TESTIMONY OF
DIANE EDQUIST DORMAN
VICE PRESIDENT
NATIONAL ORGANIZATION FOR RARE DISORDERS

before the

ENERGY AND COMMERCE COMMITTEE
HEALTH SUBCOMMITTEE

U.S. HOUSE OF REPRESENTATIVES

MAY 16, 2007

Department of Public Policy
1050 17th Street, NW
Suite 600
Washington, DC 20036
(202) 496-1296

Mr. Chairman and distinguished members of the Committee, thank you for allowing me this opportunity to testify today regarding the reauthorization of the Medical Device User Fee and Modernization Act (MDUFMA). I would also like to share my views of HR 1494, the Pediatric Medical Device Safety and Improvement Act of 2007.

I am Diane Dorman, Vice President of Public Policy for the National Organization for Rare Disorders (NORD). NORD is a non-profit voluntary health agency dedicated to the identification, treatment and cure of rare diseases through programs of education, research, advocacy and services to patients and families. Because most patients with rare diseases have no or few treatment options, our primary goal is to encourage research and development of new "orphan" drugs and biologics and "humanitarian use devices" (HUD).

NORD is also a member of the Alliance for Drug Safety and Access. ADSA members advocate on behalf of over 31 million patients, including those suffering from HIV/AIDS, Parkinson's disease, spinal cord injuries, paralysis, multiple sclerosis, leukodystrophies, Tourette syndrome, and over 6,000 known rare diseases. Our members also represent over 100,000 providers of care to pediatric patients and individuals with mental illnesses.

Reauthorization of the Medical Device User Fee and Modernization Act (MDUFMA)

NORD believes that the Food and Drug Administration (FDA), in a perfect world, should be fully funded through appropriations, but we recognize that for now user fees are inevitable and crucial to ensure that safe and effective medicines reach the public as quickly as possible. As Vice President of the FDA Alliance Board, we support the concept of user fees for medical devices as one of several measures needed to assure adequate funding for FDA.

The Need for Safe and Effective Medical and Surgical Devices for Children

For the past several years, NORD has worked in concert with the American Academy of Pediatrics, the Elizabeth Glaser Pediatric AIDS Foundation, and other stakeholders, including the device industry, in the hopes of identifying a pathway by which medical device manufacturers would be encouraged to develop and then manufacturer devices for the pediatric population.

Simply put, children need medical devices that meet their unique needs. Devices must take into account the small size of children and accommodate their growing and changing bodies and active lifestyles. Yet, doctors continue to be frustrated by the lack of modern medical devices for children.

Children deserve access to devices that are safe, effective, and made just for them. But today's devices are not made with these considerations in mind, and some vital, life-saving devices are not made at all. Because pediatric disease is generally rare, there is a relatively small market for pediatric devices and there appears to be little incentive for device manufacturers to make them.

So today, I testify before you to express NORD's strong support for the Pediatric Medical Devices Safety and Improvement Act (HR 1494), and to express my deep gratitude to Mr. Markey, Mr. Mike Rogers, Mrs. Eshoo, Mrs. Capps, Mr.Grijalva, and Mr. Ramstad, for their commitment to achieve safe and effective medical devices for all children.

This legislation is the result of the extraordinary efforts of all stakeholders, including patient and medical provider groups, and device manufacturers. This bill will help children get the safe medical and surgical devices they need by strengthening safety requirements and encouraging research, development, and the manufacture of pediatric devices.

Device manufacturers face marketplace challenges not experienced by the pharmaceutical and biotechnology sectors because new medical surgical devices quickly become obsolete. Consequently, large markets are needed to justify the development and regulatory costs of devices. As a result, children are frequently denied access to the latest technologies in life-altering or life-saving devices. Doctors are left with only one option. They are forced to jury-rig existing devices in the hopes of accommodating the needs of their young patients.

Defining the Need

This bill streamlines federal agency processes by creating a "contact point" at the National Institutes of Health (NIH and requires FDA, NIH and the Agency for Health Quality and Research to work together to identify important gaps in knowledge, and to improve pediatric medical device development. An important component of this is the ability to survey the pediatric medical providers "rank and file" in order to learn the actual unmet pediatric device need.

Facilitating Pediatric Device Development and Manufacturer through Mentorship

The bill also establishes six-year demonstration grant(s) to support a nonprofit consortium to provide critically needed support in helping the innovators with pediatric device ideas to navigate the "system" successfully. The consortium will match inventors with appropriate manufacturing partners, provide mentoring for pediatric device projects with assistance ranging from prototype design to marketing, and connect innovators with available federal resources. The consortia will also coordinate with the NIH for pediatric device development and the FDA for facilitation of pediatric device approval.

Perhaps had this nonprofit consortium existed previously, it would not have taken Dr. Robert Campbell 14 years to invent, develop and then bring to market the Vertical Expandable Prosthetic Titanium Rib (VEPTR) (Exhibit I). Dr. Campbell is a pediatric orthopaedic surgeon, and Professor of Orthopaedics at the University of Texas Health Science Center at San Antonio, Texas. The Titanium Rib was invented in 1987 to save the life of a six-month-old with scoliosis and missing ribs who was full-time ventilator-dependent. It was not until August 2004 that Synthes' Humanitarian Device Exemption application was finally approved.

Improving the Humanitarian Device Exemption (HDE)

The Humanitarian Device Exemption was meant to be a tool for approving devices intended for small populations, which often included children and those with rare conditions. The specific criteria for the approval of a humanitarian use device (HUD) are:

- Expected to benefit fewer than 4,000 people in the U.S. per year;
- No comparable device is marketed;
- Patient will not be exposed to "unreasonable or significant risk of illness or injury; and,
- The potential benefits of the device outweigh its risk.

It was originally thought that the restriction on profit would force device manufacturers to conduct full clinical trials and seek pre-market approval from the FDA. That scenario never played out. Instead, the restriction on profits proved to be a barrier to innovation, especially for children.[1] Of the 39 HUDs approved by the FDA only seven are specifically intended for use in the pediatric population.[2]

[1] Currently, device manufacturers can only recoup the costs of research and development, fabrication, and the distribution of the device.
[2] There are 41 devices listed on the FDA web site. However, two HUDs have been withdrawn.

Device Name	Incidence	Device Description/Device Indications
Karl Storz Semi-Rigid TTS Fetoscopy Instrument	3,800	The Karl Storz TTS Fetoscopy Instruments Sets are indicated for selective laser photocoagulation in the treatment of twin-to-twin transfusion syndrome for fetuses whose gestation age is between16 and 26 weeks.
Vertical Expandable Prosthetic Titanium Rib	500	For the treatment of Thorasic Insufficiency Syndrome (TIS) in skeletally immature patients. Categories include: Flail Chest Syndrome, Rib fusion and scoliosis, hypoplastic thorax syndrome, including Jeune's syndrome, Achondroplasia, Jarcho-Levin syndrome, Ellis van Creveld syndrome
DeBakey VAD Child Left Ventricular Assist System	737	For use to provide temporary left side mechanical circulatory support as a bridge to cardiac transplantation for pediatric patients who are in NYHA Class IV end stage heart failure, are refractory to medical therapy and who are listed candidates for cardiac transplantation.
CONTEGRA Pulmonary Valved Conduit	3,756	The CONTEGRA Pulmonary Valved Conduit is indicated for correction or reconstruction of the Right Ventricular Outflow Tract in patients aged less than 18 years with any of the following congenital heart malformations: pulmonary stenosis, tetralogy of Fallot, Truncus arteriosus, transposition with ventricular septal defect, pulmonary atresia.
Shelhigh Pulmonic Valve Conduit Model NR-4000 with "No-React®" Treatment	3,275	For replacement of the diseases, damaged, or absent pulmonic artery in small children or infants to age 4 years.
Kings College Hospital Fetal Bladder Drainage Catheter	2,241	For urinary tract decompression following the diagnosis of post-vesicular obstructive uropathy in fetuses 18 to 32 weeks gestational age.
Harrison Fetal Bladder Stent Set	3,112	For fetal urinary tract decompression following the diagnosis of fetal post-vesicular obstructive uropathy in fetuses of 18 to 32 weeks gestational age.

By eliminating the profit prohibition for children, the bill increases the incentive for companies to manufacture pediatric devices, especially the small manufacturers who are likely to embrace an affordable pediatric device development pathway with definable, affordable regulatory requirements.

Tracking Pediatric Device Approvals and Streamlining Device Development

HR 1494 makes improvements in the way FDA tracks the number and type of devices approved for use in children or for conditions that occur in children. At present, FDA cannot satisfactorily produce data on the number and type of devices marketed for pediatric uses. The bill requires FDA to track new devices granted pre-market approval or approved under the humanitarian devices exemption and report on the number of pediatric devices approved in each category.

Strengthening Post-market Safety

In addition to the important incentives for pediatric device development proposed in HR 1494, the bill also ensures that medical devices used in children are safe. The Institute of Medicine conducted a thorough review of pediatric medical devices and found that FDA lacked significant capacity and authority for post-market monitoring and surveillance of devices in children (Exhibit II). The legislation provides the authority for FDA to order post-market surveillance of devices used in children, only when needed, and broadens the reach of the authority to the most commonly used pediatric devices. In addition, FDA is granted important flexibility to order longer post-market surveillance if necessary to ensure that the device remains safe in children's growing bodies. The new safety protections in HR 1494 are essential to keep children safe while the incentives provisions stimulate new devices that meet their medical needs.

Reimbursement for Humanitarian Use Devices (HUDs)

I would like to address an issue not contained in HR 1494, but of great concern to the rare disease community. Humanitarian Device Exemptions (HDEs) are a special type of marketing approval granted for humanitarian use devices intended to treat fewer than 4,000 people a year in the United States. Rare disease patients benefit greatly from HDEs and need their development to be encouraged in any appropriate way.

FDA has been very sensitive to the value of HUDs and has made clear that HUDs are legally marketed products and not experimental products. I have attached a page to my testimony that illustrates the lengths the FDA has gone to clearly establish that HUDs are legally marketed (Exhibit III). For this, the rare disease community is grateful.

Nonetheless, insurers and government programs often will not reimburse the use of HUDs on the basis that they are experimental. In effect, they ignore FDA's regulations on the status of these devices. This is disheartening to the rare disease community and frustrating because FDA policy is so clear: the agency stands behind these devices by treating them as legally marketed.

We believe that the situation could be improved if the current FDA regulatory policy were to be codified in statute. This will make it more difficult for reimbursement to be denied by making clear that FDA's position is backed by Congress. NORD would welcome the opportunity to accomplish this by working with committee staff and FDA to draft appropriate language for inclusion in HR 1494.

Conclusion

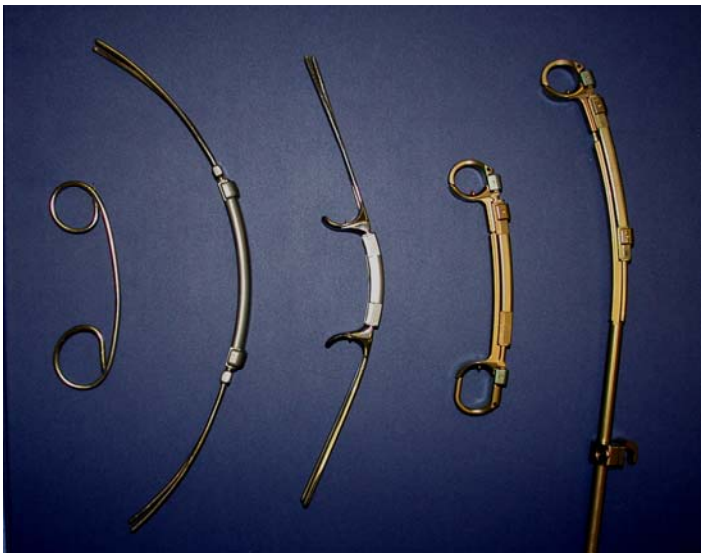
I want to thank the Committee for allowing me the opportunity to share my views on reauthorization of the Medical Device User Fee and Modernization Act (MDUFMA), and most importantly, the "Pediatric Medical Devices Safety and Improvement Act of 2007."

HR 1494 represents an historic step forward for children's medical and surgical devices similar to those steps taken on drugs. Children deserve access to devices that are safe, effective and made just for them. Children need medical devices that take into account their smaller size, growing bodies, and active lifestyles.

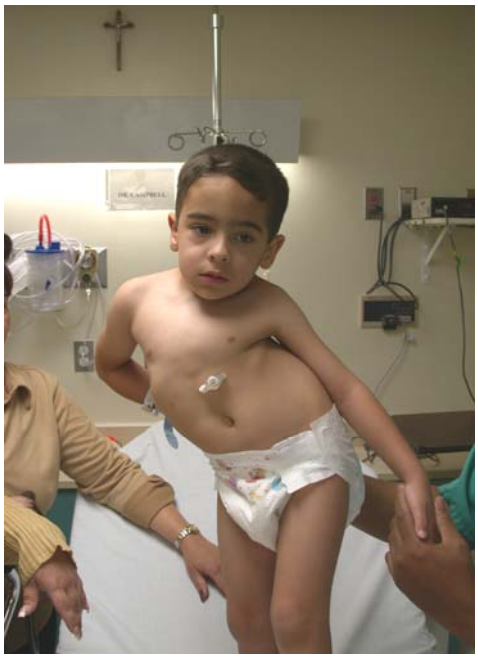
Thank you.

Exhibit I

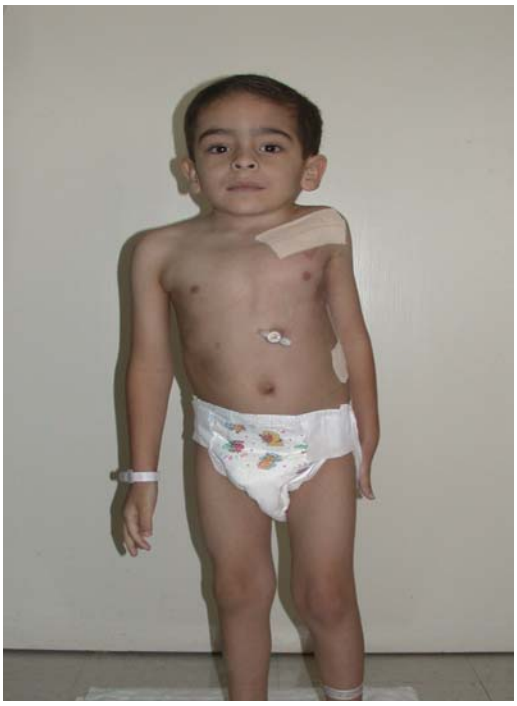
Vertical expandable Prosthetic Titanium Rib (VEPTR)



Before Surgery…



After Surgery…



Today…

Exhibit II

Institute of Medicine
"Safe Medical Devices for Children"
Complete List of Recommendations
July 18, 2005

Adverse Event Reporting

Recommendation 4.1: FDA should collaborate with industry, health care professionals and organizations, and parent and patient advocates to:

- focus more attention on adverse device events, including events involving children;
- promote linkages between adverse event reporting systems, various FDA databases, and other safety programs;
- update product labeling, patient information, and other communications to promptly reflect safety-related findings from analyses of adverse event reports; and,
- issue yearly reports on results from adverse event analyses, including findings involving children.

Recommendation 4.2: FDA should continue educational and communication programs to promote recognition and useful reporting of serious adverse device events and device problems by hospitals and other user facilities. Such encouragement should continue whether or not requirements for mandatory reporting by user facilities are eventually eliminated with the effective implementation of the MedSun program. Reporting by user facilities of events possibly related to devices should continue to include deaths, serious injuries, and device malfunctions.

Recommendation 4.3: FDA's plan for evaluating MedSun's performance as a replacement for and improvement on mandatory user facility reporting should include, among other elements:

- assessment of ongoing program and participant facility success in educating facility personnel about identifying, evaluating, and reporting adverse device events and improving the quality, timeliness, and usefulness of event reports;
- determination of the extent to which the sample of MedSun participating hospitals-including children's hospitals-represents the relevant range of facility characteristics and experiences, including representation of both academic medical centers and community hospitals and sufficient representation of facilities with device-oriented specialties and procedures;
- comparison with the mandatory user facility reporting system, including the extent to which either program produced reports for FDA or manufacturers of emerging hazards, important close calls, or other significant events (including those involving children) that were missed or delayed by the other; and
- evaluation of the active surveillance components if the program is instrumental in reducing harm to patients, promoting constructive communication between facilities and FDA, and improving timely knowledge of the nature and extent of selected device problems, including errors in the use and design of devices.

Recommendation 4.4: Within the pilot MedSun program, FDA and participating children's hospitals should serve as a resource for the broader involvement of children's hospitals in patient safety programs to identify, evaluate, respond to, or prevent problems with the use and design of medical devices. In addition, FDA should promote efforts to link or otherwise employ event reporting, device recall, safety notification, and other databases within and outside FDA to better assess and report on device safety issues involving children.

Recommendation 4.5: When FDA mandates or agrees to device labeling that requires professionals to be trained in the safe and appropriate use of a medical device, the training should include information on the identification of adverse events, voluntary adverse event reporting under Med Watch, and user facility and manufacturer medical device reporting (MDR) requirements.

Recommendation 4.6: Medical, surgical, and other organizations or societies that include health professionals who care for children should:

- establish working groups to evaluate problems as well as benefits in the pediatric use of devices of particular importance to their practice;
- collaborate with existing public and private patient safety initiatives to add or expand attention to safe and appropriate use of medical devices with children;
- establish standards for professional education and competency in the use of these devices; and
- include as professional competencies the identification and appropriate reporting of device problems and the successful communication with patients and families about how to prevent, recognize, and respond to device problems.

Recommendation 4.7: Children's hospitals and other user facilities should establish a focal point of responsibility for medical device safety. Tasks include reviewing and monitoring the adequacy of institutional programs in areas such as tracking of safety alerts and recalls, responding to safety alerts and recalls training in adverse event evaluation and reporting, and factoring safety data or evaluations into device purchased decisions.

Recommendation 4.8: FDA should continue t o improve and expand its medical device safety resources for patients and families and its focus on devices used in the home and community by:

- working with patient, family, and consumer organizations, providers, and industry to make it easier for patients or their families to report device problems to manufacturers or FDA and to learn about resources to support the safe use of medical devices;
- making online reporting and information resources more accessible by using language and directions appropriate for lay users; and
- enlisting hospitals, home care agencies and vendors and other professional and provider groups to promote patient and family understanding of how to use devices safely, when and how to seek help, and when and how to report problems.

Monitoring Study Commitments

Recommendation 5.1: Congress should require FDA to establish a system for monitoring and publicly reporting the status of post-market study commitments involving medical devices. The system should also cover voluntary studies negotiated between FDA and manufacturers as part of the device approval or clearance process. The public database should, among other features, allow easy determination of the status of post-market studies that involve questions about device use with children.

Recommendations 5.2: FDA's system for monitoring and reporting post-market study commitments should include information about the disposition of study findings: for example, a change in the labeling of a device. It should also provide for the responsible and understandable reporting of the source, methods, and findings of monitored post-market studies.

Strengthening Post-market Studies

Recommendation 6.1: FDA should develop additional guidance for its own staff as well as for manufacturers and investigators on the identification and evaluation of pediatric questions at all stages in the design and evaluation of medical devices used with children.

Recommendation 6.2: As part of the government and private health informatics initiatives, such as those supporting the electronic medical record, FDA should promote the development and adoption of common device coding and other standards and approaches for capturing and linking use and outcomes data for medical devices. FDA should also work with agencies such as the Agency for Healthcare Research and Quality university- and industry-based methodologists to strengthen methods and tools for epidemiologic research on medical device safety.

Recommendation 6.3: As a resource for itself and others, FDA should create or collaborate with others to create a registry of relevant registries, that is, a database with information about registries that are either device specific or that have the potential to provide information useful in evaluating device safety and effectiveness.

Recommendation 6.4: As part of the public commitment to post-market surveillance of device safety, the Center for Devices and Radiological Health should have its own extramural research program to support studies using external data sources.

Recommendation 6.5: Congress should amend Section 522 of the Federal Food, and Cosmetic Act to:

- permit FDA to order post-market studies as a condition of clearance for the categories of devices for which Section 522 Post-market Surveillance studies are now allowed and;
- allow FDA to tailor the duration of Section 522 studies of devices likely to have significant pediatric use so that studies can take into account children's growth and development and, if appropriate, exceed the current 3-year limit on study length.

Recommendation 6.6: FDA should collaborate with the National Institutes of Health, the Agency for Healthcare Research and Quality, and other research funding agencies and interested parties to define a research agenda and priorities for the evaluation of the short- and long-term safety and effectiveness of medical devices used with growing and developing children.

Responsibilities for Medical Device Safety

Recommendation 7.1: FDA should establish a central point of responsibility for pediatric issues within the Center for Devices and Radiological Health to evaluate the adequacy of the Center's use of pediatric expertise and its attention to pediatric issues in all aspects of its work.

Recommendation 7.2: All those engaged in improving the quality of health care and protecting patients from harm should evaluate and sharpen, as appropriate, their attention to medical device safety, including safety issues that particularly affect children.

Exhibit III

FDA Views Humanitarian Use Devices as Legally Approved Products

In the preamble of the HUD final rule (FR vol. 61, No. 124, June 26, 1996) there was a discussion of why the provision was being placed in the market regulations (21 CFR 814), rather than the Investigational Device Exemption (IDE regulation 21 CFR 812). To make the point clear, it was decided by the agency to create a new subpart H Part 814 specifically addressing HUDs, thereby further establishing these devices as legally marketed products under the Act. I have appended to this testimony a page of references from FDA regulations that make clear FDA positions that these are legally marketed devices.

The first item below is very clear that FDA considers these to be legally marketed devices and that FDA chose not to put the provision into the investigational device exemption reg. to make that point clear.

1. In the preamble of the HUD final rule (FR vol. 61,No. 124, June 26, 1996) there is a discussion of why the provision was finally being placed in the marketing regulations 21 CFR 814, instead of the Investigational device exemption (IDE) regulation 21 CFR 812. It concludes **"Accordingly, the agency has chosen to create a new subpart H under part 814 specifically addressing HUD's, thereby establishing these devices as legally marketed products under the act".**

2. In the current HUD/HUD regulation 21 CFR 814.100 includes a few citations that "marketing approval" is mentioned.

    a. For example 814.100(a) states "The subpart provides procedures for obtaining (1) HUD designation of a medical device; and (2) **Marketing approval for the HUD** notwithstanding the absence of reasonable assurance of effectiveness that would otherwise be required under sections 514 and 515 of the act.

    b. 814.100(c) mentions **"Obtaining marketing approval for a HUD involves two steps**: (1) Obtaining designation [of the HUD from OOPD] and (2) Submitting and HDE [to CDRH}

    c. 814.126(b)(1)(iii) under Post-approval requirements and reports sates that requires that "The **number of devices that have been shipped or sold since initial market approval under this subpart H"** be submitted in periodic [annual] reports.

Exhibit IV

Humanitarian Use Devices
A brief guide for clinicians, investigators and IRB members
Dale E. Hammerschmidt, M.D.
University of Minnesota; October, 2001

Introduction

Regulations governing the use of medical devices cause a lot of confusion. In part, this is because several sets of statutes and regulations may apply — those involving patient care, those involving research with human subjects, those involving development of medical devices for marketing approval, those involving insurance billing. In part, too, it is because the grey zone is so large between activity that is unambiguously research and activity that is so small a variation on standard technique that it isn't subject to regulation or special scrutiny.

A special class of devices (and a special set of regulatory provisions) causes particularly much confusion: **Humanitarian Use Devices** (HUDs). These devices (and regs) are in the *Never-never Land* between research and ordinary practice – they will probably never make it as commercial products under ordinary licensing rules, but they may be recognized standard or even preferred devices for certain circumstances. In some respects, they may be thought of as a parallel to "orphan" drugs.

What the regs define as a Humanitarian Use Device

A HUD is a medical device that has been granted (by the FDA) a special exemption from some of the requirements for approval before marketing, because its expected market is so small that the studies needed for licensure would simply never be able to be carried out. The general criteria are:

- Expected to benefit fewer than 4,000 people in the US per year (in some FDA information sheets, worded more narrowly as "is designed to treat or diagnose a disease or condition that affects fewer than 4,000 individuals in the United States.")
- No comparable device already available
- No exposure to "unreasonable or significant risk of illness or injury"
- Potential benefits of the device outweigh its risks.

Obviously, these criteria are a bit subjective, but that's not the *direct* worry of the local investigator or the IRB, as this determination is made by the FDA.

What's different about an HUD?

The main difference is a direct result of the small target group of patients. An HUD is expected never to be able to get the type of efficacy data required for an ordinary Pre-Market
Approval by the FDA, so it has its own special category of "approval," called a Humanitarian Device Exemption. This "approval" retains some of the flavor of the more usual clearance for research (the "IDE" or "Investigational Device Exemption"), including IRB oversight and limitations on the ability to charge for the device. The freedom of the clinician/investigator to use the device for other than its label indications is also restricted.

What this means in practical terms

• Before the first use of an HUD in an institution, the clinician intending to use the device must obtain IRB approval (stipulated in regs at 21 CFR 814.124(a), so not much "wiggle room" available). The applicant may request approval for several patients so that it is already in place the next time; case-by-case IRB oversight is not required unless the IRB for some special reason decides it to be necessary.
• IRB review has to be by a convened quorum; it cannot be by expedited review (even though this might at first blush seem to fit expedited review criterion 1[b][i] for those devices judged to pose no more than minimal risk).
• The informed consent requirements are the ordinary *clinical* requirements rather than the special requirements for research; most IRBs still require documentation that the patient has been told that the device has not been licensed in the ordinary manner (and/or that it has not been proven to be safe and effective by the usual criteria).
• IRB continuing review (annual or more frequent) is required, just as for other devices under development.
• Off-label uses require IRB scrutiny and notification of the manufacturer, and may require an amendment to the HDE.
• Off-label use that is an emergency, or first use that is an emergency that cannot wait for IRB action, is handled according to basically the same rules applied to the emergency use of an investigational drug or device of any other type:

- Life-and-limb-threatening emergency
- No other more standard (or already IRB-approved) intervention available with reasonable chance of success
- No preclusive regulatory barriers (*i.e.* within HDE provisions, or steps begun to obtain special approval) (usually handled by emergency communication with HDE sponsor)
- Urgency of situation does not allow time for IRB review
- (If consent must be waived) Physician uninvolved in patient's care concurs
- *Not in the regs* per se, *but both FDA policy and local policy provide that an attempt be made to screen the proposed use with an IRB officer, who can walk the applicant through the criteria and begin the required administrative process*
- Formal report to IRB within 5 working days; formal application if additional patients likely.

Conclusion

The use of Humanitarian Use Devices creates confusion, because they are in some ways regarded as not being research (consent requirements and some aspects of billing) and in other ways are regarded as research (IRB review). The simplest approach is just to treat them as though they were ordinary research devices under the usual sort of IDE, but be open to a lesser requirement for documentation of consent. Most of the other special features of HUDs pertain to aspects other than the on-site regulatory and oversight requirements faced by the IRB and the clinician/investigator.

See http://www.fda.gov/cdrh/ode/guidance/1381.pdf *for the most recent (July, 2001) FDA guidance document. An additional, more general FDA website addressing device issues is* http://www.fda.gov/cdrh/devadvice/dd_home.html

Exhibit V

POST-MARKET SURVEILLANCE

"SEC. 522. *7 [21 U.S.C. 360l] (a) IN GENERAL.—The Secretary may by order require a manufacturer to conduct post-market surveillance for any device of the manufacturer which is a class II or class III device the failure of which would be reasonably likely to have serious adverse health consequences or which is intended to be—*
(1) implanted in the human body for more than one year, or
(2) a life sustaining or life supporting device used outside a device user facility.
(b) SURVEILLANCE APPROVAL.—Each manufacturer required to conduct a surveillance of a device shall, within 30 days of receiving an order from the Secretary prescribing that the manufacturer is required under this section to conduct such surveillance, submit, for the approval of the Secretary, a plan for the required surveillance. The Secretary, within 60 days of the receipt of such plan, shall determine if the person designated to conduct the surveillance has appropriate qualifications and experience to undertake such surveillance and if the plan will result in the collection of useful data that can reveal unforeseen adverse events or other information necessary to protect the public health. The Secretary, in consultation with the manufacturer, may by order require a prospective surveillance period of up to 36 months. Any determination by the Secretary that a longer period is necessary shall be made by mutual agreement between the Secretary and the manufacturer or, if no agreement can be reached, after the completion of a dispute resolution process as described in section 562."

Exhibit VI

Few medical devices exist for sick infants

Sunday, April 22, 2007
BY ROBERT COHEN
New Jersey Star-Ledger Staff

At the Bristol-Myers Squibb Children's Hospital in New Brunswick, pediatricians have had to scramble to deliver medicine to infants with life-threatening cardiac problems when the veins of the babies were too small to use IVs and infusion pumps.

"In such cases, you have to use needles to get into the bones and many times, they are not the right size for little babies. The needles are pretty big,' said Ernest Leva, director of pediatric emergency medicine at the hospital.

"You just keep trying. If you can't get the children the medicine they need, they could become impaired or die," he said. "These situations don't happen that often, but when they do, they can be tragedies." The dilemma described by Leva is common.

There is a big availability gap when it comes to external and implanted medical devices for children, with doctors often forced to jury-rig adult devices for diagnosis and treatment that weren't designed for small bodies.

Congress is seeking to address this problem with legislation that would offer incentives to manufacturers to create medical devices designed specifically for children. The bill also would establish grants for nonprofit groups to promote pediatric device development and help link inventors with manufacturers.

"While we all know children are not simply small adults and should not be treated as such, the pediatric market is so small and pediatric diseases relatively rare, there has been little incentive for medical-device manufacturers to focus their attention on children," said Sen. Chris Dodd (D-Conn.), sponsor of the Pediatric Medical Device Safety and Improvement Act.

The measure is included in a multifaceted Senate bill that gives the Food and Drug Administration added drug safety authority, renews the user fees paid by the pharmaceutical and device industries to the FDA, and re-authorizes a law to increase the number of drugs tested and labeled for children.

The sweeping legislation was approved by the Senate Health, Education, Labor and Pensions Committee last week. A similar measure is pending in the House, with lawmakers hoping for final passage by the summer.

Jay Berkelhamer, president of the American Academy of Pediatrics, said there is a critical need for medical devices manufactured for children.

"Although children and adults often suffer from similar diseases and conditions, their medical needs and physiology differ considerably," he said.

One example of the problem, Berkelhamer said, is advanced chemotherapy catheters that are too large for infants, requiring them to use less-advanced tubing that leaves children more vulnerable to infection. Another example: Devices that keep a failing heart beating while a patient waits for a transplant, known as left ventricular assist de vices, aren't available for children age 5 and younger.

In other cases, physicians have had to resort to invasive procedures when a baby needs assistance breathing because even the smallest nasal masks on the market aren't designed to fit infants.

Ed Rozynski, vice president of Stryker, a maker of orthopedics and other medical devices, said his company makes a bone-replacement implant for children with cancerous tumors that can be elongated to account for a child's growth. Stryker also makes plates and screws specially for children undergoing skull surgery.

But Rozynski, whose company has two manufacturing facilities in Bergen County, told a Senate committee last month the market is "very small" for pediatric devices and the hurdles of developing such products are high.

"The cost of developing a new medical device and performing the required pre-market clinical studies can be enormous, often steering some manufacturers to serve larger, more established and well- known adult medical device markets," Rozynski told lawmakers.

He said provisions in the pending legislation, including allowing a profit for companies marketing products under the so-called humanitarian device exemption, will "likely spur companies to develop pediatric products they otherwise might not have."

A humanitarian device exemption is special approval given by the FDA that allows the marketing of a device that is designed to treat or diagnose a condition that affects fewer than 4,000 individuals per year. The approval is granted even though the effectiveness of the de vice hasn't been tested or proven, because it isn't financially feasible to do the usual clinical testing when so few individuals are affected. While allowing companies to recover their costs, existing law prohibits them from making a profit.

The legislation by Dodd and Rep. Ed Markey (D-Mass.) would lift the profit restriction for sales of up to 4,000 a year.

In addition, the bill would:

- Require the National Institutes of Health to designate a contact point or office to help inventors and physicians access funding for pediatric medical device development.
- Grant authority to the FDA's Pediatric Advisory Committee to monitor pediatric devices and make recommendations for improving their availability and safety.
- Incorporate recommendations of the Institute of Medicine, including improving the post-market surveillance of medical devices used in children and expanding public access to post-market studies of pediatric devices.