



American  
Association of  
Neurological  
Surgeons



CNS

**Statement**  
of the  
**American Association of Neurological Surgeons**  
**Congress of Neurological Surgeons**  
before the  
**Food and Drugs Administration**  
**Public Hearing**  
on the Subject of  
**Manufacturer Communications of**  
**Physician-Directed Uses of Approved Medical Products**  
**November 9, 2016**

My name is William Welch. I am a neurosurgeon practicing at the University of Pennsylvania Medical Center, and I am here today on behalf of the American Association of Neurological Surgeons and the Congress of Neurological Surgeons. I have been a member of the AANS/CNS Committee on Drugs and Devices for over 15 years and currently serve as its vice chair. I appreciate the opportunity to participate in today's public hearing to address issues surrounding communications regarding physician-directed — sometimes called off-label — use of FDA-approved medical products. We support the dissemination of scientifically valid information between healthcare professionals and manufacturers and urge the FDA to allow industry to provide physicians with access to such clinical information when asked.

In its notice of 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. Organized neurosurgery, along with our colleagues in the Alliance of Specialty Medicine — from whom you will hear tomorrow — believe physicians have the ability to assess and interpret clinical data appropriately. This is an essential competency for physicians and we consider the source of all information used in shared decision-making with our patients, assuring their appropriate informed consent regarding the risks and benefits of treatment.

Physician directed use of FDA-approved drugs and devices is a central part of the practice of medicine. Of course, in a perfect world, we may all prefer to have randomized control trial data for every drug and device for each indication, but the cost and the rarity of some diseases make this impractical and often impossible. The refinement of the use of FDA-approved drugs and devices is a rational process. Scientific evaluation of a product necessarily must be limited to the questions asked, and variables examined. This results in narrow FDA marketing “approval.” Once approved for sale and marketing, however, use of that product expands into areas of real-world clinical experience. As experience is gained by the medical community, physicians publish and discuss their findings on how the device performed, including its observed risks and benefits. Its use is then modified appropriately. If the manufacturer has data on uses of a drug or device that has been developed following approval, this is valuable additional information for physicians. Feedback to the manufacturers from the physician community may be useful as well and lead to future improvements of their products. Communication is a two-way street.

There are many examples of how this expansion of product indications benefits patients, relieves suffering and saves lives. In cancer care, for instance, many chemotherapy agents are approved for narrow “on-label” uses for a particular indication, but are quickly extrapolated to related cancers that have limited treatment options. In the area of spine disease, the use of screws to stabilize the back of the cervical spine was not FDA “approved” but over the years had become a medical standard as one of the best ways to securely stabilize the spine. We commend the FDA for recent efforts to classify many screws used in the spine. Off-label or physician-directed expansion is particularly important in pediatrics where few devices go through FDA clearance due to the expense, legal risk and difficulty of setting up valid studies with relatively limited numbers of potential patients. Without the application of products in off-label uses, advancement in the care of children would halt.

Neurosurgery is a very clinically diverse and device dependent specialty, and those devices hold great hope for improvement in the quality of life and reduction of pain for many patients. Neurostimulators are showing great promise for uses outside of the initially labeled indication — treating patients with secondary dystonia, essential tremor, and many conditions causing pain or dysfunction. New uses for endoscopic embolization devices are being developed, treating potentially debilitating or fatal cerebrovascular conditions. In addition to device development, the uses of drugs with other label indications have been found effective for serious nerve pain. The ability to share information about these hopeful new applications that were not part of the original label for a drug or device is beneficial and should be encouraged.

The expansion of use from the narrow on-label approval by the FDA to more broad off-label or physician-directed applications, then, is a standard part of medical practice and the advancement of patient care. As I have mentioned, in many cases, new applications are found that dramatically improve care and save lives in off-label or physician-directed ways that increasingly deviate from the original FDA approval. In those cases, best medical evidence leads to products that may have their primary use in off-label or physician-directed applications. Such refinement in patient care could not occur if government bodies, such as the FDA, regulated how professional judgment is exercised. The evaluation of evidence — including clinical trials, observational studies and registry data — is essential to improvement in patient care. Including manufacturers in this process is useful. As they and practitioners become aware of new indications, dosages, and complications about the use of a product after the label is created, sharing the information is of benefit to individual patients in particular and public health in general.

The stigma of off-label use can cause confusion and misunderstanding. Particularly for drugs and devices with long time use that differs from the labeling, we would urge the FDA to consider an expedited process to add the indications to the labeling or find another way to educate important stakeholders and dispel misinformation about physician-directed use. Some off-label uses have been in common practice and widely considered excellent medical care for decades, as was the case with some screws used in the spine for which the labeling was limited to other areas of the anatomy. We have joined the Alliance of Specialty Medicine in suggesting that one way to address these concerns would be to add a statement to drug and device labeling acknowledging that after FDA approval of a product, additional scientifically valid data may become available that would support new uses, dosages or other refinements. This would help to clarify physician-directed use for the public, payors and others. Specific language has been provided to the FDA by the Alliance and will be discussed tomorrow when Dr. Stulting speaks on behalf of the Alliance.

I have been privileged to interact with the FDA over the last 23 years — as a practicing neurosurgeon, a clinical investigator and a leader of the AANS/CNS Committee on Drugs and Devices. As such, I have stood before FDA panels as a physician innovator, as a representative of my medical specialty societies, and have, on occasion, reported device failures or malfunctions to the FDA. Based on my experiences, I have a deep respect for the dedication and intelligence of the men and women working at the FDA. Their purview is vast, they labor under a tremendously bureaucratic system, and, I believe, they are eager to foster open communication with practicing physicians and with industry to enhance patient care and reduce morbidity and mortality. As always, organized neurosurgery stands ready to continue to work with the agency to develop safe and effective drugs and devices and to improve scientific exchange for our patients.

Thank you.

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