BIOGRAPHICAL SKETCH

NAME	POSITION TITLE
Steven L. Shafer, MD	Professor of Anesthesiology, Perioperative and Pain Medicine, Stanford, Adjunct Associate Professor of Bioengineering and Therapeutic Sciences, UCSF
eRA COMMONS USER NAME (credential, e.g., agency login)	

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

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
Princeton University	A.B.	1978	Biology
Stanford University	M.D.	1983	Medicine
Hospital of the University of Pennsylvania	--	1983-1984	Internship
Hospital of the University of Pennsylvania	--	1984-1986	Anesthesia Residency
Stanford University	--	1986-1987	Fellowship in Clinical Pharmacology

A. Personal Statement

I am very excited to participate in this exciting P01 proposal. As described by Dr. Eisenach, we have collaborated on research projects for three decades, ranging from our collaboration establishing the pharmacokinetics of intrathecal administered drugs to our collaboration on the ethics of neuraxial and perineural drug studies during our tenure as Editors-in-Chief of competing journals. The papers cited below are evidence of our longstanding collaboration.

My role in this proposal is to direct the Pharmacokinetic and Pharmacodynamic Core. I bring to this project more than 30 years of experience modeling drug pharmacokinetics and pharmacodynamics. From 1998 through 2008 I conducted dozens of clinical trials of intravenous anesthetics, developed novel concepts to characterize drug behavior, and wrote computer programs to analyze drug behavior and control drug delivery. The common thread is the use of mathematics and computer science to improve drug discovery and delivery. These contributions included the program STANPUMP (a portmanteau of “Stanford” and “Infusion pump”), which infused intravenous drugs based on pharmacokinetic and pharmacodynamic models to rapidly achieve and maintain desired drug concentrations in the plasma or at the site of drug effect. STANPUMP advanced research in clinical pharmacology by allowing investigators to perform studies at “pseudo steady-state” concentrations. After placing STANPUMP into the public domain, the software was widely adopted by other laboratories for research (with over 260 references in PubMed), and became the core software in commercial “target controlled infusion” devices worldwide.

Precise drug delivery, as described in this proposal, requires accurate pharmacokinetic models. My laboratory at Stanford developed models for many intravenous anesthetic drugs, including propofol, remifentanil, dexmedetomidine, midazolam, flumazenil, sufentanil, lidocaine, and multiple experimental drugs. Products whose FDA approval directly incorporated results from my laboratory at Stanford scholarship include propofol, remifentanil, dexmedetomidine, transdermal fentanyl, inhaled fentanyl (“Staccato”), bispectral index EEG monitoring, and Sedasys (a propofol delivery system for non-anesthesiologists).

1. Eisenach JC, Hood DD, Tuttle R, Shafer S, Smith T, Tong C: Computer-controlled epidural infusion to targeted cerebrospinal fluid concentrations in humans: Clonidine. Anesthesiology 1995; 83: 33-47
2. Shafer SL, Eisenach JC, Hood DD, Tong CY. Cerebrospinal fluid pharmacokinetics and pharmacodynamics of intrathecal neostigmine methylsulfate in humans. Anesthesiology 1998;89(5):1074-1088. PMID: 9821995
3. Shafer SL, Eisenach JC: Location, location, location. Anesthesiology 2000; 92: 641-643 2. Eisenach JC, Hood DD, Curry R, Shafer SL. Cephalad movement of morphine and fentanyl in humans after intrathecal injection. Anesthesiology 2003;99(1):166-173. PMID: 12826857
4. Eisenach JC, Shafer SL, Yaksh T: The need for a journal policy on intrathecal, epidural, and perineural administration of non-approved drugs. Pain 2010; 149: 417-419
5. Yaksh TL, Eisenach JC, Shafer SL: Consent contraindicated? Science 2010; 328: 45

B. Positions and Honors

Positions:

1983-1986	Internship and Resident, Anesthesiology, University of Pennsylvania
1986-1987	Clinical Pharmacology, Stanford University
1987-2005	Staff Anesthesiologist, Palo Alto VA Health Care System
1987-1988	Clinical Instructor, Department of Anesthesia, Stanford University
1988-1994	Assistant Professor, Department of Anesthesia, Stanford University
1994-2000	Associate Professor, Department of Anesthesia, Stanford University
2000-2008	Professor, Department of Anesthesia, Stanford University
2001-present	Adjunct Associate Professor of Biopharmaceutical Science, UCSF
2008-2012	Professor, Department of Anesthesiology, Columbia University
2012-present	Professor, Department of Anesthesiology, Perioperative and Pain Medicine, Stanford University
1999-2001	Vice President, Product Development, Pharsight Corporation
2002-2006	Anesthetic & Life Support Advisory Committee, FDA, 2005-2006 Chair
2006-2016	Editor-in-Chief, Anesthesia & Analgesia

Honors:

2003	Fellowship by Election, Royal College of Anaesthetists
2007	Rovenstine Lecture, Post Graduate Assembly, New York, NY
2008	FAER Honorary Research Lecture, ASA Annual Meeting
2011	Lifetime Achievement Award, International Society of Anesthetic Pharmacology
2012	Honorary Fellow, College of Anaesthetists of Ireland
2013	Honorary Member, German Society of Anaesthesiology and Intensive Care Medicine
2013	Gold Medal, Royal College of Anaesthetists, London
2013	David M. Little Jr. Prize, Anesthesia History Association
2015	Lewis Sheiner Award, International Society of Pharmacometrics, Washington, DC
2015	Severinghaus Lecture, Annual Meeting of the American Society of Anesthesiologists, San Diego, California

Federal Government Public Advisory or Scientific Review Committees:

1993-1997	Pharmacological Sciences Review Committee (NIGMS)
1995-1999	Department of Veterans Affairs Merit Review Committee for Alcoholism and Drug Dependence
2002-2006	Anesthetic & Life Support Advisory Committee, FDA, 2005-2006 Chair

C. Contributions to science related to this application

1. Development of effective target-controlled infusion strategy for intravenous anesthetics:
    a. Hu C, Horstman DJ, **Shafer SL**. Variability of target-controlled infusion is less than the variability after bolus injection. Anesthesiology. 2005;102:639-45.
    b. Van Poucke GE, Bravo LJ, **Shafer SL**. Target controlled infusions: targeting the effect site while limiting peak plasma concentration. IEEE Trans Biomed Eng. 2004;51:1869-75.
    c. Struys MM, De Smet T, Depoorter B, Versichelen LF, Mortier EP, Dumortier FJ, **Shafer SL**, Rolly G. Comparison of plasma compartment versus two methods for effect compartment--controlled target-controlled infusion for propofol. Anesthesiology. 2000;92:399-406.
    d. **Shafer SL**, Siegel LC, Cooke JE, Scott JC. Testing computer-controlled infusion pumps by simulation. Anesthesiology. 1988;68:261-6.
2. Development of new theoretical constructs for pharmacokinetic and pharmacodynamic modeling.
    a. Struys MM, Coppens MJ, De Neve N, Mortier EP, Doufas AG, Van Bocxlaer JF, **Shafer SL**. Influence of administration rate on propofol plasma-effect site equilibration. Anesthesiology. 2007;107:386-96.
    b. Minto CF, Schnider TW, Gregg KM, Henthorn TK, **Shafer SL**. Using the time of maximum effect site concentration to combine pharmacokinetics and pharmacodynamics. Anesthesiology. 2003;99:324-33.

c. Minto CF, Schnider TW, Short TG, Gregg KM, Gentilini A, **Shafer SL**. Response surface model for anesthetic drug interactions. Anesthesiology. 2000;92:1603-16.
d. Schnider TW, Minto CF, Gambus PL, Andresen C, Goodale DB, **Shafer SL**, Youngs EJ. The influence of method of administration and covariates on the pharmacokinetics of propofol in adult volunteers. Anesthesiology. 1998;88:1170-82.

3. Disemination of practical elements of pharmacokinetics and pharmacodynamics to practicing clinicians.
   a. Hendrickx JF, Eger EI 2nd, Sonner JM, **Shafer SL**. Is synergy the rule? A review of anesthetic interactions producing hypnosis and immobility. Anesth Analg. 2008;107:494-506.
   b. Barr J, Egan TD, Sandoval NF, Zomorodi K, Cohane C, Gambus PL, **Shafer SL**. Propofol dosing regimens for ICU sedation based upon an integrated pharmacokinetic-pharmacodynamic model. Anesthesiology. 2001;95:324-33.
   c. **Shafer SL**, Stanski DR. Improving the clinical utility of anesthetic drug pharmacokinetics. Anesthesiology. 1992;76:327-30.
   d. **Shafer SL**, Varvel JR. Pharmacokinetics, pharmacodynamics, and rational opioid selection. Anesthesiology. 1991;74:53-63.

4. Development of accurate pharmacokinetic and pharmacodynamic models for the newly developed IV anesthetic agents reminfentanil and dexmedetomidine
   a. Minto CF, Schnider TW, **Shafer SL**. Pharmacokinetics and pharmacodynamics of remifentanil. II. Model application. Anesthesiology. 1997;86:24-33.
   b. Minto CF, Schnider TW, Egan TD, Youngs E, Lemmens HJ, Gambus PL, Billard V, Hoke JF, Moore KH, Hermann DJ, Muir KT, Mandema JW, **Shafer SL**. Influence of age and gender on the pharmacokinetics and pharmacodynamics of remifentanil. I. Model development. Anesthesiology. 1997;86:10-23.
   c. Dyck JB, Maze M, Haack C, Vuorilehto L, **Shafer SL**. The pharmacokinetics and hemodynamic effects of intravenous and intramuscular dexmedetomidine hydrochloride in adult human volunteers. Anesthesiology. 1993;78:813-20.
   d. Egan TD, Lemmens HJ, Fiset P, Hermann DJ, Muir KT, Stanski DR, **Shafer SL**. The pharmacokinetics of the new short-acting opioid remifentanil (GI87084B) in healthy adult male volunteers. Anesthesiology. 1993;79:881-92.

5. Testing and validation of bispectral index versus entropy as processed electroencephalographic measures of the clinical effect of anesthetics.
   a. Bouillon TW, Bruhn J, Radulescu L, Andresen C, Shafer TJ, Cohane C, **Shafer SL**. Pharmacodynamic interaction between propofol and remifentanil regarding hypnosis, tolerance of laryngoscopy, bispectral index, and electroencephalographic approximate entropy. Anesthesiology. 2004;100:1353-72.
   b. Bruhn J, Bouillon TW, Radulescu L, Hoeft A, Bertaccini E, **Shafer SL**. Correlation of approximate entropy, bispectral index, and spectral edge frequency 95 (SEF95) with clinical signs of "anesthetic depth" during coadministration of propofol and remifentanil. Anesthesiology. 2003;98:621-7.
   c. Bruhn J, Bouillon TW, **Shafer SL**. Onset of propofol-induced burst suppression may be correctly detected as deepening of anaesthesia by approximate entropy but not by bispectral index. Br J Anaesth. 2001;87:505-7.
   d. Bruhn J, Bouillon TW, **Shafer SL**. Bispectral index (BIS) and burst suppression: revealing a part of the BIS algorithm. J Clin Monit Comput. 2000;16:593-6.

D. Other Support

Project number: SPO 145193 04/01/19-06/1/21
Source: Concentric Analgesics $454,479
Title of Project: Safety and Efficacy of TRP V1 Agonists

Major goals of this project: Develop pharmacokinetic and pharmacodynamic models of novel TRP V1 receptor agonists in clinical trials. The primary focus is characterizing clinically effective goals to inform clinical studies leading to FDA approval..
Role: PI
Time: 20% FTE
Overlap: None

Project number: R01 HD070795 07/20/12 - 08/31/21
Source: NIH $582,442
Title of Project: Prevention of neonatal opioid withdrawal syndrome
Major goals of this project: Develop pharmacokinetic and pharmacodynamic models to characterize the efficacy of ondansetron in the prevention of neonatal abstinence syndrome and to guide therapeutic dosing in parturients taking opioids during pregnancy.
Role (since March, 2019) Consultant.
Time: 15% FTE
Overlap: None

Project number: 1K23GM132755 09/15/19 – 08/31/23
Source: NIH $189,972
Title: Anesthetic modulation of human memory during acute pain
Major goals of this project: This study will clarify how three distinct anesthetics affect the formation of conscious and subconscious memories during experimental painful stimulation, using a variety of measurements.
Role: Consultant
Time: 0 (no salary support)
Overlap: None