

**Public Hearing: Manufacturer Communications Regarding Unapproved
Uses of Approved or Cleared Medical Products**

Summary of Testimony

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My name is Dr. Doyle Stulting. I am testifying today on behalf of the American Society of Cataract and member organizations of the Alliance of Specialty Medicine*, a coalition of medical specialty societies representing more than 100,000 physicians and surgeons. I am also testifying on behalf of my fellow physicians and our patients.

I am a past President of the American Society of Cataract and Refractive Surgery, co-founder of the Stulting Research Center in Atlanta, Georgia, Director of Corneal Disease & Research at Woolfson Eye Institute, and Professor of Ophthalmology, Emeritus at Emory University. I have authored over 200 peer-reviewed publications and led numerous NIH-sponsored, physician-sponsored, and industry-sponsored clinical trials. I was a member of the Ophthalmic Devices Panel for 10 years and received the Food and Drug Administration Citation for Excellence Award in 1998. This diverse exposure to the regulatory process from “both sides of the table” gives me a unique perspective from which to comment on the topic of today’s session.

We appreciate the opportunity to share our concerns about regulations that limit communications regarding off-label use of approved medical products. We believe that the FDA’s current regulations unnecessarily interfere with the dissemination of scientifically valid information between healthcare professionals and manufacturers. This interference, we believe, ultimately denies physicians access to vital, current, real-world experiences and adversely affects healthcare outcomes.

In its notice for this hearing, the FDA posed questions about how clinicians might assess off-label communications, possible consequences of these communications, and ways they should be regulated. I, and my colleagues in the Alliance of Specialty Medicine, believe physicians have the ability to assess and interpret clinical data appropriately, and that access to those data will result in measurable benefits to patients through improved outcomes and new cures. Reasonable restrictions on the communications would include notification that a referenced indication is off-label as well as a requirement that communications be truthful, balanced, and not misleading.

Off-label use of drugs and devices is actually very common in the everyday practice of medicine. I do not believe a day goes by without my prescribing medications or using medical devices off-label. Off-label use of medical products is commonly found in medical textbooks. In fact, failure to prescribe medications or use devices off-label would quickly place many of us at risk for a malpractice lawsuit. In my subspecialty, routine use of postoperative antibiotics after cataract surgery, the use of mitomycin-C as a surgical adjunct, application of adhesives for the closure of wounds, and even the treatment of infectious corneal ulcers with effective topical antibiotics represent off-label use. Long after the use of intraocular implants for visual correction after cataract surgery became standard of care for all adults, their use for patients under the age of 60 years was off-label—a ridiculous label restriction by contemporary standards that stood for years before the FDA finally decided to remove it.

For certain populations, such as children, pregnant women, cancer patients, and patients with rare diseases, clinical trials are not feasible or too costly for any manufacturer to undertake. This is especially true for patients with rare diseases and those with conditions that may exclude them from FDA clinical trials. According to the National Organization for Rare Disorders (NORD), no FDA approved treatment exists for 95 percent of rare diseases. For patients such as these, who come to our offices grasping for help, off-label use of medical products is our only option—one that may be vision- or even lifesaving.

Clinical trials designed for FDA approval are rigid, well designed, monitored, appropriately analyzed, and reliable. Obtaining FDA approval for a particular indication is, however, slow, cumbersome, and expensive. In addition, the information upon which approval is based often does not reflect the full range of appropriate indications. It may also not accurately list all warnings and contraindications. Data often come to light after approval that expands the indications, supports modification of dosage, or even limits the indications for a treatment. The quality of this information may not meet the so-called “gold standard” of a randomized, double-blind, prospective, controlled clinical trial, but my colleagues and I are all skilled at analyzing scientific data, and we share our experiences among ourselves. The shared data range from early case reports to more rigorous, prospective, controlled, clinical trials. Physicians are quite capable of evaluating the reliability of scientific communications, and we can appropriately apply this information to our clinical practice. In fact, this is an important element of our training and our responsibility to patients.

The label on medical products represents the results of clinical trials that are designed by the manufacturer to obtain FDA approval in the most certain and most expeditious way possible. These motivations are not the same as our motivation to provide the best medical care to our patients. Clinical trial results, therefore, often do not represent all appropriate indications for a product. The product label not only reflects limited clinical data influenced by business considerations, but it also represents a summary of knowledge that is “frozen in time.” Invariably, practitioners become aware of new indications, dosages, complications, and cautions about the use of medical products after the label is created, and this “off-label” information is often vital to the health of our patients. There is no reason for our use of medical products to be bound by outdated information.

Current FDA regulations impede our quest for scientific knowledge and our ability to care for our patients by interfering with the flow of information from drug and device manufacturers to practitioners—and even among physicians themselves. They limit discussions in public forums and limit the ability of drug and device manufacturers to interact with physicians who request information about their products. In reality, many patients are harmed when treatment options are taken off the table for lack of information.

In fact, rising public awareness of off-label use and the stigma that FDA’s regulations have attached to it even interferes with the doctor-patient relationship. Not infrequently, patients return to us after an initial consultation, having decided not to take prescribed medications on their own because of outdated or poorly stated information they read on the product label. Not only do they fail to comply with appropriate, effective treatment, they also question the clinical skills of their doctor who prescribed a medication based on valid scientific evidence that was not available at the time the label for a product was created.

Before regulatory hurdles were erected, it was not at all uncommon for a representative of a manufacturing firm to be the first to call our attention to important new information about off-label use of a medical product. We had the opportunity to evaluate before using it to guide patient care. Now, this kind of information may go unnoticed by busy practitioners, burdened by efforts to comply

with increasing administrative and regulatory duties, for a significant amount of time—to the detriment of our patient’s health.

Physicians are savvy consumers of medical information. We have been trained to sift through information to recognize scientifically valid data and to use it appropriately. Restricted access to information about off-label use fails to recognize the limitations of FDA clinical trials or the fact that our knowledge of the effects of medical treatments continues to evolve with time. Provided there is prominent disclosure that the FDA has not approved a product for a certain indication, truthful, unbiased, communication of data should not be impaired.

We urge the FDA to open the lines of communication between manufacturers and practitioners to help facilitate the development and dissemination of accurate information about off-label use. This will allow providers to make better decisions for their patients, improve medical outcomes, minimize the lack of patient compliance caused by outdated label information, and improve the good relationship that we strive to maintain with our patients.

In fact, we believe it would be appropriate to add a paragraph to all drug and device labels stating something like the following: “The indications, contraindications, warnings, cautions, and other information contained in this label are based on data generated by the clinical trial used to obtain approval for marketing this product in the United States. After marketing approval, additional scientifically valid data may become available to justify new uses, dosages, contraindications, or other modifications of the information contained herein. Your physician will take this information into consideration when prescribing this product and can discuss it with you.” This, or similar wording would empower physicians to utilize approved products for the benefit of their patients on the basis of current, scientifically valid data without the stigma and hampered professional communication created by existing restrictions on off-label discussions.

We appreciate the opportunity to speak in front of you today. We look forward to continuing to work with the FDA to ensure the creation of policies that enhance patient care and health outcomes. At this time, I would be happy to answer any questions.

*Association of Neurological Surgeons, American College of Mohs Surgery, American Gastroenterological Association, American Society for Dermatologic Surgery Association, American Society of Cataract and Refractive Surgery, American Society of Plastic Surgeons, American Urological Association, Coalition of State Rheumatology Organizations, Congress of Neurological Surgeons, Society for Cardiovascular Angiography and Interventions, and American Academy of Facial Plastic and Reconstructive Surgery