

# Matthew M. Hutmacher

406 Arbana Dr  
Ann Arbor, MI 48103  
H: 734.332.9767  
C: 805.390.9857  
[Matt.Hutmacher@a2pg.com](mailto:Matt.Hutmacher@a2pg.com)  
[mmhutm@yahoo.com](mailto:mmhutm@yahoo.com)

## I. EXPERIENCE

- **June 2004 – present** Pfizer, Inc., Ann Arbor, MI  
*Associate Director Pharmacometrics – Clinical Pharmacology.* Develop, evaluate, and apply model- and simulation-based analyses and strategies to clinical research. Focus is on clinical trial design strategies and the evaluation of these using: trial performance metrics of clinical endpoint statistics, dose selection and go/no go decision criteria (estimating the probability of correct decision, technical success, and commercial viability), PK/PD and disease progression models, longitudinal and landmark-type meta-analytic models, and trial execution models (such as compliance and dropout models). Implemented these strategies on projects such as Lyrica and Celecoxib. Other interests include incorporation of model uncertainty into simulation strategies and model selection methodologies.
- **September 2003 – May 2004** Amgen, Inc., Thousand Oaks, CA  
*Research Scientist- Pharmacokinetics and Drug Metabolism.* Supported Enbrel in psoriasis and renal insufficiency using exposure-response modeling methodologies. Contributed to reports submitted to FDA for filing the psoriasis indication. Performed simulations to recommend and support untested dosing strategies.
- **September 1997 – September 2003** SIR, Libertyville, IL
- **July 1996 – September 1997** PAREXEL, Northbrook, IL  
*Consulting Statistician.* Advised Searle/Pharmacia/Pfizer on population pharmacokinetic/pharmacodynamic (PK/PD) issues of drug development in pre-clinical and phases I-III. Responsibilities included: simulating sampling designs to ensure model stability, efficient parameter estimation, and suitable power; and mechanism based and empirical model fitting such as standard PK, indirect response, Emax, and ordered categorical models; model inference and validation, both internal (bootstrap) and external (bridging studies). Results guided dose/regimen selection and have affected drug label formulation including defense of selection at the FDA. Participated on the PK/PD modeling task force, in the clinical trial simulation effort work group, and as an *ad hoc* member on the *in silico* technologies project team. Participated in the Celebrex, Bextra, Dynastat, and Inspra NDAs.

- **April 1996 - July 1996** Independent Consultant  
*Consulting Statistician.* Advised the Center for Retail Management in the Kellogg School of Business on the statistical aspects of marketing strategies. Formulated models and tests to optimize product-marketing profiles.
- **October 1994 - April 1996** STATCOMP, Waukegan, IL  
*Consulting Statistician.* (Clinical) Provided support to G.D. Searle in PK/PD modeling strategies. (Pre-clinical) Advised clients on experiments/research using design of experiments, response surface methodology, process capability and stability. Modeling tools used were mixed effects modeling, trend and Dunnett tests, non-parametric regression, and derivation and interpretation of mechanistic (protein binding type) models.
- **June 1993-September 1993** G.D. Searle, Skokie, IL  
*Intern.* Instructed clients on the statistical issues of animal models using logistic regression, response surface methodology, and design of experiments.
- **September 1992-June 1994** Northwestern University, Evanston, IL  
*Graduate Teaching Assistant.* Assisted outside clients with statistical issues including categorical models. Taught statistical concepts for five consecutive quarters.

## II. EDUCATION

- **September 1992-June 1994** NORTHWESTERN UNIVERSITY, Evanston, IL  
M.S. Degree in Mathematical Statistics
- **August 1987 - December 1991** UNIVERSITY OF ILLINOIS, Champaign/Urbana, IL  
B.S. Degree in Graduate School Preparatory Mathematics.  
Cum Laude, Departmental High Distinction

## III. PUBLICATIONS

### A. Professional Articles

1. Kowalski KG, Hutmacher MM. Design evaluation for a population pharmacokinetic study using clinical trial simulations: a case study. *Statist. Med.* **20**:75-91 (2001).
2. Kowalski KG, Hutmacher MM. Efficient screening of covariates in population models using Wald's approximation to the likelihood ratio test. *JPP* **28**: 253-275 (2001).
3. Kowalski KG, McFadyen L, Hutmacher MM, Frame B, Miller R. A two-stage mixture model for longitudinal adverse event severity data. *JPP* **30**:315-336 (2003).
4. A Method of obtaining starting values of kin and kout for the indirect response models. *JPP* **31**:29-42 (2004).

5. Don BR, Spin G, Nestorov I, Hutmacher M, Rose A, Kaysen GA. The pharmacokinetics of etanercept in patients with end-stage renal disease on haemodialysis. *J. Pharmac. Pharmacol.* **57**:1-7 (2005)
6. Hutmacher MM, Mukherjee D, Kowalski, KG, Jordan DC. Collapsing mechanistic models: an application to dose selection for proof of concept of selective irreversible antagonist. *JPP* **32**:501-520 (2005).
7. Hutmacher MM, Nestorov I, Ludden T, Zitnik R, and Banfield C. Modeling the exposure-response relationship of etanercept in the treatment of patients with chronic moderate to severe plaque psoriasis. *J. Clin. Pharmacol.* **47**:238-248 (2007).
8. Kowalski KG, Ewy W, Hutmacher MM, Miller R, and Krishnaswami S. Model-based drug development – a new paradigm for efficient drug development”. *Biopharmaceutical Report.* **15**:2-22 (2007).
9. Lalonde RL, Kowalski KG, Hutmacher MM, Ewy W, Nichols DJ, Milligan PA, Corrigan BW, Lockwood PA, Marshall SA, Benincosa LJ, Tensfeldt TG, Parivar K, Amantea M, Glue P, Koide H, and Miller R. Model-based drug development. *Clin. Pharmacol. Therapeut.* **82**:21-32 (2007)
10. Chapel S, Hutmacher MM, Haig G, Bockbrader H, de Greef HJMM, Agin M, and Lalonde R. Exposure-response analysis to assess the effect of asenapine, quetiapine (Seroquel®), or placebo administration on the QTc interval in patients with schizophrenia (2007, Manuscript in preparation for CPT)
11. Hutmacher MM, Chapel S, Agin M, and Lalonde R. Performance characteristics of the analysis method for “thorough QT” studies in ICH E-14. (2007 accepted in JCP).
12. Chapel S, Hutmacher MM, deGreef HJMM, Agin M, and Lalonde R. A simulation study for comparison between exposure-response analysis and the E14 statistical analysis for thorough QTc study results. (2007, Manuscript in preparation for CPT).
13. Kowalski KG, Olson S, Remmers A, and Hutmacher, MM. Modeling and simulation to support dose selection and clinical development of SC-75416, a selective COX-2 inhibitor for the treatment of acute and chronic pain (accepted in CPT).
14. Hutmacher MM, Krishnaswami S, and Kowalski, KG. Concentration-response and dose-response for the efficacy of a JAK3 inhibitor administered to rheumatoid arthritis patients (accepted in JPP).

#### B. Text Books

1. Hutmacher MM and Kowalski KG. Evaluation of random sparse sampling designs for a population pharmacokinetic study: assessment of power and bias using simulation. Kimko HC and Duffall S (eds.). New York: Marcel Dekker, Inc. (2003).
2. Hermann D, Miller R, Hutmacher MM, Ewy W, and Kowalski KG. Design and Analysis of Clinical Exposure - Response Trials. Ette E and Williams P (eds.). John Wiley & Sons, Inc. (2007)

#### IV. INVITED PAPERS AND PRESENTATIONS

1. Population PK Modeling. Northern Illinois Chapter of the American Statistical Association. Chicago, IL. October 2001.
2. Evaluation of random sparse sampling designs for a population pharmacokinetic study: assessment of power and bias using simulation. Clinical Trial Simulation in Drug Development. Washington DC. August 2002.
3. Selecting an Indirect Response Model and Dosing Implications for Proof of Concept. Midwest Users Forum for Population Approaches in Data Analysis – MUFADA. Ann Arbor, MI. May 2003
4. Pharmacometrics – Modeling and Simulation in the Pharmaceutical Industry. Department of Statistics – Cornell University. Ithaca, NY. March 2005
5. Modeling and Simulation: Examples and Current, Selected Concepts. Chemical Engineering Department Graduate Study Program – University of Michigan. Ann Arbor, MI. January 2006.
6. Minimum Hellinger Distance in Model Selection and Estimation. MUFADA. Ann Arbor, MI. May 2006.
7. Model Selection Using the Minimum Hellinger Distance Criterion (MHDC) with an Introduction to Minimum Hellinger Distance Estimation (MHDE). PAGE. Brugge, Belgium. June 2006.
8. Population Model Diagnostics and Selection. Chemical Engineering Department Graduate Study Program – University of Michigan. Ann Arbor, MI. March 2007 (*upcoming*).

#### V. ABSTRACTS AND POSTERS

1. A Population Model for Plasma Protein Binding. Poster at NONMEM short-course. San Francisco, CA. May 1997.
2. Pregabalin Exposure-Response Analysis in Patients with Post-herpetic Neuralgia. Co-author – Top Abstract Award. ASCPT. Orlando, FL. March 2005.
3. Performance Characteristics of the Analysis Method for “Thorough QT” Studies in ICH E-14. ASCPT. Baltimore, MD. March 2006.
4. An extension of the indirect response models to ordered categorical pharmacodynamic data using latent variables. ASCPT. Baltimore, MD. March 2006.
5. Population Pharmacokinetics/Pharmacodynamics (PK/PD) of Pegaptanib Sodium (Macugen<sup>®</sup>) in Patients with Age-Related Macular Degeneration (AMD). ARVO. Ft. Lauderdale, FL. May 2006.
6. An extension of the indirect response models to ordered categorical pharmacodynamic data using latent variables. PAGE. Brugge, Belgium. June 2006.
7. Population pharmacokinetic and pharmacodynamic modeling of mydriasis after administration of atomoxetine, duloxetine, and reboxetine as a potential biomarker for norepinephrine reuptake inhibitor. ASCPT – received Trainee Award – presented by Wonkyong Byon. Anaheim, CA. March 2007.

8. Examination of atypical absorption kinetics using the Weibull absorption function in population pharmacokinetics. ASCPT. Anaheim, CA. March 2007.
9. Population pharmacokinetic analysis of indiplon. ASCPT. Anaheim, CA. March 2007.

## **VI. OTHER PRESENTATIONS**

1. Secondary Protein Structures via Circular Dichromatic Spectra, a Statistical Examination. Summer intern research presentation - G.D. Searle. Skokie, IL. August 1993.
2. A Non-parametric Analysis of Secondary Protein Structures. Statistics Department - Northwestern University. Evanston, IL. May 1994
3. A Mechanistic Model Fitting Approach to  $\beta$ -cyclodextrin Complexes in Solution. Technical Expertise Group presentation - G.D. Searle. Skokie, IL. June 1995.
4. Repeated Measures and SAS: an Example Using PROC GLM and PROC MIXED. Technical Expertise Group presentation - G.D. Searle. Skokie, IL. September 1995.
5. An Overview of PK/PD Modeling. Statistical seminar series – PAREXEL. Northbrook, IL. January 1997.
6. Eliciting Diagnostics to Detect Error Structure Misspecification after Initial Attempts at Model Building. Technical Expertise Group presentation - G.D. Searle. Skokie, IL. October 1997
7. Dose Selection via Population PK/PD Modeling. Technical Expertise Group presentation – G.D. Searle. Skokie, IL. July 1998.
8. Overview of Population PK/PD Modeling Methodology. Global statistical seminar series – Pharmacia. Kalamazoo, MI. November 2002.
9. Exposure Response Analysis for TQT Studies. FDA invited discussion. Washington, DC. Co-author – Sunny Chapel presented. July 2005.
10. Exposure Response Analysis for TQT Studies. ASCPT oral presentation. Baltimore, MD. Co-author – Sunny Chapel presented. March 2006.

## **VII. EXTERNAL PROFESSIONAL DEVELOPMENT**

1. NONMEM Beginner and Intermediate Short Course. San Francisco. May 1997.
2. Sheiner-Roland Advanced PK-PD Course. San Francisco. April 2005.
3. Reviewed for *Journal of Pharmacokinetics and Pharmacodynamics*
4. Reviewed for *Pharmaceutical Statistics*

## **VIII. SKILLS**

- NONMEM population analysis software
- SAS programming language
- WinNonlin/WinNonMix software – beta-tested WinNonMix 1.0 and 2.0
- Crossgraphs software – beta-tested Crossgraphs 2.0
- S-PLUS
- PC, UNIX, and VMS environments

**IX. AFFILIATIONS**

- NONMEM Users Group
- Reviews for Journal of Pharmacokinetics and Pharmacodynamics
- ASCPT Membership
- Golden Key National Honor Society
- Phi Kappa Phi, Alpha Lambda Delta, Phi Eta Sigma Honoraries