

## About IPI

IPI seeks to improve pediatric care by stimulating development of medical products and medications designed specifically for babies and children. We do this through public, private, nonprofit, and for-profit collaboration on product innovation.

Institute for Pediatric Innovation is a nonprofit 501(c)3 organization incorporated in Massachusetts.

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## Kansas University Begins Reformulation Research on First Drug Product

Work is underway at Kansas University (KU) to reformulate a common adult medication into a pediatric formulation. This is part of IPI's Pediatric Pharmaceutical Reformulation Program.

Scott Weir, PharmD, PhD, Director of KU's Office of Therapeutics, Discovery and Development, is leading the effort at KU. He describes the program this way: "IPI and their pediatric experts identify the adult drug products they would like to reformulate into pediatric formulations. We will develop the liquid formulations in our lab, with input the IPI Pediatric Hospital Consortium and others. Then with industry experts in the region we will work with IPI to get that product manufactured and materials available for the market."

IPI Principal Investigator Stephen Spielberg, MD, PhD, says the first drug for reformulation was picked based on careful research. "We made an initial examination of where the needs are," he says. "For certain classes of medicines for children, or for certain conditions or types of infections, there are already good commercial formulations available. But for others, the pediatric marketplace is so small that good formulations haven't been made available by drug companies."

Spielberg says that one of the first target areas for this work are medications in the cardiorenal category, in part because many already have FDA approved labeling, but are not yet commercially available for children.

Scott Weir says the drug currently under development targets an unmet medical need in children, is extremely safe and effective, and has a clear and well-defined set of processes for FDA approval. "It is a straightforward, low-risk project, and has all the qualities we would like to see to generate some initial success."

Also partnering on this project is Beckloff Associates, a regulatory drug development consulting firm in Kansas City, which helps firms work with the FDA to define the criteria involved in bringing a product to market.

"IPI has the vision to identify the drugs," says Weir. "KU puts it in dose form. IPI's Consortium members conduct trials in children; and KU and Beckloff conduct any adult trials necessary for commercialization. It's a great partnership."

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# IPI Innovation Matters

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## IPI Receives Grant to Study Extemporaneous Compounding

IPI has been awarded a \$50,000 grant from University of Kansas to conduct a national research project on extemporaneous compounding. The goal is to understand how widespread the practice is, and gain an understanding of the top 20 drugs that are extemporaneously compounded in 25 different pediatric institutions or institutions with pediatric services. The results will help IPI develop a priority list for reformulation efforts, and may also point to the need for better automation in hospital pharmacies.

The participating institutions include the three hospitals in IPI's Pediatric Hospital Consortium, plus 22 members of the Pediatric Pharmacy Advocacy Group, a non-profit association dedicated to improving medication therapy in children. Consortium pharmacies are helping to evaluate and fine tune the survey tool, and are all participating in the study.

IPI Principal Investigator Stephen Spielberg, MD, PhD, is leading this effort along with Ralph A. Lugo, PharmD, Professor and Chair, Dept of Pharmacy Practice, East Tennessee State University College of Pharmacy, and Robert M. Ward, MD, Director of Pediatric Pharmacology at the University of Utah.

"This is important because over the last ten years there has been no national review of this serious issue," says Spielberg. "Extemporaneous compounding is not regulated in the same way that commercially available drugs are. This is a safety and quality issue."

## Clinical Teams Help Develop NICU Product Opportunities

Teams within each member of IPI's Pediatric Hospital Consortium are helping create several new products for neonatal care: better adhesives for use in the NICU, an improved respiratory device for intubation of newborns, and a blood vessel detection device.

IPI identified the needs for these products during the latter half of 2007 through a rigorous process involving extensive surveys, hospital visits, and a product imagination workshop.

The work at this stage is preliminary and proprietary, so details are not available for publication. But the work at Children's Mercy Hospital in Kansas City on adhesive alternatives offers a glimpse into some of the challenges.

"We are looking at adhesive products that will make attaching various devices to neonates easier," says Ross Trimby, IPI's Chief Operating Officer. "Neonates born between 26 and 30 weeks do not have fully developed skin, and they are at risk for skin damage when the adhesives that hold devices in place are peeled off. Babies younger than 26 weeks are kept in high humidity environments, so they have a lot of moisture on their skin, and the adhesives don't stick. What we need is a product that sticks well when you want it to, and comes off easily when you want it to."

Barbara Haney, RNC, MSN, CPNP-AC, Clinical Nurse Specialist at Children's Mercy Hospital, works with IPI on this program, providing clinical expertise to IPI's product development consultants. "The tiny baby is quite a challenge," she says. "Their skin is very immature and translucent. The skin develops its toughness in the first two weeks of life."

(Continued on page 2)

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## US Pharmacopia Hosting Meeting To Chart New Paths

IPI and US Pharmacopia are co-sponsoring a unique meeting where diverse stakeholders can join together to discuss the future of pediatric therapeutics. Case studies of past pediatric drug development efforts—successes and failures—will launch participants into discussions of ways to overcome formulation, regulatory, and financial challenges of the past.

"This conference is tremendously exciting," says IPI's Stephen Spielberg, MD, PhD. "We have been able to enlist the help and support of our colleagues at US Pharmacopia, and we will bring together experts in formulation development, industry people from large pharmaceuticals, and representatives from NIH, NICHD, FDA, and child advocacy groups such as the (Continued on Page 2)

## US Pharmacopia Hosting Meeting (continued from P.1)

National Organization for Rare Diseases, along with representatives from each of our hospital consortium members, IPI board members, and IPI reformulation project advisors.

The goal of the conference is to define previous impediments from a technological, regulatory and market point of view. "We hope to define new paths forward for public/private partnerships, ways that we can work with colleagues across this broad arena in industry and academia to find new ways of making sure that proper medications are available for children," says Spielberg.

Robert Poole, Pharm. D., is Director of Pharmacy at Lucile Packard Children's Hospital at Stanford. He is a founding member of the PPAG and also serves on the Pharmacy Committee of the Child Health Corporation of America.

"What sets this conference apart from so many others is that we will have regulators in the room," says Poole. "You can have the best reformulators in the world, but if you don't have a regulator in the room, there is no way forward. Regulation is not a barrier, it is an important part of the process."

"We are looking forward to having an open dialog about why it is important and appropriate to have drug formulations for infants," he continues. "My hope is that we will get past the point where we agree there is a problem, to charting a clear way forward in all the sectors involved in drug development."

The all-day invitation-only meeting is scheduled for June 23 in USP headquarters in Rockville, MD. The IPI Project Advisory Committee will meet in executive session following the meeting to incorporate findings into IPI's Drug Reformulation Program.

## NICU Product Opportunities (continued from P.1)

These tiny babies need monitors and other devices attached to their bodies while they are in the ICU. "Every baby needs an electrode monitor attached, and a temperature probe. Breathing and endotracheal tubes need an adhesive to the face, and in an emergency you have to remove it quickly. Many also have IVs in their arm, leg, or umbilica that must be secured in place."

"If the tape doesn't adhere properly, the tubes or wires can be dislodged and you are no longer able to adequately monitor or administer medications," she explains. "And if it does adhere well, but tears the skin when you remove it, then the baby has an open wound like a burn that risks infection."

To date, says Haney, there is no perfect adhesive. "If we can come up with something that sticks yet releases, it would revolutionize the way we care for these babies."

Ross Trimby says the other two products currently being explored would also have a strong positive impact on the care of neonates. "Endotracheal tubes are generally not the right size for neonates," he says. "There is an issue of size, of keeping them in place, and of infection." IPI is working with Lucile Packard Children's Hospital at Stanford to create a better respiratory device for intubations.

At Rainbow Babies and Children's Hospital in Cleveland, OH, the work is centered on developing a way to help clinicians more easily locate tiny veins and arteries in neonates, to aid in the accurate insertion of needles for blood drawing or for IVs.

"Our model involves rigorously quantifying the need," says IPI Chief Executive Officer Donald Lombardi, "and then we work with professional product development people and clinical teams to generate and develop product ideas to meet those needs. We think it is a very unique and strong model."

Preliminary results from the three product development programs are expected by early Summer 2008.

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## IPI Staff News

IPI recently welcomed a new staff member as well as two summer interns, and said goodbye to a former colleague.

Denise Wright joined IPI as Office Manager in April, having previously worked for CEO Don Lombardi for five years at Children's Hospital Boston as administrative assistant. Wright says her new job is challenging and interesting, and she was able to hit the ground running because "I already knew how to work with Don." We are very happy to have her on staff.

Zimbabwe native Chido Kativhu a junior at Amherst College studying (Continued on Page 3)

## IPI Staff News (continued from p. 2)

neuroscience, has joined IPI as a summer intern. She is working with Stephen Spielberg on the drug reformulation project with WHO, focused on treating TB in developing nations.

"Back home I work with different organizations regarding children who are affected by AIDS," she says. "IPI's mission to better medicine for children fits with my goals. I am immensely enjoying it, and learning a lot."

Kativhu plans to attend graduate school in the US before returning to Zimbabwe.

Amherst College junior Justin Park has also joined IPI for the summer as an intern. An economics and pre-med major, Park says he was attracted to the internship after studying cost-benefit analyses of medical products and policies. "The idea of medical efficiency is very interesting to me," he says. "It is the intersection between medicine and social entrepreneurship, and IPI sits at that same intersection. Academically it's a good fit."

Park is working with COO Ross Trimby on the Drug Reformulation Project, and doing market research on various medical products. A native of Champagne-Urbana, IL, Park says he is enjoying his work experience at IPI. "It's an environment where they trust you to do your work. It's very self-motivating." And, he adds, getting the chance to watch a non-profit develop from the beginning is "sweet."

And lastly, Caron D'Ambruso has left IPI to return to the medical device industry. She served as Vice President for Product Innovation, helping us analyze the current state of NICU equipment and identify needs. We wish her much success in her new endeavors.

## IPI and WHO Collaborate On Pediatric TB Drug

IPI is collaborating with the World Health Organization (WHO) to develop the first pediatric multi-drug formulation to treat tuberculosis (TB). This is part of an initiative launched by WHO called *Make Medicines Child Sized*, a global campaign to raise awareness and accelerate action to address the need for improved availability and access to safe child-specific medicines for all children under 15.

"This is a very exciting initiative with a long history," says IPI's Stephen Spielberg, MD, PhD. "Many of us in pediatric pharmacology have been working with WHO for years to include a consistent pediatric perspective in their essential drug list." This list, called The Model List of Essential Medicines, includes drugs that are important for all countries, but is particularly focused on the needs of developing countries.

WHO's new campaign aims to ensure greater access to children's medicines, with priority placed on the development are drugs targeting HIV/AIDS, malaria, pneumonia, tuberculosis, and diarrhea in children. Combined, these diseases are responsible for more than 50% of deaths under the age of five. Approximately 10 million children under five are expected to die in 2007, more than half from illnesses and diseases that can be treated with appropriate medication.

"If you look at TB therapy, for adults you have to give multiple medications at the same time for months to prevent infection," says Spielberg. "They take a tablet that contains three drugs, and for those who need a fourth drug, there is one additional tablet. For children, most people end up crushing the tablets and administering it in pudding or water. But the triple therapy for adults has the wrong formulation for children, too much of some drugs and not enough of others. We want to develop a fixed-drug combination for children."

IPI and WHO have submitted a grant proposal to the Bill and Melinda Gates Foundation for funding to develop a multi-drug combination that could be used for very young children through teenagers. Spielberg will be attending a WHO conference in July in Geneva at which he and colleagues will set the appropriate dose ratios for treatment, based on the world's literature. "Once we set those standards, we will work with colleagues in a number of different settings, including at Muhimbili University in Tanzania, to do a survey of patient preferences."

Spielberg underscores the importance of support from organizations such as the Gates Foundation for this work. "There isn't much of a significant return for commercial entities. There is no way to develop a product like this without significant philanthropic support."

A response to the grant proposal is expected in July 2008.