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"Examining Medical Product Manufacturer Communications"

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Chairman Burgess, Ranking Member Green, and Members of the Subcommittee: thank you for holding this hearing and for inviting me to testify on this important topic. My name is George Van Hare. I am Chief of Pediatric Cardiology at Saint Louis Children's Hospital and Professor of Pediatrics at Washington University School of Medicine in St. Louis, Missouri. My clinical practice is focused on caring for children with heart rhythm disorders, as well as adults who are survivors of surgery for congenital heart disease. As such, I prescribe antiarrhythmic medications, utilize medical devices such as catheters for cardiac ablation procedures, and implant pacemakers and defibrillators. This year, I have the honor of serving as the President of the Heart Rhythm Society. Founded in 1979, the Heart Rhythm Society is the international leader in science, education and advocacy for cardiac arrhythmia professionals. Its members include 6,100 physicians, scientists, nurses and other allied health professionals in more than 90 countries who specialize in electrophysiology and perform basic, clinical, and translational research science. Electrophysiology is a distinct subspecialty of cardiology, and adult electrophysiologists are board certified through the American Board of Internal Medicine.

BACKGROUND: OFF-LABEL USE

The Food and Drug Administration (FDA) approves drugs and medical devices for specific indications, which are reflected in the product's label. Off-label use refers to the utilization of an FDA-approved treatment or device for any use other than the one(s) listed in the approved labelling, or in a population not reflected in the labelling, such as children. It is important to note that these off-label uses are often not experimental uses. In fact, some are so common they have become the standard of care. Many off-label uses are well-documented in the peer-reviewed

literature, are discussed widely among physicians, and are cited as standard and accepted treatment in medical textbooks.

THE CURRENT REGULATORY PARADIGM IMPEDES SCIENTIFIC DISCOURSE.

FDA prohibits any promotion by manufacturers related to off-label uses of a drug or device. The question then becomes: what is promotion? The current regulatory approach limits the ability of a manufacturer to share data not referenced in the package insert. This means that much valuable information may never be conveyed to clinicians and other medical decision-makers. Essentially, we do not get the benefit from data that has not been derived from randomized, controlled clinical trials.

Sharing comprehensive, scientifically valid data is critical to the practice of medicine generally, and it is even more critical for particular specialties. It is sometimes claimed that the use of drugs or devices off-label is the result of a choice by physicians. While sometimes this is true, for pediatric cardiologists and electrophysiologists, this is usually not the case. This is due to the fact that very few of the medications for arrhythmias that are on the market are formally approved for use in children. Thus, using treatments off-label is often our main method of treatment. Similarly, catheters that we use for catheter ablation procedures are labelled for a limited number of specific arrhythmias, but are used by all electrophysiologists (adult and pediatric) for treating and curing all types of arrhythmias.

By way of example, I will cite the example of amiodarone, brand name Cordarone. This is one of the most important medications for the treatment of potentially life-threatening arrhythmias, particularly in patients who have undergone successful surgical repair of complex congenital heart defects but who have dangerous arrhythmias in the aftermath of surgery. The

FDA-approved label simply states “The safety and effectiveness of Cordarone Tablets in pediatric patients have not been established.”

There are an additional six months of exclusivity granted to manufacturers of medications who generate data related to pediatric populations, under the Pediatric Research Equity Act (PREA) but this has not been sufficient to produce the amount of shareable data we might like, particularly for older drugs. As such, our clinical decisions often rest on anecdotal evidence and informal information-sharing among physicians. This is not an ideal environment in which to make treatment decisions.

Another example that I might cite, not specific to children, is labelling of ablation catheters. These devices are used in performing curative catheterization procedures, and these procedures have essentially replaced open heart surgery as the best option for a curative procedure for the last 25 years. Their labelling is limited to only certain arrhythmias. For example, the Cryocath Freexor-Xtra cryoablation catheter (manufactured by Medtronic) is only labelled for treating one arrhythmia, atrioventricular node reentry tachycardia (AVNRT) despite the fact that it is ideal for treating tachycardia due to accessory pathways located close to the normal conduction system without risking inadvertent atrioventricular block. It would be absurd to use a different catheter for this indication on the basis of the labelling, and even more absurd to consider open heart surgery. However, because of the labelling, technical support representatives of the manufacturer are not allowed to discuss this indication directly, despite the fact that the use of this catheter for this indication is widely agreed to be the standard of care.

There is an important way in which this information-sharing among physicians may also be adversely affected. When a medical conference is directly sponsored by a manufacturer, these conferences do not qualify as continuing medical education (CME) events based on rules of the

Accreditation Council on Continuing Medical Education (ACCME). Consequently, physician speakers are considered to be "agents" of the manufacturer sponsoring the event, and so they are also limited to discussing only the labelled indications. Any discussion between physicians regarding experiences with drugs or devices that are off-label at such events must occur informally, rather than as part of the program, and thus these discussions do not benefit from the great potential for information sharing among physician attendees. Such discussions can occur formally at medical and scientific conferences not directly sponsored by industry, but this rule limits the opportunities for such information sharing of data related to children.

The good news is that it doesn't have to be this way. It is likely that there is a large amount of data maintained by manufacturers, which, under the current regulatory structure, manufacturers are not allowed to proactively share with clinicians. I recommend that the Committee develop ways to work with FDA to unlock this data. I also would like to respectfully suggest a few parameters to ensure this is done in a responsible manner.

REGULATION SHOULD DISTINGUISH BETWEEN PROMOTION AND DATA-SHARING.

There is a difference, in my view, between advertising an unapproved use to the public versus sharing scientifically valid data with clinicians, and this difference can be reflected in the regulatory approach to each type of activity. There is a vast space between our current regulatory approach and a "Wild West" approach. In my opinion, the appropriate and responsible regulatory approach likely lies somewhere in the middle.

I urge the Committee to explore ways to define acceptable real-world evidence that manufacturers can proactively share with medical decision-makers. These types of data may

include observational studies, pharmacoeconomic studies, or information on subpopulations. The data must be truthful, presented in context, and scientifically valid.

There is some concern that manufacturers might overwhelm physicians with data taken out of context, or data that is misleading and skewed to present a more favorable picture than is realistic. However, physicians are trained to analyze data. We know how to evaluate the validity of studies. If regulatory restrictions provide guardrails to ensure that the data is truthful and presented in context, physicians are fully capable of analyzing such data effectively.

As I noted previously, a reasonable regulatory paradigm lies somewhere between no communication and completely unrestricted communication. However, the current structure is not serving to foster the advancement of medical knowledge, and it leaves many patients and their physicians at an unnecessary disadvantage. Additionally, it seems incongruous that the manufacturer – the entity with the most robust data related to a product – cannot share the information they hold proactively, while any layperson with an internet connection can freely disseminate whatever information they like about that same product, however biased and unreliable.

CLOSING

I hope that my testimony has provided the Committee with a real-world perspective on how current FDA policy is preventing physicians from receiving valuable, clinical information in a timely fashion. In closing, I respectfully suggest that Congress should establish ways to unlock data maintained by manufacturers related to off-label conditions and populations. I thank the Committee for its time and look forward to working with you on policy proposals related to this topic.