

Emerging pediatric technologies

Pediatric Technology Watch | 2018 Volume 1



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Disclaimer: Vizient® staff attends clinical sessions at important scientific meetings throughout the year. The staff meets with suppliers, reviews new technologies and monitors data from pertinent clinical trials. The information is consolidated into this overview of product and practice trends in the various pediatric segments. This document is intended to educate nonclinical hospital staff by offering insights into new and innovative technologies. Vizient staff members have no personal financial connections with the suppliers and no conflicts of interest in the development of this document. The products and trends presented are for educational purposes. Vizient does not endorse any of the products described in this document.

Introduction

Children require specialized, compassionate and comprehensive care that supports every stage of their lives. The Vizient® Pediatric Technology Watch is intended to educate and provide insights into new and innovative technologies that support delivery of the highest-quality

pediatric care. This issue highlights the latest products and pharmaceuticals available in the market as well as emerging technologies. The Pediatric Technology Watch also features Vizient pricing projections for both products and pharmaceuticals.

Market watch

A look at legislative developments affecting the pediatric health care industry

Development of medical devices for the pediatric patient population has historically lagged behind devices for adults. Some of this lag can be attributed to a lack of technology needed for smaller-sized devices, but the lack of satisfactory return on investment for developing unique pediatric products is also a significant contributor. In December 2016, Congress passed the 21st Century Cures Act, which was designed to help accelerate medical product development and bring new innovations and advances to patients who need them. The legislation contained elements that could greatly benefit the development of pediatric devices and drugs. The legislation also established a task force on pregnancy and lactation research has already started working to improve women's health; additional efforts on behalf of the pediatric population are expected as well. Other benefits to the pediatric patient population include¹:

- Title II, Subtitle G: Promoting pediatric research
- Title III, Subtitle B: Advancing new drug therapies (includes those for rare pediatric diseases and orphan drug development)
- Title III, Subtitle F: Promoting medical device innovations
- Title X: Strengthening mental and substance use disorder care for children and adolescents

In October 2017, the Food and Drug Administration (FDA) published draft guidance titled “Breakthrough Devices Program: Draft Guidance for Industry and Food and Drug Administration Staff,”² which describes policies that the FDA intends to use to implement the new Breakthrough Devices Program established by the Cures Act. The program will help accelerate the development of pediatric devices.

In September 2016, the FDA published “Leveraging Existing Clinical Data for Extrapolation to Pediatric Uses of Medical Devices,”³ which gives the medical device industry guidance to “leverage relevant available clinical data, when appropriate, [that] may lead to more devices being granted marketing authorization for pediatric indications, which will increase the availability of medical devices with appropriate labeling to support safe and effective device use in pediatric patients.” The objective of this guidance is to ensure that devices used to treat pediatric patients are safe and effective, while ensuring that device approvals are based on valid scientific evidence. The hope is that the medical device industry will heed the call and accelerate the development of pediatric medical devices.



Economic watch

Price projections affecting the pediatric market

Overall projected price changes

Vizient expects overall national market prices for supplies to increase 1.8 percent in 2018 (Table 1). Vizient also provides estimated drug price changes for contract and noncontract products over the next 12 months (Table 2).



Table 1. Projected supply price changes through December 2018

Product category	National market price projection (%)
Business products	3.0
Capital equipment	2.1
Cardiovascular	0.9
Facilities	3.3
Food and nutrition	3.0
Imaging	1.3
Laboratory	2.2
Medical supplies	1.6
Orthopedics	3.0
Surgical supplies	1.8
Overall projected price change	1.8

Source: Vizient Budget Impact Projections Report, fourth quarter 2017.

Table 2. Projected drug price changes July 2018-June 2019

Product group	Estimated price change weighted by Vizient member purchases (%)
Vizient contracted products	0.81
Noncontract products	6.54
Total weighted average drug price inflation estimate	7.35

Source: Vizient Drug Price Forecast, January 2018.

Technology watch

New innovative technology in the pediatric pipeline

Caring for the pediatric patient population—whether neonate, infant, child or adolescent—is complex. The Center for Devices and Radiological Health of the FDA defines pediatric as birth through age 21 years, with the adolescent subgroup defined as those 12 through 21 years old.⁴ This wide age range creates unique issues in that there are simply too few devices specifically approved for the variety of pediatric applications that need these particular devices. Due to the limited availability of specialized devices, physicians have been treating pediatric patients using medical devices for indications not contained in the approved labeling, including using adult devices, as is or modified, or using implants designed for other purposes.

The FDA has implemented initiatives to increase the availability of pediatric medical devices, including identifying barriers to the development of pediatric devices and incorporating known information about other populations to support labeling of existing devices for pediatric indications. As a result, new products indicated for pediatric patients will continue to be released and physician and patient awareness of the availability of these products will increase, leading to greater penetration of pediatric devices and driving market growth.

The U.S. pediatric device market will grow at a moderate pace through 2025, primarily because the incidence of pediatric injuries will increase as the pediatric population grows.⁵ Improved physician training, increased focus on pediatric care and the development of innovative pediatric devices will also drive market growth.

Currently available products

Pivo Needle-Free Blood Draw Technology

(Velano Vascular)

Pivo is a single-use disposable device designed to take blood samples from indwelling peripheral intravenous lines to reduce the number of needle sticks and the need for central line access for blood collection. It is intended to help provide a more compassionate care experience for patients, a safer environment for caregivers and a more financially responsible alternative for health systems. This device was cleared for use by the FDA in February 2017.

Flourish pediatric esophageal atresia device

(Wilson-Cook Medical, Inc.)

(Humanitarian exempt device)

The Flourish pediatric esophageal atresia device is used to nonsurgically repair the esophagus in infants who were born with their upper esophagus disconnected from their lower esophagus and stomach (esophageal atresia) and who are therefore unable to eat by mouth. The device consists of two tubes, each of which contains a magnet at its tip. One tube is inserted through the mouth and the other through the stomach. Once in place, the magnetic ends of the catheters attract one another and pull the ends of the esophagus together. Over several days, the gap between the upper and lower esophagus is closed and the surrounding tissue grows together. Within 13 days, the tissue trapped between the magnets dies and a hole is created between the two portions of the esophagus. The device is indicated for pediatric patients up to 1 year of age, with esophageal atresia without a tracheoesophageal

fistula or with a fistula that was closed in a prior procedure. This device should be used only when the gap between the upper and lower portions of the esophagus is less than 4 centimeters. The device was cleared for use by the FDA in May 2017.

OSB lead-Flourish post-approval study⁶ (H150003/PAS001)

Wilson-Cook (supplier sponsored)

Study size: unlimited

Retrospective, nonrandomized, post-market, multicenter U.S. study

The study, mandated by the FDA, is a five-year post-marketing study of the safety and effectiveness of the device. The study has just begun enrolling patients; no clinical data is available.

Exact osteotomy system (WishBone Medical)

WishBone Medical is the newest company (founded in January 2017) focused on developing pediatric-specific orthopedic products. The Exact osteotomy system allows precise and repeatable osteotomies for all types of pediatric orthopedic surgery. The first product to launch from this system is a set of guides specifically for juvenile bunion surgery that are an accurate aid in the correction of first metatarsal phalangeal joint deformities. The system provides eight different guide types for the most popular distal metatarsal osteotomies, including Austin/Chevron and Youngswick procedures. The single-use, sterile-packed kit includes cut guide, custom saw blades and two 0.045 K-wires. The product was cleared for use by the FDA in July 2017.

FreeStyle Libre Flash glucose monitoring system (Abbott)

The FreeStyle Libre Flash glucose monitoring system is an advance in glucose-sensing technology that eliminates the need for routine finger sticks, either for calibration or to obtain samples. The patient wears a small sensor on the back of the upper arm for up to 10 days. Readings can be received through clothing and the water-resistant design allows the device to be worn in the shower and during swimming. Each scan provides the current glucose reading and those for the last eight hours, and graphically displays glucose trends and patterns. The device is indicated for aiding in the detection of episodes of hyperglycemia and hypoglycemia, facilitating both acute and long-term therapy adjustments in patients age 18 and older with diabetes. The system is intended for single-patient use and requires a prescription. The device was cleared for use in the U.S. by the FDA in September 2017.

Novel glucose-sensing technology and hypoglycemia in type 1 diabetes⁷ (NCT02232698)

Jan Bolinder, et al. (Sweden), principal investigator

Study size: 328 patients

Prospective, non-masked, randomized, multicenter, non-U.S. study

This study assesses whether a factory-calibrated, sensor-based, flash glucose-monitoring system (FreeStyle Libre) reduced exposure to hypoglycemia in patients with type 1 diabetes, as compared to self-monitored glucose testing. The study found mean time in hypoglycemia changed from 3.38 h/day at baseline to 2.03 h/day at 6 months (baseline adjusted mean change -1.39) in the intervention group, and from 3.44 h/day to 3.27 h/day in the control group (-0.14); with the between-group difference of -1.24 (SE 0.239; $P < .0001$), equating to a 38% reduction in time in hypoglycemia in the intervention group. No device-related hypoglycemia or safety issues were reported. The study did not include any adolescent patients.

Owlet Smart Sock 2 (Owlet Baby Care)

The Smart Sock 2 uses proven pulse oximetry technology to continuously track an infant's heart rate and oxygen levels. The device, which is marketed for home use, incorporates a sensor into a small wrap that fits on an infant's foot. The information collected is accessible with a smartphone tablet. The device has a range up to 100 feet and uses an innovative fabric sock to ensure comfortable fit and accurate readings. This device was cleared for use by the FDA on September 2017 and is available in retail stores.

Carnation ambulatory electrocardiogram monitor (Brady Diagnostics, Inc.)

The Carnation ambulatory electrocardiogram (ECG) monitor (CAM) is a P-wave-centric electrocardiogram monitor indicated for pediatric use for up to seven days. The small size of the sensor (approximately 7" L \times 1½" W \times ⅜" H) means that it can easily be worn by children (≥ 22 lb). The CAM monitor encompasses design criteria and state-of-the-art sensor electronics allowing for a low noise floor designed for optimal P-wave detection. Data is collected continuously and the monitor provides an executive review report focused on actionable events. The device comes in two parts, a reusable monitor and a single-use, off-the-shelf attachment system. Use of the device is reimbursable. The device is approved for use in the U.S. by the FDA.

Comparison of diagnostic value using a small, single channel, P-wave-centric sternal ECG monitoring patch with a standard 3-lead Holter system over 24 hours⁸

Warren M. Smith, et al. (New Zealand), principal investigator

Study size: 50 patients

Randomized, non-masked, single-center non-U.S. study

The study compared the diagnostic efficacy of the P-wave-centric ECG patch to a standard 3-channel (leads V1, II and V5) Holter monitor. Patients were referred to a hospital Holter clinic for standard clinical indications. Patients wore both devices simultaneously, serving as their own controls. Holter and patch reports were read in a blinded fashion by experienced electrophysiologists unaware of the findings in the other corresponding ECG recording. The P-wave-centric patch recording system identified rhythms in 23 patients (46%) that altered management; the Holter monitors identified such rhythms in 6 patients (12%; $P < .001$). The patch ECG intervals PR, QRS and QT correlated well with the Holter ECG intervals, with correlation coefficients of 0.93, 0.86 and 0.94, respectively. Finally, 48 patients (96%) preferred wearing the patch monitor.

Hummingbird TTS ear tube delivery system (Preceptis Medical)

The Hummingbird TTS uses a technology to reduce manipulations of the eardrum and reduce pain and time associated with ear tube placement. The device is intended to deliver a tympanostomy tube through the tympanic membrane, combining the separate functions of creating a myringotomy and positioning and placing a tympanostomy tube. The reduced discomfort allows physicians to use conscious sedation to keep the child comfortable and awake during the short procedure. The device is currently FDA cleared for use with conscious sedation in hospital or surgery center settings. The prospective, single-center, office-based study at Health Partners Clinic, the Hummingbird TTS Office Study, is enrolling patients. No data is available.

Products in clinical trials

Bili-Hut phototherapy system (Little Sparrows Technology)

The Bili-Hut is a lightweight, low-cost phototherapy device to treat neonatal jaundice. Infants with severe jaundice are at risk of brain damage if left untreated. The device offers a three-pound, collapsible enclosure that uses low-energy LED lights, enabling use with either line power or alternative sources such as a 12-volt battery. The device is designed for use in medically underserved areas. It has not been cleared for sale in the U.S. by the FDA.

OtoNexus ultrasound device (OtoNexus Medical Technologies, Inc.)

A new otitis media evaluation device uses air-coupled ultrasound technology to provide the data needed to instantly and accurately assess middle ear infections, and in particular to determine when to prescribe antibiotics. The device identifies not only the presence but also the type of infection. The handheld device is easy to use, highly accurate and inexpensive. It is designed to provide, for the first time, definitive, objective diagnostic data, leading to

increased accuracy, expedited diagnoses, earlier and better treatment, better patient outcomes, reduced antibiotic use and significantly reduced health care costs. The device has not received clearance for use in the U.S. from the FDA.

Pediatric coronary products (PediaVascular)

PediaVascular has been focusing on providing cardiac products indicated for use in pediatric patients since 2010. The company's Mongoose 3.3F and 4.0F angiographic catheters and its Super Sheath introducer lines are approved for use in the U.S. Earlier this year, the company began developing a 3.0F long sheath designed for peripheral artery stenting, aortic stenting (used to correct narrowing of the aorta) and Blalock-Taussig shunts (used to help increase blood flow to the lungs in babies born with defects that obstruct the flow). The company is also rumored to be developing a bioresorbable coronary stent. The long sheath has not been cleared by the FDA and is not yet available in the U.S.

Products in development

Boomcast (Fathom)

Boomcast is a 3D-printed leg cast with embedded electronics that enable a doctor to monitor a leg's physical state remotely. The cast can integrate technology from industry-leading companies and be outfitted with pressure sensors, Bluetooth speakers, LED lights, gyroscopes, accelerometers, and Wi-Fi enabled Intel Edison. The cast demonstrates how wearable technologies are evolving and can be used for innovative medical purposes. Each cast is custom fitted from a digital body scan and can be used in both adult and pediatric patient populations. The device is currently not commercialized.

Infrascanner Model 2000 (InfraScan, Inc.)

The Infrascanner is a portable screening device that uses near-infrared (NIR) technology to screen patients (adult and pediatric populations) for intracranial hematomas, identifying those who would most benefit from immediate referral for a CT scan and neurosurgical intervention. The device includes an eye-safe NIR diode laser and an optical detector. The light to and from the laser and detector is optically coupled to the patient's head through two disposable light guides. The detector signal is digitized and analyzed within the sensor. The data is further processed and the results are displayed on the screen. The device is intended to be a cost-effective, mobile and time-efficient complement to current CT systems.

Noddle communication system (Voxello, LLC)

The Noddle is a communications device designed to address the communication barriers faced by pediatric patients. The system uses patented technology to let patients with limited motor capabilities control up to three different devices with a single touch. It can also detect the smallest intentional gesture and allow patients to access the nurse call system and control a speech-generating device. Children who may only be able to produce a tongue click, head nod or other small gesture would be able to summon help and effectively communicate with their caregivers.

Roboimplant (Magnets-in-Me, Inc.)

Roboimplant uses magnetic coupling and remote pressure sensing to correct adolescent scoliosis. The implant can lengthen or shorten a rigid implanted rod in the doctor's office without further surgery. The physician can monitor the movement of any rigid rod device and the pressure exerted on the patient's spine. The device has 6-mm universal attachments at each end that can tell the orthopedic surgeon to attach a variety of rigid rods and screws. Once attached, the implant can be controlled to place tension on the rods and slowly change the shape of the patient's spine. The device has not been cleared for use in the U.S. by the FDA.

Synthetic Muscle (Ras Labs, LLC)

Ras Labs is a developer of contractile electroactive polymer called Synthetic Muscle. The polymer, an adjustable biomimetic socket liner for prosthetic limbs, is designed to improve the interface between a child's prosthetic limb and the residual limb. Without using gears or motors, the polymer contracts or expands like a muscle in response to low-voltage electricity. The company's objective is to show that using the biomimetic polymer to line the socket of a pediatric-sized artificial leg or other limb would provide a more snug fit during normal daily use and consequently improve a child's quality of life. The device is not yet available for use anywhere.

Tabla pneumonia detector (University of California, Berkley)

The low-cost Tabla device detects changes in sound waves during percussive physical examinations, providing a more accessible and affordable alternative to chest X-rays. Based on the "percussion technique" of tapping on a patient's chest and listening with a stethoscope, the device makes a "swooping" sound while a doctor holds it against the front of a patient's body and records the sound with a digital stethoscope placed on the patient's back. The design team is using machine learning to build intelligence into its smartphone app to guide the exact change in the sound depending on age, gender, height, weight and other factors.

Pharmaceutical watch

Novel drug approvals, indications and formulations

New drugs

Benralizumab (Fasenra) injection for subcutaneous use (AstraZeneca)

Benralizumab is indicated for add-on maintenance treatment of patients with severe asthma aged 12 years and older and with an eosinophilic phenotype. In pivotal, placebo-controlled phase 3 trials, benralizumab was associated with up to a 51 percent reduction in the annual asthma exacerbation rate, a 75 percent median reduction in daily oral corticosteroid use and significant improvements in forced expiratory volume in the first second (FEV1).

Benznidazole tablet for oral use (Exeltis USA Inc.)

Benznidazole is the first treatment for Chagas disease (American trypanosomiasis), a tropical parasitic disease caused by *Trypanosoma cruzi*. Chagas disease is more common in Latin America, but it is estimated that approximately 300,000 people in the United States have the disease. This antimicrobial is indicated for patients 2 to 12 years of age.

Emicizumab-kxwh (Hemlibra) injection for subcutaneous use (Genentech)

Emicizumab is a first-in-class therapy that mimics the function of factor VIII, which is absent in patients with hemophilia A, to prevent or reduce the frequency of bleeding episodes in adult and pediatric patients. Emicizumab is administered weekly, in contrast to the existing treatment, which must be administered every other day.

Gemtuzumab ozogamicin (Mylotarg) for injection for intravenous use (Pfizer Inc.)

Gemtuzumab ozogamicin is the first approved antibody drug conjugate indicated for the treatment of newly diagnosed CD33-positive acute myeloid leukemia (AML) in adults and treatment of relapsed or refractory CD33-positive AML in adults and in pediatric patients 2 years and older. Studies demonstrate that gemtuzumab in combination with chemotherapy significantly extended median event-free survival compared with chemotherapy alone (17.3 vs. 9.5 months, respectively).

Tisagenlecleucel (Kymriah) suspension for intravenous infusion (Novartis)

Tisagenlecleucel is the first FDA-approved chimeric antigen receptor T-cell (CAR-T) therapy and the first available gene therapy in the United States. Tisagenlecleucel, a genetically modified autologous T-cell immunotherapy, is indicated for the treatment of B-cell precursor acute lymphoblastic leukemia that is refractory at the second or later relapse in patients up to 25 years old. At the six-month interim analysis, complete response or remission with incomplete blood count recovery at three months was achieved in 82.5 percent of participants. Median overall survival was 16.6 months, which compares favorably with historical survival data of four months in chemotherapy-treated patients.

Vestronidase alfa-vjbk (Mepsevii) injection for intravenous use (Ultragenyx)

Vestronidase alfa is the first FDA-approved treatment for mucopolysaccharidosis type VII (MPS VII), a rare genetic condition that affects fewer than 150 patients worldwide. The efficacy of vestronidase alfa was evaluated in 23 patients ranging in age from 5 months to 25 years. The primary efficacy outcome, the six-minute walk test, improved by 18 meters in 10 patients who completed the test. The FDA has mandated an additional post-marketing study to evaluate the drug's long-term safety.

New indications

Peramivir (Rapivab) injection for intravenous use (BioCryst Pharmaceuticals, Inc.)

This approval expands the use of peramivir, previously approved only for adults, to pediatric patients aged 2 and older. Peramivir is an influenza virus neuraminidase inhibitor indicated for the treatment of acute uncomplicated influenza in patients who have been symptomatic for no more than two days.

Tocilizumab (Actemra) injection for intravenous or subcutaneous use (Genentech)

Tocilizumab is the first FDA-approved treatment to manage severe or life-threatening cytokine release syndrome in adults and pediatric patients 2 years of age and older.

New formulations

Ascorbic acid (Ascor) injection for intravenous use (McGuff Pharmaceuticals Inc.)

Ascor is the first ascorbic acid (vitamin C) formulation approved by the FDA for use in the U.S. Intravenous ascorbic acid is indicated for the short-term (up to one week) treatment of scurvy in adults and pediatric patients age 5 months and older for whom oral administration is not possible, insufficient or contraindicated. Intravenous ascorbic acid is included in a group of products that were grandfathered into use prior to the formation of the FDA, but these products are now required to meet current approval standards. American Regent and Mylan Institutional currently have unapproved ascorbic acid products on the market. The FDA will likely allow a grace period of approximately one year for their removal, after which McGuff will have a period of market exclusivity before other sponsors can file an abbreviated new drug application.

Bosentan (Tracleer) tablet for oral suspension (Actelion)

This approval of bosentan covers both a new formulation and a new indication. The drug is now the first FDA-approved medicine for the treatment of patients aged 3 years and older with idiopathic or congenital pulmonary arterial hypertension (PAH). Bosentan helps improve pulmonary vascular resistance, which is expected to result in an improvement in exercise ability.



References

- 1 21st Century Cures Act. Pub L No. 114-255, 130 Stat 1033.
- 2 Breakthrough devices program; draft guidance for industry and Food and Drug Administration staff. *Fed Regist*. 2017;82(205):49373-49375.
- 3 Leveraging existing clinical data for extrapolation to pediatric uses of medical devices; guidance for industry and Food and Drug Administration staff. *Fed Regist*. 2016;81(119):40317-40319.
- 4 Center for Devices and Radiological Health. Guidance for industry and FDA staff: Pediatric expertise for advisory panels. Food and Drug Administration website. <http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm082188.pdf>. Accessed September 21, 2016.
- 5 Pediatric medical devices. Food and Drug Administration website. <https://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/ucm135104.htm>. Accessed January 17, 2018.
- 6 OSB lead-Flourish post-approval study. Post-Approval Study Database. Food and Drug Administration website. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma_pas.cfm?t_id=585891&c_id=4376. Accessed January 17, 2018.
- 7 Bolinder J, Antuna R, Geelhoed-Duijvestijn P, Kroger J, Weitgasser R. Novel glucose-sensing technology and hypoglycemia in type 1 diabetes: a multicentre, non-masked, randomised controlled trial. *Lancet*. 2016;388(10057):2254-2263.
- 8 Smith WM, Riddell F, Madon M, Gleva MJ. Comparison of diagnostic value using a small, single channel, P-wave centric sternal ECG monitoring patch with a standard 3-lead Holter system over 24 hours. *Am Heart J*. 2017;185:67-73. doi:10.1016/j.ahj.2016.11.006.



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