Testimony of

Robert M. Campbell, Jr., M.D.

Professor of Orthopaedics
University of Texas Health Science Center at San Antonio

before the

United States Senate Committee on Health, Education, Labor, and Pensions

"Ensuring Safe Medicines and Medical Devices for Children"

March 27, 2007

Chairman Kennedy, Senator Enzi, and members of the committee, thank you for this opportunity to testify today regarding safe medicine and medical devices for children.

I am Dr. Robert Campbell, a pediatric orthopaedic surgeon, an inventor, and the father of five children. I am a Professor of Orthopedics at the University of Texas Health Science Center at San Antonio and hold the President's Council/Dielmann Chair in Pediatric Orthopaedic Surgery. I work primarily at Christus Santa Rosa Children's Hospital in San Antonio. I am a specialty surgical fellow of the American Academy of Pediatrics and serve on the Medical Advisory Committee of the National Organization of Rare Disorders. Throughout my career, I have cared for children in need of medical technology that was not readily available to them and my work has made me keenly aware of the need for better medical devices for children.

The primary reason I was invited to appear before you today is that I invented, developed, and brought to market a life saving pediatric surgical device known as the Vertical Expandable Prosthetic Titanium Rib (VEPTR), which was approved as a Humanitarian Device Exemption (HDE) device in 2004 after 14 years of FDA trials (see attached). I am here to help provide you with some insight about the problems of pediatric device development from someone who has "been in the trenches" and about how this pending legislation can help the children who need devices.

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

Mr. Chairman, as a pediatric orthopaedic surgeon, I am very pleased to hear my colleague, Dr. Gorman, describe the gains made in the field of pediatric pharmacology as a direct result of actions taken by Congress. I support his view that the Best Pharmaceuticals for Children Act and Pediatric Research Equity Act are critical laws to children and must be reauthorized. But just as the need existed in 1997 when this committee and Congress acted to help children by increasing the study of drugs, Congress now has the opportunity to take the same kind of action with an equally important need: children's medical and surgical devices.

As a surgeon who has treated the orthopaedic diseases of children for over twenty years, I have been frustrated many times that the "shelves are bare" when I need a modern device for their care. A surgeon from the 1950s would recognize many of the pediatric instruments and devices in my operating room because there has been little progress. We pediatric sub-specialists are an endangered species, with less physicians each year choosing to join our ranks for complex reasons, especially in orthopaedics,[1,2] and one reason for this may be that we don't have the up-to-date technology to care for children that is available to our adult counterparts.

[1] Huurman W. Report of the Pediatric Orthopaedic Work Force Committee of the Pediatric Orthopaedic Society of North America. 2003.

[2] Bell MJ, Catterall A, Clarke NMP, Hunt DM. "Children's Orthopaedics and Fracture Care." Special Report. British Orthopaedic Association. July 2006.

Children need medical devices that meet their unique needs. Devices for children should take into account their smaller size, accommodating their growing bodies and active lifestyles.

Children deserve access to devices that are safe, effective, and made just for them. Yet today many devices are not made with these considerations in mind, and some necessary devices are not made at all. Because pediatric disease is generally rare, there is a relatively small market for pediatric devices and there appears little incentive for device manufacturers to make them. Device manufacturers have different marketplace challenges than pharmaceutical companies. New medical and surgical devices quickly become obsolete, so large markets are needed to justify their development and regulatory costs. As a result, children are frequently denied access to the latest technology in life-changing or life-saving devices. Other times, physicians must "jury-rig" existing devices to accommodate their young patients.

But when children need a medical device that is unavailable, the consequences can be tragic. Twenty years ago, I became involved with a child that needed a pediatric device to survive that did not exist. Instead of accepting the inevitable, we decided to do whatever was necessary to provide him with a chance for life. None of us at the time had the slightest idea about how to develop a medical device, but since it was critically needed, we had to try it. None of us realized the ultimate cost of that decision, and how it would take 16 years from drawing the first blueprint to having an approved pediatric implant available on the "device shelf " for other surgeons to use. I wish to share what we learned through that experience.

The Titanium Rib Saga

The Vertical Expandable Prosthetic Titanium Rib (VEPTR) device, also known as the titanium rib, was invented to save the life of a 6-month-old full-time ventilator-dependent infant born with scoliosis and missing ribs.

In 1987, Dr. Melvin Smith, a pediatric general surgeon, was consulted by the family about tracheostomy care of this child. Although he was expected to die soon, Dr. Smith felt it might be possible to salvage the situation somehow and he asked me to get involved in a last ditch effort to safe his life. There was no known commercially available chest wall prosthesis for this age group, and there was no way to stabilize his scoliosis without stopping growth of the spine. We managed to come up with a possible solution and, with nothing to lose, the family gave us permission to operate on the child as soon as possible. At surgery we "jury-rigged" an artificial chest wall of orthopaedic fracture pins, wired vertically to support the lungs and control the scoliosis. It was a difficult surgery, but to our amazement, it worked, and days later the infant was weaned off his ventilator for the first time and went on to be weaned off oxygen. We were very happy about the initial outcome.

But since our patient survived and was growing, we were now faced with new problems. The crude "jury-rigged" chest wall device would not grow with the patient, and the lung underneath would try to grow, but would eventually be compressed with adverse effect on its growth. The non-growing fracture pins would also tend to tether the growing spine and worsen the scoliosis. We could change out the crude device frequently in major surgery, but sooner or later we would have a catastrophic complication.

A new device had to be invented for this child and it needed to be safe to implant, just as effective as the "jury-rigged" device, but expandable in a simple fashion with minor surgery to avoid major complications. And it was needed quickly. I promised Dr. Smith that I could develop such a device with my engineering background, and assumed it would be an easy matter to get an orthopaedic manufacturer to make it. The confidence of the naïve is boundless.

The engineering blueprints of the first VEPTR device were drawn up ten months later. It was a simple metal device with only two moving parts that could perform the same function as the fracture pin device, but was safer to implant and easy to expand as the child grew. I thought the job was mostly done at that point, but little did I realize that I had just made the first small step in a very long journey. I contacted multiple orthopaedic companies to make the device. They were sympathetic, but did not have the resources to make a pediatric device for one patient with a rare birth defect. I was getting discouraged as the months went by and the patient grew worse.

Finally, an orthopaedic custom device company, Techmedica Corporation of Camarillo, California, was recommended to me and they seemed receptive to making the device. Although they knew that making a completely new pediatric device would cause a substantial financial loss for them, with little hope of enough subsequent patients to recover development costs, they proved to be advocates for children and did accept the challenge. All they asked for in return was that, if the surgery proved to be successful, we would publicize their role in the surgery. We began an emergency effort to quickly produce a working device.

Six months later the first VEPTR device was manufactured and we successfully replaced our "jury-rigged" device with it in April 1989. When news of the new surgical device for rare birth defects of the spine and chest wall came out, we were inundated with desperate families trying to find treatment for their children. We were able to develop five new surgeries to help these children using the VEPTR device as its basis, but there was too much patient volume to continue treatment under the custom device provisions, so the FDA was approached for guidance. I was asked to provide a personal briefing for the FDA chief of devices. He was quite supportive of our efforts to develop a new implant for these lethal birth defects, and authorized a sole site FDA feasibility study which was began in 1991 with Techmedica Co. as the sponsor.

Things went well for the next few years with encouraging clinical results. To their credit, members of the FDA permitted several minor modifications of the device by Techmedica

Co. during this time to enhance pediatric patient safety. This was cited by the 2005 Institute of Medicine Report "Safe Medical Devices for Children" as a favorable example of pediatric device development.

During this period we received critical seed grant funding from the National Organization of Rare Disorders to support our research. Based on the preliminary clinical trial results made possible by the NORD support, we were able to secure further substantial grant support from the FDA Office of Orphan Product Development that enabled us to complete our sole site FDA study and initiate a multi-center FDA VEPTR trial.

A few years into the feasibility trial we were devastated to learn that Techmedica Corporation was to be closed by their large corporate parent. New patients needed VEPTR devices, and treated patients needed new larger devices because of growth, but we now had no way to provide them. We needed a new guardian angel to make the VEPTR, but had no idea where to find one. Incredibly, the angel found us.

Soon after the Techmedica Co. closure, I was approached during an orthopaedic trauma course by a device product manager with the Synthes Spine Company, Mr. Paul Gordon, who was interested in knowing more about the VEPTR device. We soon learned he was a champion for pediatric patients. He convinced us that his company had the resources and the commitment to children to successfully take over the development of the VEPTR device. Through his efforts, I next met with upper management of the company and, eventually, the private owner of this major spine company, Mr. Hansjorg Wyss.

Mr. Wyss proved to also be an advocate for children and, although the device had little chance of producing a profit, he gave his full support in 1994 for the engineering refinement of the VEPTR device and for involvement of the Synthes in-house regulatory division in the design of a FDA VEPTR multi-center trial. A large investment was made to upgrade the VEPTR device to a more standardized design that was easier to implant, and the multi-center Synthes VEPTR trial began in 1996.

The first new hospitals to join the VEPTR FDA multi-center trial were Children's Hospital of Pittsburgh and then Boston Children's Hospital. Another five children's hospitals eventually joined the study. These hospitals provided additional experience with VEPTR treatment to confirm the San Antonio results of safety and effectiveness, and by 2001 there appeared to be adequate experience to consider an FDA application for approval, but in 2002 FDA brought up a concern that there were no controls for the VEPTR study. Subsequently a Humanitarian Device Exemption (HDE) application was filed by Synthes in 2003 with approval by the FDA on August 24th, 2004, concluding the 14 year FDA study of the VEPTR device.

The Lessons Learned from the VEPTR Experience

I made many mistakes in developing this device over those fourteen years. I had no mentor. I had no experience in developing a device from an engineering viewpoint. I had

no knowledge of the FDA requirements for device development. It was basically a trial and error experience for many years.

I did not know which manufacturer was the best choice for VEPTR. Small companies can be responsive to small pediatric projects, but do not have large budgets for device development or the regulatory resources to secure FDA approval. Large publicly owned companies have those resources, but can't justify non-profit pediatric device projects to their stockholders. We were extremely lucky that we found companies who could be responsive to the needs of children in spite of the many obstacles. Many individuals at the FDA clearly were advocates for development of children's devices, but a clear and transparent regulatory pathway for VEPTR approval did not exist. I had limited knowledge about what financial resources were available for support of the VEPTR study. The grants of the National Organization of Rare Disorders and the Orphan Products Division of the FDA were crucial support for the success the VEPTR trial, but additional resources would have been helpful for a study that eventually took 14 years to complete. There were numerous additional problems during the VEPTR trial that could have been better addressed if we had access to resources and mentorship, but they did not exist at the time.

The VEPTR pediatric device is now available for children only through hard work by many individuals across the United States, commitment of device manufacturers without regard for their economic well-being, and luck. Many hundreds of other pediatric devices have never been developed and probably won't be under current conditions. With what I have learned from the VEPTR experience, I have gone on to personally help mentor a handful of physicians trying to develop devices for children, but really a broad, expert, well-organized national system is needed for this. Children deserve better. Legislative and regulatory changes are absolutely necessary so that others not have to have the same struggle as we did.

My chance to contribute to a new approach to pediatric device development began in June 2004, when I came to Washington, D.C. from San Antonio to participate in a series of meetings hosted by the American Academy of Pediatrics, Elizabeth Glaser Pediatric AIDS Foundation, National Organization for Rare Disorders (NORD), the National Association of Children's Hospitals, and the Advanced Medical Technology Association (AdvaMed). The "stakeholder" meetings resulted in a series of recommendations for improving the availability of pediatric devices. Those meetings were a key turning point in that they were the first broad-based dialogue that engaged stakeholders in all aspects of pediatric devices from health care providers, manufacturers, and federal government regulators.

Subsequently, the Institute of Medicine produced a strong report in 2005 entitled, "Safe Medical Devices for Children." The IOM found flaws in safety monitoring and recommended expanding the FDA's ability to require post-market studies of certain products and improving public access to information about post-market pediatric studies. IOM reported:

> [T]he committee must conclude that FDA has lacked effective procedures to monitor the fulfillment of postmarket study commitments. The agency has lacked a basic, searchable listing of devices for which further studies were specified as a condition of their approval for marketing. Furthermore, it has not maintained any system for systematically monitoring the status of these study commitments based on periodic reports or updates from either its own staff or sponsors.[3]
>
> FDA can ask for clinical studies prior to clearing devices, although clinical data are submitted for only a small percentage of devices that go through clearance. FDA cannot, however, order postmarket studies as a condition for clearance. It can (but rarely does) order studies subsequent to clearance through its Section 522 authority. Studies that are ordered subsequent to the approval or clearance of a device are limited to 3 years (which often means a shorter period of evaluation for most individual study subjects). This may be too short a period for certain safety problems or developmental effects to be revealed.[4]

In July of 2005, the American Academy of Pediatrics established the Task Force on Pediatric Medical Devices to work with Congress to advance legislation to meet medical and surgical device needs of children. I am pleased to be a member of the Task Force.

The recommendations produced by the stakeholder meetings in 2004 and the IOM report on device safety in 2005 point to the need for Congress to pass legislation that both stimulates device development and manufacture as well as increases the safety monitoring of pediatric medical devices, particularly after they are on the market. The Pediatric Medical Device Safety and Improvement Act 2007, S. 830, strikes the right balance and puts forward a comprehensive package that serves a critical step forward for children.

Support for the S. 830, the Pediatric Medical Devices Safety and Improvement Act

I am here today to express my strong support of S. 830 and to express my sincere gratitude to Senator Dodd for his commitment to achieving safe and effective medical devices for all children. This legislation is the result of huge effort put forward by present and former members of this committee, patient and 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 manufacture of pediatric devices. The following provisions address many of the obstacles we faced when developing the VEPTR device for children.

Defining the Need for Pediatric Devices.

[3] Field MJ and Tilson H. eds. Safe Medical Devices for Children, Committee on Postmarket Surveillance of Pediatric Medical Devices, Board on Health Sciences Policy; Institute of Medicine of the National Academies, 2005, p. 195.
[4] IOM, p. 226.

The 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 on identifying important gaps in knowledge and 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 needs.

Facilitating Pediatric Device Development and Manufacture through Mentorship.
The bill also establishes six-year demonstration grant(s) to support nonprofit consortia to provide critically needed support in helping the innovators with pediatric device ideas to navigate "the system" successfully and bring new pediatric devices to market. 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 "contact point" for pediatric device development and the FDA for facilitation of pediatric device approval.

Improving the Humanitarian Device Exemption (HDE).
The Humanitarian Device Exemption (HDE) was meant to be a tool for approving devices intended for a small populations (less than 4,000 patients), which often included children and those with rare conditions, but the profit restriction on HDE-approved devices limits the effectiveness of the provision by forcing device manufacturers to only recover their research and development costs. 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.
S. 830 makes needed 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 premarket approval or approved under the humanitarian devices exemption and report on the number of pediatric devices approved in each category.

Strengthening Postmarket Safety
As recommended by the IOM, this bill grants the FDA increased authority to ensure that approved medical devices are safe for children. Under this law, the FDA would be able to require postmarket studies as a condition of approval or clearance for certain devices under section 522, if used significantly in children. This legislation also allows the FDA to require a study of longer than 3 years if necessary to ensure that the study is long enough to capture the effect of a child's growth on the safety and efficacy of a medical device. A database of such studies would be made available to the public. New post-market authority can address the current limited amount of available data on devices for children and to create a mechanism for ensuring that needed pediatric studies are

conducted for a sufficient length of time. The legislation is crafted so that there is no delay in approval or clearance for a device.

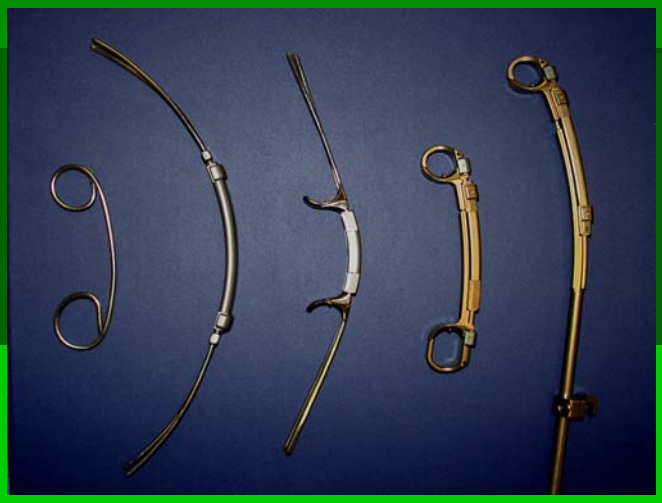
Conclusion

I would like to thank the committee for allowing me the opportunity to share my support of the Pediatric Medical Device Safety and Improvement Act, S. 830. This bill represents a historic step forward for children's medical and surgical devices similar to those steps taken on drugs. It will help future medical inventors of pediatric devices to avoid my mistakes and my frustrations so that they can get their devices "off the napkin" and into the pediatric patients who need them, in a safe and timely fashion.

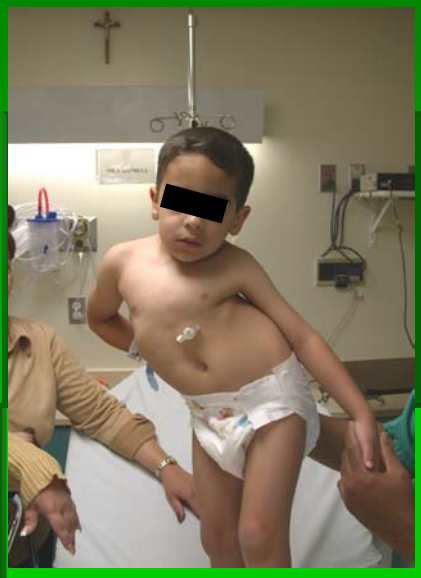
I urge the members of the committee to support this legislation. I would be happy to take any questions you may have.

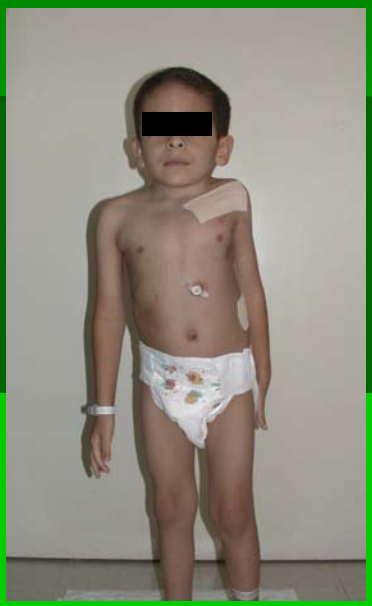
Robert M. Campbell, Jr., M.D.

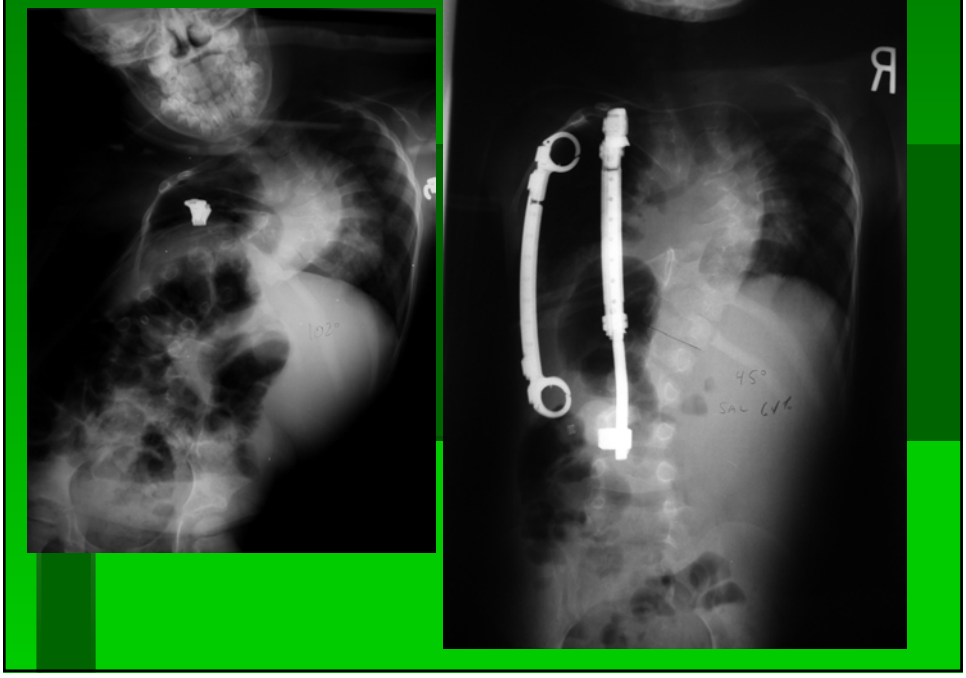
The Titanium Rib Development 1987-2005



-IOM Report, Safe Medical Devices for children, 2005






R
45°

Summary of Testimony
Robert M. Campbell, Jr., M.D.
United States Senate Committee on Health, Education, Labor, and Pensions
"Ensuring Safe Medicines and Medical Devices for Children"
March 27, 2007

Chairman Kennedy, Senator Enzi, and members of the committee, thank you for this opportunity to testify today regarding safe medicine and medical devices for children.

I am Dr. Robert Campbell, a pediatric orthopaedic surgeon, an inventor, and the father of five children. I am a Professor of Orthopaedics at the University of Texas Health Science Center at San Antonio. Throughout my career, I have cared for children in need of medical technology that was not readily available to them, but the primary reason I was invited to appear before you today is that I both invented, developed, and brought to market a life-saving pediatric surgical device known as the Vertical Expandable Prosthetic Titanium Rib (VEPTR), which was approved as a Humanitarian Device Exemption (HDE) device in 2004 after 14 years of FDA trials. I am here to help provide you with some insight from someone who has "been in the trenches" about how this pending legislation can help the children who need devices.

Children deserve access to devices that are safe, effective, and made for just for them, but they are frequently denied access to them because there is a relatively small market for pediatric devices with little incentive for manufacturers to make them. Physicians must commonly "jury-rig" existing devices for children. The VEPTR was invented to replace a "jury-rigged" device used to save the life of a 6-month-old full-time ventilator-dependent infant born with scoliosis and missing ribs.

I made many mistakes in developing VEPTR. I had no experience in device development or knowledge of FDA requirements. I had no mentor. But, learning through trial and error, supported by grants from the National Organization of Rare Disorders and the Orphan Products Division of the FDA, and luckily identifying child advocate manufacturers, we succeeded after 16 long years. Hundreds of other pediatric devices, however, have never been developed and probably won't be under current conditions. Children deserve better.

I am here today to express my strong support of S. 830 and to express my sincere gratitude to Senator Dodd for his commitment to achieving safe and effective medical devices for all children. The following provisions address many of the obstacles we faced when developing the VEPTR device for children.

The bill creates 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 on identifying important gaps in knowledge and 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 needs.

The bill also establishes six year demonstration grant(s) to support nonprofit consortia to provide critically needed support in helping the innovators with pediatric device ideas to navigate "the system" successfully and bring new pediatric devices to market. The consortium will mentor inventors and connect them to manufacturers and available federal resources. It will also coordinate with the NIH "contact point" for pediatric device development and the FDA for facilitation of pediatric device approval.

The profit restriction on Humanitarian Device Exemption (HDE)-approved devices has limited the effectiveness of the provision by forcing device manufacturers to only recover their research and development costs. 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.

The bill also will result in improvements in the way FDA tracks the number and type of devices approved for use in children and will strengthen post-market safety.

I would like to thank the committee for allowing me the opportunity to share my support of the Pediatric Medical Device Safety and Improvement Act, S. 830. It will help future innovators avoid my mistakes and my frustrations so that they can get their devices “off the napkin” and onto the shelf in a safe and timely fashion for the pediatric patients who need them. I urge the members of the committee to support this legislation.