

# Health Technology TRENDS

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► DECEMBER 2007

## Nonprofit group formed to push development of pediatric drugs and medical devices

### ► Summary

*The founder of a nonprofit organization dedicated to the advancement of pediatric drugs and medical devices spoke with Health Technology Trends about the business model he hopes will advance these needed tools to production.*

According to the American Academy of Pediatrics, approximately 75% of drugs have not been appropriately tested for use in children, leaving practitioners to estimate dose based on height, weight, and age. Similarly, a large number of devices used in pediatric medicine may not account for growth, active lifestyles, and differing metabolism associated with the pediatric population. In an aim to remedy this situation, a former hospital executive from Children's Hospital of Boston (Boston, MA, USA), founded the Institute for Pediatric Innovation (IPI)(Cambridge, MA, USA). IPI is a nonprofit organization launched in the beginning of 2007 to address the largely unmet needs of practitioners in pediatric care and their patients.

### Steep development barriers

Donald P. Lombardi, president and chief executive officer of IPI, says it doesn't have to be that way. In the 15 years that Lombardi spent leading the intellectual property office at Children's Hospital of Boston, he witnessed a lot of research and innovation. "We got 6 products onto the market, 12 more to clinical studies, and Children's is making tens of millions a year on the royalties from these products." However, Lombardi noted, the fruits of this labor never came to fruition in the pediatric market. And he knows why.

As it is, research and development in the adult population can take from 10 to 12 years. However, the development market for pediatric products is necessarily more complex with regard to ensuring patients'

safety, enrolling sufficient numbers of patients in a clinical trial, and accounting for multiple age groups with different technical and medical issues. "This means the development pathway for drugs can be onerous from the point of view of companies," says Lombardi. "It's high risk and high cost."

### Small market, small ROI

The other problem is what Lombardi calls the "traditional technology transfer paradigm." He explains, "It starts with researchers who are fundamentally biologists with grants" working in academic centers. These PhDs in labs "do very important work, and very interesting work, some of which results in ideas for treatments at a place like Children's Hospital of Boston," says Lombardi. The bulk of the work is in the biotechnology/biopharmaceutical domain. "These are high-investment ideas, so the investors who take them on are naturally interested in the adult general market uses, versus the pediatric market," he explained. "The products require long-term investment cycles."

This isn't a new problem. "Historically, companies have perceived a negative incentive to invest in the pediatric market," said Lombardi, and it has to do with size. "The pediatric market is less than a tenth the size of the general market, and it's divided into submarkets, from the preterm baby to

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the teenage mom," he notes. "Any given product may be for a fairly small number of people." In addition, companies fear the potential risks and added expense associated with testing a fragile population fraught with legal complexities over informed consent and other issues.

Finally, Lombardi points to a lack of needs assessment on the front line, about what is needed most. This requires consulting pediatric physicians and nurses who must split pills or somehow appropriately dilute medication, making educated guesses about the proper dosage. Likewise, pediatric surgeons often must adjust and "engineer" medical devices for size to fit smaller or even tiny patients.

### New business models

Lombardi's organization has developed several models designed to shepherd drugs and devices through the development pipeline to market.

One approach is to "think small." Lombardi says many products "don't require the discovery side of research, are much more development oriented, and have much shorter timelines to get to the marketplace." For example, the reformulation of compounds already in medical use has proven successful. Lombardi worked on one project at Children's Hospital that involved developing a better formulation of a drug that treats lead poisoning. "After working on a no-cost basis with a formulation company to develop a better formulation for . . . younger children, we found an investor who did the research and due diligence to determine what would be required to get the product approved," he said. The investors concluded that they were looking at less than two years for one-and-a-half million dollars, a big difference from "the \$800 million scenario touted by the pharmaceutical companies" to develop and bring to market a new drug. According to Lombardi, "the product had long ago been approved by the FDA for a different use," and with 30 years of documented use in children, "the approval process is much less onerous," he says.

Lombardi says that even though the product looks to address a market in the \$30- to \$40-million range, as opposed to the

\$3 billion range preferred by pharmaceutical companies, the lower cost of getting it to market justified an investment by a small group that felt it would get a sufficient return.

IPI plans to identify a portfolio of off-patent pharmaceutical compounds that clinicians want in different formulations. "With a very careful analysis of that portfolio, we can identify clinical need and market feasibility and match up different products with different potential sponsors, including government, foundation, and for-profit ones." Going to companies with a complete business case, developed product, and clinical data-in-hand, "We can simply say: 'Let's do it,'" Lombardi says.

One company, Children's Medical Ventures, a subsidiary of Respiroics, Inc. (Pittsburgh, PA, USA) funded IPI to conduct a needs analysis in neonatal intensive care units. "We had to find out from nurses, doctors and other staff what their problems were, where they've had to improvise equipment and devices to treat these tiny children, and then work with marketing and engineering experts and our corporate sponsors to carry out a process we call 'product imagination.'"

In addition to investors, IPI will seek funding from sources that do not require a financial return, so as to reduce risk and lower the threshold for market feasibility. Depending on the product, Lombardi says this could come from the federal government—particularly the National Institutes of Health and FDA—or a single disease-focused foundation. "Foundations such as the Epilepsy Foundation are able and willing to finance the development of certain pediatric products for certain populations through several different mechanisms," says Lombardi, adding that they'll go this route when they don't anticipate attracting "a hard nose or corporate investor" for the development phase.

Lombardi says they've already aggregated close to \$1 million in funding from stakeholders including pediatric institutions, philanthropic organizations, and the medical industry. "We think we're in a pretty good position to expand funding in these sectors, and also leverage government and investor sources." ▶

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# Will legislative incentives move pediatric drugs and devices through the development pipeline?

## Summary

*Two existing pediatric drug-testing laws have just been renewed, and a new pediatric medical device law has been enacted. This provides the U.S. Food and Drug Administration with so-called carrot-and-stick incentives for drug and device manufacturers to pursue the development and clinical study of pediatric products.*

On the legislative front, the pediatric community got some promising news. On September 27, 2007, President Bush signed the U.S. Food and Drug Administration Amendment Act into law. Included in the legislation was the renewal of both the Best Pharmaceuticals for Children Act (BPCA) and the Pediatric Research Equity Act (PREA).

### Pediatric medications

BPCA can extend a drug's patent life by three months if sales exceed \$1 billion, and six months if sales are less than that. According to the American Academy of Pediatrics (AAP), in the 10 years the law has been enacted, more than 780 pediatric studies have been conducted, resulting in more than 132 completed studies and more than 115 label changes.

Such studies have uncovered things like ineffective chemotherapy treatments that caused severe side-effects in some cases. Another case involved an epilepsy drug that caused extreme behavioral changes in children ages 3 through 12, because dosing scales did not take children's faster metabolisms into consideration.

While no comparable data are available on PREA, together with BPCA, FDA calls this a "carrot and stick" approach to incentivize research and development.

PREA gives FDA authority to require drug manufacturers to conduct pediatric studies of certain drugs. These drugs must already be on the market, must be in clinical use in a substantial number of children, and must represent a meaningful benefit over existing therapies.

However, Congress set an expiration date for PREA within five years, news that met with disappointment by both AAP and the Elizabeth Glaser Pediatric AIDS Foundation. The latter group's statement read thus: "Regrettably, one thing the law does not do is make the FDA's authority to

require pediatric drug studies permanent. Adults don't have to lobby Congress every five years to preserve their fundamental right to safe and effective medicines, and children shouldn't have to either. We hope to work together with Congress and the administration to ensure that, as we move forward, children's health will finally be put on permanent and equal footing with that of adults."

### Pediatric medical devices

On the device front, the Pediatric Medical Device Safety & Improvement Act was also passed. About \$6 million annually has been earmarked for a nonprofit consortium to stimulate device development within the next five years. It also gives FDA authority to require post-market studies of approved pediatric devices to ensure their continued efficacy and safety.

The pediatric device legislation was also largely supported by AAP, and the organization cited examples such as chemotherapy catheters, which are too large for infants and require the use of less advanced tubing that leaves them more vulnerable to infection. In addition, stapling devices used in certain pediatric surgeries often weigh more than the patients, and left ventricular assist devices, which keep a failing heart beating while a patient waits for a transplant, are not available for children ages 5 years and younger.

### Gaps in the legislation

Although BPCA has been in place for 10 years, Donald P. Lombardi, president and chief executive officer of the Institute for Pediatric Innovation (Cambridge, MA, USA) says it's not clear what impact this is making in the field yet.

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***“According to recent discussions with FDA, a substantial number of drugs have come out with pediatric labeling since the laws went into effect.”***

come out with pediatric labeling since the laws went into effect,” noted Lombardi. In these cases, “The labeled data indicate whether or not it’s appropriate for children and, if so, the amounts for dosing requirements.”

Lombardi calls this “a big step forward,” pointing out that “it does provide the data clinicians need to guide their administration of drugs; however, it does not necessarily get the drugs reformulated, and that’s what’s needed for effective treatment in many cases.”

For example, Lombardi says that young children can’t take pills. “Grinding up pills and putting them into food or a liquid suspension risks lack of uniformity and instability, and may give the drugs a foul taste. Getting products developed in proper

dosing or delivery form for children,” is a problem that must be solved, he stresses.

Lombardi adds that a large number of drug compounds were approved prior to the passing of the act. Furthermore, the legislation provides no incentives to develop off-patent generics, although he says efforts are underway at the National Institutes of Health to help finance testing of generics. His nonprofit organization has developed business models in which investors and funding could address areas the legislation doesn’t cover.

Overall, Lombardi says, “It’s an area that needs continual collaboration in the industry, in the pediatric community, and the government, and I think that’s a role we can play.”

### ABOUT ECRI INSTITUTE

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