



# Off-Label Use of Medical Devices in Children

SECTION ON CARDIOLOGY AND CARDIAC SURGERY, SECTION ON ORTHOPAEDICS

Despite widespread therapeutic needs, the majority of medical and surgical devices used in children do not have approval or clearance from the Food and Drug Administration (FDA) for use in pediatric populations. The clinical need for devices to diagnose and treat diseases or conditions occurring in children has led to the widespread and necessary practice in pediatric medicine and surgery of using approved devices for “off-label” or “physician-directed” applications that are not included in FDA-approved labeling. This practice is common and often appropriate, even with the highest-risk (class III) devices. The legal and regulatory framework used by the FDA for devices is complex, and economic or market barriers to medical and surgical device development for children are significant. Given the need for pediatric medical and surgical devices and the challenges to pediatric device development, off-label use is a necessary and appropriate part of care. In addition, because of the relatively uncommon nature of pediatric conditions, FDA clearance or approval often requires other regulatory pathways (eg, Humanitarian Device Exemption), which can cause confusion among pediatricians and payers about whether a specific use, even of an approved device, is considered experimental. This policy statement describes the appropriateness of off-label use of devices in children; the use of devices approved or cleared through the FDA regulatory processes, including through the Humanitarian Device Exemption; and the important need to increase pediatric device labeling information for all devices and especially those that pose the highest risk to children.

## INTRODUCTION

In the United States, the Food and Drug Administration (FDA) has the responsibility to approve or clear medical and surgical devices for marketing. The regulatory process required by the federal Food, Drug, and Cosmetic Act (21 US Code §301–§399d) classifies medical devices according to risk groups.<sup>1</sup> Medical and surgical devices are assigned a category according to level of complexity and necessary regulatory

## abstract

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oversight. Devices within each of the 3 categories have different regulatory requirements for approval. For example, devices included in the lowest risk category usually require the least rigorous review and often are exempt. New versions of such low-risk devices can be “cleared” using the authority defined under Part A, §360, §510(k) of the Food, Drug, and Cosmetic Act. As devices increase in complexity or risk, FDA approval requirements become more rigorous.

For new high-risk devices, a premarket approval (PMA) application is the most commonly used mechanism to obtain FDA clearance. A PMA must present laboratory and clinical data supporting a conclusion that a device is safe and effective when used as intended. The “intended” or “labeled” use of the device is the only clinical scenario for which the device can be marketed legally. Clinical trials supporting a PMA often involve large numbers of subjects and can be difficult, if not impossible, to accomplish for relatively uncommon pediatric disorders. The expense of such studies can be a barrier to device development because of expected returns from relatively small pediatric markets, in addition to other perceived barriers related to performing studies in vulnerable pediatric populations.<sup>2</sup>

To provide a pathway for approval for uncommon conditions in both children and adults, the FDA uses the Humanitarian Device Exemption (HDE) mechanism to clear or approve devices that are expected to be used in fewer than 4000 patients annually. A device can be approved through an HDE on the basis of data supporting a conclusion that the device has “reasonable safety and probable benefit.” Because of this different standard for approval, the law requires each institution to obtain permission from its institutional review board (IRB)

before the device is used clinically. This IRB requirement has led to the misconception that such devices remain investigational and are not truly FDA approved, which is not the case.<sup>3</sup>

Pediatric patients requiring medical or surgical devices have unique needs relative to adult populations. Fundamental differences in diseases and defects, growth and development, metabolic differences, physiological changes, differences in the natural history of disease, and other factors require medical and surgical interventions that account for these differences. However, unlike drugs, there is no requirement in current law that medical and surgical devices be studied in children as a routine part of device development. For a new drug or drug formulation, if the disease or condition for which the drug is indicated occurs in children, a company is required to study that drug in pediatric populations, as directed by the FDA, although under special circumstances, the studies can be deferred. The FDA also uses the process of the Best Pharmaceuticals for Children Act (21 US Code §355a, §505A [2002]) to provide an incentive for drug companies to conduct studies in children by permitting an additional 6 months of marketing exclusivity. Without an analogous requirement for device development, pediatricians and surgeons regularly are faced with a lack of available medical and surgical devices designed for children.

In the absence of needed devices, pediatricians regularly use devices that are made for adults in pediatric patients. Such “off-label” or “physician-directed” use occurs when a physician or surgeon uses a device for an indication that is not included in the FDA-approved labeling. Off-label device use is common in pediatrics because, in many instances, there is no medical or surgical device available that has

been approved or cleared by the FDA for specific pediatric indications through the PMA, HDE, or other mechanisms.<sup>4,5</sup> Off-label use is legal, is not regulated by the FDA, and is considered by the FDA to be the practice of medicine. Without such use, children may be left with no therapeutic options and, in fact, the off-label use of many devices has become the most common and appropriate practice in pediatrics, often supported by published data, professional guidelines, and expert opinion.

The American Academy of Pediatrics (AAP) supports the off-label use of devices for treatment of certain conditions in children for cases in which their use is deemed by the physician or surgeon to be in a patient’s best interest, in which such use is not being conducted as research, except under specific research protocols, and in which financial conflicts of interest have been disclosed to patients. The off-label use of a medical or surgical device is analogous to the common off-label use of many medications in children.<sup>6</sup>

For children, off-label and HDE-approved devices are often the safest and most effective therapy available. Children will be deprived access to important therapies if payment for such devices is denied.

The AAP recognizes that the use of off-label devices is not ideal, but often is necessary in children. The AAP remains firm in its commitment to specific design, testing, labeling, and market availability for devices specifically for the treatment of childhood medical and surgical conditions.<sup>7</sup> Off-label use may indicate areas in which safety data are lacking and studies about the use of off-label devices are needed. Given the lack of incentives to support device development, testing, and labeling for pediatric indications, the AAP believes that new policies and

funding mechanisms are necessary to meet the needs of children.

As with pediatric drug development, the AAP has advocated to improve the development of medical and surgical devices through advocacy with stakeholders and the federal government. Beginning in 2004, the AAP began meeting with medical societies, advocacy groups, industry, researchers, and government officials to identify and remediate barriers to pediatric device development. One result of these efforts was the passage of the Pediatric Medical Device Safety and Improvement Act (PMDSIA) in 2007 and subsequent reauthorization of the law in 2012. The law's provisions included incentives for device development, regulatory reforms designed to improve available data and facilitate device approvals, and federal funding for new pediatric device development consortia<sup>8</sup> to stimulate innovation. The provisions of the PMDSIA were intended to increase focus and capacity at the FDA to address challenges to pediatric device approval or clearance as well as economic barriers to device development. In particular, for pediatric populations, the PMDSIA repealed a profit limitation on devices approved as HDEs with the intention of improving the economic viability of this pathway for manufacturers. Even with these legislative and regulatory advancements, pediatric device development remains insufficient to meet the therapeutic needs of children across pediatric subspecialties.

## RECOMMENDATIONS

1. Pediatricians should consider off-label or physician-directed use of medical and surgical devices in children as necessary and appropriate when there is no device available that has been approved or cleared

by the FDA for the specific pediatric indication. Such use is often supported in the medical literature, and may be the most common and appropriate practice for many childhood medical and surgical conditions.

2. Policy makers, IRBs, and payers should consider the use of HDE-approved medical and surgical devices as appropriate and not investigational. The HDE mechanism often is the only pathway to FDA clearance for devices used in fewer than 4000 patients annually.
3. Public and private payers should approve payment for off-label and HDE-cleared devices when the use of such devices is directed by a physician, when the use of such devices provides effective therapy, and when equivalent therapy is not available with other specifically labeled devices.
4. Appropriate government agencies should take steps necessary to increase FDA-approved pediatric labeling for all medical devices, especially for the highest-risk devices that are used in children.
5. The FDA, National Institutes of Health, and other policy makers should vigorously explore opportunities to facilitate and encourage the design and testing of medical and surgical devices specifically for children through scientific and regulatory innovation, including increasing pediatric expertise within relevant agencies.

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## ABBREVIATIONS

AAP: American Academy of Pediatrics  
FDA: Food and Drug Administration  
HDE: Humanitarian Device Exemption  
IRB: institutional review board  
PMA: premarket approval  
PMDSIA: Pediatric Medical Device Safety and Improvement Act

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