BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors. Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Terrence F. Blaschke	Professor of Medicine and of Molecular
eRA COMMONS USER NAME (credential, e.g., agency login) blaschke.terry	Pharmacology (Active Emeritus)

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)

INSTITUTION AND LOCATION	DEGREE (if applicable)	MM/YY	FIELD OF STUDY
University of Denver	BS	1964	Mathematics
Columbia University	MD	1968	Medicine
University of California at Los Angeles		1970	Internal Medicine
Metabolism Branch, NCI, NIH		1972	Clinical Associate
University of California at San Francisco		1974	Clinical Pharmacology

Please refer to the application instructions in order to complete sections A, B, C, and D of the Biographical Sketch.

A. Personal Statement

I have been involved in research in HIV since the inception of the AIDS Clinical Trials Group in the mid-1980s. A focus of my research on drugs used in HIV-infected patients is to optimize the individual benefit/risk of pharmacotherapy of HIV or opportunistic infections by discovering and quantifying the pharmacokinetics and pharmacodynamics (PK/PD) of drugs used in such therapy; i.e., the distribution of individual-specific doseconcentration-effect relationships in the population. I have a special interest in understanding the relationships between antiviral drug exposure and virological and toxicological responses. Over the past 2 decades this has involved studies examining drug-taking behavior in HIV-infected patients, primarily using electronic monitoring techniques that provide detailed drug dosing histories in individual patients. Individual patterns of drug-taking behavior that inevitably involve partial adherence determine the exposure of that individual to antiretroviral drugs and is the major source of inter-individual variability in pharmacokinetics and drug response (pharmacodynamics). Partial adherence carries with it a high risk of promoting drug resistant variants of HIV, which could have widespread consequences over the long term. Another area of interest is identifying other sources of variability in drug disposition, such as those due to drug-drug interactions between antiretroviral drugs and drugs used to treat opportunistic infections, in particular drugs used to treat tuberculosis or malaria.

B. Positions and Honors.

Positions and Employment

1974 – 1981 Assistant Professor of Medicine and Pharmacology, Stanford University School of Medicine Chief, Division of Clinical Pharmacology, Stanford University School of Medicine 1978 - 2003 Associate Professor of Medicine and Pharmacology, Stanford University School of Medicine 1981 - 1991 1991 - 2006Professor of Medicine and of Molecular Pharmacology, Stanford University School of Medicine 2006 – Present Professor of Medicine and of Molecular Pharmacology (Active Emeritus), Stanford University 2000 - 2002Vice President, Methodology and Science, Pharsight Corporation, Mountain View, CA 2002 - 2006Associate Director, General Clinical Research Center, Stanford University School of Medicine 2001 – Present Adjunct Professor, Department of Bioengineering and Therapeutic Sciences, UCSF 2002 - Present Associate/Assistant Dean for Medical Student Advising, Stanford University School of Medicine 2005 – Present Adjunct Professor of Medicine, Indiana University School of Medicine

Other Experience and Professional Memberships

American Society for Clinical Pharmacology & Therapeutics (ASCPT) (President, 1988/89) American Soc of Pharmacology & Exp. Therapeutics (Clin Pharm Exec Comm, 1986–1989. Chair 2002–2003) Expert Consultant, Div. of Biopharmaceutics, Bureau of Drugs, FDA (1976–1980) Chairman, Generic Drugs Advisory Committee, FDA (1990–1994) Member, Nonprescription Drugs Advisory Committee, FDA (2003–2007) Associate Editor, Annual Review of Pharmacology and Toxicology (1989-)

Editorial Board, Clinical Pharmacology and Therapeutics (1981-)

Executive Editor, British Journal of Clinical Pharmacology (2008 -)

Chairman, Clinical Pharmacology Committee, MKSAP VII

Member, Pharmacology Study Section, DRG, NIH (1979–1983)

Member, VA Merit Review Committee (1984–1986)

Western Society for Clinical Research, Western Association of Physicians

Visiting Scientist, Div. Molecular Pharmacology, National Institute for Medical Research, Mill Hill, England (1980–1981)

Visiting Scholar, Center for Bio-Pharmaceutical Sciences, University of Leiden and Department of Medical Informatics, Erasmus University, The Netherlands (1991)

Visiting Professor, Moi University Faculty of Health Sciences, Eldoret, Kenya (Aug-September, 1997) Special Government Employee and Visiting Scientist, Office of Clinical Pharmacology and Biopharmaceutics,

Food and Drug Administration, Washington, DC (Nov 1997–April 1998)

<u>Honors</u>

Phi Beta Kappa

Alpha Omega Alpha (Junior Year)

Recipient, PMAF Faculty Development Award in Clinical Pharmacology

Recipient, Burroughs-Wellcome Scholar Award in Clinical Pharmacology (1977–1982)

Recipient, Research Career Development Award from NIGMS (1978–1983)

Stanford Univ. Sch. of Med Henry J. Kaiser Award for Outstanding Contributions to Medical Education – 1999 Recipient, 2002 Rawls-Palmer Progress in Medicine Lecture and Award, ASCPT

Recipient, Honorary Fellowship from the American College of Clinical Pharmacology - 2004

"Best Doctors in America", 2002, 2003, 2004, 2005, 2006, 2007, 2008, 2009

Recipient, 2006 Henry W. Elliott Award, ASCPT

Recipient, 2007 Oscar B. Hunter Award, ASCPT

C. Selected Peer-reviewed Publications (Selected from 176 peer-reviewed publications and 59 reviews, chapters and letters)

Most relevant to the current application

- Girard P, Sheiner LB, Kastrissios H, Blaschke TF: Do we need full electronic compliance data for population pharmacokinetic analysis? JOURNAL OF PHARMACOKINETICS AND BIOPHARMACEUTICS 24:265-282, 1996
- Vanhove GF, Schapiro JM, Winters MA, Merigan TC, Blaschke TF: Compliance and drug failure in protease inhibitor monotherapy. JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION 276:1955-56, 1996 [Letter]
- 3. Vanhove GF, Gries J-M, Verotta D, Sheiner LB, Coombs R, Collier AC, Blaschke TF: Exposureresponse relationships for saquinavir, zidovudine and zalcitabine in combination therapy. ANTIMICROBIAL AGENTS AND CHEMOTHERAPY 41:2433-38, 1997.
- 4. Kastrissios H, Suárez J-R, Katzenstein D, Girard P, Sheiner LB, Blaschke TF: Characterizing patterns of drug-taking behavior with a multiple drug regimen in an AIDS clinical trial. AIDS 12:2295-2303, 1998.
- Kastrissios H, Suárez JR, Hammer S, Katzenstein D, Blaschke TF: The extent of noncompliance in a large AIDS clinical trial using plasma dideoxynucleoside concentrations as a marker. AIDS 12:2305-2311, 1998.
- 6. Girard P, Blaschke TF, Kastrissios H, Sheiner LB: A Markov mixed effect regression model for drug compliance. STATISTICS IN MEDICINE 17:2313-2333, 1998
- Kshirsagar SA, Blaschke TF, Verotta D, Sheiner LB, Krygowski M, Acosta EP. Improving data reliability using a non-compliance detection method versus using pharmacokinetic criteria. (JOURNAL OF PHARMACOKINETICS AND PHARMACODYNAMICS 34:35-55, 2007; Epub 2006 Sep 27
- 8. Urquhart J, Blaschke TF: Patient compliance with anti-HIV treatments. PRACTICAL ISSUES IN HIV AND AIDS PATIENT MANAGEMENT, 1997, Issue Number 7 (August 1997), published by Van Zuiden Communications B.V., Alphen aan de Rijn, The Netherlands.
- 9. Kastrissios H, Blaschke TF: Therapeutic Implications of Nonadherence with Antiretroviral drug regimens. HIV: ADVANCES IN RESEARCH AND THERAPY **8**(2):

- 10. Osterberg L, Blaschke T: Adherence to Medication. NEW ENGLAND JOURNAL OF MEDICINE **353**:487-97, 2005 and **353**:1972-4, 2005 (Correspondence and Reply)
- 11. Blaschke TF: Variable adherence to prescribed dosing regimens for protease inhibitors: scope and outcomes. CURRENT OPINION IN HIV AND AIDS **3**:603-607, 2008
- 12. Vreeman RC, Nyandiko WM, Blaschke TF: Adherence to Antiretroviral Therapy for Adults and Children in Resource-Limited Settings. REVIEWS IN ANTIVIRAL THERAPY, pp 5-13, (2) 2009

Additional recent publications of importance to the field (in chronological order)

- Hammer SM, Katzenstein DA, Hughes MD, Gundacker H, Schooley RT, Haubrich RH, Henry WK, Lederman MM, Phair JP, Niu M, Hirsch MS, Merigan TC, Blaschke TF, Simpson D, McLaren C, Rooney J, Salgo M: A trial comparing nucleoside monotherapy with combination therapy in HIVinfected adults with CD4 cell counts between 200 and 500 per cubic millimeter. NEW ENGLAND JOURNAL OF MEDICINE **335**:1081-90, 1996
- Lu J-F, Blaschke TF, Flexner C, Rosenkranz SL, Sheiner LB, and AIDS Clinical Trials Group Protocol 378 Investigators: Model-based Analysis of the Pharmacokinetic Interactions Between Ritonavir, Nelfinavir and Saquinavir After Simultaneous and Staggered oral administration. DRUG METABOLISM AND DISPOSITION 30:1455-1461, 2002
- Washington CB, Flexner C, Sheiner LB, Rosenkranz SL, Segal Y, Aberg JA, Blaschke TF and the AIDS Clinical Trials Group Protocol 378 (ACTG 378) Study Team: Effect of Simultaneous versus Staggered Dosing on Pharmacokinetic Interactions of Protease Inhibitors. CLINICAL PHARMACOLOGY AND THERAPEUTICS 73:406-16, 2003

D. Research Support

Ongoing Research Support

None

Completed Research Support

GM07065-2807/01/77-06/30/05NIHTraining Program in Clinical PharmacologyInstitutional National Research Service Award Training Grant.

Role: Program Director

NIH/NIAIDS AACTG Pharmacology Support Laboratory

The Pharmacology Support Laboratory (PSL) of the Adult AIDS Clinical Trials Group represented 35% effort of Dr. Blaschke. The major goal of this project is to support the overall goal of the AACTG Pharmacology effort, which is to define the optimal use of current and future therapeutic modalities in the treatment of HIV infection and its associated diseases.

Role: Principal Investigator

NIH/NIAID R01 AI0588398/15/05 through 7/31/08Optimizing Efavirenz Doses in Patients with HIV and TB

This is a drug-drug interaction study examining the effects of rifampicin on the pharmacokinetics of efavirenz in patients co-infected with HIV and tuberculosis to determine whether the dose of efavirenz should be increased in this patient population.

Role: Principal Investigator