We live in an amazing age. Technological breakthroughs occur daily. The USB thumb drive I have in my pocket has 100 times more storage than my “super” computer from 25 years ago. The average cell phone can place calls, make and accept electronic payments, track stocks in real time, receive and send emails, sign contracts, track calories, monitor heart rate, obtain oxygen saturation via Bluetooth, wirelessly monitor an inpatient EKG, and effortlessly download an entire patient file in

Continued on Page 2
Reflections from the Chair  Continued from Page 1

seconds. HIPAA notwithstanding, what limits do we have on technology? On eBay, I can buy a pulse oximetry that will arrive in just days. I can buy a technology that will monitor a baby in another room or perhaps tell me if that baby has become apneic. I can go on Craigslist and purchase breastmilk. (At least, it's supposed to be breastmilk.) I don't need a prescription for a potent antibiotic; the vendor on the other end of the transaction doesn't know or care that I am a physician. The situation is getting out of hand.

As chair of the Section on Advances in Therapeutics and Technology, I know we should celebrate advances in the availability and accessibility of these wonderful therapeutic devices and medications. Technology should be available at the speed of light. But something is missing. There is no oversight. There is no responsibility. There is no credibility. And moreover, there is no pediatrician to arbitrate. Let's back this up. Yes, there is a detailed instruction book that might even be written in English. Certainly, the manufacturer or vendor will warrantee the transaction, but when a child's health is on the line, of what value is a money-back guarantee?

A couple of months ago, I had a dilemma. I was trying to send a former premature baby home from the Neonatal Intensive Care Unit, but I could not get to a point where the baby was apnea-free for more than a five-day period. I could have waited it out, perhaps another week or two. But these were good parents and although there is a real question as to whether there is good data that home apnea monitoring can provide an evidence based solution that prevents Sudden Infant Death Syndrome, I suggested to the parents that it might be best to consider sending the baby home with a monitor. To my surprise, and thanks to the miracle of Dr. Google, the parents had already investigated and had purchased one on line! I hesitated. We could not use this monitor that did not have FDA approval or an indication for the purpose that the parents intended to use it. I spoke to our discharge planners, but none of our usual suppliers had a monitor in stock. Thankfully, the baby's events improved, and she went home without a physician indicated monitor. That said, after making the investment, the parents are probably monitoring the baby with or without my imprimatur.

We have all become advocates of breastmilk being best for babies. Baby Friendly programs in hospitals have significantly increased breastfeeding rates around the country. Varied estimates of health cost savings from improved morbidities have suggested that exclusive breastfeeding can save the nation up to 3 billion dollars annually in reduction of costs from formula and improvements in infant health. Wanting the best for their babies, moms around the country have tried to exclusively breastfeed. Most are successful. For one or another reason, some are not. Although many of these moms may look to commercial milk banks, the costs may be discouraging. Enter the World Wide Web. Yes, breastmilk can be purchased in the same way as any other online product. HIV, Hepatitis, and CMV testing may or may not be stated. The proprietor may be a mom from Wisconsin wanting to help support her family or perhaps someone else from who knows where. The breastmilk may come from a mom who is deliberately health-conscious, takes prenatal vitamins, and makes sure that her own baby gets enough as well. Or perhaps, mom drinks organic tea with Fenugreek imported from some distant land (Cadmium toxicity)? Maybe she dilutes the breastmilk with just a little bit of water or formula or perhaps melamine? How can we possibly know?

I can "buy Vancomycin online without a prescription at a low price". My Google search for this term took me to a website that promised worldwide delivery for only $15. In an age of increased emphasis on antibiotic stewardship, what do my best efforts matter if my patients are able to get extremely
powerful antibiotic therapies online for viral syndromes? Who knows if this is really Vancomycin, perhaps it is some Vancomycin-like compound that is cut with some illicit substance?

The sheer volume of medical solutions that are available through alternative outlets makes it unlikely that the FDA or other government agencies could effectively reel them all in. But, this is a progressively worsening health concern that we are ill-equipped to handle in either the hospital or office setting. Even if I could, I am not sure I would know how to report these incidents. Local law enforcement may be sympathetic, but many of these transactions occur across state lines and internationally outside of their jurisdiction.

So, where are we now? I am not sure. Are we ineffectual in the face of advancing technology? I think not. But this unregulated therapeutic exuberance must be reeled in. How are we as pediatricians vested in advances in therapeutics and technologies to stand in the way of the Internet age? The answer is obvious. We must.

I am not sure that we can stop all of the madness, but anticipatory guidance has taken on a new meaning and gravity. The parents of our patients must understand the danger of buying into unconventional nutrition delivery systems, as well as newer medications and medical devices that have not been vetted by good scientific method in a controlled environment. Parents must have a defined understanding of the dangers of untested technology and beware of false claims made by unscrupulous online outlets. In as much as our section is about “advances”, in this situation, we must be the impediment.

Sincerely,

Mitchell Reid Goldstein, MD, FAAP
Greetings from SXSW in Austin, Texas!

As one example of the growing national pediatric innovation movement, at the 3rd annual Impact Pediatric Health pitch competition at SXSW in Austin, TX (impactpediatrichealth.com) in mid-March, I witnessed energetic pediatric champions touting their products as the next major disruptive technology in pediatrics. Unfortunately, there could only be one digital health winner and one medtech winner for the prizes, and they were Keriton LLC of Philadelphia, PA, which is focused on improving breast milk for NICU babies, and Luminopia of Cambridge, MA, which is focused on visual and neurological care using virtual reality technology, respectively. Of note, this event is one of several sponsored by children’s hospitals nationwide that broadly support pediatric technology development to improve children’s health through pediatric innovations.

Yet, innovation should be implemented with the safety of our pediatric patients at the forefront. This edition of the SOATT newsletter includes a call by our SOATT chair, Mitch Goldstein, MD, FAAP, for more research and clinical trials to allow for responsible introduction of pediatric innovations into the clinical realm. And this is also echoed for our NICU patients in an article from Ron Ariagno, MD, FAAP. This edition also features an update by Ed Connor, MD, MBE, FAAP on the work of the Global Pediatric Clinical Trials Network that was sponsored in part by the SOATT and which has led to the launch of the well-received Institute for Advanced Clinical Trials for Children (I-ACT for Children).

We look forward to seeing you at this fall’s NCE meeting in the “Windy City” (Chicago) and especially at the Section’s Educational program on Pediatric Innovation on Monday, September 18, 2017, 12:00 pm – 2:00 pm.

We hope that you enjoy reading this edition of the newsletter, and please share it with a colleague, patient, or friend. We welcome all suggestions for articles. It is an avenue of communication for our Section, and for those who share the passion of caring for children and improving our care for children.

**Pediatric Medical Device Resource List:**

FDA-funded Pediatric Device Consortia (PDC) – a resource for pediatricians, pediatric caregivers, and pediatric specialists in developing their innovative pediatric medical device projects. Available assistance can include consulting, project management, and seed funding.

Further details can be found in the previous editions of the newsletter at: [https://www.aap.org/en-us/about-the-aap/Committees-Councils-Sections/soatt/Pages/newsletters.aspx](https://www.aap.org/en-us/about-the-aap/Committees-Councils-Sections/soatt/Pages/newsletters.aspx)  

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From the Editor's Desk  Continued from Page 4

Atlantic Pediatric Device Consortium
(Georgia Institute of Technology / Emory University / Children's Healthcare of Atlanta / Virginia Commonwealth University Institute for Engineering and Medicine)
www.atlanticpediatricdeviceconsortium.org

Boston Pediatric Device Consortium
(Boston Children's Hospital / Harvard Medical School)
www.childrenshospital.org

National Capital Consortium for Pediatric Device Innovation
(Children's National Health System / University of Maryland)
innovate4kids.org

New England Pediatric Device Consortium
(Simbex / CIMIT / IPI / Mass General Hospital for Children / Dartmouth University)
nepd.org

Philadelphia Regional Pediatric Medical Device Consortium
(Children's Hospital of Philadelphia / University of Pennsylvania / Drexel University)
www.PhillyPediatricMedDevice.org

Southern California Consortium for Technology and Innovation in Pediatrics
(Children's Hospital Los Angeles / University of Southern California)
scctip.com

University of California San Francisco Pediatric Device Consortium
(University of California San Francisco)
pediatricdeviceconsortium.org

University of Michigan Pediatric Device Consortium
(University of Michigan)
peddev.org

FDA Pediatric Device Consortia Grants Program
(Office of Orphan Products Development)
www.FDA.gov/PDC
Achieving Parent Advocacy for Regulatory Clinical Trials Research

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Stanford University Professor Emeritus, Pediatrics,
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Neonatologists should not expect parent advocacy for therapeutic development until neonatologists have a consensus and actively participate in biomarker discovery, surrogate endpoints and the regulatory process required for approval of existing or new therapeutics.

Background
Currently, most conditions and diseases in critically-ill neonates are managed with “off label” drugs (90%) due to lack of data to support (US Food and Drug Administration (FDA) approval) safety and efficacy or decisions to determine appropriate dose and formulation. In older children, the percentage of drugs prescribed “off label” (not approved for the use intended by the FDA) has fallen from approximately 80% to 50% over the past 15 years. By comparison, the use of off label drugs in newborn intensive care clinical practices continues at 90%.

Neonatologists have a consistent history of doing clinical research regarding the use of drugs and comparisons of different treatment regimens. These studies have not usually focused on or provided the results required for drug approval and labeling due to study design limitations and lack of convincing safety and efficacy measures (acceptable biomarkers for diagnosis or disease/condition, endpoints and outcome measures for change or improvement). Currently, bedside practice and teaching is still based on clinical publications, anecdotal experience, and opinion. Therefore, “the standard of care” varies widely, not only regionally but even within practices.

The American Academy of Pediatrics (AAP) and others (e.g., FDA) have successfully lobbied for pediatric initiatives such as the Best Pharmaceuticals for Children Act (BPCA, 2002) and Pediatric Research Equity Act (PREA, 2003), and for Neonatology expertise at the FDA. The FDA Safety and Innovation Act (FDASIA), which was passed in 2012, has made BPCA and PREA permanent regulatory statutes. The BPCA authorizes the FDA to extend marketing exclusivity for six months for a product for which the manufacturer provides additional pediatric labeling information, either because the product can be anticipated to provide a meaningful therapeutic benefit or because the FDA has requested specific information. Under FDASIA, if a written request from the FDA to the sponsor does not include studies for neonates, the FDA must explain its rationale for the exclusion. PREA mandates a pediatric assessment of drugs and biologic products if the application involves a new indication or dosage form (e.g. new liquid formulation), new route of administration, dosing regimen (combination) or active ingredient. The pediatric assessment must address safety and efficacy for the clinical indication in all appropriate pediatric age groups.

The Institute of Child Health and Development (NICHD) and FDA also established the Neonatal Drug Development Initiative (NDDI). The mission of the workshop (2004) was to define a multiphase program to identify knowledge gaps in neonatal pharmacology, clinical study design, and outcome measures and to explore new study designs appropriate for preterm and term newborns with the
goal of determining whether the drugs used in the clinical management of newborns are safe and effective. The proceedings of the workshop were published in 2005 (Clin Ther. 2005: 27:796-813) and 2006 (Pediatrics Vol. 117 No. Supplement 1, 2006).

Recently, the report entitled “Drug Labeling and Exposure in Neonates” (JAMA Pediatr. 2014 Feb;168(2):130-6) reviewed the FDA pediatric data for studies submitted between 1997-2010 to identify the impact of those studies and labeling changes that included neonates. Neonates were included in 41 studies of 28 drugs, with 23 of the drugs studied, which resulted in labeling changes. There were a total of 24 neonatal labeling changes (one drug had 2).

Forty-six percent (11 of 24) of the labeling changes also included an approval as safe and effective for neonates. Of note, these drugs were studied for HIV (4), anesthesia (3) and other (4): plasma substitute volume expander, gastroesophageal reflux, reduction of blood pressure and antibiotics. In this report, they assessed the potential impact of these label changes using a clinical cohort of neonates (infants up to 28 days of age) from 2005-2010 studied for drug exposure from the Pediatrix Medical Group dataset, which had 290 NICU’s and 446,335 hospitalized infants. Three hundred and ninety-nine drugs were prescribed for more than 1.5 million exposures in the first 28 postnatal days. Of the 11 drugs with a neonatal indication, 7 were never used in the Pediatrix sample and the other four drugs (famotidine, linezolid, nevirapine and rocuronium) were used infrequently. Of the 28 drugs in the FDA study, gastroesophageal reflux drugs (ranitidine, lansoprazole and famotidine) were most frequently used in clinical practice (in spite of the lack of a clear indication or physiologic rationale) and the second most commonly used overall was inhaled nitric oxide. The authors concluded that few hospitalized neonates (<0.5%) were exposed to a drug approved for use in neonates. From these data it appears that BPCA and PREA have not increased needed study of “off patent” (“off label”) drugs for neonates. The clear message is that neonatologists and not industry alone need to take the lead in readdressing this major deficiency in knowledge and to make a commitment for change.

The conclusion is that the NIH and FDA Neonatal Drug Development Initiative (2004), the Best Pharmaceuticals for Children Act (BPCA), Pediatric Research Equity Act (PREA) and FDA Safety and Innovation Act (FDASIA, 2012) have been very important and significant efforts; however, they have not been sufficient to change neonatal clinical practice patterns in which most drugs in use are unapproved or “off labeled”.

More recent initiatives to advance therapeutic development for infants:

The Task Force for Neonatal Perinatal Therapeutic Development (NeoPeriTD) (https://www2.aap.org/sections/Perinatal/pdf/PerinatalFeb2016.pdf) (Chair: RL Ariagno) was established and approved by the American Academy of Pediatrics (AAP) Section on Neonatal Perinatal Medicine (SoNPM) Executive Committee on October 22, 2015.

The mission: To promote and facilitate neonatal-perinatal therapeutics development and FDA regulatory approval for new and established therapies to improve the care and outcome of critically ill newborn infants. The goal: use the educational, advocacy, liaison and leadership resources of the AAP and SoNPM to establish, through consensus, a culture of investigation and collaboration for all clinical neonatology practices: academic, corporate and community-based to maximize the opportunity
for infants to participate in research. *(A clinical consensus for the importance of investigation and collaboration from neonatologists, parents and intensive care nurses is critical. Neonatologists will need to establish a consensus to establish the standardization of clinical practice so that the variation within and between practices and regions is less than the difference hypothesized for an intervention, which will be studied.)*

The International Neonatal Consortium (INC) and (Global) Pediatric Trials Consortium (PTC):

Recently, the American Academy of Pediatrics, pharmaceutical companies and the FDA, through the Critical Path Institute, have launched two independent non-conflicted organizations: the International Neonatal Consortium (INC; May, 2015; http://c-path.org/programs/inc/#) and the (Global) Pediatric Trials Consortium (PTC: October 2015; http://c-path.org/programs/ptc/). Although NIH is not a formal part of these agreements, NIH has several representatives participating in these consortia. The PTC is developing national and global pediatric/neonatal interdisciplinary clinical trials networks.

The focus of the INC is on conditions commonly encountered in neonatal medical care: e.g., Neonatal Brain Injury, Neonatal Lung Injury, Neonatal Gastrointestinal Injury, Neonatal Sepsis (infections), Retinopathy of Prematurity (ROP), Treatment of Seizures, Prevention of Bronchopulmonary dysplasia (BPD), and Developing a clinical pharmacology for neonates position paper that may be used to inform the FDA and the European Medicines Agency (EMA). The INC Clinical Pharmacology working group has a publication in Pediatric Research: “Safety, Dosing and Pharmaceutical Quality for Studies that Evaluate Medicinal Products (including Biological Products) in Neonates.” (Ward RM, et al, Pediatric Research 2017, doi10.1038/pr.2016.221). An online comprehensive document is available to assist investigators and sponsors conducting studies to evaluate medicinal products and biologics in neonates.

In summary, neonatologists make drug selections based on applying the information from drugs approved for children and adult populations and on what they consider current “standard of care”, the availability of drug in the hospital formulary, their level of comfort in using the drug in the neonate based on what is known from the published literature and advice from “experts” or consultants. For many reasons there have been continuing obstacles for neonates to fully benefit from the Neonatal Drug Development approaches over the last decade plus e.g., such as prohibitive high commercial drug development cost for an orphan population (*conditions affecting < 200,000); insufficient awareness of issue, professionally (neonatologists and nurses) and publically; suboptimal enrollment in clinical trials; suboptimal research resources (trained researches and sustained laboratory infrastructure); lack of collaborative research networks working together; lack of shared archived data bases and knowledge; and not being a sufficient priority. Finally, a basic knowledge base must be established to facilitate approval of new interventions, through robust research, that can deliver the data required to prove safety and efficacy.

(*http://www.fda.gov/ForIndustry/DevelopingProductsforRareDiseasesConditions/ucm2005525.htm*)

Ultimately, the most effective approach would be for regulatory studies to be accomplished within clinical practices. Parents and families will need to be informed of the critical need for the research and the importance of their input in trial design and to learn what would be acceptable for them. Continued on Page 9
Collaboration between subspecialty pediatricians, clinical and academic/clinical physician investigators, National Association of Neonatal Nurses (NANN), FDA (utilizing BPCA and PREA), National Institute of Health (NIH), National Institute for Child Health and Development (NICHD): Pediatric Trials Network (PTN) and Neonatal Research Network; Pediatrix (MEDNAX), Kaiser Permanente, Academic Societies, AAP Section on Neonatal and Perinatal Medicine (SONPM), Section on Advances in Therapeutics and Technology (SOATT), AAP Organization of Neonatal Training Program Directors (ONTPD), AAP Training and Early Career Neonatologists (TECaN), AAP Fetus and Newborn Committee and other relevant Sections and Committees, Vermont Oxford Network (VON) and California Perinatal Quality Care Collaborative (CPQCC), National Heart Lung and Blood Institute (NHLBI) Pediatric Respiratory Outcomes Program and Pediatric Pulmonary Hypertension Network (and other relevant data and clinical trials networks), March of Dimes, Industry, Investigator Sponsors, International Neonatal Consortium, (Global) Pediatric Trials Consortium and “parents, family and community” advocates will be needed. Among this long list of stakeholders and collaborators it is important to emphasize that the support of parents will be essential to have success in the next era of advancing clinical practice and clinical trials research. When parents and the public are fully informed and appreciate the need to accomplish this research, we can add their voice and support for professional action and funding. Then we can work together to accomplish the research needed to advance the care of neonates and improve outcomes.

It is important to emphasize for neonatologists and parents that currently most neonatal clinical trials do not address research to provide data to support approval of existing or novel therapeutics for infants. To accomplish this research it will require collaborative efforts to discover biomarkers, endpoints and outcome measures so that therapeutic investigations can target specific mechanisms of a condition or disease e.g., to improve or to prevent BPD. Biomarkers will be the key to evaluating the effectiveness of new interventions.

**Conclusion**

The success of our efforts to establish parent and family group advocacy will hinge on neonatologists’ (neonatal intensive care practitioners and nurses) consensus and regulatory research involvement to make clear that we agree and support that this effort is critical for us to improve care and outcomes of neonates.
Intranasal Procedural Sedation for Diagnostic Procedures in Children

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Email: sedillo@bcm.edu

Introduction
Over the past few years, the pediatric sedation literature is replete with articles describing various sedation regimens for children who require diagnostic radiologic procedures such as MRI or CT scan, or neuro-diagnostic testing such as electroencephalogram (EEG) or ABR (auditory brainstem reflex testing). This development is having a profound impact on the sedation management of children by providing a less invasive, less painful, and more satisfying medication administration process. The primary sedative agents administered nasally in children include dexmedetomidine (DEX), midazolam (MID), ketamine (KET), and fentanyl. Worldwide, this technique is utilized in the emergency department, the sedation unit, the radiology suite, and the critical care units. This administration technique has many advantages for the medical team, the patient and their family as outlined in Table 1.

<table>
<thead>
<tr>
<th>Table 1. Advantages of Intranasal (IN) Sedative Administration in Children</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relatively non-invasive and painless</td>
</tr>
<tr>
<td>Better patient and family satisfaction</td>
</tr>
<tr>
<td>Reduced materials and equipment</td>
</tr>
<tr>
<td>Reduced expense</td>
</tr>
<tr>
<td>Reduced training requirement</td>
</tr>
<tr>
<td>Increased safety with fewer adverse events</td>
</tr>
</tbody>
</table>

Nasal Administration
The nasal cavity is the administrative route for many pharmacologic agents with either local nasal effects or wider systemic effects. Examples of nasally-administered medications with systemic effects include agents for migraine treatment (sumaltriptan), blood glucose control (insulin), smoking cessation, analgesia (fentanyl), illness prevention (influenza vaccination), opioid overdose (Naloxone), and hormonal replacement (desmopressin).

The nasal cavity can be subdivided in 3 regions: the nasal vestibule, the respiratory region, and the olfactory region (Figure 1). In the adult male, the total surface area of the nasal cavity is approximately 150 cm² with the olfactory mucosa of the roof of the nasal cavity covering only 4 cm². The respiratory region begins with a squamous epithelium that gradually transitions to a pseudostratified columnar epithelium covered with microvilli, which has a relatively high absorptive capacity and is thus a potential site for systemic drug absorption. The junctional complexes of these epithelial cells have selective permeability to hydrophilic molecules.

Intranasal medications can be administered in a variety of ways: the syringe drip method into the nares or with the use of an aerosolizing device such as the LMA MAD Nasal intranasal mucosal atomization device (Figure 2, Teleflex Incorporated, Research Triangle Park, NC). The maximal volume limit for

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intranasal administration is not clear but up to a maximum of 0.5 mL of concentrated medication in each nare in the child, and up to 1 ml in the adult may be reasonable.

The Nose-to-Brain Pathway
The olfactory mucosa is a pseudostratified respiratory epithelium with olfactory sensory neurons, which extend into the basement membrane and then through the cribiform plate to synapse in the olfactory bulb. The so-called nose-to-brain pathway for drugs may be by the axonal transport mechanism in an intracellular fashion, or by the olfactory epithelial pathway via the tight junctions. Thus, medications may reach the central nervous system either by transepithelial absorption into the blood stream with transport across the blood-brain barrier, or by the nose-to-brain pathway (Figure 3).

Dexmedetomidine Usage in Children
Dexmedetomidine (DEX) is a highly selective alph-2 receptor agonist that was approved by the FDA in 1999 for short-term sedation in the ICU.
With further patient experience, unlabeled usage for DEX has expanded to include its use as a pre-operative medication, as an anesthetic adjunct, and as a post-operative sedative. Its use in pediatrics began in the perioperative arena but now it is being used in the PICU and in the pediatric sedation suite as a safe and effective sedative agent.⁴,⁵

In one of the first reported pediatric series of the use of dexmedetomidine as a sedative agent, Nichols and colleagues of the University of Missouri reported their retrospective case series of intravenous dexmedetomidine (IV-DEX) as a rescue agent in the MRI suite following failed sedation with chloral hydrate or benzodiazepines.⁶ Many other prospective and retrospective case series then followed using dexmedetomidine by the intravenous and intranasal routes, and in combination with other agents.

Last year, the Pediatric Sedation Research Consortium (PSRC), which is a collaborative group of institutions dedicated to improving pediatric sedation and anesthesia care outside of the OR, published a study of 13,072 procedural sedation episodes in which DEX was utilized. Their study demonstrated a sedation success rate of 99.7% with an overall serious adverse event rate of 0.34% (45 of 13,072). Approximately 10% of these cases received IN-DEX, often co-administered with a benzodiazepine. It is currently the largest published series reported thus far and demonstrates the high success rate and safety of dexmedetomidine as a sedative agent.⁷

**Intranasal Dexmedetomidine and Midazolam**

IN-DEX usage in humans began with pioneering studies looking at its pharmacokinetics and pharmacodynamics in comparison with intravenous dexmedetomidine in healthy adult volunteers. With IN-DEX, peak plasma concentrations of dexmedetomidine are reached in 38 minutes with bioavailability of 82%. Onset of effects of IN-DEX was 30 to 45 minutes. The plots of dexmedetomidine plasma concentration over time are comparable between intravenous and intranasal administration (Figure 4).⁸

One of the earliest prospective pediatric studies of IN-DEX was published in 2012 in which the researchers administered 2 mcg/kg by syringe drip method 30 minutes prior to their scheduled study. They found that 60% (17 of 28) of their patients successfully completed their MRI scan without adverse events.⁹ Further studies, both prospective and retrospective case series, have refined dosing quantity, dosing technique, and the use of adjunctive sedative agents to improve the sedation success rates while still maintaining an excellent safety profile. Figure 5 offers selected case series for a variety of diagnostic procedures in intranasal sedative agents.

**Summary**

In summary, there are now many well-studied intranasal sedation regimens available to the clinician providing procedural sedation services to children. These regimens have good efficacy and a strong safety profile, if the pediatric sedation services are rendered within an environment that has the appropriate personnel, policies, support systems, supplies, equipment, and monitoring. There are still areas of intranasal sedation administration that require further research to include determining the maximal administration volume for a given child’s age or size, the proper patient positioning, and the optimal medication administration device.

Continued on Page 13
### Table 2. Selected Pediatric Intranasal Sedation Studies – Therapeutic & Diagnostic Procedures

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Study Author &amp; Year</th>
<th>Study Design</th>
<th>Study Size</th>
<th>Sedative Regimen</th>
<th>Admin. Technique</th>
<th>Sedation Success (1st dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT Scan</td>
<td>Mekitarian Filho, 2013</td>
<td>Prospective Observational</td>
<td>60</td>
<td>IN MID 0.4 mg/kg Rescue with IN MID 0.1 mg/kg</td>
<td>LMA MAD</td>
<td>1 dose: 75% 1-2 doses: 93.3%</td>
</tr>
<tr>
<td></td>
<td>Mekitarian Filho, 2015</td>
<td>Prospective Observational</td>
<td>60 (ED patients)</td>
<td>IN DEX 2.5 mcg/kg Rescue with IN DEX 1 mcg/kg</td>
<td>LMA MAD</td>
<td>95%</td>
</tr>
<tr>
<td>MRI Scan</td>
<td>Ibrahim, 2014</td>
<td>Prospective RCT</td>
<td>58 (29 each group)</td>
<td>IN DEX 3 mcg/kg vs IN Ketamine 7 mg/kg Rescue as needed</td>
<td>Syringe drip</td>
<td>IN DEX: 86.3% IN KET: 79.4%</td>
</tr>
<tr>
<td></td>
<td>Tug, 2015</td>
<td>Prospective RCT</td>
<td>60</td>
<td>IN DEX 3 vs 4 mcg/kg Rescue with IV Propofol</td>
<td>Syringe drip</td>
<td>3 mcg/kg: 30% 4 mcg/kg: 70%</td>
</tr>
<tr>
<td>ABR/EEG</td>
<td>Baier, 2016</td>
<td>Retrospective</td>
<td>169 (EEG – 117, ABR – 52)</td>
<td>IN DEX 2.5-3 mcg/kg Rescue with IN DEX 1-1.5 mcg/kg</td>
<td>LMA MAD</td>
<td>1 dose: 90% 1-2 doses: 99%</td>
</tr>
<tr>
<td>ABR</td>
<td>Reynolds, 2016</td>
<td>Prospective RCT</td>
<td>90</td>
<td>Oral chloral hydrate vs IN DEX 3 mcg/kg</td>
<td>LMA MAD</td>
<td>IN-DEX: 89%</td>
</tr>
<tr>
<td></td>
<td>Reynolds, 2016</td>
<td>Retrospective</td>
<td>300 (100 IN DEX)</td>
<td>PO CH 50 mg/kg vs IN DEX 4 mcg/kg</td>
<td>LMA MAD</td>
<td>IN-DEX: 91%</td>
</tr>
<tr>
<td></td>
<td>Li, 2015</td>
<td>Prospective Observational</td>
<td>115</td>
<td>IN DEX 3 mcg/kg</td>
<td>LMA MAD</td>
<td>87%</td>
</tr>
<tr>
<td></td>
<td>Li, 2016</td>
<td>Prospective RCT</td>
<td>279</td>
<td>IN DEX 3 mcg/kg by LMA MAD vs syringe drip method</td>
<td>Both</td>
<td>LMA MAD: 82.5% Syringe drip: 84.5%</td>
</tr>
<tr>
<td></td>
<td>Miller, 2016</td>
<td>Retrospective</td>
<td>63</td>
<td>IN DEX 2.5-3 mcg/kg Rescue with IN DEX 1 mcg/kg</td>
<td>LMA MAD</td>
<td>90%</td>
</tr>
<tr>
<td></td>
<td>Miller, 2016</td>
<td>Prospective RCT</td>
<td>150</td>
<td>PO CH 70 mg/kg vs IN DEX 2-3 mcg/kg</td>
<td>Syringe drip</td>
<td>N-DEX: 98%</td>
</tr>
</tbody>
</table>

Fig.5. Chart of selected pediatric intranasal sedation studies for diagnostic procedures.
Legend: IN DEX, Intranasal dexmedetomidine; IN KET, Intranasal ketamine; IN MID, Intranasal midazolam; PO CH, Oral chloral hydrate; LMA MAD, LMA® MAD Nasal™ Mucosal Atomizer, Teleflex Inc., Research Park, NC, USA
References:
17. Li BL, Ni J, Huang JX, Zhang N, Song XR, Yuen VM. Intranasal dexmedetomidine for sedation in 

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Intranasal Procedural Sedation for Diagnostic Procedures . . . Continued from Page 14


We’re New and Need You!
How to Join . . .
It’s easy! There are NO DUES to join the SOATT if you are an AAP member.
Send an e-mail to Jackie Burke at jburke@aap.org to request to be added to the Section.

SOATT Milestones
The Section has created a document that catalogs important highpoints for the Section since its creation in 2010.
During the last year, Critical Path Institute’s Pediatric Trials Consortium (PTC) has finalized its Advisory Report, providing advice and guidance for a new independent non-profit designed to advance information regarding new innovative therapeutics for children (www.c-path.org). Based on this Advisory Report, the new non-profit, the Institute for Advanced Clinical Trials for Children (aka I-ACT for Children) was established as a 501(c)3, received verification of its tax-exempt status, and appointed its initial Board of Directors (Ed Connor MD, MBE, FAAP, Robert Ward, MD, FAAP, Martha Brumfield, PhD, and Caroline Dorsa, MBA) www.iactc.org.

The leadership team at I-ACT for Children is now working diligently to build core policies and operational support, complete its seed funding campaign, establish advisory and review committees, and identify vanguard projects and collaborating institutions. Currently we are focused on establishing the Institute’s core competencies in the following four areas:

**Strategy and Planning.** This involves providing independent, expert advice and guidance to trial sponsors and other stakeholders to help them develop pediatric plans and protocols – doing our best to get them “right the first time.” Core components include facilitating the identification of unmet therapeutic needs of children; advancing scientific knowledge about strategies to close gaps in diseases and conditions that affect children; and mobilizing stakeholders in action-planning to address important clinical trial design challenges.

**Capabilities, Tools, Best Practices.** In this area, the Institute will lead, or participate in, cross-sector teams that streamline and improve clinical trial processes and systems to enhance the quality and timeliness of regulatory-quality data and reduce administrative burden. Education regarding standardized approaches and tools, particularly in those administrative areas that cause the most significant delays, are important outcomes of this work.

**Infrastructure and Clinical Trials Execution.** This involves supporting a network of pre-qualified trial-ready sites and collaborating with regional and diseased-focused networks to ensure that we reach children across the world.

**Leadership.** Here the I-ACT for Children will work to catalyze efforts that assure early and continuous engagement of patients, caregivers, investigators, nurses, pharmacists and other research delivery staff; creating awareness and disseminate information and research regarding unique opportunities to address diseases and conditions that impact children; enhancing the application of innovative trial designs and quantitative science research methods; improving clinical trial design; and streamlines trial conduct for all stakeholders.

Continued on Page 17
The Institute will build these capabilities and demonstrate the value and proof-of-principle of the *I-ACT for Children* model. Subsequently, it will build on this established core, scale the work and establish a sustainable infrastructure for clinical trials research, education, and leadership as a collaborative element of the global pediatric trials ecosystem.

I-ACT for Children is based on a foundational set of values, including

**Addressing Children's Unmet Medical Needs.** Children's unmet medical needs drive our agenda and all our work supports the development of innovative medicines and devices for children that are most needed to improve and preserve children's health and wellness.

**Independence.** We are an independent voice in innovative medicines and devices development, focused on optimal impact on child health.

**Collaboration.** We are collaborative and synergistic with other elements of the clinical research ecosystem – finding common ground and aligning common values, with children at the center.

**Quality.** Our standards are grounded in regulatory requirements, providing the basis upon which we deliver scientifically strong, clinically relevant and ethically sound advice and manage high-quality, timely conduct of clinical trials.

**Actionable Data.** We are focused on creating actionable data – meaning data that can be utilized to improve the safe and effective use of therapies, support robust regulatory submissions and enhance the information used by pediatric healthcare providers.

**Efficiency and Timeliness.** Because children are waiting, we must shorten the time it takes to bring innovative medicines and devices to them. Streamlining operations, reducing burdensome processes and optimizing the use of resources are fundamental principles that guide us.

**Trial Innovation.** We are committed to utilizing innovative clinical trials design and execution to maximize the value and impact of clinical trials for children's health.

*I-ACT for Children* will formally launch its work in 2017 and in anticipation of this, welcomes interested individuals, institutions, and research sponsors to become members of the Institute. Membership information is found on the *I-ACT for Children* website, [www.iactc.org](http://www.iactc.org) along with information about other ways by which you can support the Institute's mission. We look forward to the realization of the work that was started in 2014 at the AAP Stakeholder’s Forum on Pediatric Clinical Trials. We thank Critical Path Institute, members of the Pediatric Trials Consortium, and countless others who have contributed to getting us to this milestone.

For more information, please contact Ed Connor, MD, MBE, FAAP at ed.connor@iactc.org.
On August 5, 2015, the FDA approved the first drug to be manufactured on a 3D Printer. Spritam® (levetiracetam) was approved for adjunctive therapy of several forms of epilepsy in both pediatric patients and adults. The pill’s porous, layered composition allows it to disintegrate more rapidly than previously approved dosage forms, and may be particularly helpful for patients who have trouble swallowing. This is but one example of how 3D printing technology is dramatically altering the development space for drugs, biologics, medical devices and combination products. Opportunities for applying 3D printing technology to pediatric medical products abound, and are highlighted below.

3D printers create an object from a three-dimensional digital frame—such as that created by MRI or CT imaging, using 3D software. The printer creates a precise representation of the computer-generated structure by laying down successive layers of a raw material into the programmed 3D form. The material may consist of biocompounds and/or cells. The layered form may be composed of a single compound or tissue, or a combination of compounds. Also, known as additive manufacturing, 3D printing offers tremendous opportunity to transform how drugs, medical devices, biologicals and combination products are developed and manufactured.

The term “Additive Manufacturing” describes the process for creating an object with a 3D printer. By interpreting computer coded MRI and/or CT digital images, the printer translates those digital pictures into a 3-dimensional representation. The object is created by precise horizontal layering of the printer material (for example, photopolymer resin) into the object, such as a child’s defective heart, skull or limb. These models support surgical planning with creations that are anatomically precise.

Consider for example, how a pediatric neurosurgeon or cardiac surgeon prepares for a specific surgical procedure. Prior to 3D printing technology, the surgeon relied on imaging studies and visual reconstruction on a computer screen. Now, the surgeon can create a 3D model of the defective heart or limb or skull, and use that model to prepare for the patient-specific procedure or to create customized devices for each patient.
Examples of custom devices created through 3D printing include implants (such as cranial plates, external prostheses, hip joints or dental implants).

Both FDA and the National Institutes of Health websites provide guidance, video resources and available design modules. The NIH 3D Print Exchange provides 3D Print models and tools related to biomedical science, including collections for prosthetics, neuroscience, a heart library, and a “Molecule of the Month” Protein Data Bank. This exchange invites you to add to the available collection and tools. See the weblinks below:

- FDA’s role in 3D Printing: [https://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/3DPrintingofMedicalDevices/ucm500548.htm](https://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/3DPrintingofMedicalDevices/ucm500548.htm)
- Process of 3D Printing of Medical Devices: see: [https://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/3DPrintingofMedicalDevices/ucm500544.htm](https://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/3DPrintingofMedicalDevices/ucm500544.htm)
- Video: The 3Rs of #D Printing: FDA’s Role: [https://www.youtube.com/watch?v=kXWKF-PzEF8](https://www.youtube.com/watch?v=kXWKF-PzEF8)
- NIH 3D Print Exchange: [https://3dprint.nih.gov/](https://3dprint.nih.gov/)
- E-Nable: [http://enablingthefuture.org/](http://enablingthefuture.org/): a global network of volunteers who have developed models for 3D Printed assisted hand devices; see [https://www.youtube.com/watch?v=3ZyDLGgSj60](https://www.youtube.com/watch?v=3ZyDLGgSj60)
**Orlando, Florida**- The 2017 iCAN Research & Advocacy Summit will take place July 10-14, 2017 at Loews Sapphire Falls Resort, and will be hosted by iCAN and our local KIDS Florida chapter. This year's Summit will be larger than ever before, with a projected 175+ attendees, a highly interactive agenda, and our first-ever iCAN Partner Expo. Our numerous councils, committees, Boards and partners are all working together to build educational hands-on workshops and sessions that will cover a wide range of topics in the realm of pediatric research and medicine. The goal of this year's Summit is to promote innovative thinking and to send each and every attendee home with valuable information and tangible skills to inspire, as well as to fuel the momentum of our expanding global network.

Like years before, iCAN's third-annual Summit will deliver a world-class educational experience to all iCAN leaders, delegates and partners as we engage with one another, learn about different aspects of healthcare, research and innovation, and have a global impact on the future of pediatric medicine.

*The 2016 iCAN Research & Advocacy Summit at the Hospital Sant Joan de Déu in Barcelona, Spain, July, 2016*

Since last year's Summit, iCAN has been working diligently to expand the network and adjust its foundational elements accordingly, increase awareness of the importance of youth involvement in clinical research, and create more opportunities for our youth members to take part in patient advocacy and pediatric research initiatives. iCAN has continued to develop its committees and produce many deliverables to both benefit the youth involved and fortify the growing network. Among these initiatives are multiple abstracts, publications and posters, and contributions to iCAN's website. Youth representatives from many of iCAN's global chapters have attended numerous international conferences for medical innovation and research, including the International Pediatric Association's (IPA) 28th International Congress of Pediatrics, the AAP National Conference & Exhibition, Peds2040,
and numerous forums in the US and Europe. At each conference, youth members represented iCAN at an exhibit booth at which they conducted various surveys that were created by the iCAN Youth Council (topics included Centralized Electronic Medical Records Systems and Opinions on Genomic Testing in Pediatrics). The Youth Council has collated and analyzed the data from these surveys, submitted abstracts, and will hopefully present their posters at future conferences. Youth members have also participated in round table discussions, panel sessions, and a Young Innovators workshop.

With the new year, iCAN’s website received a complete overhaul in order to help establish consistent branding for the organization, offer more information to the general public and potential partners, and provide more opportunities for youth members to collaborate. iCAN is also working to develop its first-ever Special Interest Chapter in collaboration with childhood cancer research organization, Live Like Bella (www.livelikebella.org), which will offer youth the opportunity to participate

Continued on Page 22
in a virtual iCAN chapter made up of other kids and families with different forms of cancer across the globe. This Special Interest Chapter will be the first of its kind for iCAN, focusing on diseasespecific initiatives and offering an international representation of cancer patients and survivors in the iCAN network. iCAN leadership also met in Hartford, Connecticut with representatives from Tokyo, Japan to establish first steps towards iCAN’s first Asian chapter! For more updates on iCAN and the upcoming Summit, follow @iCANResearch on Facebook, Twitter and Instagram, or #iCANSummit2017.

iCAN members from KIDS Florida and childhood cancer research organization, Live Like Bella at the Young Innovators Workshop at Peds2040 in Miami, Florida, January 2017

iCAN leadership met in Connecticut with Dr. Hide Nakamura, Dr. Tsutomu Harada, and Child Life Specialist Kana Harada to discuss the possibility of establishing a KIDS chapter in Tokyo, Japan, January 2017
2016 AAP SOATT Award for Pediatric Innovation at the AAP NCE

The AAP Section on Advances in Therapeutics & Technology Award for Pediatric Innovation recognizes an individual who has greatly contributed to the field of pediatrics, pediatric therapeutics or pediatric technology through hard work and innovation.

We are delighted to nominate **Linda Ulrich, MD, FAAP** for the 2016 AAP Award for Pediatric Innovation. Dr. Ulrich is a pediatrician who works in the FDA's Office of Orphan Products Development (OOPD) and is the Director of the FDA's Pediatric Device Consortia Grant Program. As a member of the AAP, she meets all eligibility requirements for this award.

*Congratulations Dr. Ulrich!*

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2017 AAP NCE Update

*If you are attending the 2017 AAP National Conference (NCE), the Section on Advances in Therapeutics & Technology has several exciting and interesting programs sponsored by SOATT during the conference:*

**Sunday, September 16, 2017**

8:30 – 10:00 AM, repeat at 4:00 - 5:30 PM
Gadgets and Gizmo's for the Pediatric Office Workshops (2)

**Monday, September 18, 2017**

Noon – 12:05 PM Welcome
12:05 – 1:00 PM Top Three Research Paper Presentations (podium) plus Q & A
  TOPIC # 1 (tbd)
  TOPIC #2 (tbd)
  Topic # 3 (tbd)
1:00 – 1:30 PM Section Award for Pediatric Innovation Presentation
  (2017 Recipient: tbd)
1:30 – 2:00 PM Reception
CALL FOR ABSTRACTS
for the
American Academy of Pediatrics
SECTION ON ADVANCES IN THERAPEUTICS AND TECHNOLOGY
for the
AAP National Conference and Exhibition
September 16-19, 2017
Chicago, IL

Submission deadline:
April 7, 2017 at 11:59pm EST
(Abstracts must be received by this date)

The AAP Section on Advances in Therapeutics and Technology is providing a research forum for the discussion of research related to advances in medicine for children, innovations in pediatrics and pediatric devices.

Abstracts may cover such diverse topics as clinical trials of vaccines/drugs/devices, vaccine/drug/device safety, public policy and law related to drug and device development, practicalities of device/technology utilization in pediatric office settings, use of electronic devices for information sharing with patients and families, etc.

Abstracts will be accepted for poster presentations ONLY.
The top 3 posters may be permitted to have a short oral presentation.
Employees of commercial interests will not be permitted to present orally.

Industry authors cannot present/be first author, but they can be a non-first author. No need to be a member of AAP or SOATT specifically, but must register for meeting if selected.

Both original research and case reports will be considered for presentation. Abstracts will be published in Pediatrics, if accepted and authors comply with submission rules.

Submit your abstract at
http://www.aapexperience.org/abstracts/

Questions about the submission process or technical support should be directed to YMAmjad@aap.org

Questions about abstract content can be submitted to either Abstract Chairperson, Paul Wang, MD, FAAP (paul.wang@autismspeaks.org) or Susan Cummins, MD, MPH, FAAP (susan.cummins@gmail.com)
A Message from the Membership Committee

Chris Rizzo, MD, FAAP
SOATT Membership Committee Chair
crizzo624@gmail.com

It is an exciting time to be involved in generating new information on pediatric technology, devices and medications.

Those of you reading this newsletter are likely SOATT members. We rely on your help to recruit others to the Section. Members of the Section do not need to be eligible for AAP membership. See below for membership categories and eligibility.

Our Section continues to grow and now has 629 members!

Who Can Join?

1. AAP Members

Membership in the section is open to AAP Fellows, Specialty Fellows, Candidate Members, Post Residency Training Members, Honorary Fellows, Residents, Medical Students, Senior Members, and Corresponding Fellows with an interest in advances in therapeutics and technology. There is no fee for AAP members.

2. SOATT Affiliate Members

Affiliates are those who are not eligible for membership in the AAP and hold a Masters degree or Doctorate (or equivalent) in pharmacy or other health science concentration. Affiliates must submit an application (see “How to Join” below) and have a signed letter of support from an AAP fellow in good standing. There is a $40 annual fee for section affiliate members.

How To Join?

If you are already a member of the AAP and would like to become a SOATT member, join online by:

1. Going to Member Center of the AAP website and use your AAP login and password.
2. Click on “Join a Section or Council” under Member Community
3. Choose “Advances in Therapeutics and Technology”, answer a few questions, and click “Submit”.

Membership applications can be found at:
Members: http://membership.aap.org/Application/AddSectionChapterCouncil
Affiliates: http://membership.aap.org/Application/SectionAffiliate

If you have any questions about membership, please contact Chris Rizzo MD FAAP at crizzo624@gmail.com or the section staff at jburke@aap.org.
Welcome New Members
(October 2016 to February 2017)

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<td>Elham Alhifthy, MD</td>
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Section Produces Patient Education Brochure on Clinical Trials in Conjunction with the AAP Department of Marketing and Publications

Should My Child Join a Clinical Trial? Patient education brochure was finalized and published in February 2014. The brochure covers:

- Why are clinical trials for children needed?
- How are clinical trials done?
- What are the benefits and risks of a clinical trial?
- What do I need to know before I sign up my child for a clinical trial?
- What questions should I ask about a clinical trial?
- Words to Know
- For more information

For a free sample copy of the brochure, please contact AAP Customer Services at 866/843-2271.


* * *

AAP News
December 27, 2016

Personalized medicine evolving into precision medicine

J. Steven Leeder, Pharm.D., Ph.D. and Richard L. Gorman, M.D., FAAP

Precision medicine is a much bandied about term. During his 2015 State of the Union address, President Barack Obama launched a precision medicine initiative “to bring us closer to curing diseases like cancer and diabetes.”

Precision medicine is a model that is not very different from personalized medicine. Both stress that therapeutic and treatment decisions are based on information about an individual. What continues to evolve is the amount of diagnostic and individual information that is available.

The rapid development of genomics, proteomics, metabolomics, cellular assays, diagnostic radiology and diagnostic sonography is a potential game changer in individual care. The ability to analyze large data sets at the population level and apply results to an individual patient also is evolving rapidly.

Continued on Page 28
The concept of precision medicine is not new to pediatricians. The treatment of infections was based on symptoms, readily available lab results (white blood cell counts, erythrocyte sedimentation rate, C-reactive protein), patient age, likely organisms and potential outcomes of both the disease and the therapy. Treatment became more precise with better diagnostics such as gram stains, cultures and sensitivities. Similarly, the ability to measure blood types and Rhesus factors enabled blood transfusion to become more individualized, safer and more effective.

The same tools transforming personalized medicine to precision medicine are transforming pharmacokinetic thinking and research. In the clinical arena, the question asked is “What dose should we give?” In the pharmacokinetic arena, the answer is “What response do you want?” Linking the clinical question and pharmacokinetic answer is the concept of how much drug needs to be in the body — the “systemic exposure” — to elicit the desired response.

Working back from the desired response and the exposure required to elicit that response, drug developers and pharmacokineticists can devise the correct dose to achieve the exposure based on a patient’s individual characteristics. Information needed to predict and measure the responses to therapeutic agents includes things that pediatricians are aware of such as age and weight. However, the next level of understanding requires knowledge of drug absorption, changes in expression of drug metabolism enzymes during growth and development, and the developmental trajectory of the drug target itself.

A simple example is the metabolism of ethyl alcohol by children. Infants are born with approximately 10% of an average adult’s ability to metabolize alcohol. By 2 years of age, the ability reaches only about 30% of the adult ability. The recognition of the development of alcohol dehydrogenases ontogeny led to the removal of alcohol from virtually all pediatric medications.

In addition to genomics, proteomic, metabolomics and the like, pediatric pharmacologists and drug developers need to deal with the ontogeny of both the metabolic pathway and the drug target. Pediatricians have been practicing personalized or precision medicine for generations by dosing drugs in terms of milligrams of drug per kilograms of weight. However, to get to the next level of rational drug use, pediatricians need to become familiar with projects like the GOLDILOKs Project at Children’s Mercy Hospital in Kansas City, Mo.

The project starts with the desired response, taking into account the variables mentioned above to model and project the optimal dose for a specific pediatric patient. Consider giving a “slow metabolizer” of an active drug one-tenth of the recommended dose or a “fast metabolizer” with a highly expressed drug target 20 times the recommended maximum dose. While pediatricians are comfortable with the “one size does not fit all” concept, old conventions will be difficult to shatter until they become comfortable with the data and science behind precision dosing of drugs.

Fortunately, such changes likely will be rolled out for drugs where metabolic pathways and drug targets are well-understood. Most likely, drugs with the highest therapeutic index (potential benefit/potential adverse event) will ease pediatric clinicians into this therapeutic tomorrow so they can provide the best possible care for their patients.

Announcements from the AAP

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Announcements from the AAP  Continued from Page 28

Dr. Leeder is Marion Merrell Dow/Missouri endowed chair in pediatric clinical pharmacology and director of the Division of Clinical Pharmacology and Therapeutic Innovation at Children's Mercy, Kansas City. Dr. Gorman is interim chair of the AAP Section on Clinical Pharmacology and Therapeutics Executive Committee.

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* * *

21st Century Cures Act Signed into Law

On December 13, 2016, President Obama signed the 21st Century Cures Act (H.R. 34) into law, a sweeping piece of legislation that includes several strong protections for children across a range of issues. Prior to consideration by President Obama, the legislation overwhelmingly passed the House and Senate respectively by votes of 392-26 and 94-5. The Academy released a press statement following House passage of the bill.

The following are key takeaways from the legislation:

• Mental health reform priorities:
  ◦ A $9 million grant program modeled after child psychiatry access programs that operate in more than 30 states. The language, originated by the AAP, supports state and regional pediatric mental health teams to provide support, training, technical assistance, and referrals to pediatric primary care sites.
  ◦ A new $5 million grant program for maternal depression screening, assessment, and treatment services for pregnant women and those who have given birth within the last 12 months.
  ◦ A new $20 million grant program to human services agencies or nonprofit institutions to operate evidence-based infant and early childhood mental health programs for children who are at significant risk of mental illness.

• Effective January 1, 2019, children receiving Medicaid-covered inpatient psychiatric hospital services are also eligible for the full range of early and periodic screening, diagnostic, and treatment (EPSDT) services. Currently, children in institutions for mental disease have difficulty receiving EPSDT due to the antiquated Medicaid Institutions for Mental Disease exclusion.

• New funding for initiatives at both the National Institutes of Health (NIH) and the Food and Drug Administration (FDA) that goes above any annual appropriations funding:
  ◦ A total of $4.8 billion to the NIH Office of the Director for fiscal years 2018 - 2026. This includes $1.4 billion for the Precision Medicine Initiative, $1.6 billion for the BRAIN Initiative, $1.8 billion for cancer research, and $30 million for clinical research to further the field of regenerative medicine using adult stem cells.
  ◦ $500 million for the FDA.

• An AAP-championed requirement that the NIH track and report on the number of children enrolled in clinical trials. Although the NIH has had a formal policy since 1998 requiring this, it has failed to track and publish data on the numbers of children actually enrolled. The AAP has fought for years for such a provision to better understand diseases impacting children and their treatments.

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• $1 billion over two years to expand access to opioid treatment, training, and prevention. The AAP supported the *Comprehensive Addiction and Recovery Act* (CARA), which was recently signed into law and authorizes numerous programs to help combat the opioid epidemic. Since CARA did not include supplemental funding, this additional funding is a major step forward in providing the resources necessary to combat the epidemic.

• Reauthorization of the AAP-supported *Sober Truth on Preventing (STOP) Underage Drinking Act*. The STOP Act reauthorization creates a new grant program to train child healthcare providers about screening, brief intervention, and referral to treatment, which is strongly supported by the AAP and has been shown to help identify alcohol and other substance use disorders early on. The STOP Act authorized several crucial programs to fight underage drinking, including funding for a Centers for Disease Control and Prevention program that has collected valuable data on underage drinking activity nationwide.

• A provision similar to the AAP-supported *Promise for Antibiotics and Therapeutics for Health Act* (PATH), which would establish a new approval pathway at FDA for antibiotics to treat serious infections with unmet medical needs.

• The establishment of a Task Force on Research Specific to Pregnant and Lactating Women to provide advice and guidance to the Department of Health and Human Services (HHS) Secretary. The goal is to address gaps in knowledge and research regarding safe and effective therapies for pregnant and lactating women, and the Secretary is required to update regulations and guidance after considering the task force’s recommendations.

• A provision that directs the HHS Secretary, within two years, to make recommendations for the voluntary certification of health information technology for use by pediatric health providers to support the health care of children.

Although the *Family First Prevention Services Act of 2016*, a bipartisan effort to improve how the child welfare system serves children and families in adversity, was originally connected to the 21st Century Cures Act, the final package did not include the bill. The AAP will continue to work to ensure passage of *Family First* in the 115th Congress.
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