Cecilia Fosser, Ph.D.
Curriculum Vita

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SUMMARY:

Cecilia Fosser works as a Principal Statistician within the Full Service Provider division of Ctyel supporting clinical drug development. Previously she led the Quantitative Pharmacology and Pharmacometrics group within Strategic Consulting at Cytel. She got her Ph.D. in applied mathematics from The University of Arizona while on a national fellowship. There she focused on modeling and simulation of systems of nonlinear differential equations. She worked as a clinical statistician at Pfizer for 4 years on early and late phase clinical research projects across several therapeutic areas. In 2010, she began working in Pfizer's pharmacometrics group across many therapeutic areas with a focus on inflammation. In July of 2014, Cecilia joined Cytel Inc. to work in a hybrid position where she combines statistical and pharmacometrics techniques for quantitative drug development.

Cecilia has presented at several large international conferences (ASCPT, and ACoP), worked and published on exposure-response analyses of multiple endpoints, and in particular on multivariate Cox proportional hazards modeling of clinical risk factors for safety and efficacy endpoints. She has provided comparative effectiveness analysis in the form of model-based meta-analysis of psoriasis treatments, as well as, for chronic kidney disease endpoints and treatments. As both a statistician and a pharmacometrician Cecilia provides industry-leading approaches, including advanced modeling and simulation techniques, that contribute to quantitative decision making.

EDUCATION:

Ph.D. in Applied Mathematics (Biomathematics)
University of Arizona, Tucson, Arizona 85721.   **G.P.A. 3.9**

Dissertation: *Statistical Analysis of a Stochastic Automata Model for the Spread of Disease Among Mobile Individuals*.

Advisor: C. David Levermore
- Developed technique for controlling macroscopic statistics by altering microscopic behavior in a discrete model.
- Created a simulation (written in C) tailored for infectious disease but adaptable to numerous scenarios.
- The biomathematics program was extremely interdisciplinary and helped develop a number of important skills: a strong scientific background that spanned many disciplines, the ability to identify and understand relevant scientific literature, the ability to apply knowledge gained from these sources, the ability to work in scientific teams with people of diverse backgrounds, and the ability to communicate (both in writing and orally) knowledge and ideas to diverse audiences.

Master of Science in Applied Mathematics

University of Central Florida, Orlando, Florida 32816.   G.P.A. 3.9

Master's Thesis: *Turing Bifurcations in Nonlinear Competition Models with Delay*.

Advisor: Roy Choudhury.

- Published: Quarterly of Applied Mathematics, Vol. LIV, No. 1, March 1996.
- Derived the necessary and sufficient conditions for a Turing Bifurcation.

Bachelor of Science in Mathematics

University of Florida, Gainesville, Florida 32611.   G.P.A. 3.9

Senior Honors Thesis: *Program for Determining Conjugacy Classes of a Group of Permutations of a Finite Set*.

Advisor: Rick Smith.

- Graduated First in Class from the Mathematics Department.

PROFESSIONAL EXPERIENCE:

July 2014 – Present

Cytel, Inc., Cambridge, MA
Principal Biostatistician, Clinical Services
(September 2019 – Present)

Provide statistical leadership and statistical expertise into clinical development plans, concept sheets and protocols for clinical development projects. Lead statistical teams on clinical development projects, ensuring alignment of objectives and delivery of statistical output on time and meeting project requirements, coordinating all statistical aspects across clinical trials of each assigned project. Provide statistical input into study protocols, Case Report Forms, data management plans, write statistical analysis plans, review or create analysis dataset specifications, and perform statistical analyses. Review and contribute to study reports and clinical and statistical sections of regulatory submission dossiers, lead electronic submissions of clinical data to regulatory authorities, and participate to meetings with regulatory authorities. Generate the use of innovative statistical methodology approaches by identifying, adapting, developing or using optimal statistical research methodologies and techniques appropriate to each project, and contribute internally and externally to the development and visibility of the company and of the Clinical Services department through her expertise and customer orientation. Develop strong collaboration

and communication with sponsor cross-functional teams and sponsor Biostatistics management.

Director, Strategic Consulting and Pharmacometrics, Strategic Consulting *(September 2017 – August 2019)*

Provided strategic, quantitative, drug development consultation including guidance and expertise with model informed drug development, study designs, and sample size calculations. Areas of focus included adaptive designs, model-based, meta-analysis, and performing exposure-response modeling and simulation of pre-clinical and clinical data, including translational modeling to inform on dose ranges for First In Human studies.

Director, Head Quantitative Pharmacology and Pharmacometrics and Phase 1 Biostatistics *(April 2017 – September 2017)*

Led a global group that performed 4 distinct functions: 1). Pharmacometrics 2). Quantitative Pharmacology including Non-Compartmental Analysis (NCA) 3). Phase 1 Biostatistics 4). Creation of Comparator Databases. In addition, provided model informed drug development consultation and performed exposure-response modeling and simulation of pre-clinical and clinical data, including translational modeling and model-based, meta-analysis.

Director, Quantitative Pharmacology and Pharmacometrics *(September 2016 – March 2017)*
Provided model informed drug development consultation and perform exposure-response modeling and simulation of pre-clinical and clinical data, including translational modeling and model-based, meta-analysis.

Director, Biostatistics *(July 2014 – September 2016)*

Provided statistical input into Phase I - IV clinical trial development, write statistical analysis plans (SAPs), performed the analysis of clinical trial data, and provided statistical input into the reporting of clinical trial results. Responsible for collaborating and consulting with clients on statistical issues. Worked closely with statistical programmers and provided oversight of statistical programming.

November 2010 – July 2014

Pfizer, Inc., Groton, CT
Associate Director, Pharmacometrics, Global Clinical Pharmacology, Primary Care Business Unit

- Member of the Rheumatoid Arthritis Phase 3 Pharmacometrics team for Xeljanz (tofacitinib) Submission:
    - o Provided exposure-response analyses of multiple endpoints including blood pressure, serious infections, and opportunistic infections.
    - o Provided multivariate Cox proportional hazards modeling of clinical risk factors for safety endpoints.
    - o Provided technical and scientific assistance/consulting/scientific programming in the backroom of the advisory committee meeting at the FDA.
    - o Assisted on safety, time-to-event and exposure-response analyses as part of regulatory queries.
    - o Developed a technique for identifying an optimal threshold value of a continuous predictor of clinical outcomes

- Member of the Psoriasis Phase 3 Pharmacometrics team for Xeljanz (tofacitinib) Submission:
    - o Provided comparative effectiveness analysis in the form of model-based meta-analysis of psoriasis treatments.
    - o Led data structure development for the pooled Phase 3, long-term extension study dataset.
    - o Simulated time-to-event data and estimated operating characteristics associated with exposure-response analyses of rare safety events using Cox proportional hazards models.
- Provided modeling strategy for model-based, meta-analyses for chronic kidney disease endpoints and treatments. Provided a model-based, meta-analysis of urinary albumin to creatinine ratio (UACR). Quantitatively assessed biomarker to registration endpoint relationship for predictive value and trial designs.
- Provided population exposure-response modeling analyses for ECG data and PANNS negative efficacy data for a compound being developed for schizophrenia.

October 2008 – November 2010

Pfizer, Inc., New London, CT
Biostatiscian, Associate Director, Inflammation Statistics, Specialty Care Business Unit

- Member of the Rheumatoid Arthritis Phase 3 Statistical team for Xeljanz (tofacitinib): Primary author of the pooled Phase 3 safety, statistical analysis plan for global submission packages. Contributed to study designs for both confirmatory and exploratory studies; analyzed phase 2 safety data; specified randomizations; developed statistical analysis plans; ensured reported findings were statistically accurate; addressed regulatory queries.

- Volunteered to assist with Bayesian analysis of Phase 2 psoriasis CP-690,550 (Xeljanz) data to be used for Phase 3 dose selection. (Note: subsequent decision to not pursue this analysis)
- Tibco Spotfire Subject Matter Expert. Organized and facilitated Lunch and Learn sessions to provide support and education to Spotfire users across all Pfizer lines.

June 2007 – October 2008

Pfizer, Inc., New London, CT
Biostatistician, Manager, Cardiovascular and Metabolic Diseases Statistics

- Statistical consultant: Contributed to study design; primary liaison between statistics line and study team; specified randomizations; developed statistical analysis plans; conducted statistical analyses; ensured reported findings were statistically accurate; and contributed to Clinical Study Reports in Diabetes and Osteoporosis.
- Promoted and applied ECTD/EQDD (Enhanced Clinical Trial Designs/Enhanced Quantitative Drug Development) principals to derive quantitative Go/No Go decision criteria for drug development strategies.
- Ran extensive simulations under multiple scenarios to contribute to quantitative decision making.
- Took initiative and leadership and began work on proposing an ECTD drug development plan for 3rd Calcium Receptor Angtagonist (for Osteoporosis) back-up compound that combined a 4 week POM study with a 6 month POC study and potentially saved 1.5 years off of development timelines.

May 2006 – May 2007

Pfizer, Inc., Groton, CT
Biostatistician, Manger, Clinical Pharmcology Statistics

- Statistical consultant: Contributed to study design, including proposing dose-response modeling during protocol development; primary liaison between statistics line and study team; specified randomizations; developed statistical analysis plans; conducted statistical analyses; ensured reported findings were statistically accurate; and contributed to Clinical Study Reports of clinical pharmacology studies covering most therapeutic areas.
- Derived and presented statistical and mathematical results that are relevant to the statistical analysis of pharmacology studies.
- Responded to regulatory queries regarding the Exubera 1st Generation global filings, often involving reanalyzes of data.

- Worked as a Project Statistician on the Exubera 2nd Generation Early Development Team by providing statistical support and advising on drug development strategy.
- Contributed to machine vs manual QT measurements meta-analyses.
- Continually showed leadership in finding ways to increase efficiency and build morale within the study teams and among the clinical pharmacology statisticians.

May 2004 – May 2006

Pfizer, Inc.(contracted by Sigma Systems, Inc.), Clinical Pharmacology Group, Groton, CT
Biostatistician, Biostatistics & Reporting, Nonclinical Biostatistics

- Statistical consultant: Contributed to study design during protocol development, primary liaison between statistics line and study team, specied randomizations, developed statistical analysis plans, conducted statistical analyses, ensured reported findings are statistically accurate, and contributed to Clinical Study Reports of clinical pharmacology studies covering most therapeutic areas.
- Derived and presented statistical and mathematical results that are relevant to the statistical analysis of pharmacology studies.
- Contributed to the development of enhanced reporting displays of first-in-human safety data in early development studies.

June 1997 – July 1997

Los Alamos National Laboratory, Los Alamos, NM
Visiting Researcher, Theoretical Division, Mathematical Modeling & Analysis

- Collaborated with the Epidemiological Modeling Group on model development and numerical analysis for statistical behavior of infectious disease.
- Developed computer simulation using cellular automata and mathematical analysis.

May 1995 – August 1995

Xerox Research Center of Canada, Toronto, Canada
Researcher, Simulation Laboratory

- Developed a numerical model for the diffusion of heat through a multi-level medium.
- Created a cellular automata model for the formation of oxidation-induced facets on the surface of platinum.

May 1993 – September 1993

> **Xerox Research Center, Pasadena, CA**
> **Researcher, Color Systems Technology Group**
>
> Developed and programmed mathematical transformations to provide interchangeability of color printing formats.

1987 – 1989

> **Sprint Corporation, Orlando, FL**
> **Analyst, Revenue Planning and Pricing**
>
> - Tracked and forecasted (using both linear and nonlinear regression analysis) revenues, costs and profits for a regulated utility.
> - Developed rates and assisted in FCC filings.
> - One of four employees picked to participate in an in-house "think tank" to develop new services.

LANGUAGES:

Fluent in Spanish

COMPUTER SKILLS:

- Pharmacometrics Analysis Software: Phoenix NLME, nlmixr, Stan, NONMEM, PsN, Xpose
- Statistical Programming Languages/Tools: R, S-plus, SAS (SAS Certified Base Programmer), nQuery Advisor
- Programming Languages and Graphing Tools: C, Fortran, Spotfire
- Operating Systems: Windows, MacOS, Linux, UNIX
- Scientific Computing: Matlab, Maple, and Mathematica
- Other: MS Office Suite, Lotus Suite, LaTex, HTML

AWARDS AND ACTIVITIES:

- Pfizer Individual Performance Award, Nominated by Tong Zhu, Clinical Pharmacology, Worldwide Research and Development   2013
- Pfizer Individual Performance Award, Nominated by Pankaj Gupta, Clinical Pharmacology, Specialty Care Business Unit 2013

- Pfizer Individual Performance Award, Nominated by Sriram Krishnaswami, Clinical Pharmacology, Specialty Care Business Unit 2012
- Pfizer Individual Performance Award, Nominated by Pankaj Gupta, Clinical Pharmacology, Specialty Care Business Unit 2012
- Pfizer Individual Performance Award, Nominated by Mike Brown, Head of Inflammation Statistics, Specialty Care Business Unit 2010
- Pfizer Individual Performance Award, Nominated by Mohan Beltangady, Global Head of Statistics 2009
- National Physical Science Consortium Fellow 1993-1999
  - Awarded one of 26 national six-year full fellowships that included tuition and a stipend.
- Flinn Foundation Scholarship in BioMathematics   1995-1996
- Finalist for National Science Foundation Research Fellowship (removed when awarded NPSC fellowship).
- Finalist for Bell Labs Research Fellowship for Minorities and Women (removed when awarded NPSC fellowship).
- Awarded (but declined) University of California – Los Angeles University Fellowship.
- Awarded (but declined) University of Maryland – College Park University Fellowship.
- Second Place Graduate Teaching Award, University of Central Florida. 1993
- University of Florida's President's Honor Roll (4.0 GPA), Summer 1985, Fall 1985, Spring 1986
- Florida Teachers Scholarship/Loan 1985-1987
- Applied Mathematics Graduate Representative, University of Arizona.
- Started a Women's Issues Discussion Group in the Mathematics Department, University of Arizona.

Professional Organizations:
- Member of International Society of Pharmacometrics (ISoP) 2011-Present; Member Special Interest Group for Statistics; Member Special Interest Group for Mathematics and Computation
- Member of American Society of Clinical Pharmacology and Therapeutics (ASCPT) 2011-Present; PMK Steering Committee member April 2017–Present
- Community Outreach Chair, Pfizer Hispanic Network, 2008-2010
- Member of the American Mathematical Society. 1993-2006
- Member of the Society for Industrial and Applied Mathematics (SIAM). 1996-2006

Teaching Experience:

2002 - 2003

Old Saybrook Senior High School, Old Saybrook, CT
High School Math Teacher

Full teaching duties for Advanced Placement Calculus (AB & BC) and Statistics.

1999 - 2000

Golden West Community College, Huntington Beach, CA
Adjunct Instructor

Full teaching duties for Introduction to Statistics.

Fall 1998

University of Arizona, Tucson, AZ
Undergraduate Research Project Mentor

Mentored an undergraduate student on a research project involving cellular automata.

Fall 1997

Southwest Regional Institute in the Mathematical Sciences, Tucson, AZ
Volunteer High School Workshop Instructor

- Planned and ran two all-day workshops on Fourier Series and Harmonic Analysis for high school students in the Tucson area.
- Web page: http://www.math.arizona.edu/~rims/

Fall 1996

University of Arizona, Tucson, AZ
Volunteer Graduate Teaching Assistant

- Full teaching duties for a reform Calculus II course.
- Volunteer status was required due to National Physical Science Consortium Fellowship.

1991 - 1993

University of Central Florida, Orlando, FL
Graduate Teaching Assistant

Full teaching duties for subjects ranging from College Algebra through Calculus.

1990 - 1993

Valencia Community College, Orlando, FL
Adjunct Instructor

Full teaching duties for subjects ranging from College Preparatory Algebra through Calculus.

1984 - 1987

University of Florida, Gainesville, FL
Private Math Tutor

Tutored approximately 20 students per semester in a variety of math courses.

CERTIFICATIONS & PROFESSIONAL TRAINING:

- SAS Certified Base Programmer
- Mango Solutions Introduction to R programming
- Spotfire Training
- Certara University's Phoenix NLME Introduction to Population Modeling and Advanced Population Modeling
- NONMEM 7 Training by ICON

PUBLICATIONS & PRESENTATIONS:

Publications:

1. L. Greenbaum, G. Deschenes, E. Levtchenko, M. Besouw, C. Fosser, N. Confer, S. Zheng, G. Checani. *Quantification of Dimethylsulfide Associated With Cysteamine Bitartate-Induced Halitosis Using Breath Analysis in Cystinosis Patients Treated with Delayed-Release and Immediate-Release Cysteamine Bitartrate. Nephrology Dialysis Transplantation*, Volume 32, Issue suppl_3, 1 May 2017, Pages iii114, https://www.postersessiononline.eu/173580348_eu/congresos/54ERA/aula/-SP_26_54ERA.pdf
2. C. Fosser, G. Duczynski, M. Agin, P. Wicker, and B. Darpo. Comparison of Manual and Automated Measurements of the QT Interval in Healthy Volunteers: An Analysis of Five Thorough QT Studies. Clinical Pharmacology & Therapeutics, Vol. 86, No. 5, pp. 503–506,

2009.

3. Bharat Damle, Cecilia Fosser, Kaori Ito, Anh Tran, Pamela Clax, Howard Uderman and Paul Glue. Effects of Standard and Supratherapeutic Doses of Nelfinavir on Cardiac Repolarization: A Thorough QT Study. J. Clin. Pharmacol, Vol 49; pp 291-300, 2009.
4. S. Roy Choudhury and C. Fosser. Turing Bifurcations in Nonlinear Competition Models with Delay. Quarterly of Applied Mathematics, Vol. LIV, No. 1, March 1996.
5. C. Fosser and C. D. Levermore. Statistical Analysis of a Stochastic Automata Model For the Spread of Disease Among Mobile Individuals. In preparation.
6. C. Fosser and C. D. Levermore. A Reactive-Diffusive Lattice Automata. In preparation.

Seminars & Conferences:

1. Poster: C. Fosser, J. Bhattacharyya, P. Jain, H. Kulkarni. *Optimizing Dose Selection in the Face of Model Uncertainty with Proc MCPMod,* ACoP9, October 2018
2. Poster: P. Zhang, C. Fosser, J. Roberts, A. Brainsky, Y. Li, W. McKeand, J. Sidhu. *Identifying Efficacious Thresholds for Bleeding Risk Reduction in Relation to Factor VIII Levels in Hemophilia A Patients Receiving rVIII-SingleChain*, ISTH SSC June 2018
3. Poster: C. Fosser, J. Roberts, M. Tortorici, I. Jacobs, J. Sidhu. *Identifying Efficacious Thresholds for Bleeding Risk Reduction in Relation to Factor IX (FIX) Levels in Hemophilia B Patients Receiving IDELVION* ACoP8, October 2017
4. Poster: C. Fosser, L. Mattheakis, R. Saralaya, K. Horsch, N. Rao, L. Bai, L. Zhao, T. Annamalai, D. Liu. *Model Based Predictions of the PTG-100 Pharmacodynamic Responses in Ulcerative Colitis Patients.* PAGE June 2017
5. Presentation: "Asking the Right Questions of Your Data: Experiences with Model-informed Development Approaches": Chief Medical Officer's Summit, Boston, May 2017
6. Chaired Session "Using Biomarkers to Predict Registration Endpoints: A Look Inside the Crystal Ball": ASCPT, March 2017
7. Chaired Session "Pharmacometric Approaches for Analysis of Categorical Safety Data for Improved Risk Assessment": ACoP6, October 2015
8. Poster: M. Gopalakrishnan, J. Bolognese, J. Bhattacharya, C. Fosser, N. Patel. *Leveraging Biomarkers, Clinical Endpoints, and Exposure-Response Modeling and Simulation to optimize Phase 3 Dose Selection* ACoP6, October 2015
9. Poster: C. Fosser, M. Huttmacher, P. Gupta, S. Krishnaswami, M. Tortorici. *An Assessment of the Operating Characteristics (OCs) of Time-to-Event (TTE) Exposure-Response (ER) Analyses of Adverse Events (AEs).* Selected for Oral Presentation ASCPT March 2014
10. Poster: JJ Gomez-Reino, A Hazra, C Fosser, S Menon, SH Zwillich, R Riese, S Krishnaswami. *Post-Hoc Analysis Of Serious Infection Events and Selected Clinical Factors In Rheumatoid Arthritis Patients Treated With Tofacitinib*. ACR. October 2013
11. Poster: C. Fosser, M. Huttmacher, S. Krishnaswami. *A Technique for Identifying an Optimal Threshold Value of a Continuous Predictor of Clinical Outcomes*. ACoP4 May 2013
12. Poster: A. Hazra, C. Fosser, S. Riley, S. Menon, V. Purohit, A. Mukherjee, J. French, M. Huttmacher, M. Peterson, M. Lamba, S. Krishnaswami. *An R function to efficiently screen*

for relationships between drug and/ or disease parameters and rare adverse events. ACoP4. May 2013

13. Poster: C. Fosser, P. Gupta, M. Peterson, S. Ahadieh, J. Mandema. Competitive *Landscape for Psoriasis Treatments: March 2013 Update*. Specialty Care Business Unit, Medicines Development Group, Pfizer. April 2013

14. Poster: R. van Vollenhoven, R. Riese, S. Krishnaswami, T. Kawabata, C. Fosser, S. Rottinghaus, M. Lamba, S. H. Zwillich, J. Bradley. *Relationship Between Lymphocyte Count and Risk of Infection in Rheumatoid Arthritis PatientsTreated with Tofacitinib*. EULAR 2013 and ACR 2013 (Encore). March and October 2013

15. Poster: C. Fosser, A. Hazra, A. Mukherjee, M. Peterson, V. Purohit, M. Lamba, M. Hutmacher, S. Menon, S. Krishnaswami, R. Riese, S. Rottinghaus, and the Tofacitinib Team. *Exposure-Response and Biomarker-Response Analysis of Opportunistic Infections in the Tofacitinib RA Program.* Specialty Care Business Unit, Medicines Development Group, Pfizer.   November 2012

16. Presentation: ”*Spotfire as a Quick Visualization Tool for Data Cleaning”*. East Coast Scientific Forum, Global Clinical Pharmacology, Pfizer. October 2012

17. Presentation: “Converting Confidence Intervals Under Nonlinear Transformations”. Global Pharmacometrics Meeting. January 2012

18. Presentation: “Fluctuation Statistics in an Individual-Based Model of Disease Spread” Mathematics Colloquium, *California State University,* Long Beach, California. February 2000

19. Poster: “Continuum Limits of Convective-Diffusive Lattice Boltzmann Methods”

20. Fourth SIAM Conference on Applications of Dynamical Systems. May 1997

21. Presentation: “Modeling Infectious Disease via Diffusive Automata” Dynamics in Populations Seminar, *University of Arizona.* November 1997

22. Presentation: “Continuum Limits of Lattice Boltzmann Methods”

23. Dynamics in Populations Seminar, *University of Arizona.* October 1997

24. Presentation: “Macroscopic Limit of a Nonlinear Transport Equation” Applied Mathematics Brown Bag Seminar, *University of Arizona.* April 1997

25. Presentation: “Lattice Boltzmann Methods: Numerical Schemes for Solving Convective-Diffusive PDEs” Applied Mathematics Brown Bag Seminar, *University of Arizona.* February 1996