the product is being used in an off-label manner and discuss the benefit/risk profile for that use. This approach not only serves the patient's best interests, but also limits the physician's liability risk.

### **Benefits and Risks of Physician-Directed Applications**

Benefits and risks exist with off-label use. Benefits include the ability to provide care to patients who would not receive treatment without off-label use, such as many pediatric patients. Risks include the potential for limited effectiveness and unexpected side-effects from uses that have not been adequately studied for the specific indication or patient population.

It is well-established that physicians who use a product for an indication not in the approved or cleared labeling have the responsibility: (1) to be well informed about the product; (2) to base its use on a firm scientific rationale and sound medical evidence; and (3) to maintain awareness of the product's uses and effects.

### **Conflicts of Interest**

Conflicts of interest should be disclosed in compliance with all state and federal laws and regulations. Specialty physicians engaging in compensated arrangements with industry should disclose their financial arrangements in medical education, research, and professional activities. Physicians who are involved in product development and/or testing should disclose this role to patients. Physicians should avoid interactions and activities where discussions of off-label use could be considered promotional in nature.

### **Statement of Policy (Conclusion)**

**The Alliance of Specialty Medicine recognizes that a specialty physician may prescribe or administer any legally-marketed product for an off-label use within the authorized practice of medicine where the physician exercises appropriate medical judgment and it is in the best interests of the patient.** If specialty physicians use a product for an indication not in the approved or cleared labeling, they have the responsibility: (1) to be well informed about the product; (2) to base its use on a firm scientific rationale and sound medical evidence; and (3) to maintain awareness of the product's use and effects. Specialty physicians should appropriately counsel patients about the benefits and risks of the proposed treatment, and alternative treatments that might be available. Specialty physicians are encouraged to notify the relevant agency or institution of adverse events related to the use of medical products.