

# Pediatric Pharmacology Research Unit

## DIVISION PROFILE

Number of Faculty	5
Number of Other Students (full and part-time)	1
Number of Support Personnel	6
Annual Total Grant Support (direct)	\$305,330
Annual Total Industry Contracts (direct)	\$10,951
Number of Peer Reviewed Publications	4

## FACULTY LISTING

**Alexander A. Vinks, PharmD, PhD**, Research Professor, Director

**Tracy A. Glauser, MD**, Associate Professor, Director, Comprehensive Epilepsy Program

**Daniel W. Nebert, MD**, Professor, UC Department of Environmental Health and Center for Environmental Genetics (CEG)

**Floyd R. Sallee, MD, PhD**, UC Department of Psychiatry

**Philip D. Walson, MD**, Professor of Pediatrics

## OVERVIEW

The Pediatric Pharmacology Research Unit (PPRU) at Cincinnati Children's is one of 13 PPRUs established by the National Institute of Child Health and Human Development in response to the need for appropriate drug therapy for pediatric patients. The 13 PPRUs form a network of research centers for federally sponsored pediatric pharmacology studies across the United States. The network has access to large all-inclusive pediatric population, ranging in age from birth through young adulthood, with approximately 177,000 pediatric inpatient admissions and over two million outpatient visits per year.



**S. Vinks**

The network's mission is to facilitate and promote age-specific pediatric labeling of new drugs or drugs already on the market to support their safe and effective clinical use in children. The PPRU provides a locus for expertise in pharmacokinetic and drug metabolism studies, pharmacogenetics, population pharmacokinetic and pharmacodynamic modeling, and clinical trials methodology.

During this fiscal year, our site was directly involved in 8 new protocols ranging from specific drug class evaluations (e.g. antiepileptic drugs), pharmacokinetics (e.g. atypical neuroleptics), and safety and efficacy trials (e.g. proton pump inhibitors). Besides efforts associated with sponsorship from the pharmaceutical industry, several investigator initiatives by the PPRU including pharmacogenetics, therapeutic drug monitoring/biomarker studies were key to network success in the current year. Direct involvement includes everything from dissemination of protocols to appropriate researchers and divisions, to attending off-site start-up meetings commencing protocols, to actual patient recruitment and enrollment. The PPRU participates in these collaborative efforts through interaction with other Clinical and Research Divisions on the CCHMC campus.

The PPRU has taken an active role in the development and application for registration of a Clinical Pharmacology Fellowship Program through the American Board of Clinical Pharmacology, Inc. Critical to the implementation of such a training program is the attainment of a critical mass of faculty with expertise in Pediatric Clinical Pharmacology. At the faculty level, the PPRU also seeks a mentorship role in the research training of junior faculty in pediatric clinical pharmacology and the performance of clinical trials.

The PPRU has moved from the main campus to the Oak Campus as part of the 53,500 sq. ft., Cincinnati Center for Clinical Research (CCCR). This facility, located five minutes from the main campus, also houses the PPRU's Laboratory of Applied Pharmacokinetics and Therapeutic Drug Management (LAP-TDM).

## HIGHLIGHTS

In January 2004 the competitive PPRU grant was renewed for a second 5-year cycle with Dr. Vinks as the principal investigator. The PPRU team continues to fulfill the mission to facilitate and promote clinical pharmacology studies and investigator initiated and industry sponsored PPRU network studies at CCHMC. Programmatic resources currently include laboratory support (drug levels determinations, pharmacokinetic analysis and pharmacokinetic-pharmacodynamic modeling), time-shared study coordinators, and study design support. This fiscal year, the PPRU has participated with 21 protocols in the network. Placement of studies has been in therapeutic areas of neuropharmacologic agents, antibiotics, contrast agents, sleep, and gastrointestinal agents.

### **TDM/GLP Laboratory**

Laboratory of Applied Pharmacokinetics and Therapeutic Drug Management (LAP-TDM) opened as one of three laboratories following Good Laboratory Practice (GLP) guidelines at the Cincinnati Center for Clinical Research (CCCR). The laboratory develops and provides high quality chromatography-based assays for drug monitoring to support pharmacokinetic studies and clinical trials on a contract or fee-for-service basis. The laboratory also provides pharmacokinetic and clinical pharmacology consultation. The laboratory has collaborated with Drs. Phil Walson, Paul Steele, Ken Setchell and Tracy Glauser to establish a Clinical and Research Therapeutic Drug Monitoring Service. Assays that were developed and validated include amantadine (collaboration with Physical Medicine & Rehabilitation), Mycophenolate Mofetil (Cellcept®), and most recently six anti-HIV protease inhibitor drugs (amprenavir, efavirenz, indinavir, nelfinavir, ritonavir and saquinavir). The laboratory is further collaborating with the Division of Nephrology (Dr. Goebel) and the transplant group at UC (Drs. Alloway and Woodle) in both clinical and laboratory research involving immunosuppressant assays. Dr. Vinks has performed industry supported TDM laboratory studies (in collaboration with Dr. Walson at the Division of Clinical Pharmacology).

### **Genetic Pharmacology Service**

In collaboration with the Divisions of Human Genetics (Dr. Wenstrup and Cindy Prows, MSN, RN) and Neurology (Dr. Glauser) the PPRU was actively involved in the development and implementation of a Genetic Pharmacology Service at Cincinnati Children's. Scientific evidence indicates that pharmacogenetic testing for some medications may improve patient safety, can reduce the incidence of side effects and/or can reduce the time to reach a therapeutic dose. Adding genetic information to the usual considerations of patient age, weight, disease process, use of other medications, health behaviors and environment will help physicians and nurse practitioners choose and dose medication that best meets the needs of the individual patient. A GPS consult service will be provided by faculty members participating in the PPRU.

### **Teaching Activities**

Ongoing teaching activities included a weekly seminar series and journal club in collaboration with the Division of Clinical Pharmacology. General themes include "Pharmacogenetics", "Population pharmacokinetic and pharmacodynamic (PK-PD) modeling", and "Therapeutic Drug Monitoring" of drugs such as anticonvulsants, immunosuppressants and protease inhibitors.

## TRAINING

Diego Morita, MD

University of Buenos Aires, Buenos Aires,  
Argentina

Ivana Kcirova, MD  
 Michelle Eckerle  
 Roberto Santos  
 Kristin Carlsson  
 Sandrine Derkene

University of Ostrava, Czech Republic  
 University of Louisville, Louisville, Kentucky  
 Upstate Medical University, Syracuse  
 University of Oslo, Norway  
 UC Dept. of Environmental Health and Center  
 for Environmental Genetics

## GRANTS, CONTRACTS AND INDUSTRY AGREEMENTS

<b>Grant and Contract Awards</b>	<b>Annual Direct/Project Period Direct</b>
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Vinks, A	
<b>CHMC Clinical Pharmacology Research Unit</b>	
National Institutes of Health	
U10 HD 37249	02/15/04 – 12/31/08
	\$205,330/\$1,076,177
<b>Risperidone Pharmacokinetics in Children with Pervasive Development Disorder</b>	
National Institutes of Health	
R21 HD 42440	09/30/01 – 08/31/04
	\$100,000/\$300,000
<b>Current Year Direct</b>	
	<b>\$305,330</b>

### Industry Contracts

Vinks, A	
Enzon Pharmaceuticals	\$10,951
<b>Current Year Direct Receipts</b>	
	<b>\$10,951</b>
<b>TOTAL</b>	
	<b>\$316,281</b>

## PUBLICATIONS

1. de Wildt SN, de Hoog M, **Vinks AA**, van der Giesen E, van den Anker JN. Population pharmacokinetics and metabolism of midazolam in pediatric intensive care patients. Crit Care Med 2003;31(7):1952-8.
2. Sallee FR, Gilbert DL, **Vinks AA**, Miceli JJ, Robarge L, Wilner K. Pharmacodynamics of ziprasidone in children and adolescents: impact on dopamine transmission. J Am Acad Child Adolesc Psychiatry 2003;42(8):902-7.
3. Touw DJ, Neef C, **Vinks AA**. [Better treatment for less money. Rationale and cost-effectiveness of therapeutic drug monitoring. Part I.]. Pharm Weekbl 2003;138(30):1061-66.
4. Touw DJ, Neef C, **Vinks AA**. [Better treatment for less money. Rationale and cost-effectiveness of therapeutic drug monitoring. Part II.]. Pharm Weekbl 2003;138(35):1212-1216.