Eunice Kennedy Shriver
National Institute of Child Health and Human Development (NICHD)
National Institutes of Health (NIH)

2023 Best Pharmaceuticals for Children Act (BPCA) Meeting & Trainee/Scholar Orientation

July 17-18, 2023

Meeting Summary

Purpose: The purpose of this meeting was to (1) provide an introduction and update on the Best Pharmaceuticals for Children Act (BPCA) Clinical Program at the National Institutes of Health (NIH), (2) familiarize Fellows and Scholars with the organization's history, current undertakings, and resources, and (3) foster successful integration into the BPCA-funded Clinical Pharmacology Training Network.

Day 1: Monday, July 17, 2023

Welcome, BPCA Overview and Updates
Perdita Taylor-Zapata, MD - Medical Officer, Obstetric and Pediatric Pharmacology and Therapeutics Branch (OPPTB), NICHD, NIH

Dr. Taylor-Zapata welcomed participants to the 2023 Best Pharmaceuticals for Children Act Trainee and Scholar Orientation. She provided an overview of the BPCA legislation, which was enacted in 2002 as a follow-up to the FDA Modernization Act. The Act gives pharmaceutical companies six months of exclusivity to conduct pediatric clinical trials under the oversight of the FDA's Pediatric Division. It also includes a mandate for NIH to develop a pediatric drug development program and conduct studies with off-patent drugs. Under the BPCA Program, NICHD is required to prioritize pediatric therapeutic needs, conduct trials through the Pediatric Trials Network (PTN), sponsor translational research, and promote pharmacology training. The goals are to improve pediatric drug labels, improve pediatric health, establish a pipeline of investigators in pediatric therapeutics research, and engage with all stakeholders in the pediatric drug development space, including other Institutes and Centers (ICs), industry, patients, families and societies, FDA regulators, and academia.

In 2021, NICHD developed the BPCA Framework, which is a list of resources, articles, and guidelines related to pediatric drug development. Dr. Taylor-Zapata summarized several trials that the BPCA Program has conducted, including trials in the special population of neonates, pharmacokinetic (PK) data in children with special needs, and PK data of drugs in breastfeeding mothers and infants. With the help of the Network, the Program has incorporated novelty and innovation in its approach to designing and conducting trials, with the goal of generating evidence for use by future researchers. As of July 2023, the PTN has enrolled over 12,000 participants in 46 studies and has achieved 18 label changes. Dr. Taylor-Zapata shared an example of an impactful label change in the case of acyclovir, which lacked dosing in preterm neonates; and two novel PTN studies: the CUDDLE study, which looked at PK data for medicines used during breastfeeding and the extent of transfer into breastmilk, and the opportunistic POPS study on the pharmacokinetics of understudied drugs. She also shared translational impacts in areas such as the Clinical Trials on a Chip study, the Maternal and Pediatric Precision Therapeutics Hub (MPRINT), and the PTN methods.

The 2022 BPCA meeting focused on the current state and future direction of pediatric drug development. The need for training was a major theme that emerged during discussions and informed the focus of the 2023 meeting. Future directions for the program include collaborations with other networks and programs, developing innovative ways to build evidence registries, better engagement with patients and providers, toolkits for future researchers, and non-competitive spaces to identify scientific and training needs and programs. Dr. Taylor-Zapata encouraged participants to share thoughts about their training programs and how the BPCA Program can improve.

Session I: Introduction to Training and Workforce Development

Moderator: Lesly Samedy Bates, PharmD, PhD

Welcome to NICHD and OPPTB Updates

Aaron Pawlyk, PhD - Branch Chief, OPPTB, NICHD, NIH

Dr. Pawlyk noted that the passage of the BPCA legislation led to the creation of NICHD's Obstetric and Pediatric Pharmacology and Therapeutics Branch (OPPTB). Both NIH and NICHD are assessing training and career programs with the goal of establishing a more robust pipeline. For many years NICHD has considered making changes to its multi-site clinical trial networks, which play an important role in training, and they have recently redone both the Maternal-Fetal Medicine Units (MFMU) Network and the Neonatal Research Network. NICHD is reflecting on the work done under the 2020-2024 Strategic Plan and looking ahead to future efforts with the assistance of staff, including 40 new staff members hired since the beginning of the COVID-19

pandemic. NICHD is also maintaining stewardship of existing programs, including the PTN, and renewing activities in areas such as pediatric medical devices and 3D printing for novel therapeutic constructs in pediatric populations. A K12 scholar program for career development will be launched in 2023, led by Dr. Samedy Bates, as well as a translational research platform added to the MPRINT Hub, and an effort focused on transporter proteins and the placenta to improve the understanding of drug transport from mother to infant. Dr. Pawlyk added that NICHD is also pursuing efforts to address equity, justice, and poverty, and to foster a robust environment for trainees, who represent the future of science.

Introduction to NICHD Clinical Pharmacology Training Network & Updates
Lesly Samedy Bates, PharmD, PhD - Program Officer, OPPTB, NICHD, NIH

Dr. Samedy Bates began her talk by noting that she herself was a product of the Clinical Pharmacology Training Network (CPTN), which was originally known as the Pediatric Clinical and Developmental Pharmacology Training Network. The change in name reflects NICHD's intent to include a maternal and obstetric pathway along with the pediatric focus. The purpose of the CPTN program is to ensure a diverse and highly trained clinical pharmacology and therapeutics workforce. It includes T32, F32, and K12 grant mechanisms and provides a comprehensive training experience with collaboration, career development, mentorship, research experiences, a virtual network, and a lecture series. Dr. Samedy Bates highlighted the collaboration component, which includes team science within and outside of the network, and the Principles of Pediatric Clinical Pharmacology lecture series, which was designed to meet the needs of students and trainees without a formal education curriculum in clinical pharmacology. In addition to didactic sessions, the lecture series includes fellows-only workshops on career development. She listed the sites that are included in the current network, highlighting the Duke University/University of North Carolina (UPTiC) program and an F32 fellow at Boston Children's Hospital with a specialty in surgery and medical devices.

Over the last several years CPTN made it a point to develop its alumni network, successfully transitioned their T32 annual meeting to a virtual and then hybrid format, and introduced an orientation meeting to help fellows build a foundation as they begin their training experiences. Fellows are also encouraged to participate in collaborations outside of the network, such as FDA rotations and multi-site paper collaborations. Dr. Samedy Bates shared post-fellowship career path data gathered through the alumni network, with the majority of respondents pursuing careers in the academia and hospital settings. In 2022, OPPTB supplemented its existing program with the Pediatric Clinical Pharmacology Research Career Development Program (the K12). The purpose of including the K12 is to foster the development and productivity of early career researchers and support independent opportunities for fellows to move into. The K12 allows individuals who do not have formal clinical pharmacology programs to conduct clinical pharmacology research; it is currently pediatric-focused, without a maternal component. Moving forward, CPTN will continue to build on pediatric workshops, modify the lecture series, improve

resources with toolboxes for postdocs and scholars, and encourage applications through the T32 mechanism for maternal pharmacology training.

Current State of Training
Joe Gindhart, PhD - Deputy Director, Division of Extramural Activities, NICHD, NIH

Dr. Gindhart spoke about NICHD's commitment to training, how the Institute analyzes its extramural training activities, and how its activities fit into the bigger picture within and beyond the NIH. NICHD has a $1.3 billion budget to fund grants, contracts, and cooperative agreements, and approximately 6% of the budget is invested in training. That training budget is broken down into funding for individual fellowships (15%), training grants (24%), career development K awards (59%), and diversity and re-entry supplements (2%).

In 2015, NICHD engaged in a multi-year effort to analyze its training activities by reviewing its support of training, the balance of support to different career stages and training mechanisms, the relationship between NICHD's training activities and its scientific mission, and how to define successful training outcomes. Additional studies were conducted and resulted in research publications, including a paper in *JAMA Pediatrics* which showed that scientists supported by individual K awards applied to the NIH for research grants at higher rates than those supported by institutional K awards. In an effort to design training activities that are forward-thinking, NICHD formed an Extramural Training & Career Development Working Group. The working group revisited many of the topics addressed in the 2015 analysis, including the definition of a successful training outcome, and developed a concept of training as a pathway rather than a pipeline.

NICHD's work around training activities aligns with several NIH-wide initiatives. Both the NICHD and NIH strategic plans establish goals and provide a framework to track their progress, including in the area of training. The UNITE Initiative is one of several NIH-wide efforts to strengthen diversity, equity, and inclusion (DEI) in the biomedical workforce, and a similar program in NICHD (STtrategies to EnRich Inclusion and AchieVe Equity, or STRIVE) addresses DEI in NICHD's intramural workforce, the extramural workforce, and NICHD's role in health disparities research.

Training Clinician-Scientists: A Call for a Shift
Christoph P. Hornik, MD, PhD, MPH - Associate Professor of Pediatrics, Duke University

Dr. Hornik began his presentation with some general comments for clinician-scientists:

- Total independence is not necessary to be an excellent researcher.
- Career development is a continuous process for anyone who wants to be successful in academia.

- It is better to be a strong researcher, clinician, or educator than to be weak in all three areas.
- True innovation develops when different backgrounds, ideas, and skills mix.
- Clinical research is a career that requires great time and effort, but it is not a way out of clinical commitments.

In order to be successful, clinician-scientists need training that addresses quantitative skills, team science and collaboration, academic skills, and career development. Quantitative skills are learned through a combination of degree programs and hands-on experiences; establishing a theoretical foundation and then applying it in the research space. Clinical research training programs (CRTPs) are a key tool in acquiring quantitative skills, which must then be demonstrated through publications. Trainees can access some of these programs through their home institution or online, and they can also continuously self-teach by applying those quantitative skills within the clinical environment where they already have expertise. All high-impact clinical research programs are team-based environments, and in order to lead those programs one must be able to function as part of a team. This also involves a combination of formal training and hands-on experience; the sooner a clinician-scientist can begin contributing to a team, the better positioned they will be to lead when the time comes. Research networks, collaborators, and government programs provide excellent opportunities for team contribution. For many scientists with clinical backgrounds, the time to join a team environment is during a fellowship, when protected time ensures that they can be present and contribute to the team consistently.

Academic skills include the ability to write grants and papers and present findings in order to have an impact on clinical care, and these are skills that can be learned iteratively and continuously. Career development is key to the success of clinician-scientists and requires a great investment of time and effort. A team of mentors with one person acting as the primary mentor is often the most successful model for trainees, rather than asking one person to assume all mentoring responsibility. In the training environment, the two main NIH funding mechanisms are the T32 and K awards, both of which cover dedicated research time. With respect to the time it takes to build a clinical research career, starting early is better, and protected time is a scarce resource even as a trainee. Dr. Hornik suggested using that protected time to pursue degree programs, acquire foundational skills, and establish or solidify mentorships. When considering faculty positions and other career pathways, clinician-scientists should consider the duration versus amount of protected time offered, opportunities for bridge funding, flexibility and longevity of funds versus the size of a startup package, available opportunities versus expertise in a specific domain, and early career awards. As the landscape of clinical work and pressures on clinicians evolve, clinical researchers currently embarking on their careers must consider how clinical care and clinical research will be integrated in the future.

Session II: Reshaping Training and Reigniting Workforce Development

Moderator: Perdita Taylor-Zapata, MD

Workforce Building Supported by NIH

Robert Tamburro, MD, MSc - Senior Adviser for Clinical Research, Division of Extramural Research, NICHD, NIH

Dr. Tamburro shared NICHD's new approach to clinical research networks and the Institute's objective to further enhance diversity in multi-site clinical research. NICHD formed its first two clinical research networks [the Neonatal Intensive Care Units (now the Neonatal Research Network) and the Maternal-Fetal Medicine Units] in 1985, and since then it has continued to create networks to address essential areas of healthcare relevant to its mission. Each network consists of a funded Data Coordinating Center (DCC) and multiple individual Clinical Research Centers where participants are recruited and enrolled. Each center receives funding for research infrastructure to support a part-time principal investigator (PI), a full-time research coordinator, and a data manager, and centers are often made up of multiple ancillary or recruitment sites. The DCC and centers apply to join the network in response to specific funding opportunity announcements (FOAs), and their applications undergo NIH peer review.

In 2016, the NIH proposed several reforms to enhance clinical trial stewardship and transparency, and ICs were asked to develop their own clinical trial FOAs and notices of funding opportunity (NOFOs). Many of the concerns about the clinical trial ecosystem persist today, including that trials are expensive, cumbersome, and slow; that numerous reviews have found that at least 80% of standard medical guidelines do not have high-quality evidence behind them; and that most NIH-supported trials have small sample sizes. NICHD conducted an extensive assessment of its clinical trial networks and published a Request for Information (RFI) to solicit the public's input on its vision for supporting multi-site clinical trial infrastructure. This RFI received a robust response, and common themes included: sponsoring many clinical sites to ensure diversity of enrollment, increasing diversity of researchers that can access network infrastructure, and providing an environment for research training and mentoring of young investigators. NICHD also conducted a landscape analysis of best clinical research practices across the NIH.

NICHD has reaffirmed its commitment to conducting rigorous multi-site clinical trials, and identified four guiding principles of that research: to enhance the rigor and reproducibility of clinical trial protocols; to promote greater availability of multi-site clinical trial infrastructure to support trials from a wider range of investigators; to facilitate data sharing and access to biospecimens to efficiently expand research capacity for all investigators; and to facilitate greater involvement of diverse populations in multi-site clinical trials. To operationalize these principles, NICHD opted for a centralized approach wherein network infrastructure will continue to be supported, any qualified investigator can use the infrastructure, and all applications and

protocols will undergo NIH peer review. In November 2022, NICHD published a dedicated FOA to solicit clinical research applications to leverage the network infrastructure (PAR-23-037). NICHD also instituted a five-step rigorous pre-application assessment process, which is posted on the Institute's website. NICHD has received over 30 letters of inquiry to-date, with one-third coming from non-network investigators, and approximately one-third with pharmacologic intervention.

Dr. Tamburro highlighted the NICHD Data and Specimen Hub (DASH), which is a centralized resource for researchers to share de-identified data from NICHD-funded studies. He also touched on the importance of networking for young investigators; interviews conducted with prior applicants to NICHD's Pediatric Critical Care and Trauma Scientist Development Program highlighted the value of community-building through mentoring and peer mentorship, which led to their growth, success with grants, and improved career trajectory.

Dr. Philip Walson asked if the data in DASH was vetted for quality. Dr. Tamburro said that DASH was overseen by the Office of Data Science and Sharing (ODSS), and assuring top quality of public-use datasets was a high priority for ODSS. **Dr. Rohan Hazra** added that the DASH group does not conduct a quality review, but does give feedback to DCCs in an iterative fashion as the DCC prepares datasets for submission to DASH. **Dr. Ravinder Anand** added that DASH is primarily focused on ensuring that data is adequately redacted, and verifying data quality must be done at the program level when studies are being conducted. DASH is moving into creating dashboards and mechanisms to generate summary data, which could highlight outliers and nuances for investigators.

Exploring Diversity and Improving Educational Opportunities
Anne Zajicek, MD, PharmD, FAAP - Program Director, Office of Clinical Research Education and Collaboration Outreach, Office of Intramural Research, Office of the Director, NIH

Dr. Zajicek spoke about the current state of access, opportunity, and exposure to research and how it can be improved. She compared the definitions of diversity, equity, inclusion, and accessibility set forth in Executive Order 14035 and the federal definition of a disadvantaged background. She then shared data from the U.S. Census on the U.S. education pipeline by race/ethnicity and gender that showed a steeper drop-off in the numbers of non-white students earning advanced degrees. She also shared data from the American Association of Medical Colleges (AAMC) showing higher rates of attrition for U.S. medical school matriculants of low socioeconomic status (SES), and higher amounts of medical education debt for students with low family income. AAMC data on racial demographics of active physicians does not align with race and ethnicity data from the Census, and more data is needed on income and poverty.

Opportunities for students to consider a career in medicine come from many places: parents and home environment, personal strengths and experiences, healthcare experiences, and teachers/schools. A paper by Shuler et al. on producing Black professionals in STEM highlighted

several ways to encourage students, including practicing holistic mentoring that supports all aspects of student education and wellness, meeting students where they are, and taking into account factors that make up their personal as well as education lives. In this vein, NIH has developed the Institutional Development Award (IDeA) States to improve the amount of money and research to states that do not otherwise receive as much NIH funding. The NIH also has a competitive Loan Repayment Program and an R25 Research Education Program intended to support research education activities that enhance the diversity of the biomedical, behavioral, and clinical research workforce. Researchers with grants can also apply for an administrative supplement to provide funding to improve diversity. Dr. Zajicek highlighted a group of medical students at the University of Pittsburgh's School of Medicine who started an organization to provide free application assistance to aspiring medical students. Role models and a mentorship system are important aspects of early experience, and several years ago NIH established master partnership agreements with regional medical centers to expand their use of NIH Intramural Research Program resources. Howard University has been the most active agreement site, with several research collaborations and clinical training collaborations.

Leveraging Untapped Talent Pools: A Regulatory Perspective
Gilbert Burckart, PharmD - Associate Director for Pediatrics, Center for Drug Evaluation and Research, Office of Translational Sciences, Office of Clinical Pharmacology, FDA

Regulatory professionals are a strategic resource in healthcare industries, and they are relatively specialized and rare. Governmental agencies also rely on highly trained specialists who have or gain expertise in regulatory affairs, and companies and agencies face a continuing challenge of filling open positions. The COVID-19 pandemic exacerbated shortages in every office at the FDA as professional staff retired, took jobs in industry, or moved away. Scientific research and regulatory policy are both crucial to the FDA, and each area informs and encourages the other. It is common for the FDA to recruit individuals with a scientific background who gain regulatory skills during their time at the agency. The science of drug development is complicated, which is reflected in the wide knowledge base of the application review team, and this requires complex training.

Dr. Burckart noted that there is a link missing between PharmD and PhD education and the job skills needed for regulatory science and drug development (RS/DD). An increasing number of PharmD students are graduating but cannot find postgraduate training programs; this is reflected by requests for P4 pharmacy student rotations at the FDA, where approximately 800 students apply for 200 spots with mentors each year. While there is a shortage of physicians nationally and this may limit entry into the regulatory area, some medical students are interested, and advertising could potentially increase interest in a regulatory drug development career.

Dr. Burckart listed the regulatory research programs that the Office of Clinical Pharmacology currently offers, including 30 summer internships per year and a Visiting Pediatric Clinical

Pharmacology Fellows Program. He noted that in order to improve the U.S. supply of RS/DD professionals it is important to stimulate early interest in drug development through tuition and loan incentives and programs to expose students to the regulatory environment during their academic years. It is also crucial to invest in team science training programs and provide incentives for retention of staff and for participation in and expansion of pre- and postdoctoral training.

Session III: Bridging the Gap

Moderator: Katie Vance, PhD

Looking Across Network Sites & Centers: Successes & Challenges

Research Training within the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)
Victoria Spruance, PhD - Program Director, NIDDK, NIH

Dr. Spruance gave a presentation about the work that NIDDK's Division of Kidney, Urologic, and Hematologic Diseases (KUH) is doing to re-imagine institutional training. Nephrology and urology research are historically dominated by MD-trained physician-scientists, and as interest in the fields of nephrology and urology has decreased in recent years, KUH has faced an impending research workforce shortage. In response, they have made efforts to think about ways to increase the number of people entering the field and to ensure that physicians who enter their pipeline are given the necessary resources to succeed in research careers.

NIDDK offers a range of individual and institutional training mechanisms. The latter category includes the T32 mechanism, which is awarded to institutions to pay for stipend, tuitions, and training-related expenses for pre- and postdoc students in mission areas relevant to NIDDK. KUH's evaluation found that trainees supported by T32s have the lowest retention rates in their research workforce, with roughly 15% of T32 trainees receiving subsequent NIH or VA support over a 15-year timespan. In 2019, NIDDK held a T32 best practices meeting, convening program directors, NIH staff, and trainees to discuss lessons learned and ways to improve T32 programs. Trainee feedback included a need for more networking and community-building opportunities and better career development opportunities.

NIDDK took the feedback from the best practices meeting and created the Institutional Network Award, which is a U2C cooperative agreement award with a networking core, a professional development core, and an administrative core. The cooperative agreement is linked to a TL1-NRSA training award similar to the T32. The overarching goal of the Institutional Network Award is to cultivate a highly integrated community of people and innovative resources to propel kidney, urologic, and hematologic training and research, and to build a national community of interdisciplinary trainees. There is a limit of one award per institution - encouraging institutions

in the same geographic area to form partnerships - and a minimum requirement of five trainees per year. There are currently seven active sites, representing 44 institutions, including limited-resource institutions. Successful institutional partnerships have integrated leadership and governance structures, shared U2C resources across institutions, expanded peer-to-peer networks, dedicated TL1 slots, and outreach/pipeline building activities. The concept was introduced in 2020 and renewed in May 2022, and preliminary data shows that sites are filling their slots with diverse representation and forming new collaborations and partnerships. The cooperative agreement also allows for ongoing evaluation and continuous improvement.

KUH also has the Summer Undergraduates R25 Programs, which are geared toward early pipeline efforts. They provide 10 weeks of hands-on research experiences in KUH science, paired with didactic training, culminating in a national research symposium. In FY2023, 22 programs were included, with 40% of participants considered underrepresented populations.

Maternal and Pediatric Precision in Therapeutics (MPRINT) Hub
Adriana Tremoulet, MD, MAS - Professor of Pediatrics, University of California, San Diego

The MPRINT Hub is a service center and scientific catalyst that combines the intramural and extramural communities. It is comprised of several centers: the Indiana University-Ohio State University Data and Model Knowledge Research Coordination Center, which is a centralized collection of pharmacology knowledge; the UC San Diego Center, which is focused on antibiotics and the maternal-milk-infant triad; and the Vanderbilt Integrated Center of Excellence in Maternal and Pediatric Precision Therapeutics (VICE-MPRINT), which has expertise in pharmacogenomics and maternal opioid use. MPRINT also has a partnership with the Bill and Melinda Gates Foundation (BMGF).

MPRINT offers funding opportunities once per year, and funded projects have spanned a wide range of therapeutic regions. Applicants are asked to focus on maternal and pediatric pharmacology and to engage with the centers to grow collaborations. These projects include opportunity pool projects, BMGF and NICHD T32 fellows, and researchers working in the three centers' cores. They also host a webinar series that covers topics across pediatric and maternal pharmacology as well as career development. Recently, the MPRINT team and Dr. Samedy Bates have discussed ways to combine the MPRINT and T32 programs and build a more integrated network. The first day of the Annual MPRINT Hub Meeting in April 2023 was dedicated to trainees and early-career individuals, and **Dr. Tremoulet** noted that everyone from the MPRINT program will be invited to the Clinical Pharmacology Training Network meeting in September 2023.

Dr. Tremoulet also highlighted the K12 Program in Pediatric Clinical Pharmacology, which is currently under consideration for funding. The program is led by the University of North Carolina and Duke University and seeks to train the next generation of leaders and mentors in pediatric

clinical pharmacology by combining expertise and resources across a nationally dispersed group of leading academic institutions. She concluded by noting that it is ideal to work on streamlining training programs and maximizing the number of trainees, as the current demand for MPRINT funding by trainees exceeds the funding that is available.

NIH Blueprint for Neuroscience Research Short Courses in Neurotherapeutics Development
Oreisa O'Neil-Mathurin, MPH - Health Program Specialist, National Institute of Neurological Disorders and Stroke (NINDS), NIH

Ms. O'Neil-Mathurin shared information about the Training in Neurotherapeutics Discovery and Development for Academic Scientists, an initiative put forth by the NIH Blueprint for Neuroscience Research. Industry engagement in central nervous system (CNS) drug discovery has diminished in recent years, and there is an increased need for university researchers to participate in developing new therapies for nervous system disorders. This course is designed to provide academic researchers with the skills to compete successfully for translational drug discovery and development grant opportunities and lead an academic drug discovery and development effort.

Neurological disorders are collectively the leading cause of disability globally, and the magnitude of this burden will likely rise due to population growth and aging. The training program's objective is to train academic researchers to discover and develop new treatments to reduce disability and lead to improved quality of life for those affected by neurological disorders. The NIH Blueprint for Neuroscience Research Short Course for Academic Neuroscientists is offered yearly and most recently took place in March of 2023. Attendees explore various topics critical to discovery and development of neurotherapeutic agents and are provided with individualized mentoring and assessment and opportunities to interact with topic experts. During the four-day intensive course, trainees acquire the knowledge to discover and advance a neurotherapeutic agent to investigational new drug (IND) application. The course combines didactic lectures with active engagement in activities where the students work through their own drug discovery project with the guidance of faculty members.

The course is designed for advanced postdoc researchers and faculty members who are engaged or would like to become engaged in neurotherapeutics discovery and development. Individuals from racial and ethnic groups underrepresented in biomedical research, individuals with disabilities, and women are particularly encouraged to apply. The training is designed to be applicable to multiple diseases of the nervous system and will equip students with a broad understanding of the various component steps in the neurotherapeutics drug discovery and development process. Continual engagement with faculty is one of the key components of the course, with contact between students and their mentors continuing at least once a quarter during the two-year period following the course. The 2024 course offering will be held March 12th through March 15th at the Hyatt Regency in Bethesda, Maryland. Ms. O'Neil-Mathurin

shared several reviews from past participants which highlighted the course's comprehensive overview of the drug discovery and development process and the productive discussions with mentors and fellow trainees.

Questions and Answers & Final Comments
Roundtable Discussion

Dr. Sonya Tang Girdwood asked if there were partnerships between T32 networks across Institutes. Dr. Spruance said that her group in NIDDK was interested in standing up a separate award intended to link all of the institutional network awards together and provide infrastructure to build a national cohort. She agreed that linking their efforts with other Institutes and other divisions within NIDDK was an important concept but noted that it was often challenging to get people to work together even within one discipline. Dr. Samedy Bates added that it often comes down to infrastructure and funding, but NICHD is always in communication with other Institutes to discuss possible collaborations. Dr. Pawlyk added that one reason the T32 clinical pharmacology program has been so successful is the fact that training is included in the BPCA mandates.

Dr. Vance noted that one of the recurring themes of the day's discussions was the need for collaboration, networking, and mentoring. She asked Dr. Spruance about the model for KUH's networking core and what they were doing to help trainees learn how to network. Dr. Spruance clarified that each institution funded through the mechanism has its own networking core that is linked to their TL1. Each institution is responsible for including creative ways to approach the networking core in their application, and a key component is providing a virtual platform, designed with trainees' input, through which the trainees can be in constant communication with one another. Dr. Tamburro added that the Collaborative Pediatric Critical Care Research Network (CPCCRN) runs an annual retreat that is open to anyone interested in applying to the national K12 program, and this has been a very successful initiative that allows young investigators to form connections. Dr. Walson asked if these types of collaborations could be international. Dr. Spruance said that nothing prohibits foreign collaborators from participating in networks in the U2C/TL1 mechanism, though they are subject to National Research Service Award (NRSA) policy, which prohibits researchers who are not U.S. citizens or permanent residents from being appointed to the TL1 portion of the grant.

Dr. Taylor-Zapata asked if there was any thought of universally including drug development and regulatory components as part of all residency program curricula. Dr. Burckart said that that would be a good idea, as both clinical studies and clinical care are dependent on drug development in the U.S. He added that many programs do include those as components of their training programs, and fellows who have rotated through the FDA have benefitted from the regulatory insight. Dr. Samedy Bates asked Dr. Tamburro if DASH was accessible to trainees. Dr. Tamburro said that the pediatric critical care datasets in DASH are the same datasets that the

network used when writing their papers, and they are a good resource for trainees to get publications on their CVs quickly and begin to build a body of research. Dr. Burckart added that there is a large amount of publicly available FDA data available on the agency's website. Dr. Vance asked if meeting participants from the networks had any ideas of other technologies or infrastructure that could be used to diversify the workforce and bring more people into the fold of clinical pharmacology and research training. Dr. Spruance said that it was important to make sure that their outreach is beyond the scope of higher-resourced institutions.

Dr. Taylor-Zapata asked participants to weigh in on the difference between mentorship and sponsorship and their importance in career trajectory, and Dr. Samedy Bates asked if any of the trainees at the meeting currently had a sponsor. **Dr. Rose Gelineau-Morel**, a T32 fellow, said that while there can be overlap between mentors and sponsors, in her experience sponsors were more involved in the administrative aspect of her work while mentors were more involved in the research and scientific areas. She added that peer mentorship would be a valuable tool for trainees. Dr. Spruance said that it was important for institutions and NIH ICs to provide support for the training of mentors and sponsors. Dr. Tang Girdwood asked if there were any plans for a platform where trainees could contribute datasets related to clinical pharmacology. Dr. Vance said that DASH could be an appropriate place for a clinical dataset of that nature, and there was a role for groups like MPRINT to inform other investigators about those data. Dr. Taylor-Zapata added that the PTN has decades' worth of data that are on DASH, and it would be helpful to have a centralized way of advertising what data is available, where it is, and how to find it.

Day 1 Summary & Adjournment
Perdita Taylor-Zapata, MD

Dr. Taylor-Zapata thanked the presenters and attendees for their time and adjourned the meeting at 4:59 p.m.

Day 2: Tuesday, July 18, 2023

Session IV: Welcome to NICHD & Navigating the Network

Moderator: Lesly Samedy Bates, PharmD, PhD

History of the Clinical Pharmacology Training Network (CPTN) & Updates
Lesly Samedy Bates, PharmD, PhD

Dr. Samedy Bates welcomed participants to the second day of the BPCA meeting. She summarized several opportunities presented on Day 1 and encouraged trainees to apply to MPRINT's support and opportunity pools and the FDA summer experience and to look at networks with publicly available data.

Getting to Know CPTN & Network Expectations
Debbie Stein and Emily Peters, INFINITY

INFINITY Conference Group provides logistical support for the T32 fellowship program and BPCA prioritization for pediatric therapeutics. **Ms. Peters** and **Ms. Stein** highlighted several fellowship activities: the Fellows Flash newsletter, which is distributed monthly and includes information on upcoming meetings, featured fellow research, and a congratulations corner; networking activities such as closed Zoom networking sessions that are moderated by peers; the Principles of Pediatric Clinical Pharmacology Lecture Series; and the CPTN Meeting, which will take place on September 12th and 13th, 2023 and feature fellow presentations. The SharePoint site for fellows can be found at www.PedPharmHub.org and includes Pediatric Clinical Pharmacology Lecture Series discussion boards, a Fellow Directory, and recordings of past T32 meetings. This year's chief fellow is Rose Gelineau-Morel, MD, from Children's Mercy Hospital in Kansas City.

Session V: Navigating NIH

Moderator: Lesly Samedy Bates, PharmD, PhD

Tips on Working with NIH Program Officers
Ronna Popkin, PhD - Program Officer, Populations Dynamics Branch, NICHD, NIH

Grant applications that are submitted to the NIH must speak to the agency's mission: to seek fundamental knowledge about the nature and behavior of living systems and apply that knowledge to enhance health, lengthen life, and reduce illness and disability. The Center for Scientific Review (CSR) screens all incoming applications and assigns them to ICs and study sections, and it also administers scientific review for 70% of NIH applications. Study sections are comprised of scientific peers who are experts from outside the NIH who review the scientific and technical merit of grant applications. An NIH official, the scientific review officer (SRO), oversees study section meetings. Program officials (POs) set funding priorities and make decisions about funding, as well as providing scientific consultation and guidance. POs are located within the funding Institute and should be contacted before submission of applications and after the review meeting. POs know their Institute's scientific priorities, the gaps in the scientific literature, and the technical details of applying for grants, and they regularly observe peer review meetings and can often offer insights from their own scientific background. They know what kinds of questions tend to arise about applications and thematic issues across study sections and scientific domains, and can use this experience to help investigators.

The most effective way to contact a PO is through email. **Dr. Popkin** recommended that investigators either email one PO or send one email addressed to multiple POs at the same Institute. Before contacting a PO, investigators should read the funding notices, key dates, and instructions, check RePORTER to see what else has been funded on their topic, and draft a

description of their project. NOFOs can be found in the NIH Guide for Grants and Contracts, and Dr. Popkin summarized the four different types of announcements: Parent Announcements, which announce the use of a mechanism and which ICs participate for investigator-initiated applications; Program Announcements with Review (PARs), which announce areas of scientific interest for one or more ICs and include special receipt, referral, and/or review criteria; Requests for Applications (RFAs), which focus on specific program objectives and areas of scientific interest and are issued for one or more ICs, include set-aside funds, and are reviewed by a specially convened study section; and Notices of Special Interest (NOSIs), which announce areas of scientific interest for one or more ICs and refer applicants to existing Parent Announcements or PARs.

Dr. Popkin gave an overview of how to read a NOFO, which indicates important information such as the participating ICs and eligibility criteria for foreign applicants. NIH RePORTER is an important resource for investigators to find out what NIH has funded in the past, and it has a Matchmaker tool where investigators can enter a description of their project and find similar projects that have been funded, which ICs have funded similar research, and potential POs to contact. A draft of specific aims is the best information to send a PO as a starting point for a conversation; at minimum, an investigator should send a project description. This project description should communicate the research topic, primary research question, and the gap that it is to be addressed; the relevance of their research to public health; specific hypotheses, with dependent and independent variables; what methodologies are used and why they are appropriate; sampling strategies; and an estimated budget and timeline. If investigators are interested in submitting an individual fellowship or career development application, they should highlight their disciplinary background, previous training and institutional affiliations, information about mentors and other advisors, and how the training and development they are applying for will bring them to the next stage of their career.

Tips on Working with NIH Scientific Review Officers
Dianne Hardy, PhD - Scientific Review Officer, Division of Physiological and Pathological Sciences, NICHD, NIH

The Scientific Review Officer is a designated federal official with doctoral-level expertise relevant to an investigator's field. They manage the overall peer review process and are responsible for administrative and technical review of applications to ensure their completeness and compliance. SROs recruit reviewers and manage their assignments, and they are responsible for giving reviewers access to their assignments six to eight weeks before the study section meets. When investigators submit grant applications, they are received by the CSR Division of Receipt and Referral and sent to the Institutes or, as in most cases, are reviewed by CSR study sections. SROs have access to the applications once they are added to the Scientific Review Group docket, and at the end of a four- to eight-week period they release the reviewer assignments. Three or more reviewers then evaluate the application, after which the study section meets. In order to

assign a study section, one or more CSR Referral Officers examine the application and assign it to the most appropriate Review Branch to assess its scientific and technical merit, and then to one of the Review Branch's study sections.

Referral Officers follow guidelines that define the review boundaries of each study section. They seriously consider assignment requests in the cover letter or Assignment Request Form of an application, which should be used to suggest an IC or review group assignment, identify individuals in potential conflict or possessing areas of expertise needed to evaluate the application, and discuss any special situations. The Review Branch is a cluster of related study review groups, and investigators can view the study section guidelines and roster on the CSR website.

When applications arrive, the SRO is responsible for checking the application for appropriateness of topic, completeness, and compliance with policies. They then assemble a roster of reviewers consisting of standing members (in the case of Chartered Study Sections) and temporary members. Every roster must include representation of women and minorities, geographic distribution, and career stages. The size of the roster depends on the number of applications, with an assignment load of approximately eight per reviewer. When selecting reviewers, SROs look for demonstrated scientific expertise, a doctoral degree or equivalent, mature judgement, an ability to work in a group context, breadth of perspective, and impartiality. The SRO must check for conflicts of interest, and they assign three reviewers to each application, with consideration of the entire group of applications.

Each CSR standing study section has 12 to 22 regular members, plus temporary reviewers from the scientific community. About 70 applications are usually reviewed by each study section in one- to two-day meetings. At these meetings, the SRO's role is to make sure that each application receives a review that is thorough, balanced, and fair. This includes reminding the panel of discussion procedures and the review criteria and ensuring that the NIH rules are followed. The study section chair works with the SRO to conduct the meeting, guides discussion, and ensures that all opinions are given careful consideration. Discussions focus on the best applications, and reviewers typically discuss the top half of the applications. Investigators can communicate with SROs before they submit applications to ask about the appropriateness of their topic for a study section, as well as after submission but before the review, when they may submit post-submission materials. **Dr. Hardy** highlighted the Early Career Reviewer (ECR) Program, which early stage investigators can apply for through CSR. She noted that serving as a reviewer is the best way for investigators to fully understand the review process.

Tips on Working with Grants Management
Robin Kurtz - Senior Grants Management Specialist, NICHD, NIH
Sarah Lee, MPH - Senior Grants Management Specialist, NICHD, NIH

The Grants Management Branch (GMB) performs management, internal control, and acquisition functions for all NICHD grant programs. They handle the administration of traditional funding mechanisms, manage Other Transaction Authority (OTA) and other mechanisms, contribute to the development of policies and procedures, and help interpret NIH and HHS policies related to funding programs and management. The Grants Management Officer (GMO) whose name appears in the Notice of Award (NoA) is the NIH official responsible for the business management and non-programmatic aspects of the award. The Grants Management Specialist (GMS) whose name appears in the NoA serves as the agent of the GMO and is assigned responsibility for the day-to-day management of a portfolio of grants. The GMS manages business-related activities associated with the negotiation, award, and administration of grants and cooperative agreements, both prior to and after award.

The Authorized Organizational Representative (AOR) is the designated representative of a recipient organization in matters related to the award and administration of its NIH grants, including those that require NIH approval. AORs are a good first resource for any questions that investigators may have, and they can also email or call the GMS listed on the NoA. **Ms. Lee** noted that it is very important to read and understand the NoA in its entirety and she highlighted Section IV, where applicants can find NICHD-specific terms. **Ms. Kurtz** emphasized the importance of submitting materials on time, including any changes to the award and/or prior approval requests. She outlined the NRSA stipend levels for fellowships and training grants, which are provided by fiscal year, and advised investigators to look at the NoA comments to find the most up-to-date GMS assigned to the award.

NIH Jargon and Acronyms
Dennis Twombly, PhD - Deputy Director, Office of Extramural Policy, NICHD, NIH

NIH has a number of funding mechanisms targeted to different stages of research training and career development. Graduate and medical students can apply for various fellowships and career awards, including the T32 Institutional Training Grants, F30 Pre-doctoral Fellowships for MD/PhD and other dual degree students, and two F31 pre-doctoral fellowships: the Parent F31 grants and Diversity Pre-doctoral Fellowships. Post-doctoral fellows can apply for the T32 grant and for F32 Individual Post-doctoral Fellowships. Career development awards include the K22 Career Transition Award, which some ICs participate in (though NICHD does not); the K99-R00 Pathway to Independence Award; the K12 Institutional Career Development Award; the K01, K08, K23, and K25 individual career development awards, which support release time and research expenses for early stage investigators; and the K02 Independent Scientist Award and K24 Mid-career Award in Patient-Oriented Research, neither of which NICHD participates in. **Dr. Twombly**

noted that these awards are not the only way for investigators to get experience in research, and the majority of training occurs in other settings, such as on networks and in laboratories funded by research project grants.

The goal of the fellowship and career awards is to give researchers enough experience to apply for research grants such as the R03 Small Grant, the R21 Exploratory-Developmental Grant, and the R01 Research Project Grant. Dr. Twombly noted that FOAs often have multiple versions, including one where a clinical trial is required and one where a clinical trial is not allowed. The term "new investigator" refers to an applicant who has not previously competed successfully as a PD/PI for a substantial NIH independent research award. "Early-stage investigator (ESI)" refers to a new investigator who is within 10 years of the terminal doctoral degree or end of post-graduate clinical training.

Session VI: Making the Most of Your Training

Moderator: Katie Vance, PhD

Planning Your Training & Drafting Your Career Development Timelines
Sonya Tang Girdwood, MD, PhD - Assistant Professor, Department of Pediatrics, Cincinnati Children's Hospital Medical Center

Dr. Tang Girdwood shared some of her educational and training background and presented a suggested timeline based on her experience, emphasizing that trainees should make their fellowships work for them and their career goals. She advised trainees who have not yet chosen their specific area of study or mentors to meet with many PIs in various divisions, as clinical pharmacology applies to all pediatric subspecialties. Echoing comments from the previous day about the benefits of a team of mentors, she suggested considering some potential mentors for assistance with content and others for methodology. Once a trainee has a sense of their research study, they should begin work on the IRB protocol because the drafting and approval process always takes longer than expected. Depending on the type of study, data collection and analysis may not be completed by the end of the fellowship. In this case, trainees should proactively talk to their mentors about how the study will continue or transfer to a new institution. Manuscripts from the fellowship may not be published for years after the fellowship is completed.

There are many opportunities to publish and present during a fellowship, even if the trainee's research is not complete. IRB protocols can be turned into narrative or systematic reviews or methodology papers in journals, and T32 fellows can collaborate to write white papers about the state of clinical pharmacology in their subspecialties. Fellows can also look for workshops or special sessions to join or co-lead with PIs in their institutions or throughout the NICHD network and present interim analyses and research-in-progress at conferences. Dr. Tang Girdwood suggested that all fellows take the time to write a grant, even if they do not end up submitting it, as grantsmanship is a very specific and useful writing skill. Drafting the career development

portion of a grant also helps fellows to gain clarity on their future career goals. Grant opportunities for fellows include the F32 award, Institutional Internal Awards, and grants offered by the Gerber Foundation and the Thrasher Foundation. The CPTN meeting in September will also include grant workshops.

Fellowship is also a good time to pursue career development opportunities. Most institutions have a Scholarship Oversight Committee or Career Development Committee which provides career guidance. These committees are composed of research mentors, divisional members, and outside divisional members who can also serve as sponsors during job searches. Dr. Tang Girdwood also recommended several classes and workshops for trainees to take during their fellowships, including the NIH Principles of Clinical Pharmacology Course, available on YouTube, and the NICHD/BPCA Principles of Pediatric Clinical Pharmacology webinars. Fellows who take both of these courses, along with the didactic and research training at their home institutions, should be prepared for the American Board of Clinical Pharmacology (ABCP) certification exam. They can also pursue leadership and service opportunities such as the T32 Chief Fellow role and the trainee committees for local and national societies. Dr. Tang Girdwood concluded her presentation by noting that it is never too early or too late for trainees to figure out their mission statement, which can then help them plan and adjust their timeline.

Lessons Learned Along the Long, Winding Road of an Early Research Career
Thalia Robakis, MD, PhD - Associate Professor of Psychiatry, Women's Mental Health Program, Icahn School of Medicine at Mount Sinai

In order to conduct scientific research, investigators need protected time, money, and expertise, and these may be more or less available in different career stages. Because they have protected time, money, and access to the expertise of their committee during doctoral training, this stage is an important time for researchers to be productive and set themselves up for success in the next steps of their career. Protected time and money during clinical residency are limited; some researchers are able to enter into specified research tracks or negotiate with their chairs for support, while others accept that research will be limited and focus on developing clinical interests and expertise. In fellowship, time is protected and researchers have both their own expertise and that of collaborators, but funds are usually limited. In this phase, researchers can apply for funds to support research expenses, work in an established lab, or design a project within their constraints.

Dr. Robakis shared her own trajectory in perinatal and reproductive psychiatry, including her work exploring the risks and benefits of maternal psychiatry and maternal pharmacology on infants. She used examples from her research to illustrate the questions that funders will ask: why is this question important; will your study design answer it; and do you have the capacity to carry out the study? With respect to the last question, it is important for early career researchers to focus on representing their capacity to carry out their proposed project. Dr. Robakis presented

a proposed timeline for success, beginning one year before submission when researchers should decide on a question, draft specific aims, and assemble a team, and concluding a week before the NIH deadline, when research strategy details have been finalized and the researcher has incorporated feedback from their institution's grants office.

Navigating the Path to Medical Education
Brooks McPhail, PhD - Assistant Professor of Pharmacology, Wake Forest University School of Medicine - Charlotte

Dr. McPhail spoke about her path through medical education, including her background, training, and career. After personal life circumstances pushed her to study the activity of drugs in children, she completed an interdisciplinary toxicology program at the University of Georgia College of Pharmacy. After realizing the gap in physicians' knowledge of pediatric pharmacology, she decided to pursue a career educating medical students, and after completing a postdoc at the Centers for Disease Control and Prevention (CDC), she applied to teach at several medical schools, but was unsuccessful in securing a position. She taught anatomy at a community college to gain teaching experience, then became a forensic toxicologist for the State of North Carolina before a mentor that she had maintained contact with connected her to Cincinnati Children's Hospital Medical Center, where she became a T32 fellow. After her fellowship, she reapplied to teach at the University of South Carolina Greenville and was accepted. After five years there, she moved to her current job at Wake Forest University, where she helped to build the new curriculum for their medical school in Charlotte.

Dr. McPhail shared several tips and lessons learned from her educational journey:

- It is important to find a mentor that listens to your thoughts without pushing their own agenda.
- For those who want to teach in a medical school, start with the end goal first, plan, and start teaching as soon as possible.
- Network within national organizations.
- Some medical schools focus mostly on medical education and do not require extensive research and grant-writing.
- Different schools use different types of curricula, including traditional didactic lectures and problem-based, case-based, and team-based learning (PBL, CBL and TBL).
- When applying to a school, put effort into crafting a good personal statement in the application packet.
- Some schools require a research statement, which outlines past and potential future research and/or a teaching philosophy, which allows the applicant to showcase their beliefs about and passion for teaching.
- The screening process to teach at a medical school will consist of a phone interview followed by a virtual and then an in-person interview. The in-person interview will include

a job talk or chalk talk where the applicant presents a teaching demonstration and a passion project.
- Faculty workload consists of teaching, research, and service, and it is important to ask about the distribution of these core responsibilities during the interview process.

Questions and Answers (Panel)

Dr. Vance asked presenters how they found and approached their mentors and collaborators. Dr. McPhail said that it is important to be proactive. She researched and emailed her mentor when she was in graduate school. If trainees are not comfortable approaching a potential mentor directly, she suggested networking with that mentor's fellows and asking questions about their mentorship style. Dr. Samedy Bates said she reflected on her own weaknesses and identified a mentor who could help her improve in those areas, then persisted in reaching out to them to ask for assistance. Dr. Tang Girdwood noted that it was important to be clear about expectations and commitments when asking someone to be a mentor in order to avoid confusion or miscommunication. Dr. Robakis added that people should not be afraid to switch mentors if a relationship is not working out.

Dr. Vance asked the speakers what they knew now that they wish they had known at the beginning of their careers. Dr. McPhail said that her biggest life lesson was that it was okay to change her mind and to try different things. Dr. Tang Girdwood said that there was no perfect time to fit family planning into a career, and that it was important to find mentors who support mentees as they try to strike a balance. The topic of family planning and work/life balance as a researcher was not discussed when she was in the early stages of her career; it is a conversation that she would like to hear discussed more prominently moving forward. Dr. Samedy Bates noted that there is an allotment for childcare within the T32 program in order to promote good work/life balance for trainees.

Day 2 Adjournment & Meeting Closing

Dr. Samedy Bates thanked the presenters and attendees for their time. Speakers' contact information would be made available for any follow-up questions and discussion after the meeting. With no further business, the meeting was concluded at 3:54 p.m.