UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

MYLAN PHARMACEUTICALS INC.

Petitioner

v.

ASTRAZENECA AB

Patent Owner

Case IPR2016-01325

U.S. Patent No. 8,329,680

DECLARATION OF RONALD J. SAWCHUK, Ph.D. IN SUPPORT OF PATENT OWNER'S PRELIMINARY RESPONSE

I. INTRODUCTION

1. I have been retained by AstraZeneca AB ("AstraZeneca") in connection with this *inter partes* review proceeding (IPR2016-01325) before the United States Patent and Trademark Office Patent Trial and Appeal Board ("Board").

2. I understand that Mylan Pharmaceuticals Inc. ("Mylan") has challenged AstraZeneca-owned U.S. Patent No. 8,329,680, which relates to a method of treating hormonal dependent disease of the breast or reproductive tract, and, more specifically, hormonal dependent breast cancer.

3. I further understand that Mylan has petitioned institution of this *inter partes* review proceeding on the basis of several references identified in its Petition (IPR2016-01325, Paper 1) ("Petition").

4. I am being compensated $750 per hour for my time consulting in this matter. I have no financial interest in the outcome of this proceeding and my compensation is in no way contingent upon my opinions or the outcome of this proceeding.

II. QUALIFICATIONS

5. I am a Professor of Pharmaceutics, Emeritus, and Morse Alumni Distinguished Teaching Professor at the University of Minnesota. I also served as the Director of the Bioanalytic and Pharmacokinetic Services Laboratory at the

University of Minnesota until August of 2014. I have studied and carried out clinical and pre-clinical research in the field of pharmacokinetics and biopharmaceutics for over forty years.

6. I joined the University of Minnesota in 1971 as an Instructor in Pharmaceutics after having obtained a Bachelor and Masters of Science Degree from the University of Toronto in 1963 and 1996, respectively, and completing my Doctoral Degree (Ph.D.) in Pharmaceutical Chemistry (pharmacokinetics emphasis) at the University of California, San Francisco, which was granted in 1972.

7. At the University of Minnesota I served as an Assistant Professor of Pharmaceutics from 1972 to 1977, an Associate Professor of Pharmaceutics from 1977 to 1983, and a full Professor of Pharmaceutics from 1983 until my retirement in July of 2010. During this period, I was course director for instruction in pharmacokinetics, clinical pharmacokinetics, advanced pharmacokinetics, and pharmacokinetic modeling and simulation. I was also a participating instructor in biopharmaceutics, and advanced pharmacokinetics. I continue to provide lectures relating to preclinical and clinical pharmacokinetics to scientists in the pharmaceutical industry.

8. I also served as a member of the graduate programs in Pharmaceutics, Neurosciences, and Experimental and Clinical Pharmacology. From 1983 to 1989

and 1991 to 1994, I was the Director of Graduate Studies in Pharmaceutics at the University. From 1982 to 1995, I also served as Director of the Clinical Pharmacokinetics Laboratory at the College of Pharmacy at the University of Minnesota. From 1998 to 1999 I served as the Head of the Department of Pharmaceutics at the University of Minnesota.

9. Although I have formally retired from the University, my Graduate Faculty appointment in the Department of Pharmaceutics is still in effect, allowing me to teach graduate students in the program. I have advised on the order of forty graduate students, postdoctoral fellows, and visiting scholars, on projects relating to preclinical and clinical pharmacokinetics, biopharmaceutics, and bioanalytical chemistry.

10. A major focus of my research was preclinical and clinical pharmacokinetics. I have been involved with many different preclinical and clinical human trials, and in particular with the analysis of the pharmacokinetic and other data generated during those trials. I also focused my research on drug bioavailability and bioequivalence. I have taught, and continue to teach, pharmacokinetics, and pharmacokinetic modeling and simulation in professional, graduate, and elective courses at the University of Minnesota and to the pharmaceutical industry. This instruction includes lectures on the assessment of bioavailability and bioequivalence.

11. I have expertise in the determination of pharmacokinetic parameters and metrics for orally administered drugs, bioanalytical chemistry, biopharmaceutics, and pharmacodynamics. I have devoted a large part of my career to the study of the pharmacokinetics of drugs. And, in addition to authoring numerous publications in this area, I have received funding from various sources in the public and private sector to support my research in pharmacokinetics, including support from the National Institutes of Health ("NIH") and the U.S. Food and Drug Administration ("FDA").

12. During my career, I received several honors, scholarships and awards, including the Weaver Medal of Honor in 2001, the Meritorious Manuscript Award from the American Association of Pharmaceutical Scientists in 1999 and the Hallie Bruce Memorial Lecture Award in 1996. In 2007, I received the American Pharmacists Association (APhA) Research Achievement Award in the Basic Pharmaceutical Sciences.

13. I have been a member of numerous scientific and clinical societies. I am a Fellow of the American Association of Pharmaceutical Scientists and of the American Association for the Advancement of Science. I have been a member of the International Society of Anti-infective Pharmacology and the International Society for the Study of Xenobiotics (ISSX). I served a three-year term as a

member-at-large on the American Association of Pharmaceutical Scientists (AAPS) Executive Council.

14. I have served on the editorial boards of scientific journals such as the Journal of Pharmaceutical Sciences. I am currently on the Editorial Board of the AAPS Journal, and on the ISSX Journal, Xenobiotica. I have also served on numerous advisory committees and review panels.

15. I am a named author on over 100 refereed scientific publications, several book chapters and over 170 abstracts, which have been presented at scientific meetings. I have also co-edited a book on drug bioavailability and given hundreds of invited lectures.

16. I have significant experience in the areas of pharmaceutical research, pharmacokinetics, and drug development. Therefore, I believe that I am qualified to render the opinions set forth in this declaration.

17. My academic background and work experience are summarized in my *curriculum vitae*, attached to this declaration as Exhibit A.

III. ISSUES CONSIDERED

18. In this declaration, I was asked to provide opinions concerning:

i. The qualifications of a person of ordinary skill in the art as of January 10, 2000;

ii. The state of the art as of January 10, 2000;

iii. The construction of the claim terms "wherein the method achieves a therapeutically significant blood plasma fulvestrant concentration of at least 2.5 $ngml^{-1}$ for at least four weeks" (independent Claims 1 and 9) and "wherein the therapeutically significant blood plasma fulvestrant concentration is at least 8.5 $ngml^{-1}$" (dependent Claims 2 and 10); and

iv. The declaration of Dr. Laird Forrest, Ph.D. (**Ex. 1003**) ("Forrest Decl.").

IV. MATERIALS CONSIDERED

19. In preparing this declaration, I reviewed the IPR Petition submitted by Mylan; Howell 1996 and McLeskey (**Ex. 1005** and **Ex. 1006**, respectively); the '680 Patent (**Ex. 1001**); the declaration of Dr. Forrest (**Ex. 1003**); and the other exhibits listed in Exhibit B.

V. SUMMARY OF APPLICABLE LEGAL CONSIDERATIONS

20. Counsel for AstraZeneca requested that I express my opinions with certain guidelines in mind, which are set forth below.

21. For this declaration I have been asked to use January 10, 2000 as the relevant date for my analysis.

22. AstraZeneca's counsel informed me that my analysis must be done through the eyes of the "person of ordinary skill in the art" as of January 10, 2000.

I understand from AstraZeneca's counsel that a person of ordinary skill in the art is a hypothetical person, who has the characteristics of an ordinary artisan including ordinary creativity.

23. Factually, in my opinion, a person of ordinary skill in the art in 2000 would have been a person having a bachelor's or advanced degree in a discipline such as pharmacy, pharmaceutical sciences, endocrinology, medicine or related disciplines, and having at least two years of practical experience in drug development and/or drug delivery, or the clinical treatment of hormonal dependent diseases of the breast and/or reproductive tract. Because drug formulation and development is complicated and multidisciplinary, it would require a team of individuals including, at least, medical doctors, formulators and pharmacokineticists.

24. Unless I expressly state otherwise, all of the opinions provided in this declaration are made from the perspective of a person of ordinary skill in the art as of January 10, 2000.

VI. THE STATE OF THE ART AS OF JANUARY 10, 2000

A. Drug Delivery And Pharmacokinetics

25. Drug targeting and duration of delivery are two important aspects of drug delivery. Drug targeting concerns identifying a specific organ or tissue to

which the drug is to be delivered, while duration of delivery refers to how long the drug is present in the target organ or tissue.

26. Here, the point of the formulations set forth in the challenged patent claims is to deliver specified blood plasma levels of the drug fulvestrant for specified times.

27. In terms of duration, one conventional distinction involves the difference between immediate and sustained released formulations.

28. "Immediate release" means the active pharmaceutical ingredient is released without a delay from its dosage form after it is administered. Most conventional oral formulations, such as tablets or capsules, are designed for immediate release of active pharmaceutical ingredients upon administration in order to rapidly obtain complete absorption.

29. Characteristic of immediate release formulations is a relatively rapid rise in the blood plasma drug levels—to an early and high peak—followed by a relatively rapid decrease in those levels.

30. In contrast, sustained-release formulations are characterized by a relatively slow rise in blood plasma drug levels which peak later, and are followed by a relatively prolonged decrease in those levels. These formulations are also often referred to as extended-release formulations.

31. With "sustained release" "blood level oscillation characteristic of multiple dosing of conventional dosage forms is reduced, because a more even blood level is maintained." Ex. 2134 (Lachman's) at 5. "*Sustained-release* systems include any drug delivery system that achieves slow release of drug over an extended period of time. . .The objective in designing a sustained-release system is to deliver drug at a rate necessary to achieve and maintain a constant drug blood level." Ex. 2080 (Remington's) at 6.

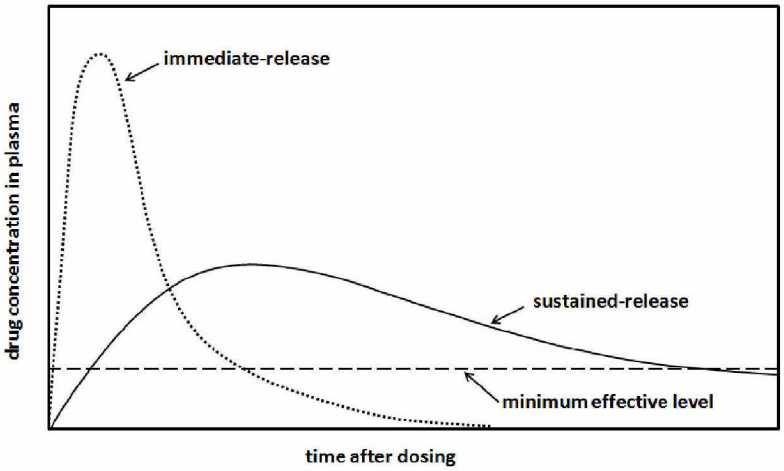
32. Without question, a person of ordinary skill would have understood that a "sustained-release" formulation is "designed to achieve a prolonged therapeutic effect by continuously releasing medication over an extended period of time after administration of a single dose. In the case of injectable dosage forms, this period may vary from days to months." Ex. 2134 (Lachman's) at 5. In other words, sustained release formulations are "designed to achieve a prolonged therapeutic effect by continuously releasing medication over an extended period of time after administration of a single dose." *Id.*

33. Many sustained-release formulations are described in terms of a specific minimum drug concentration ("at least concentration X") that is achieved and maintained over a particular period of time (e.g., hours, a day, a week, two weeks, a month).

34. The study of the time-course of blood plasma levels of a drug following administration of a particular formulation/active pharmaceutical ingredient is called pharmacokinetics. Amongst other things, pharmacokinetics offers a means by which to compare the rate and extent of drug exposure provided by different formulations and/or dosing of the same active pharmaceutical ingredient.

35. This rate and extent of drug exposure requires *in vivo* pharmacokinetic studies. In a clinical study setting, pharmacokinetists determine the concentration of drug in a subject's plasma over time (by periodically drawing blood) in order to understand how the body processes the drug as it is being absorbed from a given formulation after it has been administered. Typically a graph of plasma drug concentrations as a function of time is generated. This graph is referred to as a "concentration-time course" or "concentration-time curve." And, a variety of analytical methods can then be used to study the results.

36. The figure below illustrates the difference between the time-course of a sustained-(solid curve) and immediate-release (dotted curve) formulation for a single dose. In contrast to an immediate-release formulation, the sustained-release formulation exhibits a prolonged period during which plasma concentrations are maintained in a specified range (e.g., above some minimum effective level).



B. Pharmacokinetics, Pharmacodynamics, And The Development Of Drugs Through Clinical Trials

37. Clinical trials are conducted in a series of steps, referred to as Phases. If a drug is found to be "successful" in a given Phase, it is permitted to continue to the next. Typically there are three such Phases, referred to as Phase I, II and III, respectively.

38. The disciplines of pharmacokinetics and pharmacodynamics are important areas of activity throughout clinical development.

39. Pharmacokinetics involves studying the relationship between the dose and/or dosing regimen used and the resulting plasma or serum concentrations of the drug. The plasma concentration-time profile or levels observed depend upon the rate and extent of absorption of the drug from its dosage form into the bloodstream, in addition to how it is distributed within the body, and how rapidly

and efficiently it is clear from the body by the organs of elimination (e.g., kidney and/or liver).

40. Related to pharmacokinetics are bioavailability and bioanalytical chemistry. Bioavailability is a measure of the rate and extent of absorption of a drug into systemic blood, in animals or humans. The extent of absorption is typically characterized by the area under the curve ("AUC") in the blood plasma following either a single dose or upon multiple dosing over a specified duration. The rate of absorption is usually characterized by the maximum concentration of the drug observed in plasma, and the time at which this maximum is observed. These parameters or metrics are referred to as "C_{max}" and "T_{max}," respectively. Bioanalytical chemistry involves the quantitative analysis of biological fluids (e.g., plasma, whole blood, urine, and cerebrospinal fluid) for endogenous, e.g., hormones, and exogenous compounds, e.g., drugs and metabolites. This field includes the measurement and analysis of drug levels in plasma, which provides data used to calculate many pharmacokinetic parameters or metrics, such as AUC, C_{max}, and T_{max}.

41. Of note, systemic exposure to a drug may be described in terms of the blood serum or plasma concentrations of the drug during continuous therapy (e.g., the steady-state plasma concentration, C_{ss}), or the area under the blood plasma concentration-time curve (the "area under the curve", or AUC).

42. Pharmacodynamics involves the study of the potential relationship between plasma levels of a drug and the biological effects produced. These include both the desired therapeutic responses (efficacy) and side effects or adverse events. Although efficacy (the desired therapeutic response) may be linked to plasma levels, this relationship is often very difficult to identify for a variety of reasons including the complex and usually unknown mechanisms of action for many drugs. Other complicating factors include both the potential disequilibrium in the concentrations of a drug at the measurement site (i.e. the blood plasma or serum) with those in what is referred to as the "effect compartment" and the cascade of events that may need to occur over time before a response to the drug is observed.

43. Significant data (usually including data from Phase III clinical trials) and a careful analysis of the relationship between plasma drug levels and the effects that a drug produces is required to establish any "pharmacokinetic-pharmacodynamic" link.

C. Targeted Blood Plasma Drug Concentrations During Therapy

44. If a relationship between plasma concentrations and response—efficacy and/or adverse effects—can be established for a drug, that may allow for the development of a strategy involving achieving and maintaining a target concentration or a target range of concentrations for individual patients.

45. This target(s) corresponds with the greatest likelihood of therapeutic success. Stated differently, ranges of serum or plasma concentrations of a drug which are known to be therapeutically significant can be used prospectively to establish a dosing regimen for patients.

46. It may be important to monitor plasma concentrations in individual patients during therapy if one wishes to ensure that those levels are within the therapeutic range, in particular if for some reason the patient's medical condition or genomic class warrants it. However, this is not always necessary, for example, if the field's experience with the drug product and dosing regimen has established the typical blood plasma drug concentrations obtained.

VII. CLAIM CONSTRUCTION

47. I have been asked to consider Claims 1, 2, 9 and 10 of the '680 Patent, and specifically the limitations directed to therapeutically significant blood plasma fulvestrant concentrations and durations.

Claim 1	A method for treating a hormonal dependent benign or malignant disease of the breast or reproductive tract comprising administering intramuscularly to a human in need of such treatment a formulation comprising: about 50 $mgml^{-1}$ of fulvestrant; about 10% w/v of ethanol; about 10% w/v of benzyl alcohol; about 15% w/v of benzyl benzoate; and a sufficient amount of castor oil vehicle; **wherein** the method achieves a therapeutically significant blood plasma fulvestrant concentration of at least 2.5 $ngml^{-1}$ for at least four weeks.

Claim 2	The method of claim 1, **wherein** the therapeutically significant blood plasma fulvestrant concentration is at least 8.5 $ngml^{-1}$.
Claim 9	A method for treating a hormonal dependent benign or malignant disease of the breast or reproductive tract comprising administering intramuscularly to a human in need of such treatment a formulation consisting essentially of: about 50 $mgml^{-1}$ of fulvestrant; about 10% w/v of ethanol; about 10% w/v of benzyl alcohol; about 15% w/v of benzyl benzoate; and **wherein** the method achieves a therapeutically significant blood plasma fulvestrant concentration of at least 2.5 $ngml^{-1}$ for at least four weeks.
Claim 10	The method of claim 9, **wherein** the therapeutically significant blood plasma fulvestrant concentration is at least 8.5 $ngml^{-1}$.

48. In my opinion, the "wherein" clauses of these claims are essential in order to practice the claims.

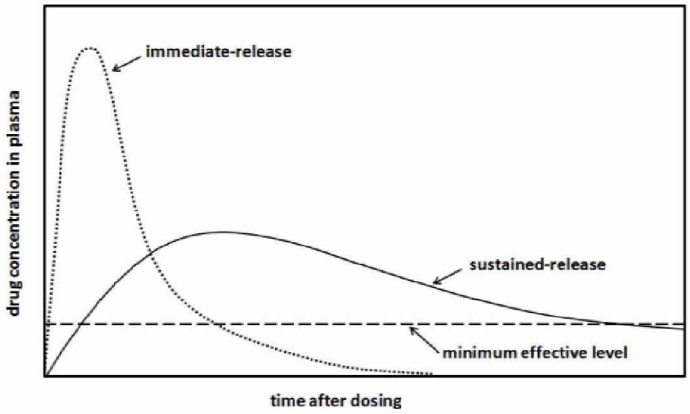
49. The claimed methods do not specifically set forth the dose of fulvestrant that is to be administered nor the frequency of administration. Rather, these claims allow for both to be varied so long as the resultant blood plasma fulvestrant concentration and duration limitations are satisfied—that is more than a desired result, it is the result that *must* be obtained in order to practice the claims.

50. Moreover, these therapeutically significant blood plasma fulvestrant concentration and duration limitations characterize and distinguish the claimed methods as involving the use of a "sustained release pharmaceutical formulation." Ex. 1001, at abstract.

51. As explained above, a *sustained release formulation* slowly releases drug over an extended period of time to achieve and maintain a prolonged therapeutic effect (also often described as an extended release formulation). *Supra* at ¶¶ 30-33, 36.

52. This stands in contrast to conventional or *immediate release formulations*, which result in a rapid rise in blood plasma drug levels—to an early, high peak—followed by a relatively rapid decrease in those levels. *Supra* at ¶¶ 28-29, 36.

53. The objective of a sustained release formulation is completely different than that for an immediate release formulation: "[t]he objective in designing a sustained-release system is to deliver drug at a rate necessary to achieve and maintain a constant drug blood level" for an extended period of time. *Supra* at ¶ 31. Moreover, again, as can be seen from the image below, a sustained release formulation exhibits a completely different concentration-time course than an immediate release formulation.



54. It is clear that the invention here involves use of "sustained release" formulations—a characteristic now firmly set forth in the wherein clauses that would be removed from the claims if those clauses were to be ignored. As such, from the perspective of a pharmacokinetist, it makes no sense to ignore those clauses.

55. The inventors repeatedly identify "the invention" as concerning a "sustained release" formulation. For example, in the Abstract the invention is described as a "novel *sustained release pharmaceutical formulation* adapted for administration by injection containing the compound 7α-[9-(4,4,5,5,5-pentafluoropentylsulphinyl)nonyl]oestra-1,3,5(10)-triene-3,17β-diol, more particularly to a formulation adapted for administration by injection containing the compound 7α-[9-(4,4,5,5,5-pentafluoropentylsulphinyl)nonyl]oestra-1,3,5(10)-triene-3,17β-diol in solution in a ricinoleate vehicle which additionally comprises at least one alcohol and a non-aqueous ester solvent which is miscible in the

ricinoleate vehicle." Ex. 1001, at abstract (emphasis added). The "Field of the Invention" states: "[t]he invention relates to a novel sustained release pharmaceutical formulation adapted for administration by injection containing the compound 7α-[9-(4,4,5,5,5-pentafluoropentylsulphinyl)nonyl]oestra-1,3,5(10)-triene-3,17β-diol." Ex. 1001, at col.1, ll. 17-21.

56. The sustained release properties and characteristics of the formulation are, in fact, discussed throughout the specification. For example, the specification explains that the inventors "surprisingly found that the . . . formulations of the invention provide, after intra-muscular injection, satisfactory release of fulvestrant over an *extended period of time*." Ex. 1001, at col.8, ll.58-60. (emphasis added). Additionally, the inventors explain "[w]e have found that despite the rapid elimination of the additional solubilizing excipients . . . from the formulation vehicle and the site of injection after injection of the formulation, *extended release at therapeutically significant levels*[1] of fulvestrant *over an extended period* can still be achieved by the formulation of the invention." Ex.

---

[1] Of note, the inventors also state, "[b]y use of the term 'therapeutically significant levels' we mean that blood plasma concentrations of at least 2.5 $ngml^{-1}$, ideally at least 3 $ngml^{-1}$, at least 8.5 $ngml^{-1}$, and up to 12 $ngml^{-1}$ of fulvestrant are achieved in the patient." Ex. 1001, at col.9, ll.24-27.

1001, at col.9, ll.17-23 (emphasis added). Further, the formulation is taught to achieve a "*particularly even release profile*," (Ex. 1001, at col.10, ll.49-50 (emphasis added)), which as explained above is decidedly *not* what is achieved using an immediate release formulation. *Supra* ¶¶ 28-33, 36.

57. The patent specification even defines "extended release": "[b]y use of the term 'extended release' *we mean* at least two weeks, at least three weeks, and, preferably at least four weeks *of continuous release of fulvestrant is achieved.* In a preferred feature *extended release is achieved* for 36 days. Preferably *extended release of fulvestrant is for at least 2-5 weeks* and more preferably *for the following periods (weeks)* 2.5-5, 2.5-4, 3-4, 3.5-4 and most preferably *for at least* about 4 weeks." Ex. 1001, at col.9, ll.29-36 (emphasis added).

58. Consistent with the specification, the formulation set forth in the method of use claims is likewise described as a sustained release formulation throughout the prosecution history. For example:

i. Ex. 2132 (Dec. 3, 2002 Office Action), at 6-7 (noting the claim limitations missing from the prior art, including the limitations found in the wherein clause: "Dukes does not expressly teach the *plasma concentration of fulvestrant* herein") (emphasis added);

ii. Ex. 2133 (Aug. 21, 2008 Amendment), at 8-9 ("The invention therefore addresses the objective of defining (a) a pharmaceutically acceptable solvent or mixture of solvents (b) that will dissolve a sufficient quantity of fulvestrant [at least 250 mg] (c) to form a small enough volume of formulation that is acceptable for injection [6 ml or less] and will provide (d) a fulvestrant concentration of at least 45 $mgml^{-1}$ [claim 36] and/or (e) the *sustained release* of fulvestrant whereby a therapeutically significant *blood plasma fulvestrant concentration of at least 2.5 $ngml^{-1}$ is attained for at least 2 weeks* [claim 35]") (emphasis added);

iii. Ex. 2133 (Aug. 21, 2008 Amendment), at 14 ("The *invention* is focused in particular on the discovery of a novel and unobvious formulation for this extremely difficult to formulate molecule, which formulation is suitable for intramuscular injection to a human patient and is capable of dissolving the therapeutic target amount of fulvestrant in a small enough volume for IM administration, and which formulation provides for the satisfactory *sustained release* of fulvestrant *over an extended*

period of time as specified in the present claims") (emphasis added);

iv. Ex. 2133 (Aug. 21, 2008 Amendment), at 15 ("However, developing an IM injectable formulation for fulvestrant that would achieve the satisfactory *sustained release* of the drug over an *extended period of weeks* presented a particularly difficult challenge to the experienced formulator") (emphasis added);

v. Ex. 2135 (Aug. 21, 2008 Declaration), at 4 (explaining the goal of the research was "to formulate an intramuscular (IM) injection that would provide for the satisfactory *sustained release* of fulvestrant over a period of at least two weeks and preferably over a period of at least four weeks to reduce the frequency of administration") (emphasis added);

vi. Ex. 1002 (Dec. 21, 2010 Office Action), at 253 (noting the claim limitations missing from the prior art, including the wherein clause: "Dukes does not expressly teach the *plasma concentration of fulvestrant herein*") (emphasis added);

vii. Ex. 1002 (June 20, 2011 Amendment), at 286-287 ("The recitation regarding 'a therapeutically significant blood plasma

fulvestrant concentration of at least 2.5 $ngml^{-1}$ for at least two weeks' finds support, for example, in the specification at ¶¶ [0027] and [0051]");

viii. Ex. 1002 (Jan. 17, 2012 Amendment), at 335 ("Applicants also amended claim 24 to recite that the method achieves a therapeutically significant blood plasma fulvestrant concentration 'for at least four weeks.' Support for this amendment can be found, for example, in the specification at ¶ [0052]");

ix. Ex. 1002 (Jan. 17, 2012 Amendment), at 338 ("The Office acknowledges that *McLeskey* does not expressly teach 'the use of fulvestrant in treating hormonal dependent diseases of breast', 'the dosing regimen to be once a month, intramuscular administration', 'the volume administered', or '*the herein claimed serum concentration of fulvestrant*'") (emphasis added);

x. Ex. 1002 (Jan. 17, 2012 Amendment), at 348, 352 ("The POSITA would not have had a reasonable expectation that the *McLeskey* castor oil composition would have been e*ffective to administer fulvestrant intramuscularly to achieve a therapeutic effect for at least four weeks, as instantly recited.* Two

independent reasons are set forth below supporting a lack of expectation of success for the combination of the references cited by the Office. . . [a] POSITA would not have had an expectation that the results from subcutaneous injection in *McLeskey* would have been applicable to the intramuscular administration of fulvestrant . . . [and n]umerous variables affect the efficacy of an intramuscular formulation (e.g.,. [sic] identity and proportion of cosolvents) and a POSITA would have understood that the resulting variability precludes a POSITA from having an expectation a priori that a given formulation would be successful in a given method of treatment until actual suitable in vivo experiments are performed") (emphasis added);

xi. Ex. 1002 (Jan. 17, 2012 Declaration), at 376-377 ("Moreover, the examples above underscore the fact that efficacy of a given drug administered by a given route of dosing (e.g., intramuscular) cannot be known until appropriate comparative studies are performed in a suitable animal model. For some drugs, the desired effect might be achieved following a particular route of dosing, but for other drugs it might not. The rate and extent of drug absorption, and the associated

pharmacodynamics (e.g., the achievement of a desired drug effect) may differ greatly depending on the properties of the drug, the choice of an animal model, and the site of drug administration. Consequently, one of ordinary skill in the art having the very limited experimental subcutaneous data from *McLeskey* would not have had an expectation that the intramuscular administration of fulvestrant using the *McLeskey* castor oil composition would have been effective following intramuscular administration, such as in the method described in the claims. *This is especially true because* McLeskey *did not disclose plasma or blood levels of fulvestrant in mice after subcutaneous administration of the formulation, nor any information regarding the rate and/or extent of absorption of fulvestrant from the subcutaneous injection site. Additionally, the claims recite achieving a given therapeutic plasma concentration for at least four weeks, and there is no information in any of the references cited in the Office Action that would have suggested that such long-term efficacy* associated with a single dose would be exhibited using the *McLeskey* castor oil composition by any route of administration.

Thus, one of ordinary skill in the art would not have had an expectation that the castor oil composition disclosed in *McLeskey*, which was administered subcutaneously to mice, would have been therapeutically effective upon intramuscular administration of fulvestrant, for example, by following the method described in the claims") (emphasis added); and

xii. Ex. 1002 (Jan. 17, 2012 Declaration), at 378-379 ("Regardless of how high or low the cosolvent concentrations are in a given formulation, the preparation of formulations in which a drug such as fulvestrant can be solubilized is not sufficient to ensure the desired therapeutic effect when such formulation is administered to patients. As explained in the '887 application '[s]imply solubilising fulvestrant in an oil based liquid formulation is not predictive of a good release profile or lack of precipitation of drug after injection at the injection site.' Exhibit 7 at [0054]. *Thus, suitable experiments are needed to determine the pharmacokinetic performance of any candidate formulation(s).* In that regard, it is understood that an animal model for drug dosage form performance may provide some discrimination among candidate dosage forms in development.

Thus, the *plasma concentration profile should reflect changes in the release characteristics of the drug from the formulation. That type of pharmacokinetic data could be used to characterize important variables in the development of a suitable method of treatment*") (emphasis added).

59. Given the identification of the invention as a sustained-release formulation throughout the specification and the prosecution history, which is also replete with arguments that distinguish the prior art by reference to the claimed blood plasma fulvestrant levels and durations, a person of ordinary skill would have understood that the sustained-release characteristics—including the plasma drug concentrations and durations produced by these formulations when administered to a patient—are critical to practicing the claims.

60. Moreover, this fact is clear given the concentration amounts *differ* amongst the claims (i.e., "at least 2.5 $ngml^{-1}$" in Claims 1 and 9, and "at least 8.5 $ngml^{-1}$" in Claims 2 and 10). Logically the wherein clauses are meant to impart features of the claimed methods that must be practiced and are not simply an intended result.

61. Dr. Forrest states: "[t]he term 'wherein the method achieves a therapeutically significant blood plasma fulvestrant concentration of at least 2.5 $ngml^{-1}$ for at least four weeks,' merely expresses an intended result of the

administration of the fulvestrant formulation recited in the claims of the '680 patent. Likewise, the term 'wherein the method achieves a therapeutically significant blood plasma fulvestrant concentration [of] at least 8.5 $ngml^{-1}$,' merely expresses the intended result of the administration of the fulvestrant formulation recited in the claims of the '680 patent." Ex. 1003, at ¶ 40. Dr. Forrest offers no proof that is the case and offers no scientific explanation in support.

62. To the contrary, a person of ordinary skill in the art would have known and expected that even minor variations to formulation components or their specific proportions could significantly impact the rate of release of fulvestrant from the site of administration, the duration of the release of fulvestrant and ultimately, therefore, fulvestrant's blood plasma concentration-time profile.

63. Indeed, the prior art demonstrates how variations in formulation impact fulvestrant's blood plasma concentration-time profile. For example, the plasma concentration-time profiles obtained with a short-acting formulation of fulvestrant administered once a day for seven days are drastically different from those obtained using a long-acting formulation administered once every four weeks. *Compare* DeFriend (Ex. 1027) (18 mg dose fulvestrant in short-acting formulation) *with* Howell (Ex. 1006) (250 mg dose fulvestrant in long-acting formulation). The lower dose used in DeFriend results in *greater* mean serum concentrations one day after a first dose of 18 mg (8.13 ng/mL in DeFriend) when

compared to the much higher dose used in Howell, which results in much *lower* mean serum concentrations measured one day after a first dose of 250 mg (4.47 ng/mL in Howell).

64. Further still, DeFriend (Ex. 1027) and Howell (Ex. 1006) illustrate that even with the *same* formulation, there is variability amongst fulvestrant blood plasma concentrations. DeFriend actually notes: "[t]he mean serum drug levels versus time achieved in patients receiving the 6-mg and 18-mg daily doses of ICI 182780 are shown in Fig. 1. The serum concentration of ICI 182780 was dose dependent but showed *some variation between individual patients*." Ex. 1027, at 3 (emphasis added). Likewise, as is evident from Table II inserted below, Howell 1996 reports significant variability among individuals who received different dose amounts of the same formulation (i.e., 100 mg or 250 mg), as well as those who received the same dose and same formulation (compare, for example the C_{max} on entry for Patient 11 (29.9 $ngml^{-1}$) to that of Patient 16 (4.4 $ngml^{-1}$)). Ex. 1006, at 4.

Table II Results of C_{max} and AUC during months 1 and 6 according to response categories. There were no significant differences in drug kinetics between responders and non-responders

		On entry		*At month 6*	
Response	*Patient*	C_{max} *(ng ml^{-1})*	*AUC (ng day ml^{-1})*	C_{max} *(ng ml^{-1})*	*AUC (ng day ml^{-1})*
Progressive disease	1	4.4[a]	53.1[a]		
	4	1.6[a]	25.1[a]		
	7	5.5	105.7		
	9	9.7	138.2		
	11	29.9	289.3		
	13	5.6	36.7	15.8	243.7
	Median	5.6	79.4		
No change	2	1.8[a]	23.2[a]	7.5	135.8
	12	7.2	143.6	12.2	179.3
	15	9.0	107.8	15.8	201.7
	17	9.5	125.5	14.9	297.6
	18	10.3	183.2	10.2	156.1
	19	11.0	137.8	17.2	308.0
	Median	9.3	131.6	12.8	190.9
Partial response	3	2.9[a]	56.2[a]	9.9	139.5
	5	17.4	188.4	17.6	203.0
	6	7.7	118.3		
	8	5.9	118.7	10.0	175.2
	10	14.8	206.6	9.1	191.7
	14	9.1	134.6	13.5	266.0
	16	4.4	72.8	12.0	190.8
	Median	7.7	118.7	11.0	191.0

[a] Patients 1–4 received 100 mg dose at entry and 250 mg dose from month 2 onwards.

65. Clearly the plasma levels are variable. Again, this is shown, at least, by the very significant variability in maximum concentrations of fulvestrant and areas under the curve reported in Howell, Table II, reproduced above. Ex. 1006, at 4.

66. Dr. Forrest also states: "[n]one of this language informs how the method of administering the fulvestrant formulation to a human patient is carried out." Ex. 1003, at ¶ 40. To the contrary, column 9 of the specification indicates that an injection is to be given intramuscularly, and a dosing interval of 4 weeks is intended. Ex. 1001, at col.8, l.58-col.9, l.36. That is also clear from the language

of the claims themselves, which refers to intramuscular administration of minimum ("at least") drug level durations. Ex. 1001, at claims 1, 2, 9, 10.

67. Based on the clear statements in the specification and prosecution history that the invention pertains to a method of treatment involving a sustained-release formulation, a person of ordinary skill would have understood that the claimed therapeutically significant blood plasma fulvestrant concentrations must be achieved and maintained above those levels for at least the specified period of time in order to practice the invention.

68. The term "therapeutically significant" would also have been understood by the person of ordinary skill in the art—based on the specification—to refer to the specified blood plasma fulvestrant concentrations set forth in the respective claims. This is clear from the specification, which states: "[b]y use of the term 'therapeutically significant levels' we mean that blood plasma concentrations of at least 2.5 $ngml^{-1}$, ideally at least 3 $ngml^{-1}$, at least 8.5 $ngml^{-1}$, and up to 12 $ngml^{-1}$ of fulvestrant are achieved in the patient." Ex. 1001, at col.9, ll.24-27.

69. A person of ordinary skill in the art would have understood the term "achieves" as used in the claims to mean that the plasma fulvestrant concentration is "achieved for [a period of time]." That is, after injection the minimum specified

blood plasma level is achieved and then maintained for the specified period of time.

70. Dr. Forrest's construction of "attained" to mean "achieved an average concentration (C_{avg}) in a patient over the specified time period" (Ex. 1003, at ¶ 42) is wrong. To begin, the term C_{avg} is *not* mentioned in the claims, specification or prosecution history. Second, importing C_{avg} into the claims eviscerates another *explicitly used* claim term: "at least." The claims describe blood plasma fulvestrant concentrations of "*at least* 2.5 $ngml^{-1}$" and "*at least* 8.5 $ngml^{-1}$." Use of C_{avg} permits concentrations *less* than those set forth in the claims (so long as other values are higher and the average is above the value delineated). Simply put that makes nonsense of the "at least" claim limitation. Last and relatedly, the reason to employ a sustained-release profile—which is also explicitly described in the specification—is to avoid release profiles that fluctuate below the stated blood plasma level. *See supra* Section VI.

VIII. CONCLUSION

71. For the foregoing reasons, it is my opinion that Mylan has not shown a reasonable likelihood that claims 1-20 of the '680 Patent are unpatentable.

72. I declare under penalty of perjury under the laws of the Unites States of America that the foregoing is true and correct.

Dated: October 5, 2016

Ronald J. Sawchuk

Ronald J. Sawchuk, Ph.D.

EXHIBIT A

RONALD J. SAWCHUK, Ph.D.

PERSONAL DATA

Present Address:	Department of Pharmaceutics College of Pharmacy Room 9-149A Weaver-Densford Hall University of Minnesota 308 Harvard Street S.E. Minneapolis, MN 55455 E-mail: sawch001@umn.edu
Home Address:	14934 Pixie Point Circle SE Prior Lake, MN 55372 Telephone: (952) 226-6507 E-mail: sawch001@umn.edu
Born:	May 29, 1940, Toronto, Ontario, Canada
Marital Status:	Married, three children
Citizenship:	Dual: U.S. and Canadian

EDUCATION

1959	(High School)	Oakwood Collegiate Institute, Toronto Secondary School Grade XIII)
1963	B.Sc. Phm.	University of Toronto, Toronto Ontario College of Pharmacy Licentiate No. 10748
1966	M. Sc. Phm.	University of Toronto, Toronto
1972	Ph.D.	University of California, San Francisco Pharmaceutical Chemistry (Pharmacokinetics)

PROFESSIONAL AND ACADEMIC EXPERIENCE

1963 - 1965	Teaching Assistant, University of Toronto
1966	Community Pharmacist (part-time), Toronto
1966 - 1968	Teaching Assistant, University of California
1971 - 1972	Instructor in Pharmaceutics, University of Minnesota
1972 - 1977	Assistant Professor of Pharmaceutics, University of Minnesota
1977 -1983	Associate Professor of Pharmaceutics, University of Minnesota
1974 - 1982	Associate Director, Clinical Pharmacokinetics Laboratory, U of Minnesota
1982 - 1995	Director, Clinical Pharmacokinetics Laboratory, College of Pharmacy, U of Minnesota
1983 - 2010	Professor of Pharmaceutics, University of Minnesota
1983 - 1989	Director of Graduate Studies in Pharmaceutics, University of Minnesota
1983 - 1986	Acting Head, Department of Pharmaceutics, University of Minnesota
1984 (summer)	Quarter Leave, Sandoz Pharma, Pharmacokinetics and Drug Metabolism Dept., Basel, Switzerland (M. Lemaire)
1991 - 1994	Director of Graduate Studies in Pharmaceutics, University of Minnesota
1992 (Summer)	Quarter Leave, Sandoz Pharma, Drug Safety, Basel, Switzerland (W. Niederberger)
1996 - 1999	Member, Board of Directors, Century Mortar Club
1997 (Spring)	Semi-Quarter Leave, Toyama Medical and Pharmaceutical University, Japan (H. Sato)
1997 (Summer)	Semi-Quarter Leave, Novartis AG, PKDM, Basel, Switzerland (J. Vonderscher)
1998 - 1999	Head, Department of Pharmaceutics, University of Minnesota
2001 (Summer)	Faculty Development Leave, Novartis AG, PKDM, Basel, Switzerland (M. Lemaire)
2010 - present	Professor Emeritus of Pharmaceutics, University of Minnesota
2010 - 2014	Research Professor, Part-time, Pharmaceutics, University of Minnesota
2015- present	Adjunct Professor of Pharmaceutics

APPOINTMENTS AND PROFESSIONAL RESPONSIBILITIES

1972 - present	Member, Graduate Program in Pharmaceutics, University of Minnesota
1982 - present	Consultant to the pharmaceutical industry
1995 - present	Director, Bioanalytic and Pharmacokinetic Services, University of Minnesota
1995 - present	Editorial Board, *Saudi Pharmaceutical Journal*
1996 - 2007	Editorial Board, *Journal of Pharmaceutical Sciences*
1996 - present	Member, Graduate Program in Neurosciences, University of Minnesota
2001 - present	Member, Graduate Program in Experimental and Clinical Pharmacology, U of M
2002 - present	Member, Graduate Program in Social, Administrative and Clinical Pharmacy, U of M
2008 - present	Editorial Advisory Board, *AAPS Journal*
2009 - present	Editorial Board, *Xenobiotica*

OTHER PROFESSIONAL ACTIVITIES

Prepared two videotapes on "Pharmacokinetics" for undergraduate instruction, 1974
Co-editor of a book with James Blanchard, Ph.D. and B.B. Brodie, Ph.D., entitled "Principles and Perspectives in Drug Bioavailability." S. Karger, Publisher, 1979
Assistant Director, Clinical Pharmacokinetics Laboratory, 1974-82
Consultant in the Establishment and Implementation of the Drug Quality Assurance Program, United Hospitals, St. Luke's Division, St. Paul, 1975
Participant in Critical Incidents Workshop, PDI - College of Pharmacy, 1977
Assessor in the Pharmacy Assessment Exercises, 1978
Coordinator for Continuing Education in Pharmacy, TV Series 1978, 1980
Expert, Bureau of Drugs and Biologics, Food and Drug Administration, 1982-84
Screening Committee, Abstracts, Basic Pharmaceutics Section, APS, APhA, 1981
Review of Grants, Medical Research Council (Canada) 1980-86
Review of Grants, British Columbia Health Care Foundation, 1981-84
Advisory Consultant, Site Visit Team NIH (NINCDS) Yale University School of Medicine, October 1979
Member, Site Visit Team NIH (NINCDS) University of Utah School of Medicine, January 1983
Member, Special Pharmacology Study Section NIH, April-June 1988
Review of Grants, Idaho State Board of Education, 1989-91
Review of Grants, Greater Minnesota Corporation, 1990-91
Organizer and Symposium Co-Chair, "Microdialysis in Drug Metabolism and Disposition Studies", for the Annual AAPS Meeting, San Antonio TX, 1992
Symposium Co-Chair, "Kinetic and Dynamic Challenges of the 90's", for the Annual AAPS Meeting, San Diego, CA, 1994
Organizing Committee Member for the NATO Advanced Study Institute, "Pharmacokinetics: From Theory to Practice", Erice, Italy, April 5-16, 1994
Co-organizer and Participating Instructor, "Pharmacokinetics for the Pharmacist and Pharmaceutical Scientist" University of Milan, Varese, September 10 -15, 1995.
Member, Board of Directors, Century Mortar Club, 1996-present.
National Advisory Committee, FAMU RCMI Program, Tallahasse, FL 1996-present
Co-organizer and Participating Instructor, "Pharmacokinetics for the Biomedical and Pharmaceutical Scientist", University of Milan, Varese, September 7 -12, 1997.
Scientific Advisory Committee, 1st Symposium on Microdialysis and Pharmacokinetics, Leiden, The Netherlands April 1998
Organizer and Participating Instructor, "Pharmacokinetics for the Biomedical and Pharmaceutical Scientist", University of Malta, Msida, September 6 -15, 1998.
Founder, Microdialysis Focus Group, American Association of Pharmaceutical Scientists, 1998.
Scientific Advisory Committee, 2nd International Symposium on Microdialysis in Drug Research and Development, Stockholm, Sweden, June 2000
Chair, Microdialysis Focus Group, American Association of Pharmaceutical Scientists, 1998-2000.
Co-Chair, Organizing Committee, 3rd International Symposium on Microdialysis in Drug Research and Development, Minneapolis, MN, USA, June 2002
Visiting Professor, Guilin Medical College, Guilin PRC (2002-2007)
Scientific Advisory Committee, 4th International Symposium on Microdialysis in Drug Research and Development, Vienna, Austria, June 2004

Scientific Advisory Committee, Abbott Laboratories, for the FDA Critical Path Initiative, September 2004
Scientific Advisory Committee, 5th International Symposium on Microdialysis in Drug Research and Development, Leiden, The Netherlands, June 2006
GLP-1 Scientific Advisory Panel, Medtronic, Minneapolis, MN, April 2009-present

CURRENT AND PAST MEMBERSHIP IN PROFESSIONAL AND SCIENTIFIC SOCIETIES

American Association of Pharmaceutical Scientists (Fellow)
American Association for the Advancement of Sciences (Fellow)
American Pharmacists Association (APhA)
American Society for Pharmacology and Experimental Therapeutics
International Society of Anti-Infective Pharmacology
International Society for the Study of Xenobiotics
Technology Park, Heidelberg, Germany
Century Mortar Club (Board of Directors, 1996-98)
Rho Chi Honor Society

SCHOLARSHIPS, HONORS AND AWARDS

1964	Scholarship, Canadian Foundation for the Advancement of Pharmacy
1965-66	National Research Council of Canada
1965	Warner-Lambert Research Fellowship
1968-70	National Institute of Health (NIH) Training Grant
1981-82	Teacher of the Year, College of Pharmacy, University of Minnesota
1986	Recipient of Horace T. Morse-Amoco Foundation Award
1988	Fellow, American Association of Pharmaceutical Scientists
1990	Fellow, American Association for the Advancement of Sciences
1996	Hallie Bruce Memorial Lecture Award
1997	Fellowship, Japanese Society for the Promotion of Science
1999	Meritorious Manuscript Award, American Association of Pharmaceutical Scientists
2001	Weaver Medal of Honor
2004	Distinguished Lecture, Creighton University School of Pharmacy and Health Professions
2005	Academy of Distinguished Teachers, University of Minnesota
2006	Distinguished Lecture, Temple University School of Pharmacy
2007	APhA Research Achievement Award in the Basic Pharmaceutical Sciences

COMMITTEE APPOINTMENTS

COLLEGE OF PHARMACY

1972-73, 1973-74	Student American Pharmaceutical Association Minnesota Chapter (Faculty Advisor)
1972-75	Student Admissions and Academic Standing Committee, College of Pharmacy
1972-73	Task Force on College of Pharmacy Organization
1973-74	Continuing Education Committee
1972-78	Admissions Committee for Pharm.D. Program, College of Pharmacy (Chair 1973-74; 1977-78)
1974-75	University of Minnesota Health Sciences B/C Implementation Committee
1974-77	Constitution and By-laws Committee
1974-75	Unit K Committee, Graduate School
1975-76	Task Force on Pharm.D. Admissions
1976-78	Professional Education Committee
1977-78	Task Force on Travel
1977-78	Anatomy, Physiology, Pathology Study Group
1977-78	Drug Product Design and Evaluation Study Group
1976-78	Search Committee for Biopharmaceutics Faculty Member
1977-78	Search Committee for Assistant Director HCMC
1977-78	Search Committee for Research Associate, CEP Project D-1 (Chairman)
1978-79	Pharm.D. Program Planning Committee (Chairman)
1978-79, 1979-80	Computer Systems Committee (Chairman)
1979-80	Professional Education Committee (Chairman)

1980-81	Educational Policy Committee (Chairman)
1980-82	Externship Committee
1981-82	Academic Standing Committee
1981-83	Health Sciences Policy and Review Council
1981-82	Graduate Faculty Nominations and Course Proposals Committee
1982-83	Academic Standing Committee (Chairman)
1982-83	Advisory Committee on Animal Care Facilities
1983-85	Council of Directors of Graduate Studies
1982-83	Task Force on Computers
1983	Search Committee for Department Chairman (Chairman)
1983	Search Committee for Clinical Faculty at HCMC
1984	Ad Hoc Committee on External Pharm.D. Program
1984	Executive Committee (Chairman)
1984	Search Committee for Dean of College of Pharmacy
1984	Search Committee for Psychiatry Position, St. Paul-Ramsey Medical Center
1984	Search Committee for Clinical Faculty at Hennepin County Medical Center
1985	Endowed Chair in Pharmaceutics Search Committee (Chair)
1985	Assistant Professor in Pharmaceutics Search Committee (Chair)
1985	Appointments, Promotion and Tenure Committee
1985	Space Committee
1985	Clinical Assistant Professor (MMC) Search Committee
1985-89	Executive Committee
1986-87	Appointments, Promotion and Tenure Committee (Chair)
1986-90	Educational Policy Committee
1986-87	Subcommittee of Educational Policy Committee
1986	Search Committee for Endowed Chair (Chair)
1986-87	College of Pharmacy Strategic Planning Committee
1986-87	Subcommittee of Strategic Planning Committee to Develop College Goals and Objectives
1987-90	Continuing Pharmacy Education Advisory Committee (Chair)
1987-88	Admissions Committee
1988-89	Admissions Committee (Chair)
1989-91	Promotion and Tenure Committee
1991-92	Promotion and Tenure Committee (Chair-Elect)
1991-92	General Research Support Committee
1992-93	Promotion and Tenure Committee (Chair)
1992-93	General Research Support Committee
1993-94	Academic Standing Committee (Chair-Elect)
1994-95	Academic Standing Committee (Chair)
1994-98	College Computer Committee
1995-96	Promotion and Tenure Committee
1995-96	Internal Organization and Leadership Task Force
1996-97	Non-traditional Pharm.D. Task Force
1997-98	Search Committee for Endowed Chair in Geriatric Pharmacotherapy
1997-98	Admissions Committee
1997-98	Search Committee for Immunotherapy Faculty Position (Chair)
1998-2000	Search Committee for Pharmaceutics Faculty Position
2000-2001	Educational Policy Committee
2001-2002	Search Committee for ECP Faculty Position
2001-2002	Educational Policy Committee (Chair)
2001-2002	Search Committee for Pharmaceutics Faculty Position
2001-2002	College of Pharmacy Phar. Sci. 2020 Committee, Capital Campaign (Co-Chair)
2001-2004	College of Pharmacy Faculty Consultative Committee
2002-2003	Educational Policy Committee (Past Chair)
2002-2003	College of Pharmacy Collegiate Review Committee (Chair)
2002-2003	College of Pharmacy Central Council (Faculty Representative)
2002-2003	College of Pharmacy Instructional Development Working Group for the Duluth Expansion
2003-2005	Search Committee for Pharmaceutics Faculty Position at UMD (Chair)
2004-2007	College of Pharmacy Assessment Committee
2005-2006	Search Committee for Endowed Chair in Geriatric Pharmacotherapy

2006-2007 Search Committee for Pharmaceutics Faculty Position

UNIVERSITY COMMITTEE APPOINTMENTS

1974-78	Subcommittee on Academic-Industrial Interface, Academic Relations Committee, 3M Technical Forum
1975-76	Health Sciences Primary Health Care Program Committee (Alternate), Solicitor for the University of Minnesota Consolidated Fund Drive
1977-78	Alternate Senator (U. of Minnesota)
1978-81	Senator (U. of Minnesota)
1984-85	Health Sciences Learning Resources Committee
1986	College Delegate to All-University Single Quarter Leave Working Group, Academic Affairs
1989	Health Sciences Policy and Review Council, Graduate School
1989-91; 1991-93	Biological Sciences (formerly Plant and Animal Sciences) Policy and Review Council, Graduate School
1991-93	Graduate Faculty Nominations Subcommittee, Biological Sciences Policy and Review Council, Graduate School
1992-93	Graduate Faculty Nominations Subcommittee (Chair), Biological Sciences Policy and Review Council, Graduate School
1995-1998	Biological Sciences Policy and Review Council, Graduate School
1997-98	Faculty Research Development Proposal Review Committee for the Academic Health Center
2001-2004	Academic Health Center Faculty Consultative Committee
2001-2002	SCFP Subcommittee on Twin Cities Facilities and Support Services (STCFSS)
2003	AHC Seed Grant Review Committee
2003	AHC FCC Internal Screening Committee for Academy of Excellence Nominees
2004-2007	All-University Honors Committee, University of Minnesota

STATE, NATIONAL, AND INTERNATIONAL COMMITTEE APPOINTMENTS

1974-76	Representative to AACP Council of Faculties
1977-78	AACP Task Force on Guidelines for Pharm.D. Accreditation
1980-82	Academic Advisory Committee, Kellogg Pharmaceutical Scientist Program
1981	Screening Committee for Academy of Pharmaceutical Sciences, Basic Pharmaceutics Section
1989-present	Member, Scientific Committee, International Pharmaceutical Technology Symposium (FIP)
1990	Academic Affairs Committee, AACP (Member)
1990	Program Committee, Controlled Release Society Annual Meeting (Member)
1989-91	Continuing Education Committee, State Board of Pharmacy (Member)
1990-95	USP Committee of Revision (Member)
1991-93	NIH/NINDS Antiepileptic Drug Development Program (Consultant)
1995	Fellows Nominations Committee for AAPS, PPDM Section
1995	Screening Committee for AAPS PPDM Section Abstracts
1997-2000	Fellows Nominations Committee for AAPS, PPDM Section
1999-2000	Committee on AAPS Section Structure and Procedure Guideline
2000-2001	PPDM Vice Chair, American Association of Pharmaceutical Scientists
2000-2002	Co-Chair, Organizing Committee, 3rd International Symposium on Microdialysis in Drug Research and Development
2001-2002	PPDM Chair Elect, American Association of Pharmaceutical Scientists
2001-2002	Annual Program Planning Committee, American Association of Pharmaceutical Scientists
2001-2002	Program Coordinating Committee, American Association of Pharmaceutical Scientists
2002-2003	PPDM Section Chair, American Association of Pharmaceutical Scientists
2002-2003	PPDM Committee for Graduate Student Symposium Awardees, American Association of Pharmaceutical Scientists
2002-2003	Short Course Program Review Team, American Association of Pharmaceutical Scientists
2003-2004	PPDM Section Past-Chair, American Association of Pharmaceutical Scientists
2004-2007	Member-at-Large, American Association of Pharmaceutical Scientists Executive Council
2004-2006	Clinical and Operational Working Group (CORWG), NASA
2004-2005	AAPS Executive Council Liaison to the Clinical Sciences section of AAPS
2005-2006	AAPS Executive Council Liaison to the DDD section of AAPS
2005-2006	AAPS Executive Council Liaison to the PDD section of AAPS

2005-2006	AAPS Executive Council Liaison to the 2006 Annual Meeting Program Committee
2005-2006	AAPS Executive Council Liaison to the 2006 Annual Meeting Screeners
2005-2006	AAPS Executive Council Liaison to the 2006 Program Coordination Committee
2006	AAPS Reference Resources Task Force
2006-2007	AAPS Executive Council Liaison to the APQ section of AAPS
2006-2007	AAPS Executive Council Liaison to the PT section of AAPS
2006-2007	AAPS Executive Council Liaison to the International Affairs Committee
2009-2011	Epilepsy NINDS Steering Committee
2009-2011	NINDS Consortium to Study Bioequivalence of AED Products

INVITED PRESENTATIONS

Continuing Education Program (6 hours) Minneapolis, MN, 1973.
Upper Midwest Hospital Conference, 1974.
Continuing Education Program (6 hours) Rochester, MN, 1974.
University of Illinois, Chicago, IL, 1974.
Department of Clinical Pharmacology, University of Minnesota, 1974.
AACP Annual Meeting and Teachers' Seminar (Workshop Leader), Lake Kiamesha, NY, 1975.
Debate Symposium, "Drug Product Selection," St. Paul, MN, 1977.
Continuing Education for Minneapolis Veteran Pharmacists (2 hours), Minneapolis, MN, 1978.
Continuing Education in Pharmacy (2 hours), Mankato, MN, 1978
Continuing Education in Pharmacy "Seminar at Sea" (4 hours of instruction), 1978.
HPLC Workshop, Invited Lecturer, Bloomington, MN, 1978.
University of Kentucky, Lexington, KY, 1979.
American Association of Clinical Chemists, Midwest Section, Minneapolis, MN, 1979.
University of Illinois, Chicago, IL, 1979.
Smith Kline Corp., Philadelphia, PA, 1979.
Department of Pathology, St. Cloud Hospital, St. Cloud, MN, 1979.
Comprehensive Epilepsy Program, Minneapolis, MN, 1979.
University of North Carolina, Chapel Hill, NC, 1979.
Burroughs Wellcome Co., Research Triangle Park, NC, 1979.
St. Paul-Ramsey Medical Center, St. Paul, MN, 1989.
Continuing Education in Pharmacy (4 hours) Minneapolis, MN, September-October, 1981.
Medical Research Council of Canada, Visiting Professor, University of British Columbia, Vancouver, 1982.
Invited Lecturer, National Institutes of Health, Epilepsy Branch, Bethesda, MD, 1982.
Geriatric Research, Education and Clinical Center, Bloomington, MN, September, 1982.
Continuing Education in Pharmacy (6 hours), Duluth, MN, September, 1982.
Ciba-Geigy, Pharmaceuticals Division, Ardsley, December 2, 1982.
Swiss Federal Institute of Technology, Zurich, Switzerland, June 19, 1984.
Biopharmacy Division, Sandoz AG, Basel, Switzerland, June 22, 1984.
Biopharmacy Division, Sandoz AG, Basel, Switzerland, July 24, 1984.
"Cyclosporine Pharmacokinetics in the Rabbit: In Vivo Disposition and In Situ Absorption Studies," Rhone-Poulenc Visiting Professor, University of Toronto, Ontario, February 5, 1985.
"Pharmacokinetics and Pharmacodynamics," Drug Therapy Symposium VI, St. Paul, MN, February 27, 1985.
"Absorption and Disposition Studies with Cyclosporine," Sandoz, AG, Basel, Switzerland, July 15, 1985.
"Absorption of Cyclosporine from Rabbit Small Intestine Using an In Situ Perfusion Model," Vorstand des Instituts fur Pharmazie U. Lebensmittlechemie der Ludwig-Maximilians-Universitat, Munich, West Germany, July 17, 1985.
"Analytic considerations in the Investigation of the Pharmacokinetics of Cyclosporine," Medizinischen Hochschule, Hanover, West Germany, September 11, 1985.
"Mixed-Order Absorption of a Sustained Release Carbamazepine Tablet in Humans," Institut fur Pharmazeutische Technologie der Johann Wolfgang Goethe-Universitat, Frankfurt am Main, West Germany, May 15, 1986.
"Simultaneous First- and Zero-order Absorption of Commercial Carbamazepine Tablets," 5th Symposium on Biopharmaceutics and Pharmacokinetics, Piestany, Czechoslovakia, May 22, 1986.
"Simultaneous First- and Zero-order Absorption of Tegretol in Human Volunteers," National Institutes of Health, Epilepsy Branch, NINCDS, Bethesda, MD, November 6, 1986.
"Comparison of Plasma AUCs using the Traditional Point-by-Point and Pooled Sample Methods: Application in the Analysis of Human Pharmacokinetics of Carbamazepine and its metabolites," Food and Drug Administration, Rockville, MD, July 20, 1987.

"Pharmacokinetics in Contemporary Pharmacy Practice," Minneapolis Veteran Pharmacists Association, Richfield, MN, September 15, 1987.

"The Absorption and Disposition Kinetics of Carbamazepine and its Metabolites in Humans," Ciba-Geigy, Summit, NJ, July 23, 1987.

The following four lectures were given in Beijing, Chengdu, and Guilin, China during a visit sponsored by the Chinese Academy of Medical Sciences in late October/early November 1987:

1. "Theory and Application of a Pharmacokinetic Model in Individualizing Dosing Regimens for the Aminoglycosides."
2. "First- and Zero-order Absorption of Carbamazepine from Commercial Tablets in Epileptic Patients and Normal Volunteers."
3. "Significance of Nonlinear Disposition Kinetics in the Adjustment of Dosing Regimens."
4. "Relative Bioavailability of Phenytoin Formulations: Problems in Assessment Due to Michaelis-Menten Elimination Kinetics."

"Does Tegretol need to be Dosed TID?" Comprehensive Epilepsy Program, Minneapolis, MN, March 21, 1988.

"The Kinetics of Absorption of Carbamazepine (Tegretol) and its Metabolism in Humans," Vorstand des Instituts der Pharmazie, Ludwig-Maximilians Universitat, Munich FRG, June 8, 1988.

"Pharmacokinetic and Physiologic Considerations in Oral Controlled Drug Delivery," Novel Drug Delivery Symposium, Minneapolis, MN, September 20, 1988.

"Clinical Applications of the Two-Compartment Open Model," Regional Kidney Disease Program, Hennepin County Medical Center, Minneapolis, MN, November 16, 1988.

The following five lectures were presented in a Continuing Education in Pharmacy Program: "Concepts and Applications in Pharmacokinetics, Parts I and II"; "Therapeutic Response and Toxicity"; "Monitoring Drug Therapy"; and "Bioavailability and Bioequivalence", St. Thomas, Virgin Islands, March 8-13, 1989.

"The Pharmacokinetics of Zidovudine (AZT) with Some Observations on the Interaction with Probenecid," Queen's University of Belfast, Belfast, North Ireland, June 15, 1989.

"Pharmacokinetic and Analytical Considerations in Monitoring Zidovudine (AZT) Levels in Children with Aids," Fourth International Congress on Pediatric Laboratory Medicine, Washington, DC, August 23, 1989.

"Inhibition of Zidovudine Metabolism and Excretory Transport," Department of Pharmacodynamics, Semmelweis University of Medicine, Budapest, Hungary, September 13, 1989.

"Evaluating Bioequivalence," Western Michigan Society of Hospital Pharmacists, Grand Rapids, MI, March 2, 1990.

"Effect of Temperature and Medium of Analysis on Cyclosporine Concentration," Canadian Consensus Meeting on Cyclosporine Monitoring, Minaki Lodge, Canada, May 11, 1990.

"Studies of the Interaction between Zidovudine (AZT) and Probenecid in Animals and Humans." Pharmaceutics and Process R & D, Ayerst Laboratories Inc., Rouse's Point, NY, August 17, 1990.

"Mechanistic Studies to Examine the Effect of Probenecid on the Brain Uptake of Zidovudine," Shanghai Medical University, Shanghai, P.R.C., October 13, 1990.

A lecture series (16 hrs) on the topic of "Clinical Pharmacokinetics and Therapeutic Drug Monitoring" was given to staff members of the Chinese Academy of Medical Sciences and Hospital Pharmacists, Beijing, P.R.C., October 15-20, 1990.

"Comparative Intestinal Absorption of Compounds of Varying Lipophilicity, and the Effect of Absorptive Water Flux." Lederle Laboratories, Pearl River, NY, September 12, 1991.

"Analysis of Zidovudine Distribution into Specific Brain Regions Utilizing Microdialysis," Bristol Myers-Squibb Research Institute, Princeton, NJ, September 17, 1991.

"Distribution of AZT Into Specific Brain Regions in the Rabbit Utilizing Microdialysis," University of Illinois College of Medicine, Peoria, IL, October 9, 1991.

"Studies on the Transport of Nucleosides into Specific Brain Regions Using Microdialysis with *In Vivo* Calibration." University of Florida, College of Pharmacy, Gainesville, FL, December 6, 1991.

"Analysis of Zidovudine Distribution into Specific Brain Regions Utilizing Microdialysis," University of Arizona College of Pharmacy, Tucson, AZ, February 17, 1992.

"Regional Considerations in the In Situ Intestinal Absorption of Glycylcycline and Minocycline, and the Effect of Solvent Drag," Lederle Laboratories, Pearl River, NY, May 11, 1992.

"Comparative Absorption of Fluorothymidine and Related Nucleosides in Different Anatomic Intestinal Regions," Lederle Laboratories, Pearl River, NY, May 11, 1992.

"Microdialysis Techniques for the Study of Drug Distribution, and the Problem of Recovery *In Vivo*," Europhor Toulouse, France, June 19, 1992.

"The Use of Microdialysis in Studying the Distribution of Exogenous Substances in Biological Tissues," Sandoz Pharma, Basel Switzerland, June 24, 1992.

"Inhibition of Brain Distribution and Systemic Clearance of AZT by Probenecid," Sandoz Pharma, Basel Switzerland, June 30, 1992.

"Uptake of Zidovudine (AZT) into Rabbit Brain Using Microdialysis with *In Vivo* Calibration," Knoll AG, Ludwigshafen, Germany, July 1, 1992.

"Microdialysis in the Study of the Distribution and Metabolism of Exogenous Substances," Pharmaceutical Chemical Institute, University of Heidelberg, Heidelberg, Germany, July 2, 1992.

"The Relationship Between Urine and Plasma Concentrations of Lipophilic Drugs: Implications for Therapeutic Drug Monitoring," Sandoz Pharma, Basel Switzerland, July 8, 1992.

"Estimation of the Elimination Rate Constant for Metabolites which Exhibit Formation-Rate Limited Disappearance," Sandoz Pharma, Basel Switzerland, July 23, 1992.

"Experimental Determination of Free Tissue Levels Using Microdialysis," 4th Biennial Conference on Chemotherapy of Infectious Diseases and Malignancies, Prague, Czechoslovakia, August 31, 1992.

"*In Situ* Intestinal Absorption of Tetracycline Derivatives and the Effect of Absorptive Water Flux," Lederle Laboratories, Pearl River, NY, November 13, 1992.

"Reversibility of Carbamazepine Autoinduction upon Dose Termination in Normal Volunteers," Abbott Laboratories, Abbott Park, IL, December 2, 1992.

"Barriers to the Oral Delivery of Drugs," Wyeth-Ayerst Research, Radnor, PA, February 23, 1993.

"Preliminary Results of Studies which Examine the Distribution of the NMDA Antagonist, EAB 515, to Rat Brain," Sandoz Pharma, Basel Switzerland, April 26, 1993.

"Microdialysis Calibration Using the Zero-Net Flux Method and Retrodialysis in Studying the Distribution of Exogenous Substances to Rat Brain," Sandoz Pharma, Basel Switzerland, April 26, 1993.

"Investigation of the Pharmacodynamics of the NMDA Antagonist, EAB 515, in the Rat During Intravenous and Intracerebroventricular Administration." Sandoz Research Institute, Berne, Switzerland, April 28, 1993.

"Comparative Distribution of AZT to Brain Tissue Extracellular Fluid During Intravenous and Intracerebroventricular Infusion." Food and Drug Administration, Rockville, MD, May 21, 1993.

"Interspecies Scaling of Pharmacokinetics in the Evaluation and Development of New Antiepileptic Drugs." Natural Resources Research Institute, University of Minnesota—Duluth, Duluth, MN, August 11, 1993.

"Application of Pharmacokinetic Principles in Practice." Minneapolis Veteran Pharmacists Association, St. Louis Park, MN, September 21, 1993.

"Microdialysis as a Tool to Study Drug Delivery to the Brain." North Jersey American Chemical Society Drug Metabolism Discussion Group, Somerset, NJ, October 7, 1993.

"Graduate Studies and Research Careers in Pharmaceutics." University of Minnesota—Duluth Department of Chemistry, Duluth, MN, December 3, 1993.

"Microdialysis in Pharmacokinetic and Drug Metabolism Studies." 95th Annual Meeting, American Society for Clinical Pharmacology and Therapeutics, New Orleans, LA, April 1, 1994.

"Modeling and Simulation of Complex Pharmacokinetic Systems." NATO Advanced Study Institute, Erice, Italy, April 12, 1994.

"Microdialysis in the Study of Drug Distribution." NATO Advanced Study Institute, Erice, Italy, April 13, 1994.

"Pharmacokinetic Studies Utilizing Microdialysis." Department of Pharmaceutical Chemistry, University of Kansas, Lawrence, KS, May 2, 1994.

"Pharmacokinetic Studies Utilizing Microdialysis and On-Line HPLC." 4th International Workshop in Bioanalysis, Lawrence, KS, July 12, 1994.

"Application of Microdialysis in Pharmacokinetic Studies." Gordon Research Conference in Drug Metabolism, Holderness School, Plymouth, NH, July 20, 1994.

"Microdialysis and its Application in Pharmacokinetic Studies." Ciba-Geigy, Pharmacokinetics and Bioanalytics Division, Ardsley, NY, July 25, 1994.

"Assessing Drug Transport in the Brain with Microdialysis." 9th Annual Meeting, American Association of Pharmaceutical Scientists, San Diego, CA, November 6-10, 1994.

"Applications of Microdialysis in Preclinical Pharmacokinetic Studies." 3M Pharmaceuticals, 3M Center, St. Paul, MN, November 29, 1994.

"Problems in Assessing the Absorption of Carbamazepine from Sustained Release Dosage Forms in Epileptic Patients." Pharmavene, Inc., Gaithersburg, MD, February 23, 1995.

"Selected Preclinical Pharmacokinetic Studies with Tacrine." Parke-Davis Pharmaceuticals, Ann Arbor, MI, May 5, 1995.

"Brain Distribution and Metabolism Studies with Tacrine and Two Hydroxylated Metabolites." Department of Pharmaceutics and Pharmacodynamics, University of Illinois, Chicago, IL, July 28, 1995.

"Microdialysis and its Application in Preclinical Drug Distribution and Absorption Studies." Chiron Corporation, Emeryville, CA, August 18, 1995.

"The Principle of Quantitative Microdialysis and its Application in Preclinical Drug Distribution Studies." Genentech, Inc., South San Francisco, CA, October 9, 1995.

"Graduate Programs and Research Opportunities in Pharmaceutics." 13th Annual Symposium on Pharmaceutical Sciences Graduate Programs, Merrillville, IN, October 21, 1995.

"Principles of Microdialysis and Applications in Preclinical Drug Distribution and Absorption Studies," Wyeth-Ayerst, Pearl River, NY, December 6, 1995.

"Microdialysis in Preclinical Drug Distribution Studies." Dupont Merck, Newark ,DE, December 8, 1995.

"Microdialysis and its Application to the Study of Drug/Metabolite Distribution in the Central Nervous System," University of Pittsburgh, Pittsburgh, PA, January 25, 1996.

"Therapeutic Drug Monitoring: A Fodor's Guide." Hallie Bruce Memorial Lecture Award, Minnesota Society of Health-Services Pharmacists, Minneapolis, MN, April 13, 1996"

"Preclinical Studies of Drug Distribution to the Brain using Microdialysis." Pharmaceutical Peptides Inc, Cambridge, MA, May 2, 1996.

"Microdialysis and its Application in Nonclinical Studies of Drug Distribution and Absorption." Bristol-Myers Squibb, Pinceton, NJ, June 24, 1996.

"Continuous Monitoring by Microdialysis in Neuropharmacokinetic Investigations." Faculty of Pharmacy, University of Tanta, Tanta, Egypt, March 5, 1997.

"Preclinical Studies of Drug Distribution to the Brain using Microdialysis," Toyama Medical and Pharmaceutical University, Toyama, Japan, April 11, 1997.

"Application of Pharmacokinetic Principles in Individualizing Aminoglycoside Dosing," Toyama Medical and Pharmaceutical University, Toyama, Japan, April 11, 1997.

"Preclinical Studies of Drug Distribution to the Brain using Microdialysis," Meiji College of Pharmacy, Japan, April 18, 1997.

"Individualizing Aminoglycoside Dosing and Once-a-Day Aminoglyocosides," Meiji College of Pharmacy, Japan, April 18, 1997.

"Education of Pharmacists and Pharmaceutical Scientists at the University of Minnesota," 260th Meeting on Continuing Education of Pharmacists, Okuda-Shinmachi, Toyama, Japan, April 26, 1997.

"Pharmacokinetic Basis of Drug-drug Interactions," Novartis Workshop on Metabolic Drug-Drug Interactions, Schluchsee, Germany, October 14, 1997.

"Microdialysis and its Application in Preclinical Pharmacokinetic Studies," Merck Research Laboratories, West Point PA, December 16, 1997.

"Microdialysis and its Application in Preclinical Pharmacokinetic Studies," Merck and Co, Inc. Rahway NJ, December 17, 1997.

"Brain Distribution Studies employing Microdialysis and Crossover Designs," *1st International Symposium in Drug Research and Development*, Noorwijkerhout, Netherlands, April 3, 1998.

"Application of Sample Pooling in the Time Domain to Estimate CL, Vss and MRT in the Search for Lead Compounds." Chiron Corporation, Emeryville, CA, May 5, 1998.

"Microdialysis as a Sampling Technique in Preclinical Pharmacokinetic Studies." Pfizer Inc, Groton CT, June 18,1998

"Assessing Drug Delivery to the CNS Using Microdialysis Sampling." School of Medicine, University of Minnesota, Duluth, October 19,1998.

"Pharmacokinetic Studies Using Microdialysis Sampling." American Association of Pharmaceutical Scientists Annual Meeting, San Francisco CA, November 18, 1998.

"Applications of Microdialysis in Pharmacokinetics: Brain, Blood, and Middle Ear Fluid." Bristol-Myers Squibb, Wallingford CT, May 14, 1999.

"Applications of Microdialysis in Preclinical Pharmacokinetics: Brain, Blood and Middle Ear Fluid." Parke-Davis, Ann Arbor, MI, May 21, 1999.

"Blood Sample Pooling and the Determination of Mean Residence Times in High-Throughput Pharmacokinetic Screening"." Parke-Davis, Ann Arbor, MI, May 21, 1999.

"Role of controlled release formulations in the steady-state pharmacokinetics and pharmacodynamics of anticonvulsants" Impax Pharmaceuticals, Inc, Hayward CA, June 9, 1999.

"Investigating Neuropharmacokinetics and Drug Delivery to the CNS using Microdialysis." *8th International Conference on In Vivo Methods: Monitoring Molecules in Neuroscience.* Stony Brook NY, June 19-23, 1999.

"Use of Microdialysis in Pharmacokinetics" at the 8th BMSR Workshop on *Advanced Methods of Pharmacokinetic and Pharmacodynamic System Analysis,* Marina del Rey, CA June 25-26, 1999.

"Applications of Microdialysis in Preclinical Pharmacokinetics." Amgen, Inc., Thousand Oaks, CA, June 28, 1999.

"Pharmacokinetic –Pharmacodynamic Principles in Drug Development." Chiron Corporation, Emeryville, CA, August 20, 1999.

"Microdialysis and its Application in Pharmacokinetics: Brain, Blood, and Middle Ear Fluid." Abbott Labs, Abbott Park IL Aug 27, 1999.

"Distribution kinetics of antibiotics to the chinchilla middle ear" Department of Biopharmaceutical Sciences, Uppsala University, Uppsala, Sweden, March 16, 2000.

"In Vivo Microdialysis as a Tool to Study Site Specific Drug Delivery" *Millennial World Congress of Pharmaceutical Sciences.* San Francisco CA, April 17, 2000.

"In Vivo Microdialysis as a Tool to Study Site Specific Drug Delivery" *Engebretson Symposium on Drug Discovery and Development.* Minneapolis, MN. May 18, 2000.

"In Vivo Microdialysis as a Tool to Study Drug Delivery". *19th Annual Robert S. Rozman Memorial Symposium,* Langhorne PA , May 25, 2000.

"Basic Principles of Microdialysis, Experimental Setup". *Course on Basic and Advanced Aspects of In Vivo Microdialysis*", Stockholm, Sweden, June14, 2000.

"Recovery: Basic Idea and Practical Methods". *Course on Basic and Advanced Aspects of In Vivo Microdialysis*", Stockholm, Sweden, June14, 2000.

"Studies of Distribution of Antibiotics to the Middle Ear by Microdialysis" *2nd International Symposium on Microdialysis in Drug Research and Development*, Stockholm, Sweden, June15, 2000.

"Basic Concepts in Clinical Pharmacokinetics" A 2-Day Course. Abbott Laboratories, Abbott Park IL and Victory Hospital, Waukegan, IL, July 18-19, 2000

"Microdialysis and its Application in Preclinical Pharmacokinetics: Brain, Blood, and Middle Ear Fluid." Dupont Pharmaceuticals, Wilmington, DE July12, 2000.

"Pharmacokinetic –Pharmacodynamic Principles in Drug Development." Abbott Labs, Abbott Park IL Jan 9, 2001

"Biopharmaceutical and Pharmacokinetic Considerations in Delivering Drug to the CNS" Medtronic Neuro Division, Minneapolis. January 25, 2001

"Clinical Pharmacokinetic Principles in Drug Development." Novartis Pharma, Tokyo, April 12, 2001

"In Vivo Microdialysis as a Tool to Study Site Specific Drug Delivery" Showa University, Tokyo, Japan, April 13, 2001

"In Vivo Microdialysis as a Tool to Study Drug Delivery in Preclinical Studies". Xi'an Medical College, Xi'an, PRC. April 25, 2001

"Principles of Pharmacokinetics and their Application in Drug Development" Novartis Pharma, Basel, Switzerland, July 3, 2001.

"Microdialysis and its Application in Preclinical Studies of Drug Delivery to Target Tissues" Boehringer-Ingelheim Pharma KG, Dept. of Pharmacokinetics & Drug Metabolism, Biberach, Germany, July 5, 2001.

"Estimation of Intrinsic Clearances and Organ Partition Coefficients in an Organ Perfusion Model" Novartis Pharma, Basel, Switzerland, July 26, 2001.

"Pharmacodynamic Modeling of the Sigmoid Emax Model" Novartis Pharma, Basel, Switzerland, July 31, 2001.

"Prediction of the Pharmacokinetics of Cefdinir in Children from the Results of Animal Studies. Omnicef® Clinical Advisory Meeting, Dallas, TX, February 9, 2002.

"Applications of Microdialysis in Studying Drug Delivery to Specific Targets". Guilin Medical School, Guilin PRC, March 28, 2002

"Microdialysis: A Tool to Study Brain Uptake?" Gordon Research Conference on the Barriers of the CNS, Tilton School, Tilton NH, June 25, 2002

"A Model for the Distribution of Drugs between Plasma, CSF and Parenchyma", Workshop on Microdialysis Techniques in the CNS, Gordon Research Conference on the Barriers of the CNS, Tilton School, Tilton NH, June 26, 2002

"Microdialysis in the Study of Drug Delivery to the Central Nervous System", Department of Pharmaceutics, Seoul National University, Seoul, South Korea, November 25, 2002.

"Investigating Antibiotic Delivery to the Middle Ear". Chong Kun Dang Pharma, Cheonan, South Korea, November 27, 2002.

"Microdialysis and its Application in Preclinical Pharmacokinetic and Drug Delivery Investigations", 32nd Annual Meeting of the Korean Pharmaceutical Society, Seoul, South Korea, November 28, 2002.

"Applications of Pharmacokinetic Principles in Drug Development". Schering-Plough Research Institute. Kenilworth, NJ. December 19, 2002

"A Course in Pharmacokinetics in Pharmaceutical Development". Abbott Laboratories. Harrison Conference Center, Lake Bluff, IL. May 15-16, 2003

"Characterizing Antibiotic Delivery to the Middle Ear for the Treatment of Otitis Media. Biomedical Simulations Resource Workshop: Advanced Methods of PK/PD Systems Analysis. Marina del Rey, CA. June 20-21, 2003.

"Cerebrospinal Fluid Distribution of Intrathecally Administered Antiviral Nucleosides". Monitoring Molecules in Neuroscience. 10th International Conference on In Vivo Methods. Department of Neuroscience, Karolinska Institutet Stockholm, Sweden. June 24-27, 2003

"Microdialysis Sampling in Drug Development: Applications in Preclinical Research." Sunrise School, American Association of Pharmaceutical Scientists Annual Meeting, Salt Lake City, UT, October 26, 2003.

"Clinical Pharmacokinetics in Pharmaceutical Development." Abbott Laboratories. Harrison Conference Center, Lake Bluff, IL. July 23-24, 2003.

"Microdialysis Sampling in Drug Development: Applications in Preclinical Research." Sunrise School, American Association of Pharmaceutical Scientists Annual Meeting, Salt Lake City, UT. October 26, 2003.

"The Role of Pharmacokinetics in Drug Discovery." Abbott Laboratories. Harrison Conference Center, Lake Bluff, IL. March 18, 2004.

"Microdialysis and its Application in Preclinical Pharmacokinetic and Drug Delivery Investigations." CDER, Food and Drug Administration, Rockville, MD. March 29, 2004.
"Interspecies Scaling, PB-PK modeling and Microdialysis in Antibiotic Drug Development." Novartis Institute for Biomedical Research, Cambridge, MA. April 9, 2004.
"Does it get to the Target Site? Microdialysis as a Tool to Study Preclinical Drug Distribution and Delivery" Amgen Inc., Thousand Oaks, CA. April 30, 2004.
"Microdialysis of Antibiotics." 4th International Symposium on Microdialysis in Drug Research and Development, Vienna, Austria, June 19, 2004.
"The Chinchilla Microdialysis AOM Model" Pfizer Global Pharmaceuticals, New York, NY. June 25, 2004.
"Advantages of the Chinchilla Microdialysis Model" Scientific Basis for Tissue-Directed Antimicrobial Therapy Symposium, Boston MA, July 21-22, 2004.
"Evaluating Drug Distribution to the Target Site and Predicting Tissue Exposure in Humans from Animal Data" Scientific Advisory Committee, Abbott Laboratories. The FDA Critical Path Initiative and the Role of Modeling/Simulation in Improving the Efficiency of Drug Development. Lake Forest, IL. September 8-9, 2004.
"Assessing Drug Delivery to the Target Site: The Role of Microdialysis in Measuring Tissue Exposure in Animals and Humans." Distinguished Lecture, Creighton University School of Pharmacy and Health Professions, Omaha NE, November 30, 2004.
"Microdialysis—Introduction to Basic Principles and Applications". AAPS Workshop on Microdialysis Principles, Application, and Regulatory Perspectives, Nashville TN, November 4, 2005.
"A Phase I Open-Label, Dose-Ranging Study to Investigate the Safety and Tolerability of Gabapentin Injection Administered Intrathecally in Individuals with Chronic, Intractable Pain: A Pharmacokinetic Report". Medtronic WHQ, Fridley, MN, February 16, 2006.
"Public Outreach and AAPS: Students are the Future of Our Association". Temple University School of Pharmacy, Philadelphia, PA. February 20, 2006.
"Assessing Drug Delivery: Using Microdialysis to Measure Target Site Exposure in Animals and Humans". Wyeth Distinguished Lecture Series, Temple University School of Pharmacy, Philadelphia, PA. February 20, 2006.
"Pharmacokinetics for Scientists Engaged in Drug Discovery". Lundbeck Research, USA. Paramus NJ. February 24, 2006.
"Pharmacokinetic Issues related to Intrathecal Drug Dosing". Medtronic WHQ, Fridley, MN, March 15, 2006.
"TTM Technology: Antibiotic Distribution to Middle Ear Fluid" Abbott Laboratories, Abbott Park, IL. May 16, 2006.
"Trans-tympanic Membrane (TTM) Drug Delivery to the Middle Ear" Alcon Laboratories, Fort Worth TX. Feb 2, 2007.
"Bugs and Drugs: Does the Anti-infective Agent get to the Target Site?". Science Luncheon Presentation. APhA Annual Meeting. Atlanta, GA. March 18, 2007
"Future Perspectives on the Contributions of Microdialysis in Drug Research and Development" Keynote Address. Fifth International Symposium on Microdialysis in Drug Research and Development. Leiden, NE. April 25, 2007.
"Drug Delivery to the Middle Ear across the Tympanic Membrane for Therapy of Acute Otitis Media". Global Gators 6th Symposium on Clinical Pharmacy and Clinical Pharmacology. Munich, Germany. June 9, 2007.
"The Pharmacokinetics of Hydrophilic Drugs during Intrathecal Infusion: the Concept of a Targeted Delivery Advantage". Novartis Pharma AG, Basel, Switzerland. June 13, 2007.
"Trans-tympanic Membrane Delivery of an Antibiotic into Chinchilla Middle Ear" Alcon Laboratories, Fort Worth TX. October 15, 2008.
"A Phase I Study to Investigate the Safety and Pharmacokinetics of Intrathecal Gabapentin Injection in Individuals with Chronic Pain". University of Poitiers, Poitiers, France, April 29, 2009.
"Cerebrospinal fluid flow, and the convective/diffusive transport of drugs in the CSF" Abbott GmbH and Co., Ludwigshafen, Germany. Oct 15, 2010.
"The Neuropharmacokinetics of Hydrophilic Drugs during Intrathecal Infusion: the Concept of a Targeted Brain Delivery Advantage" Abbott GmbH and Co., Ludwigshafen, Germany. Oct 15, 2010.
"A Brief Introduction to Pharmacokinetics" Upsher-Smith Laboratories, Inc., Maple Grove, MN. December 2, 2010.
"CSF flow, and convective/diffusive transport of drugs" Upsher-Smith Laboratories, Inc., Maple Grove, MN. December 2, 2010.
"Modeling the delivery of drugs to target sites in the CNS" Upsher-Smith Laboratories, Inc., Maple Grove, MN. December 2, 2010.

TEACHING AT THE UNIVERSITY OF MINNESOTA

Undergraduate

1971 - 1972	Co-instructor in Phar 5680 "Pharmacokinetics"
1971 - 1975	Discussant in Pharm.D. Conferences
1972 - 1973	Participating instructor in Phar 5670
1972 - 1978	Discussion leader in Pharm.D. I conferences
1972 - 1985	Course director, Phar 5680 "Pharmacokinetics"
1975 - 1995	Course director, Phar 5685 "Clinical Pharmacokinetics"
1991 - 1999	Course director, Phar 5681 "Basic Pharmacokinetic Modeling"
1996 - 1998	Course director and Participating instructor, Phmc 5460 "Pharmacokinetics"
1998 - 2003	Course director and instructor, Phar 6216 "Pharmacokinetic Simulation and Data Analysis using SAAM"
1999 - 2004	Course director and Participating instructor, Phar 6163 "Pharmacokinetics"
1998 - 2004	Participating instructor in Phar 6164 "Biopharmaceutics"
2004 - 2010	Participating instructor, Phar 6163 "Pharmacokinetics"

Graduate

1972 - 1999	Course director in Phm 8420 "Modeling Approaches in Pharmacokinetics" Participating instructor in Phm 8421, Phm 8425
1972 - 2005	Participating instructor in Phm 8100 (Seminar) and Phm 8101 (Pharmaceutics Readings)
1984 - 1999	Participating instructor in Phm 8425 "Advanced Topics in Pharmacokinetics"
1986 - 1999	Course co-director in Phm 8105 "Pharmacokinetics Research Seminar"
2000 - 2006	Course co-director in Phm 8150 "Pharmacokinetics Research Seminar"
2000 - 2006	Course Co-director and Participating instructor in Phm 8421 "Advanced Pharmacokinetics"
2004 - 2010	Participating instructor in Phm 8481 "Advanced Neuropharmaceutics"
2006 - 2010	Participating instructor in Phm 8421 "Advanced Pharmacokinetics"
2016-present	Participating instructor in Phm 8421 "Advanced Pharmacokinetics"

TEACHING AT OTHER SITES

"An Introduction to Clinical Pharmacokinetics" Abbott Laboratories. Abbott Park, IL. January 9-10, 2001.
"An Introduction to Clinical Pharmacokinetics" Abbott Laboratories. Abbott Park, IL. March 29-30, 2001.
"An Introduction to Clinical Pharmacokinetics" Abbott Laboratories. Abbott Park, IL. May 17-18, 2001.
"An Introduction to Clinical Pharmacokinetics" Abbott Laboratories. Harrison Conference Center, Lake Bluff, IL. November 8-9, 2001.
"An Introduction to Pharmacokinetics" Abbott Laboratories. Harrison Conference Center, Lake Bluff, IL. March 14-15, 2002.
"An Introduction to Pharmacokinetics" Abbott Laboratories. Abbott Park, IL. July 22-23, 2002.
"An Introduction to Pharmacokinetics" Abbott Laboratories. Parsippany, NJ. Aug 26-27, 2002.
"An Introduction to Pharmacokinetics" Bristol-Myers Squibb. Wilmington, DE. September 19-20, 2002.
"Applications of Pharmacokinetic Principles in Drug Development". Schering-Plough Research Institute. Kenilworth, NJ. December 19-20, 2002
"A Course in Pharmacokinetics in Pharmaceutical Development". Abbott Laboratories. Harrison Conference Center, Lake Bluff, IL. May 15-16, 2003
"An Introduction to Pharmacokinetics" Abbott Laboratories. Harrison Conference Center, Lake Bluff, IL. July 23-24, 2003.
"Short Course in Pharmacokinetics for Drug Discovery" Abbott Laboratories. Lake Bluff, IL. March 17-18, 2004.
"Preclinical Pharmacokinetics in Pharmaceutical Discovery." Bristol-Myers Squibb, Princeton, NJ. May 6-7, 2004.
"Introduction to Pharmacokinetics" Abbott Laboratories. Abbott Park, IL, July 27-28, 2004.
"Introduction to Clinical Pharmacokinetics" Millennium Pharmaceuticals, Inc. Cambridge, MA, December 2-3, 2004.
"Introduction to Clinical Pharmacokinetics" Gilead Sciences, Foster City, CA. December 8-9, 2005.
"Basic Pharmacokinetic Concepts for the Pharmaceutical Scientist" Co-instructor. Boehringer-Ingelheim Pharmaceuticals, Inc., USA. Ridgefield, CT, April 13-14, 2006
"An Introduction to Pharmacokinetics" Lundbeck Research, USA, Inc. Paramus, NJ, February 24, 2006.
"Basic Pharmacokinetic Concepts for the Pharmaceutical Scientist" Co-instructor. Abbott Laboratories. Abbott Park, IL. June 4-5, 2007.

"Basic Pharmacokinetic Concepts for the Pharmaceutical Scientist" Co-instructor. Theravance, Inc. South San Francisco, CA. August 20-21, 2007.
"Basic Pharmacokinetic Concepts" Co-instructor. US Patent and Trademark Office. Alexandria, VA. October 4, 2007.
"Basic Pharmacokinetic Concepts for the Pharmaceutical Scientist" Co-instructor. Allergan, Inc. Irvine, CA. July 24-25, 2008.
"Basic Pharmacokinetic Concepts for the Pharmaceutical Scientist". Co-instructor. Abbott Laboratories, Abbott Park, IL. August 19-20, 2008.
"Basic Pharmacokinetic Concepts for the Pharmaceutical Scientist". Co-instructor. Gilead Sciences, Foster City, CA. October 9-10, 2008.
"Basic Pharmacokinetic Concepts for the Pharmaceutical Scientist". Co-instructor. Genentech, South San Francisco, CA. July 23-24, 2009.
"Basic Pharmacokinetic Concepts for the Pharmaceutical Scientist". Co-instructor. Abbott Laboratories. Abbott Park, IL. July 30-31, 2009.
"Neuropharmacokinetic Concepts for CNS Drug Delivery". Co-instructor. Abbott Laboratories. Abbott Park, IL. January 8, 2010.
"Basic Pharmacokinetic Concepts for the Pharmaceutical Scientist". Co-instructor. Abbott Laboratories. Abbott Park, IL. August 4-5, 2010.
"Basic Pharmacokinetic Concepts for the Upsher-Smith Pharmaceutical Scientist". Co-instructor. Upsher-Smith Laboratories, Maple Grove, MN. September 21-23, 2011.
"Basic Pharmacokinetic Short Course for Pharmaceutical Scientists". Co-instructor. Novartis Pharma, Florham Park, NJ. November 17-18, 2011.
"Basic Pharmacokinetic Concepts for the Pharmaceutical Scientist". Co-instructor. Abbott Laboratories. Independence Grove, IL. April 12-13, 2012.
"Basic Pharmacokinetic Short Course for Pharmaceutical Scientists". Co-instructor. Novartis Institutes for Biomedical Research, Emeryville, CA. September 16 -17, 2013.
"Basic Pharmacokinetic Concepts for the Pharmaceutical Scientist". Co-instructor. Genentech, South San Francisco, CA. May 7-8, 2014.
"Basic Pharmacokinetic Concepts for the Pharmaceutical Scientist". Co-instructor. Abbvie. Independence Grove, IL. July 16-17, 2014.
"Basic Pharmacokinetic Concepts for the Pharmaceutical Scientist". Co-instructor. Genentech, South San Francisco, CA. May 27-28, 2015.
"Basic Pharmacokinetic Concepts for the Pharmaceutical Scientist". Co-instructor. Abbvie. Independence Grove, IL. June 17-18, 2015.
"Basic Pharmacokinetic Concepts for the Pharmaceutical Scientist". For non-pharmacokineticists . Co-instructor. Abbvie. Independence Grove, IL. June 1, 2016.
"Basic Pharmacokinetic Concepts for the Pharmaceutical Scientist". For pharmacometricians. Co-instructor. Abbvie. Independence Grove, IL. June 2, 2016.
"Basic Pharmacokinetic Concepts for the Pharmaceutical Scientist". Co-instructor. Vertex Pharmaceuticals Inc. Boston, MA, Oct 11-12, 2016.

GRADUATE STUDENTS SUPERVISED AS PRIMARY ADVISOR

Graduate Students supervised as Primary Advisor and Year of Degree Award

1978	Wargin, W.A.	Ph.D.
1978	El-Yazigi, A.	Ph.D.
1980	Mugure Pyron	M.S.
1981	Sue-Chi Wu	M.S.
1983	Hsuehling Su	M.S.
1984	Dale Yu	Ph.D.
1984	Walid Awni	Ph.D.
1985	Lillian Riad	M.S.
1985	Rose Eggerth	Ph.D.
1987	Hisham Abou-Auda	Ph.D.
1989	Mohsen Hedaya	Ph.D.
1989	Ajit K. Shah	Ph.D.
1989	Lillian Riad	Ph.D.
1991	Helen Chan	Ph.D.
1992	William Elmquist	Ph.D.
1992	Shekman Wong	Ph.D.
1994	Yanfeng Wang	Ph.D.
1994	Bimal Malhotra	Ph.D.
1996	Richard Brundage	Ph.D.
1997	Zheng Yang	Ph.D
1998	Belinda Cheung	Ph.D.
2001	Yue Huang	Ph.D
2001	Guanfa Gan	Ph.D.
2002	Joanna Peng	Ph.D
2002	Tong Zhu	Ph.D.
2004	Ji Ping	Ph.D
2004	Wei Liu	Ph.D.
2005	Yan Song	Ph.D.
2007	Nael Mostafa	Ph.D.
2007	Zhihong Li	Ph.D.

GRANTS , CONTRACTS, and OTHER SUPPORT

1972-73	University of Minnesota Graduate School
1973-74	University of Minnesota Media Production Fund
1975-78; 1978-80	NIH/NINCDS Comprehensive Epilepsy Program Contract (Principal Investigator, Project D-1)
1976; 1977	Medical Education and Research Foundation Grant (Co-investigator with John W. McBride, M.D.)
1976-78	FDA Contract to Study the Pharmacokinetics and Toxicology of Phenytoin Sodium Products in Clinical Patients
1980-81; 1981-83	Grant to Support Research Involving the Analysis of Cyclosporin A in Biological Fluids (Sandoz, Inc.)
1982-83; 1983-84	"Pharmacokinetics and Biopharmaceutic Studies of Cyclosporin A in Selected Animal and *In Vitro* Systems" (NIH; Principal Investigator; Co-investigator, R.P. Enever)
1984	Comparative Bioavailability of Sodium Phenytoin in Normal Volunteers (Zenith Labs)
1984	Relative Bioavailability of Carbamazepine in Chewable and Conventional Tablets (Ciba-Geigy)
1984	Transdermal Delivery of Propranolol (Medtronics)
11/84 - 1/85	Absorption and Metabolism of Carbamazepine in Normal Volunteers (Ciba-Geigy)
1/85 - 4/85	Transdermal Absorption of β-Blockers (Medtronics, Inc.)
11/85 - 4/86	Relative Bioavailability of Sustained Release Oral Dosage Forms of Carbamazepine (Ciba-Geigy)
1/86 - 6/86	Analysis of Analgesics in Receptor Media (Medtronics)

8/86 - 12/86	Bioequivalence of Carbamazepine Oral Dosage Forms (Ciba-Geigy)
1/86 - 12/88	Pharmacokinetics of Diltiazem in the Rabbit (Marion)
2/87 - 9/87	Bioequivalence of Carbamazepine Dosage Forms Demonstrating Varying Dissolution Rates (Ciba-Geigy)
6/1/87 - 10/15/87	Effect of Urine Flow on the Renal Clearance of Carbamazepine and its Metabolites in Humans (Ciba-Geigy)
1/88 - 6/88	Effect of Fasting on the Absorption of Diclofenac Sodium in Normal Human Volunteers (Ciba-Geigy)
4/1/89 - 3/31/92	Enhancing Brain Uptake of AZT by Transport Inhibition, (NINCDS / NIH)
7/1/89 - 6/30/90	Induction of Carbamazepine Metabolism as a Function of Dosing Rate in Normal Volunteers (Ciba-Geigy)
9/91 - 6/92	Brain Distribution of EAB-515 in the Rabbit (Sandoz, Ltd.)
11/91 - 5/92	*In Situ* Absorption from Rabbit Intestine (Lederle Laboratories)
3/92 - 8/92	Clinical Studies of the Absorption of an Oral Immunosuppressant (Apotex Laboratories)
11/92 - 10/93	Brain Distribution of an NMDA-Receptor Antagonist in the Rat (Sandoz, Ltd).
10/92 - 5/93	Brain Uptake of a CNS-Active Agent (Warner-Lambert)
11/92 - 3/93	*In Situ* Absorption from Rabbit Intestine (Lederle Laboratories)
9/94 - 5/95	Population Pharmacokinetic Analysis of A General Anesthetic in Man (Abbott Laboratories)
7/94 - 5/95	Brain Uptake of a Cholinesterase Inhibitor and its Metabolites (Warner-Lambert)
10/94 - 9/95	Distribution of Antiviral Nucleosides into Rat Cortex (Bristol-Myers Squibb)
9/95 - 8/96	Bioanalytical Methods Development of Selected Drugs and Metabolites (MedTox)
1/96 - 9/96	Pharmacokinetic Analysis of IL-2 in the Pig (Chiron)
1/96 - 6/98	Analysis of Selected Macrolides by High-pressure Liquid Chromatography (TAP)
4/96 - 10/97	Brain Penetration of Fosphenytoin and Phenytoin in the Rabbit (Warner-Lambert)
4/96 - 9/96	Analysis and Brain Uptake of PPI-457 (Pharmaceutical Peptides, Inc)
7/97 - 3/98	Regional Intestinal Absorption of Anti-CMV agents (Bristol-Myers Squibb)
8/97 - 6/98	EM574 Absorption in the Rabbit in situ (TAP)
7/97 - 9/97	Pharmacokinetics of Macrolides in Protocol EM-97-006 (TAP)
11/97 - 12/97	Drug Interaction Pharmacokinetic Analysis (McNeil)
8/97 - 3/98	Analysis and Pharmacokinetics of Macrolides in EM-97-008 (TAP)
10/97 - 12/97	Pharmacokinetics of Slow Release Agents in the CNS (Chiron)
1/98	LC/MS/MS Equipment Grant (TAP)
2/98 - 12/99	Analysis of Macrolides and Metabolites in EM-97-013 (TAP)
3/98 - 12/99	Chemical Stability of Selected Agents (Medtronic)
5/98	Validation of Analysis of Macrolides in Dog Plasma (TAP)
8/98	Validation of Analysis of Macrolides in Rabbit Plasma (TAP)
8/98	Stability of Anticancer Drugs in Solution (Medtronic)
8/98	EM574 Toxicokinetics in the Dog (TAP)
12/98	EM574 Toxicokinetics in the Rabbit (TAP)
1/99	Pharmacodynamics of EM574 on LES Pressure (protocol 004) (TAP)
3/99	Effect of Time of Dosing on Absorption of EM574 (protocol 007(TAP)
4/99	Effect of Gastric Emptying on the Pharmacokinetics of EM574 and its Metabolites (protocol 002) (TAP)
2/99	Stability of FUDR and Heparin in Solution (Medtronic)
2/99	Pharmacodynamics and PKs of EM574 and its Metabolites During Chronic Dosing (protocol 029) (TAP)
3/00 - 8/01	Pharmacokinetics of CDTR and Distribution to Middle Ear Fluid (TAP)
8/00 - 6-01	Distribution of Ketolides to Middle Ear Fluid (Abbott)
10/01 - 09/03	Pharmacokinetics of Ketolides (Abbott)
12/01 - 11/03	Pharmacokinetics and Distribution of cefdinir (Abbott)
12/02 – 12/03	Effect of a P-Glycoprotein Inhibitor on the Middle Ear Distribution of Clarithromycin (Abbott)
12/02 – 6/04	Distribution a Cephalosporin into Middle Ear Fluid in Children with Otitis Media (H LaRoche)
12/02 – 12/04	Development and Testing of Formulations for Delivery of Antibiotics to the Middle Ear (Abbott)
5/03 - 4/05	A New Approach for the Therapy of Otitis Media (Abbott)
8/04 - 7/05	Distribution of Macrolide Antibiotics to tissue sites (Pfizer)
5/05 - 11/05	Testing the Distribution of Amoxicillin into Middle Ear Fluid in the Chinchilla following Pulsatile Dose Administration (Advancis)
1/06 – 9/06	Distribution of Macrolide antibiotics to Pulmonary Tissue and Skeletal Muscle (Pfizer)
9/07 – 10/08	Transtympanic Membrane Delivery of an Antibiotic to the Middle Ear (Alcon)
11/07 – 12/08	Development of an Acute Otitis Media Middle Ear Microdialysis Model in the Chinchilla with

	Implanted Tympanostomy Tube (Alcon)
1/10 – 12/10	Testing the Penetration of an Antibiotic into Chinchilla Middle Ear using Transtympanic Membrane Delivery Formulations – Phase II (Alcon)
1/11 – 12/11	Testing the Penetration of an Antibiotic into Chinchilla Middle Ear using Transtympanic Membrane Delivery Formulations – Phase II B (Alcon)
1/12 – 6/12	Testing the Penetration of Moxifloxacin into Chinchilla Middle Ear– Phase II, Supplement II (Alcon)
7/12 – 12/12	Testing the Penetration of Moxifloxacin into Chinchilla Middle Ear– Phase III (Alcon)
1/13 – 8/14	Testing the Penetration of Fluoroquinolones into Chinchilla Middle Ear– Phase IV (Alcon)

PATENTS

United States Patent. Number 7,220,431 "METHODS AND COMPOSITIONS FOR APPLYING PHARMACOLOGIC AGENTS TO THE EAR." UMN Docket # Z01159. RJ Sawchuk and BW Cheung. Issue Date: May 22, 2007. Filing Date: November 27, 2002: #06,306,517

PUBLICATIONS

BOOKS AND CHAPTERS

J. Blanchard, R.J. Sawchuk and B.B. Brodie, Editors. Principles and Perspectives in Drug Bioavailability. S. Karger, Basel, 1979.

J. Blanchard and R.J. Sawchuk, "Drug Bioavailability: An Overview" in Principles and Perspectives of Drug Bioavailability, J. Blanchard, R.J. Sawchuk and B.B. Brodie (Editors), S. Karger, Basel, 1979.

I.E. Leppik, J. Shope, R.J. Sawchuk, W.A. Hauser and B. Van Dyne, "Variability of Antiepileptic Drug Levels During Chronic Therapy" in Epileptology, M. Dam, L. Gram and K. Penry (Editors), Raven Press, NY, 1981.

R.J. Sawchuk, "Drug Absorption and Disposition in Burn Patients" in The Pharmacokinetic Basis of Drug Treatment, N. Massoud, L.Z. Benet, and J.G. Gambertoglio (Editors), Raven Press, NY, 1984.

"Use of Microdialysis in Drug Delivery Studies." Theme Issue. W.F. Elmquist and R.J. Sawchuk (Editors) *Advanced Drug Delivery Reviews* 45, Nos. 2-3 (2000).

R. J. Sawchuk and B.W.Y. Cheung, "Application of Microdialysis in Pharmacokinetic Studies." in Handbook of Microdialysis: Methods, Applications and Clinical Aspects , B.H.C. Westerink and T.I.F.H. Cremers (Editors), Academic Press, Amsterdam, 2007.

PROFESSIONAL PUBLICATIONS

R.J. Sawchuk, "The Plateau Principle in Drug Therapy. Part 1: The Principle and Its Application." *Minn. Pharmacist* 27(6): 19 (1973).

R.J. Sawchuk, "The Plateau Principle in Drug Therapy. Part 2: Factors Governing Plateau Levels During Chronic Drug Therapy." *Minn. Pharmacist* 27(7): 8 (1973).

M.C. Meyer, A.B. Straughn, L.J. Leeson, R.H. Levy and R.J. Sawchuk, "Meprobamate Bioavailability Monograph." *JAPhA* NS17, 173 (1977).

R.J. Sawchuk and T.S. Rector, "Burn-Induced Alterations in Drug Absorption and Disposition." *Minn. Pharmacist* 35: 6-9 (1981).

SCIENTIFIC PUBLICATIONS (NON-REFEREED)

I.E. Leppik, J. Cloyd and R.J. Sawchuk, "Coefficient of Variation as a Measure of Compliance" Letter. *Lancet*, October 14, 1978.

SCIENTIFIC PUBLICATIONS (REFEREED)

1. R.J. Sawchuk, J.M. Anderson and J.G. Nairn. "Stirring apparatus for the investigation of unstable strongly adsorbing chemicals." *J. Pharm. Sci.* 55: 1463 (1966).

2. R.J. Sawchuk and J.G. Nairn. "Rate studies on the binding of bilirubin by ion-exchange resins." *J. Pharm. Sci.* 57: 1896 (1968).

3. R.J. Sawchuk, J. Robayo and K.W. Miller. "The distribution of propranolol between blood and plasma in hypertensive patients." *Br. J. Clin. Pharmacol.* 1: 440 (1974).

4. R.J. Sawchuk and D.E. Zaske. "Pharmacokinetics of dosing regimens which utilize multiple intravenous infusions: gentamicin in burn patients." *J. Pharmacokin. Biopharm.* 4: 183 (1976).

5. D.E. Zaske, R.J. Sawchuk, D.N. Gerding and R.G. Strate. "Increased dosage requirements of gentamicin in burn patients." *J. Trauma* 16: (1976).

6. R.J. Sawchuk, D.E. Zaske, R.J. Cipolle, W.A. Wargin and R.G. Strate. "Kinetic model for gentamicin dosing with the use of individual patient parameters." *Clin. Pharmacol. Therap.* 21: 362 (1977).

7. J.C. Cloyd, D.E. Bosch and R.J. Sawchuk. "Concentration-time profile of phenytoin after admixture with small volumes of intravenous fluids." *Am. J. Hosp. Pharm.* 35: 45-48 (1978).

8. J.D. Wirtschafter, C.R. Volk and R.J. Sawchuk. "Trans-aqueous diffusion of acetylcholine to denervated iris sphincter muscle: A hypothetical mechanism for the tonic pupil syndrome (Adie's Syndrome). *Annals of Neurology* 4: 1-5 (1978).

9. D.E. Zaske, R.J. Sawchuk and R.G. Strate. "The necessity of increased doses of amikacin in burn patients." *Surgery* 84: 603-608 (1978).

10. S.M. Ehlers, D.E. Zaske and R.J. Sawchuk. "Massive theophylline overdose: rapid removal by charcoal memoperfusion. *JAMA* 240: 474 (1978).

11. I.E. Leppik, V. Ramani, R.J. Sawchuk and R.J. Gumnit. "Increased clearance of phenytoin during mononucleosis." *NEJM* 300: (1979).

12. H.G. McCoy, R.J. Cipolle, S.M. Ehlers, R.J. Sawchuk and D.E. Zaske. "Severe methanol poisoning: application of a pharmacokinetic model for ethanol therapy and hemodialysis." *Am. J. Med.* 67: 804-807 (1979).

13. R.J. Sawchuk, T.S. Rector, J.J. Fordice and I.E. Leppik. "Effect of influenza vaccination on plasma phenytoin concentrations." *Therap. Drug Monitoring* 1: 285-288 (1979).

14. R.J. Sawchuk and T.S. Rector. "Steady-state plasma concentrations as a function of the absorption rate and dosing interval for drugs exhibiting concentration-dependent clearance: consequences for phenytoin therapy." *J. Pharmacokin. Biopharm.* 7: 543-555 (1979).

15. S. Pancorbo, R.J. Sawchuk, C. Dashe and M. Schallock. "Use of a pharmacokinetic model for individualizing intravenous doses of aminophylline." *Eur. J. Clin. Pharmacol.* 16: 251-254 (1979).

16. I.E. Leppik, J.C. Cloyd, R.J. Sawchuk and S.M. Pepin. "Compliance and variability of plasma phenytoin levels." *Therap. Drug Monitoring* 1: 475-483 (1979).

17. R.L. Kriel, J.C. Cloyd, K.H. Green, R.J. Sawchuk, L.A. Lockman and R. Eggerth. "The pharmacokinetics of valproic acid in children." *Ann. Neurology* 6: 179 (1979).

18. R.J. Sawchuk and L.L. Cartier. "Liquid-chromatographic method for simultaneous determination of phenytoin and 5-(4-hydroxyphenyl)-5-phenylhydantoin in plasma and urine." *Clin. Chem.* 26: 835-839 (1980).

19. N.K. Kouchenour, M. Emery and R.J. Sawchuk. "Phenytoin absorption and metabolism in pregnancy." *Obstetrics and Gynecology* 56: 577-582 (1980).

20. S.E. Chen, R.J. Sawchuk and E.J. Staba. "American ginseng. III. Pharmacokinetics of ginsenosides in the rabbit." *Eur. J. Drug Metab. Pharmacokin.* 5: 161-168 (1980).

21. D. Baker, J.C. Rotschafer, R.J. Sawchuk, K.B. Crossley and L.C. Solem. "Vancomycin pharmacokinetics." *J. Pediatr.* 97: 502-503 (1980).

22. R.J. Sawchuk* and T.S. Rector. "Drug kinetics in burn patients." *Clin. Pharmacokinetics* 5: 548-556 (1980).

23. G.R. Matzke, J.C. Cloyd and R.J. Sawchuk. "Acute phenytoin and primidone intoxication, a pharmacokinetic analysis." *J. Clin. Pharmacol.* 21: 92-99 (1981).

24. A. El-Yazigi and R.J. Sawchuk. "Theophylline absorption and disposition in the rabbit: oral, intravenous, and concentration-dependent kinetic studies." *J. Pharm. Sci.* 70: 452-456 (1981).

25. J.H. Fischer, J.C. Cloyd, R.L. Kriel, R. Eggerth and R.J. Sawchuk. "The effect of concomitant antiepileptic therapy on valproic acid pharmacokinetics." *Epilepsia* 22: 237 (1981).

26. R.J. Sawchuk and L.L. Cartier. "Liquid-chromatographic determination of cyclosporin A in blood and plasma." *Clinical Chemistry* 27: 1368-1371 (1981).

27. G.R. Matzke and R.J. Sawchuk. "Elevated serum phenytoin concentrations in a uremic patient when measured by enzyme-multiplied immunoassay." *Drug Intell. Clin. Pharm.* 15: 386-387 (1981).

28. R.J. Sawchuk, S.M. Pepin, I.E. Leppik and R.J. Gumnit. "Rapid and slow release phenytoin in epileptic patients at steady state: comparative plasma levels and toxicity." *J. Pharmacokin. Biopharm.* 10: 365-382 (1982).

29. R.J. Sawchuk, S.M. Pepin, I.E. Leppik and R.J. Gumnit. "Rapid and slow release phenytoin in epileptic patients at steady state: assessment of relative bioavailability utilizing Michaelis-Menten parameters." *J. Pharmacokin. Biopharm.* 10: 383-391 (1982).

30. J. Rotschafer, K. Crossley, D. Zaske, K. Mead, R.J. Sawchuk and L.D. Solem. "Pharmacokinetics of vancomycin: observations in 28 patients and dosage recommendation." *Antimicrob. Ag. Chemother.* 22: 391-394 (1982).

31. R.J. Sawchuk and L.L. Cartier. "Liquid-chromatographic method for simultaneous determination of carbamazepine and its epoxide metabolite in plasma." *Clin. Chem.* 28: 2127-2130 (1982).

32. W.A. Wargin, R.J. Sawchuk, J.W. McBride, H.G. McCoy and M.L. Rylander. "Variable first-pass elimination of propranolol following single and multiple oral doses in hypertensive patients." *Eur. J. Drug Metab. Pharmacokin.* 7: 183-189 (1982).

33. J.C. Cloyd, R.L. Kriel, J.H. Fischer, R.J. Sawchuk and R.M. Eggerth. "Pharmacokinetics of valproic acid in children. I. Multiple antiepileptic drug therapy." *Neurology* 33: 185-191 (1983).

34. R.M. Ferguson, R.K. Fidelus, R.J. Sawchuk and K. Gajl. "The mechanism of action of cyclosporine in man." *Transpl. Proc.* 15(1): (1983).

35. D.K. Yu and R.J. Sawchuk. "Gas-liquid chromatographic determination of propylene glycol and plasma and urine." *Clin. Chem.* 29: 2088-2090 (1983).

36. R.J. Sawchuk and G.R. Matzke. "Contribution of 5-(4-hydroxyphenyl)-5-phenylhydantoin to the discrepancy between phenytoin analyses by EMIT and high pressure liquid chromatography." *Ther. Drug Monit.* 6: 97-103, (1984).

37. R.K. Sylvester, B. Lewis, K. Caldwell, M. Lobell, R. Perri and R.J. Sawchuk. "Phenytoin malabsorption secondary to cisplatinum, vinblastine and bleomycin." *Ther. Drug Monit.* 6: 302-305 (1984).

38. W. Awni and R.J. Sawchuk. "The pharmacokinetics of cyclosporine. I. Single-dose and constant-rate infusion studies in the rabbit." *Drug Metab. Disposition* 13(2): 127-132 (1984).

39. W. Awni and R.J. Sawchuk. "The pharmacokinetics of cyclosporine. II. Blood-plasma distribution and binding studies." *Drug Metab. Disposition* 13(2): 133-138 (1984).

40. K.H. Chan, R.J. Sawchuk, T.A. Thompson, E. Redalieu, W.E. Wagner, Jr., A.R. LeSher, B.J. Weeks, N.R. Hall and A. Gerardin. "Bioequivalence of carbamazepine chewable and conventional tablets: single dose of steady-state studies." *J. Pharm. Sci.* 74(8): 866-870 (1985).

41. A. El-Yazigi and R.J. Sawchuk. "*In vitro* - *in vivo* correlation and dissolution studies with oral theophylline dosage forms." *J. Pharm. Sci.* 74(2): 161-164 (1985).

42. D.K. Yu, W.F. Elmquist and R.J. Sawchuk. "Pharmacokinetics of propylene glycol in humans during multiple dosing regimens." *J. Pharm. Sci.* 74(8): 876-878 (1985).

43. R.J. Sawchuk and W. Awni. "Absorption of cyclosporine from rabbit small intestine *in situ*." *J. Pharm. Sci.* 75(12): 1151-1156 (1986).

44. G.R. Matzke, R.C. Brundage and R.J. Sawchuk. "Protein binding of phenytoin, p-hydroxyphenytoin, and p-hydroxy phenytoin glucuronide." *J. Clin. Pharmacol.* 26: 677-679 (1986).

45. R.M. Ferguson, D.M. Canafax, R.J. Sawchuk and Simmons R.L. Cyclosporine blood level monitoring: the early posttransplant period. *Transplantation Proceedings.* 18(2 Suppl 1):113-22, (1986).

46. C. Fletcher, R.J. Sawchuk, B. Chinnock, P. de Miranda and H.H. Balfour. "Human pharmacokinetics of the antiviral drug DHPG." *Clin. Pharmacol. Therap.* 40: 281-286 (1986).

47. L.E. Riad, K.K.H. Chan, W.E. Wagner and R.J. Sawchuk. "Simultaneous first- and zero-order absorption of carbamazepine tablets in humans." *J. Pharm. Sci.* 75(9): 897-900 (1986).

48. D.K. Yu and R.J. Sawchuk. "Pharmacokinetics of propylene glycol in the rabbit." *J. Pharmacok. Biopharm.* 15: 1-8 (1987).

49. A.K. Shah and R.J. Sawchuk. "Liquid chromatographic determination of cyclosporine and its metabolites in blood." *Clinical Chemistry* 34: 1467-1471 (1988).

50. M.A. Hedaya and R.J. Sawchuk. "A sensitive liquid chromatographic method for the determination of 3'-azido-3'-deoxythymidine (AZT) in plasma and urine." *Clinical Chemistry* 34:1565-1568 (1988).

51. L.E. Riad and R.J. Sawchuk. "A sensitive method for the simultaneous determination of carbamazepine, its epoxide and transdiol metabolites in plasma by microbore liquid chromatography." *Clinical Chemistry* 34: 1863-1866 (1988).

52. M.A. Hedaya and R.J. Sawchuk. "Effect of probenecid on the renal clearance of zidovudine (AZT) and its distribution into cerebrospinal fluid." *J. Pharm. Sci.* 78: 716-722 (1989).

53. R.J. Sawchuk and M.A. Hedaya. "Modeling the enhanced uptake of zidovudine (AZT) into cerebrospinal fluid: the effect of probenecid." *Pharmaceutical Research* 7: 332-338 (1990).

54. M.A. Hedaya, W.F. Elmquist and R.J. Sawchuk. "Probenecid inhibits the metabolic and renal clearance of zidovudine (AZT) in human volunteers." *Pharmaceutical Research* 7: 411-417 (1990).

55. R. Padmanabhan, J.B. Phipps, G.A. Lattin, and R.J. Sawchuk. "*In vitro* and *in vivo* evaluation of transdermal iontophoretic delivery of hydromorphone." *J. Contr. Rel.* 11: 123-135, (1990).

56. M.A. Hedaya and R.J. Sawchuk. "A sensitive and specific liquid-chromatographic assay for determination of ganciclovir in plasma and urine and its application to pharmacokinetic studies in the rabbit." *Pharmaceutical Research* 7: 1113-1118 (1990).

57. W.F. Elmquist, L.E. Riad, I.E. Leppik and R.J. Sawchuk. "The relationship between carbamazepine urine and plasma concentrations: implications for therapeutic drug monitoring." *Pharmaceutical Research* 8: 282-284 (1991).

58. L.E. Riad and R.J. Sawchuk. "Effect of polyethylene glycol 400 on the intestinal permeability of carbamazepine in the rabbit." *Pharmaceutical Research* 8: 491-497 (1991).

59. L.E. Riad, K.K. Chan, and R.J. Sawchuk. "Determination of the relative formation and elimination clearance of two major carbamazepine metabolites in humans: a comparison between traditional and pooled sample analysis." *Pharmaceutical Research* 8: 541-543 (1991).

60. S.L. Wong and R.J. Sawchuk. "High performance liquid chromatographic determination of 2',3,-didehydro-3'-deoxythymidine (D4T) in human and rabbit plasma and urine and its application to pharmacokinetic studies in the rabbit." *Pharmaceutical Research* 8: 619-623 (1991).

61. A.K. Shah and R.J. Sawchuk. "Effect of coadministration of intralipid on the pharmacokinetics of cyclosporine in the rabbit." *Biopharm. Drug Disp.* 12: 457-466 (1991).

62. L.E. Riad and R.J. Sawchuk. "Absorptive clearance of carbamazepine and selected metabolites in rabbit intestine." *Pharmaceutical Research* 8: 1050-1055 (1991).

63. A.K. Shah, R. C. Brundage, A. Gratwohl and R.J. Sawchuk. "Pharmacokinetic model for the subcutaneous absorption of cyclosporine during chronic dosing in the rabbit." *J. Pharm. Sci.* 81: 491-495 (1992).

64. S.L. Wong, M.A. Hedaya and R.J. Sawchuk. "Competitive inhibition of zidovudine clearance by probenecid during continuous co-administration." *Pharmaceutical Research* 9: 228-235 (1992).

65. S.L. Wong, Y. Wang and R.J. Sawchuk. "Analysis of zidovudine distribution to specific regions in rabbit brain using microdialysis." *Pharmaceutical Research* 9: 332-338 (1992).

66. S.L. Wong, K.S. Van Belle and R.J. Sawchuk. "Distributional transport kinetics of zidovudine between plasma and brain extracellular fluid/cerebrospinal fluid in the rabbit: investigation of the inhibitory effect of probenecid utilizing microdialysis." *J. Pharmacol. Exp. Therap.* 264: 899-909 (1993).

67. Y. Wang, S.L. Wong, and R.J. Sawchuk. "Microdialysis calibration using retrodialysis and zero-net flux: application to a study of the distribution of zidovudine to rabbit cerebrospinal fluid and thalamus." *Pharmaceutical Research* 10: 1411-1419 (1993).

68. L.E. Riad and R.J. Sawchuk. "Transient steady state analysis: application in the determination of the relative formation and elimination clearances of two major carbamazepine metabolites in humans." *Pharmaceutical Research* 10: 1090-1092 (1993).

69. E.H. Abdennebi, N. Khales, R.J. Sawchuk and C.M. Stowe. "Thiamphenicol pharmacokinetics in sheep." *J. Vet. Pharmacol. Therap.* 17: 12-16 (1994).

70. R.L. Oberle, H. Das, S.L. Wong, K.K.H. Chan, and R.J. Sawchuk. "Pharmacokinetics and metabolism of diclofenac sodium in Yucatan miniature pigs." *Pharmaceutical Research* 11: 698-703 (1994).

71. B.K. Malhotra, M. Lemaire, and R.J. Sawchuk. "Investigation of the distribution of EAB 515 to cortical ECF and CSF in freely moving rats utilizing microdialysis." *Pharmaceutical Research* 11: 1223-1232 (1994).

72. E.H. Abdennebi, R.J. Sawchuk and C.M. Stowe. "Thiamphenicol pharmacokinetics in beef and dairy cattle." *J. Vet. Pharmacol. Therap.* 17: 365-368 (1994).

73. W.F. Elmquist, K.K.H. Chan, V.A. John and R.J. Sawchuk. "Transsynovial distribution: synovial mean transit time of diclofenac and other non-steroidal antiinflammatory drugs." *Pharmaceutical Research* 12: 1689-1697 (1994).

74. L.E. Riad, R.J. Sawchuk, M.M. MacAlary, and K.K.H. Chan. "Effect of food on the multiple peak behavior of diclofenac sodium slow release tablets in humans." *Amer. J. Therap.* 2: 1-6 (1995).

75. A.K. Shah, R.C. Brundage, K.D. Lake and R.J. Sawchuk. "The estimation of the plasma free fraction of cyclosporine in rabbits and heart transplant patients: the application of a physiologic model of renal clearance." *Biopharm. Drug Disp.* 16: 59-70 (1995).

76. R.J. Sawchuk, J.A. Maloney, L.L. Cartier, R.J. Rackley, K.K.H. Chan and H.S.L. Lau. "Analysis of diclofenac and four of its metabolites in human urine by HPLC." *Pharmaceutical Research* 12: 756-752 (1995).

77. Y. Wang and R.J. Sawchuk. "Zidovudine transport in the rabbit brain during intravenous and intracerebroventricular infusion." *J. Pharm. Sci.* , 84: 871-876 (1995).

78. E.D. Kharasch, M.D. Karol, C. Lanni and R.J. Sawchuk. "Clinical sevoflurane metabolism and disposition; I. Sevoflurane and metabolite pharmacokinetics." *Anesthesiology* 82: 1369-1378 (1995).

79. B.K. Malhotra, M. Lemaire, J.F. Brouillard, and R.J. Sawchuk. "High-performance liquid chromatographic Analysis of (S)-□□ amine5-phosphonomethyl[1,1'-biphenyl]-3-propanoic acid □EAB 515) microdialysate (on-line) and in plasma ultrafiltrate of freely moving rats" *J. Chromatog B: Biomed Appl.* 679: 167-176 (1996).

80. B.W.Y. Cheung, Y. Wang, M. Brewster, and R.J. Sawchuk. "Brain delivery of carbamazepine during intravenous administration of polyethylene glycol and hydroxyprpyl-□-cyclodextrin formulations. *s.t.p. pharma sciences* 7: 78-84 (1997).

81. Z. Yang, RC Brundage, R.H. Barbhaiya, and R.J. Sawchuk "Microdialysis studies of the distribution of stavudine into the central nervous system in the freely-moving rat. *Pharmaceutical Research*. 14: 865-72 (1997)

82. J.W. Bartges, C.A. Osborne, L.J. Felice, L.A. Koehler, L.K. Ulrich, K.A. Bird, M. Chen, and R.J. Sawchuk. "Bioavailability and pharmacokinetics of intravenously and orally administered allopurinol in healthy beagles" *American Journal of Veterinary Research*. 58: 504-10 (1997)

83. R. Dvorsky, S. Balaz, and R.J. Sawchuk. "Kinetics of subcellular distribution of compounds in simple biosystems and its use in QSAR. J. Theoretical Biology. 185: 213-22 (1997).

84. W.F. Elmquist and R.J. Sawchuk. "Application of microdialysis in pharmacokinetics. (Invited Review) Pharmaceutical Research 14: 267-288 (1997).

85. M. Brewster, W.R. Anderson, D. Meinsma, D. Moreno, A.I. Webb, L. Pablo, K.S. Estes, H. Derendorf, N. Bodor, R.J. Sawchuk, B.W.Y. Cheung, and E Pop. "Intravenous and Oral Pharmacokinetic Evaluation of a 2-hydroxyprpyl-β-cyclodextrin-based Formulation of Carbamazepine in the dog: Comparison with Commercially Available Tablets and Suspensions. J. Pharm. Sci. 86: 335-339 (1997)

86. B.K. Malhotra, R.C. Brundage, M. Lemaire, and R.J. Sawchuk. "Modeling the route of administration-based enhancement in the brain delivery of EAB 515, studied by microdialysis" .J Drug Targetting 4: 277-288 (1997).

87. L.E. Riad and R.J. Sawchuk. "A partial area difference method for estimating elimination rate constants and distribution volumes of metabolites." J. Pharm Sci. 87: 769-773 (1998).

88. Z. Yang and R.J. Sawchuk "Investigation of distribution, transport and uptake of anti-HIV Drugs to the central nervous system." *Advanced Drug Delivery Reviews* 39: 5-31 (1999).

89. S.C. Chen, R. J. Sawchuk, R.C. Brundage, C Horvath, H.V. Mendenhall, R.A. Gunther, and R.A. Braeckman. "Plasma and lymph pharmacokinetics of recombinant human interleukin-2 and PEG-modified interleukin-2 in pigs.". *JPET* 293: 248-259 (2000).

90. M,. Davidson, A. Marwah, R.J. Sawchuk, K. Maki, P. Marwah, C. Weeks, and H. Lardy,. "Safety and pharmacokinetics of escalating doses of 3-acetyl-7-oxo-dehydroepianrosterone in healthy male volunteers" *Clin Invest. Med.* 23: 300-310 (2000).

91. W.F. Elmquist and R.J. Sawchuk. "Use of microdialysis in drug delivery studies." *Advanced Drug Delivery Reviews.* 45: 123-124 (2000).

92. R.J. Sawchuk and W.F. Elmquist. "Microdialysis in the study of drug transporters in the CNS." *Advanced Drug Delivery Reviews.* 45: 295-307 (2000).

93. R.J. Sawchuk, D.J. Mulford, and M.D. Mayer. "Pharmacokinetics of a new cephalosporin." *J. Resp. Dis.* 22: No. 8 Suppl. S43-S51 (2001).

94. Y. Huang, P. Ji, A. Inano, Z. Yang, G.S. Giebink, and R.J. Sawchuk. "Microdialysis studies of the middle ear distribution kinetics of amoxicillin in the awake chinchilla." *J. Pharm. Sci.*, 90: 2088-2098 (2001).

95. G. Gan, L.L. Cartier, Y. Huang, Z. Yang, and R.J. Sawchuk. "Intestinal absorption and presystemic elimination of the prokinetic agent, EM574, in the rabbit." *J. Pharm. Sci.*, 91: 218-228 (2002).

96. T. Zhu, B.W.Y. Cheung, L.L. Cartier, G.S. Giebink, and R.J. Sawchuk. "Simultaneous Intravenous and Intramiddle-Ear Dosing to Determine Cefditoren Influx and Efflux Clearances in Middle Ear Fluid in Freely Moving Chinchillas." *J. Pharm. Sci.*, 92: 1947-1956 (2003).

97. J.Z. Peng, R.P. Remmel, and R.J. Sawchuk. "Inhibition of murine cytochrome P4501A by tacrine: in vitro studies." *Drug Metab Dispos* 32: 805-812 (2004).

98. B.W.Y. Cheung, L.L. Cartier, H.Q. Russlie and R.J. Sawchuk. "The Application of Sample Pooling Methods for Determining AUC, AUMC and Mean Residence Times in Pharmacokinetic Studies" *Fundamental & Clinical Pharmacology*, 19, 347-354 (2005).

99. Z.Yang, Y. Huang, G. Gan, and R. J. Sawchuk. "Microdialysis Evaluation of the Brain Distribution of Stavudine Following Intranasal and Intravenous Administration to Rats." *J Pharm. Sci.* 94, 1577-88 (2005).

100. P. Jacobson, J. Rogosheske, J. N. Barker, K. Green, J. Ng, D. Weisdorf, Y. Tan, J. Long, R. Remmel, R. Sawchuk, P. McGlave. Relationship of mycophenolic acid exposure to clinical outcome after hematopoietic cell transplantation. *Clin Pharmacol Ther.* 78: 486-500 (2005).

101. R.J. Sawchuk, B.W.Y. Cheung, P. Ji, and L. L. Cartier. "Microdialysis Studies of the Distribution of Antibiotics to Chinchilla Middle Ear Fluid." *Pharmacotherapy* 25 (12): Part 2 140S-145S (2005)

102. B. W. Y. Cheung, W. Liu, P. Ji, L. L. Cartier, Z. Li, N. Mostafa, and R. J. Sawchuk. "The Chinchilla Microdialysis Model for the Study of Antibiotic Distribution to Middle Ear Fluid." *AAPSJ* 8 (1), E41-E47 (2006)

103. Z. Yang, P. Manitpisitkul and R. J. Sawchuk. "In Situ Studies of Regional Absorption of Lobucavir and Ganciclovir from Rabbit Intestine and Predictions of Dose-Limited Absorption and Associated Variability in Humans *J. Pharm. Sci.*, 95: 2276-2292 (2006).

104. Z. Yang, G. Gan and R. J. Sawchuk. "Correlation between Net Water Flux and Absorptive Clearance Determined from In Situ Intestinal Perfusion Studies Does Not Necessarily Indicate a Solvent Drag Effect." *J. Pharm. Sci.*, 96: 517-21 (2007).

105. Chaurasia CS. Muller M. Bashaw ED. Benfeldt E. Bolinder J. Bullock R. Bungay PM. DeLange EC. Derendorf H. Elmquist WF. Hammarlund-Udenaes M. Joukhadar C. Kellogg DL Jr. Lunte CE. Nordstrom CH. Rollema H. Sawchuk RJ. Cheung BW. Shah VP. Stahle L. Ungerstedt U. Welty DF. Yeo H. AAPS-FDA Workshop White Paper: microdialysis principles, application, and regulatory perspectives. *Journal of Clinical Pharmacology.* 47(5): 589-603 (2007).

106. Y. Huang, Z. Yang,, L. Cartier, B. Cheung, and R. J. Sawchuk "Estimating Amoxicillin Influx/Efflux in Chinchilla Middle Ear Fluid and Simultaneous Measurement of Antibacterial Effect" *Antimicrobial Agents and Chemotherapy*, 51 (12): 4336-4341 (2007).

107. J. Karjagin, S. Lefeuvre, K. Oselin, K. Kipper, S. Marchand, A. Tikkerberi, J. Starkopf, W. Couet and R. J. Sawchuk. "Pharmacokinetics of Meropenem Determined by Microdialysis in the Peritoneal Fluid of Patients With Severe Peritonitis Associated With Septic Shock" *Clin Pharmacol Ther*. 83 (3): 452-459 (2008).

108. D.P. Scher, R. J. Sawchuk, B. H. Alexander, and J. L. Adgate. "Estimating Absorbed Dose of Pesticides in a Field Setting using Biomonitoring Data and Pharmacokinetic Models. *J Toxicol Environ Health A.* 71 (6): 373-83 (2008).

109. R. J. Sawchuk. Liquid-Chromatographic Determination of Cyclosporin A in Blood and Plasma. Citation Classic. *Clin Chem* 54: 2076-2077 (2008).

110. C. Dahyot-Fizelier, S. Lefeuvre, L. Laksiri, S. Marchand, R. J. Sawchuk, W. Couet, and O. Mimoz. Kinetics of Imipenem Distribution into the Peritoneal Fluid of Patients with Severe Peritonitis Studied by Microdialysis. *Clin Pharmacokinetics* 49(5): 323-334 (2010).

ABSTRACTS

1. R.J. Sawchuk and T.N. Tozer. "Mixed first-order and capacity-limited elimination of 4-aminoantipyrine in the rabbit under steady-state conditions." Fifth International Congress of Pharmacology, Abstracts of Volunteer Papers, p. 202, 1972.

2. D.E. Zaske, R.B. Johnson, M.T. Spiline, R.J. Sawchuk and K.W. Miller. "Utilization of total body clearance calculations in the determination of I.V. dose therapy of theophylline in asthmatic patients." The Pharmacologist 15, 206 (1973)

3. R.J. Sawchuk, O.A. Olusanya, D.E. Zaske and K.W. Miller. "Evaluation of the bioequivalence of three theophylline preparations." Proceedings of the Minnesota Society of Internal Medicine, p. 2, October 1974.

4. K.W. Miller, P.B. Johnson, D.E. Zaske and R.J. Sawchuk. "Clinical usefulness of measuring serum theophylline levels." Proceedings of the Minnesota Society of Internal Medicine, p. 2, October 1974.

5. D. Schuppan, R.J. Sawchuk, C.S. Hansen, M.L. Funk, R.E. Ober and L.A. Fernandez. "Comparative study of plasma levels produced by two formulations of R-802, a new synthetic urinary tract anti-bacterial agent: pharmacokinetics during single and multiple dosing." APhA Academy of Pharmaceutical Sciences. Abstract. Atlanta, GA, November 1975.

6. D.E. Zaske, D.N. Gerding, R.G. Strate, R.J. Sawchuk and R.M. Jager. "Rapid elimination of gentamicin in burn patients." Annual Meeting of the American Burn Association. Abstract. Denver, CO, 1975.

7. M.L. Rylander, W.A. Wargin, R.J. Sawchuk, J.W. McBride, E. Haus and D.E. Zaske. "The clinical efficacy and pharmacokinetics of propranolol in hypertensive patients." Eleventh Mid-Year Clinical Meeting of the American Society of Hospital Pharmacists, December 1976.

8. D.L. Uden, D.E. Zaske, R.J. Sawchuk and R.G. Strate. "Gentamicin kinetics in burn patients." Eleventh Mid-Year Meeting of the American Society of Hospital Pharmacists, December 1976.

9. D.E. Zaske, R.G. Strate and R.J. Sawchuk. "The necessity of increased doses of amikacin in burn patients." Eleventh Mid-Year Meeting of the American Society of Hospital Pharmacists, December 1976.

10. W.A. Wargin, R.J. Sawchuk, R.J. Cipolle, D.E. Zaske and R.G. Strate. "Application of a kinetic model for establishing gentamicin dosing regimens based on individual patient parameters." American Pharmaceutical Association Academy of Pharmaceutical Services, November 1976.

11. R.J. Cipolle, R.J. Sawchuk, R.G. Strate and D.E. Zaske. "The clinical application of a kinetic model for individualizing gentamicin dose and dosing interval." Interscience Conference on Antimicrobial Agents and Chemotherapy, October 1976.

12. K.W. Miller, R.J. Sawchuk, J.J. Fordice and D.E. Zaske. "The clinical pharmacokinetics laboratory of the University of Minnesota College of Pharmacy." American Association of Colleges of Pharmacy, July 1976.

13. R.J. Cipolle, R.J. Sawchuk and D.E. Zaske. "Computer-assisted individualized gentamicin dosing." The Second Annual Mid-Western Conference for Clinical Pharmacy Residents, Preceptors and Teachers, 1976.

14. J.W. McBride, M.L. Rylander, W.A. Wargin, R.J. Sawchuk and D.E. Zaske. "Propranolol kinetics in hypertension: a single dose study." Minnesota Society of Internal Medicine, October 1976.

15. R.A. Whyte, D.L. Larson, R.J. Sawchuk and P.S. Portoghese. "Relationships of mouse brain-plasma transfer constants of N-substituted normeperidines to their partition coefficients." Fourteenth Annual Medicinal Chemistry Meeting-in-Miniature, Minneapolis, MN, 1976.

16. D.E. Zaske, R.G. Strate and R.J. Sawchuk. "Increased dosage requirements of amikacin in burn patients." Ninth Annual American Burn Association, Anaheim, CA, March 1977.

17. H.G. McCoy, R.J. Cipolle, S.M. Ehlers, R.J. Sawchuk and D.E. Zaske. "Severe methanol poisoning: pharmacokinetic basis for successful treatment with ethanol." 12th Annual ASHP Midyear Clinical Meeting, Atlanta, GA, December 1977.

18. J.C. Cloyd, D.E. Bosch and R.J. Sawchuk. "Concentration-time profile of phenytoin after admixture with small volumes of intravenous fluids." 12th Annual ASHP Midyear Clinical Meeting, Atlanta, GA, December 1977.

19. R.J. Sawchuk, S.M. Pepin, J.C. Cloyd, I.E. Leppik and R.J. Gumnit. "Steady-state analysis of phenytoin kinetics applied to dose adjustments in epileptic patients with comparison to nomogram." 12th Annual ASHP Midyear Clinical Meeting, Atlanta, GA, December 1977.

20. G.R. Matzke, J.C. Cloyd, R.J. Sawchuk. "Acute phenytoin and primidone intoxication: A pharmacokinetic analysis." 12th Annual ASHP Midyear Clinical Meeting, Atlanta, GA, December 1977.

21. J.C. Rotschafer, C. Foley, D. Zaske and R. Sawchuk. "Glutethimide overdose: clinical and kinetic observations of glutethimide and a metabolite." 12th Annual ASHP Midyear Clinical Meeting, Atlanta, GA, December 1977.

22. R. Carter, D. Zaske, S. Ehlers and R. Sawchuk. "Charcoal hemoperfusion: an effective method for removal of theophylline in a severe overdose." 12th Annual ASHP Midyear Clinical Meeting, Atlanta, GA, December 1977.

23. R.J. Sawchuk, I.E. Leppik and R.E. Cranford. "Pharmacokinetics of large dose intravenous phenytoin therapy." 11th World Congress of Neurology Meeting, Amsterdam, The Netherlands, September 11-16, 1977.

24. J.D. Wirtschafter, C.R. Volk and R.J. Sawchuk. "Trans-aqueous diffusion of acetylcholine to denervated iris sphincter muscle: a hypothetical mechanism for the tonic pupil syndrome (Adie's Syndrome)." Association of Research in Vision and Ophthalmology, Sarasota, FL, May 1978.

25. W.A. Wargin, M.L. Rylander, R.J. Sawchuk and J.W. McBride. "The pharmacokinetics of orally administered propranolol in hypertensive patients." APhA Academy of Pharmaceutical Sciences, Phoenix, AZ, 1977.

26. R.J. Sawchuk, J.C. Cloyd, I.E. Leppik, S.M. Pepin and R.J. Gumnit. "Steady-state analysis of phenytoin kinetics applied to dose adjustments in epileptic patients." APhA Academy of Pharmaceutical Sciences, Phoenix, AZ, 1977.

27. R.J. Cipolle, R.G. Strate, D.E. Zaske and R.J. Sawchuk. "Amikacin pharmacokinetics: effect of age on elimination." Inter-Science Conference on Antimicrobial Agents and Chemotherapy, New York, 1977.

28. D.E. Zaske, K.B. Crossley, R.J. Sawchuk, D.L. Uden and K.E. Mead. "Vancomycin kinetics: excessive steady-state serum levels resulting from recommended dosages." Interscience Conference on Antimicrobial Agents and Chemotherapy, New York, 1977.

29. D.E. Zaske, R.J. Sawchuk and R.G. Strate. "Increased dosage requirements of amikacin in burn patients." American Burn Assoc., 9th Annual Meeting, Anaheim, CA, April 1977.

30. S.E. Chen, R.J. Sawchuk and E.J. Staba. "Pharmacokinetics of ginseng compounds." 2nd International Ginseng Symposium, Seoul, Korea, 1978.

31. J.C. Cloyd, R.J. Sawchuk, I.E. Leppik and S.M. Pepin. "The direct linear plot: use in estimating Michaelis-Menten parameters and individualizing phenytoin dosage regimens in epileptic patients." Epilepsy International Symposium, Vancouver, Canada, September 10-14, 1978.

32. I.E. Leppik, V. Ramani, R.J. Sawchuk and R.J. Gumnit. "Seizures and altered phenytoin metabolism in mononucleosis." Epilepsy International Symposium, Vancouver, Canada, September 10-14, 1978.

33. I.E. Leppik, J. Cloyd, R. Sawchuk and D. Fryd. "Coefficient of variation as an objective measure of compliance." Epilepsy International Symposium, Vancouver, Canada, September 10-14, 1978.

34. E. Ramsay, I. Leppik, R. Strauss, B.J. Wilder and R.J. Sawchuk. "Plasma clearance and volume of distribution of phenytoin during pregnancy." Epilepsy International Symposium, Vancouver, Canada, September 10-14, 1978.

35. R.L. Kriel, J.C. Cloyd , K.H. Green, R.J. Sawchuk, L.A. Lockman and R.M. Eggerth. "The pharmacokinetics of valproic acid in children." Child Neurology Society, Hanover, NH, September 1979.

36. P. Subronto, C.M. Stowe and R. Sawchuk. "Pharmacokinetics of aminophylline in dairy cattle." Sixtieth Conference of Research Workers in Animal Diseases, Chicago, IL, November 26-27, 1979.

37. I.E. Leppik, J. Shope, R.J. Sawchuk, W.A. Hauser and B. Van Dyne. "Variability of antiepileptic drug levels during chronic therapy." American Academy of Neurology, New Orleans, April 28-May 3, 1980.

38. R.M. Eggerth, J.C. Cloyd, R.L. Kriel and R.J. Sawchuk. "Valproic acid pharmacokinetics in epileptic children." 12th Annual Graduate Student Pharmaceutics Research Meeting, Columbus, OH, June 25, 1980.

39. R. Sylvester, R.J. Sawchuk and R. Perri. "Decreased phenytoin absorption with cis-platinum, vinblastine and bleomycin therapy." American Society of Clinical Oncology Abstracts, 1981.

40. I.E. Leppik, J. Fischer, R. Kriel and R.J. Sawchuk. "Altered phenytoin clearance during febrile illness." American Academy of Neurology, Toronto, Ontario, April 1981.

41. W.M. Awni and R.J. Sawchuk. "Preliminary pharmacokinetic studies of cyclosporin A in animals." Fourteenth Annual Graduate Student Pharmaceutics Research Meeting, Morgantown, WV, June 1982.

42. R.M. Ferguson, R. Fidelus-Gort, J.J. Rynasiewicz, K. Gajl-Peczalska, and R.J. Sawchuk. "The immunosuppressive action of cyclosporin A (CSA) in man." Annual Meeting of the American Society of Transplant Surgery, London, August 1982.

43. J.H. Fischer, I.E. Leppik, R.L. Kriel, J.D. MacDonald and R.J. Sawchuk. "Clinical significance of absorption differences between carbamazepine tablet and suspension formulations." Fourteenth Epilepsy International Symposium, London, August 1982.

44. L.E. Riad and R.J. Sawchuk. "The pharmacokinetics of carbamazepine in the rabbit." The Second University of Minnesota/3M Research Poster Session, Minneapolis, MN, May 1984.

45. W.M. Awni and R.J. Sawchuk. "Cyclosporine pharmacokinetics in the rabbit." The Second University of Minnesota/3M Research Poster Session, Minneapolis, MN, May 1984.

46. W.F. Elmquist, D.K. Yu and R.J. Sawchuk. "Propylene glycol pharmacokinetics." The Second University of Minnesota/3M Research Poster Session, Minneapolis, MN, May 1984.

47. C. Fletcher, R. Sawchuk, B. Chinnock, C. Vicary, L.E. Kirk, P. De Miranda, and H.H. Balfour, Jr. "Human pharmacokinetics of 9-[2-Hydroxy-1-(hydroxymethyl)ethoxymethyl]guanine." Interscience Conference on Antimicrobial Agents and Chemotherapy, Minneapolis, MN, September 28, 1985.

48. R.J. Sawchuk, L. Riad and K.K.H. Chan. "Simultaneous first- and zero-order absorption of carbamazepine (Tegretol) tablets in humans." 16th Epilepsy International Congress, Hamburg, West Germany, September 6, 1985.

49. W.M. Awni and R.J. Sawchuk. "Differential absorption of cyclosporine from two consecutive anatomic regions of the small intestine using an *in situ* perfusion model." Academy of Pharmaceutical Sciences Meeting, Minneapolis, MN, October 20, 1985.

50. H.A. Abou-Auda and R.J. Sawchuk. "Absorption and metabolism of salicylate esters in rabbit small intestine." Academy of Pharmaceutical Sciences Meeting, Minneapolis, MN, October 18-24, 1985.

51. L.E. Riad, K.K.H. Chan and R.J. Sawchuk. "Contribution of epoxide pathway to induction of carbamazepine metabolism during multiple dosing in humans." Academy of Pharmaceutical Sciences meeting, Minneapolis, MN, October 18-24, 1985.

52. L.E. Riad and R.J. Sawchuk. "Contribution of epoxide formation to the auto-induction of carbamazepine in the rabbit." Academy of Pharmaceutical Sciences Meeting, Minneapolis, MN, October 18-24, 1985.

53. R.M. Eggerth and R.J. Sawchuk. "Investigation of the dose-dependent elimination of phenytoin in the rabbit." Academy of Pharmaceutical Sciences Meeting, Minneapolis, MN, October 18-24, 1985.

54. L.E. Riad and R.J. Sawchuk. "Determination of the relative formation of elimination clearance of carbamazepine metabolites in humans: a comparison of traditional and pooled sample analysis." Third European Congress of Biopharmaceutics and Pharmacokinetics, Freiburg, Germany, April 21, 1987.

55. W.F. Elmquist, D.K. Yu, G. Solis and R.J. Sawchuk. "Physiological modelling of the dependence of renal clearance on urine flow: propylene glycol pharmacokinetics in man." Third European Congress of Biopharmaceutics and Pharmacokinetics, Freiburg, Germany, April 21, 1987.

56. A.K. Shah, K.D. Lake and R.J. Sawchuk. "Blood levels of cyclosporine A and its metabolites in rabbit and man." American Association of Pharmaceutical Scientists Annual Meeting, Boston, MA, June 1987.

57. K.D. Lake, Pharm.D.*, A.K. Shah, Ph.D., R. Emery, M.D. and R.J. Sawchuk, Ph.D. "Measurement of cyclosporine metabolites in the blood of heart transplant recipients." American College of Clinical Pharmacy Annual Meeting, May 1987.

58. A.K. Shah, A. Gratwohl and R.J. Sawchuk. "Subcutaneous absorption of cyclosporine in rabbits." 2nd International Congress on Cyclosporine, Washington, DC, November 4-7, 1987.

59. M.A. Hedaya and R.J. Sawchuk. "The effect of probenecid on the renal excretion of azidothymidine (AZT) in the rabbit." Third Annual Meeting, AAPS, Orlando, FL, October 29-November 4, 1988.

60. W.F. Elmquist, K.K.H. Chan, V.A. John and R.J. Sawchuk. "Transsynovial distribution of diclofenac. " Third Annual Meeting, AAPS, Orlando, FL, October 29-November 4, 1988.

61. L.E. Riad and R.J. Sawchuk. "Administration of site-related differences in carbamazepine disposition in the rabbit." Third Annual Meeting, AAPS, Orlando, FL, October 29-November 4, 1988.

62. A.K. Shah and R.J. Sawchuk. "Effect of urine flow on the renal clearance of cyclosporine in rabbit." Third Annual Meeting, AAPS, Orlando, FL, October 29-November 4, 1988.

63. W.F. Elmquist, L.E. Riad, I.E. Leppik and R.J. Sawchuk. "Physiological modelling of the dependence of renal clearance on urine flow: carbamazepine and two metabolites in man." Third Annual Meeting, AAPS, Orlando, FL, October 29-November 4, 1988.

64. M.A. Hedaya and R.J. Sawchuk. "Pharmacokinetic analysis of the enhanced distribution of zidovudine into rabbit cerebrospinal fluid caused by probenecid." V. International Conference on AIDS, Montreal, June 4-9, 1989.

65. Y. Wang, M.A. Hedaya and R.J. Sawchuk. "Effect of mannitol IV infusion on distribution of zidovudine between plasma and cerebrospinal fluid in rabbits." V. International Conference on AIDS, Montreal, June 4-9, 1989.

66. M.A. Hedaya, W.F. Elmquist and R.J. Sawchuk. University of Minnesota, Minneapolis, Minnesota, USA. "Probenecid inhibits the metabolic and renal clearances of zidovudine in human volunteers." V. International Conference on AIDS, Montreal, June 4-9, 1989.

67. M.A. Hedaya and R.J. Sawchuk. "A sensitive and specific HPLC method for the determination of zidovudine and zidovudine glucuronide in plasma and urine." V. International Conference on AIDS, Montreal, June 4-9, 1989.

68. M.A. Hedaya and R.J. Sawchuk. "A simple and specific liquid-chromatographic method for determination of ganciclovir (DHPG) in plasma and urine." Fourth Annual Meeting, AAPS, Atlanta, GA, October 21-26, 1989.

69. L.E. Riad and R.J. Sawchuk. "Intestinal absorption of carbamazepine in the rabbit." Fourth Annual Meeting, AAPS, Atlanta, GA, October 21-26, 1989.

70. A.J. Shah and R.J. Sawchuk. "The effect of altering blood lipids on the pharmacokinetics of cyclosporine in the rabbit." Fourth Annual Meeting, AAPS, Atlanta, GA, October 21-26, 1989.

71. M.A. Hedaya, W.F. Elmquist and R.J. Sawchuk. "Mechanism of zidovudine (AZT) dose-sparing by probenecid in humans." Fourth Annual Meeting, AAPS, Atlanta, GA, October 21-26, 1989.

72. W.F. Elmquist and R.J. Sawchuk. "Tissue mean transit time determination from steady-state partition coefficients and tissue/plasma concentration ratios in the post-distributive phase." Fourth Annual Meeting, AAPS, Atlanta, GA, October 21-26, 1989.

73. L.E. Riad and R.J. Sawchuk. "Relative bioavailability and effects of food on plasma levels of diclofenac sodium following a single oral dose of Voltaren 100-mg SR tablet." Fourth Annual Meeting, AAPS, Atlanta, GA, October 21-26, 1989.

74. O.H. Chan and R.J. Sawchuk. "Intestinal absorption of diltiazem in the rabbit." Fourth Annual Meeting, AAPS, Atlanta, GA, October 21-26, 1989.

75. R.J. Sawchuk. "Pharmacokinetic and analytical considerations in monitoring zidovudine (AZT) levels in children with AIDS." The Fourth International Congress on Pediatric Laboratory Medicine, Washington, DC, August 23, 1989.

76. K.D. Lake, A.K. Shah, R.W. Emery, D.R. Holder and R.J. Sawchuk. "The effect of urine flow rate on the renal clearance of cyclosporine in heart transplant recipients." International Society for Heart Transplantation, Tenth Annual Meeting, Fort Lauderdale, FL, April 4-6, 1990.

77. R.J. Sawchuk. "Effect of temperature and medium of analysis on CsA concentration." Canadian Consensus Meeting on Cyclosporine Monitoring, Minaki Lodge, Ontario, May 10-13, 1990.

78. H. Das, S.W. Wong, K. Chan, R.J. Sawchuk and R.L. Oberle. "Pharmacokinetics and metabolism of diclofenac sodium (Voltaren) after IV and oral administration to Yucatan miniswine." Eastern Regional AAPS meeting, New Brunswick, NJ, June 3-5, 1990.

79. S.M. Wong and R.J. Sawchuk. "Interaction of zidovudine and probenecid at steady state." NATO Advanced Study Institute Symposium "New Trends in Pharmacokinetics." Erice, Sicily, September 4-15, 1990.

80. W.F. Elmquist and R.J. Sawchuk. "Tissue mean transit time determination from steady-state partition coefficients and tissue/plasma concentration ratios in the postdistributive phase." NATO Advanced Study Institute Symposium "New Trends in Pharmacokinetics," Erice, Sicily, September 4-15, 1990.

81. A.K. Shah, R.J. Sawchuk, A. Gratwohl and R.C. Brundage. "Modeling subcutaneous absorption of cyclosporine A in rabbits." NATO Advanced Study Institute Symposium "New Trends in Pharmacokinetics," Erice, Sicily, September 4-15, 1990.

82. L.E. Riad, K.K.H. Chan and R.J. Sawchuk. "Effects of dosing rate on carbamazepine enzymatic induction in normal volunteers." NATO Advanced Study Institute Symposium "New Trends in Pharmacokinetics," Erice, Sicily, September 4-15, 1990.

83. W.F. Elmquist, L.E. Riad, I.E. Leppik and R.J. Sawchuk. "The relationship between carbamazepine urine and plasma concentrations: implications for therapeutic drug monitoring." AAPS Fifth Annual Meeting, Las Vegas, NV, November 4-8, 1990.

84. S.M. Wong, L.E. Riad, P. Degen, V. John, K. Chan and R.J. Sawchuk. "Comparison of plasma concentrations of diclofenac sodium and its metabolites during single and multiple dosing of Voltaren SR tablet in humans." AAPS Fifth Annual Meeting, Las Vegas, NV, November 4-8, 1990.

85. O.H. Chan and R.J. Sawchuk. "Saturable first-pass elimination of diltiazem during intestinal absorption in the rabbit." AAPS Fifth Annual Meeting, Las Vegas, NV, November 4-8, 1990.

86. L.E. Riad and R.J. Sawchuk. "Carbamazepine enzymatic induction: extent and effects of dosing rate in normal volunteers." AAPS Fifth Annual Meeting, Las Vegas, NV, November 4-8, 1990.

87. Y.-F. Wang, M.A. Hedaya and R.J. Sawchuk. "Comparative absorption and disposition pharmacokinetics of AZT and AZddU in rabbits." AAPS Fifth Annual Meeting, Las Vegas, NV, November 4-8, 1990.

88. S.L. Wong and R.J. Sawchuk. "Investigation of distribution of zidovudine into the brain by microdialysis." AAPS Fifth Annual Meeting, Las Vegas, NV, November 4-8, 1990.

89. S.L. Wong and R.J. Sawchuk. "Interaction of zidovudine and probenecid at steady state." AAPS Fifth Annual Meeting, Las Vegas, NV, November 4-8, 1990.

90. S.L. Wong, Y.-F. Wang and R.J. Sawchuk. "Brain/plasma distribution kinetics of zidovudine (AZT) in the rabbit using microdialysis." 1991 Symposium on Microdialysis and Allied Analytical Techniques, Indianapolis, IN, May 16-17, 1991.

91. K. Van Belle, S.L. Wong, Y.-F. Wang and R.J. Sawchuk. "Comparative delivery and distribution kinetics of zidovudine (AZT) and AZddU into the rabbit brain by microdialysis." 1991 Symposium on Microdialysis and Allied Analytical Techniques, Indianapolis, IN, May 16-17, 1991.

92. Y.-F. Wang, S.L. Wong and R.J. Sawchuk "*In vitro* and *in vivo* calibration of microdialysis probes using retrodialysis." 1991 Symposium on Microdialysis and Allied Analytical Techniques, Indianapolis, IN, May 16-17, 1991.

93. B.W. Cheung, L.E. Riad and R.J. Sawchuk. "Comparative uptake of selected anticonvulsant drugs into rabbit brain." 1991 Symposium on Microdialysis and Allied Analytical Techniques, Indianapolis, IN May 16-17, 1991.

94. L.E. Riad, K.K. Chan, J.A. Maloney and R.J. Sawchuk. "Reversibility of carbamazepine autoinduction upon dose termination in normal volunteers." AAPS Sixth Annual Meeting, Washington, DC, November 17-21, 1991.

95. S.L. Wong, M.A. Hedaya and R.J. Sawchuk. "Modeling the competitive inhibition of renal and nonrenal clearance of zidovudine by probenecid." AAPS Sixth Annual Meeting, Washington, DC, November 17-21, 1991.

96. K. Van Belle, S.L. Wong, Y.-F. Wang and R.J. Sawchuk. "Comparison of pharmacokinetics and CNS distribution of coadministered AZT and AZddU by microdialysis." AAPS Sixth Annual Meeting, Washington, DC, November 17-21, 1991.

97. Y.-F. Wang, S.L. Wong and R.J. Sawchuk. "*In vitro* and *in vivo* calibration of microdialysis probes using retrodialysis: application to the study of brain/plasma distribution of zidovudine." AAPS Sixth Annual Meeting, Washington, DC, November 17-21, 1991.

98. W.F. Elmquist, L.E. Riad, I.E. Leppik and R.J. Sawchuk. "The relationship between urine and plasma concentrations of carbamazepine and phenytoin in epileptic patients on chronic therapy." AAPS Sixth Annual Meeting, Washington, DC, November 17-21, 1991.

99. S.L. Wong, Y.-F. Wang, and R.J. Sawchuk. "Effect of dose on distribution of zidovudine (AZT) into rabbit brain using microdialysis with *in vivo* calibration." AAPS Sixth Annual Meeting, Washington, DC, November 17-21, 1991.

100. W.F. Elmquist, I.E. Leppik and R.J. Sawchuk. "Physiological modeling of the dependence of renal clearance on urine flow II: phenytoin and HPPH in humans." American Association of Pharmaceutical Scientists Annual Meeting, Washington, DC, November 17-21, 1991.

101. R.J. Sawchuk. "Study of zidovudine distribution into the CNS utilizing microdialysis." 25th Annual Higuchi Research Seminar, Lake of the Ozarks, MO, March 8-11, 1992.

102. Y.F. Wang and R.J. Sawchuk. "Microdialysis studies of brain/plasma distribution of AZT during intraventricular and intravenous infusion." AAPS Seventh Annual Meeting, San Antonio, TX, November 15-19, 1992.

103. S.L. Wong, K. Van Belle, and R.J. Sawchuk. "A microdialysis study of probenecid's effect on the transport kinetics of zidovudine in rabbit brain." AAPS Seventh Annual Meeting, San Antonio, TX, November 15-19, 1992.

104. S.L. Wong, and R.J. Sawchuk. "Pharmacokinetic interaction of zidovudine and salicylic acid during continuous infusion." AAPS Seventh Annual Meeting, San Antonio, TX, November 15-19, 1992.

105. S.L. Wong, and R.J. Sawchuk. "Effect of salicylic acid on the distribution of zidovudine between plasma and cerebrospinal fluid." AAPS Seventh Annual Meeting, San Antonio, TX, November 15-19, 1992.

106. R.C. Brundage, K.K.H. Chan, and R.J. Sawchuk. "Population pharmacokinetic modeling of nicotine following transdermal drug administration." AAPS Seventh Annual Meeting, San Antonio, TX, November 15-19, 1992.

107. R.C. Brundage, K.K.H. Chan, and R.J. Sawchuk. "Population pharmacokinetics of diclofenac potassium using routinely collected experimental data." AAPS Seventh Annual Meeting, San Antonio, TX, November 15-19, 1992.

108. W.F. Elmquist and R.J. Sawchuk. "Simulation of the effect that the time delay in sampling from the bladder has on urine concentrations: implications for therapeutic drug monitoring using urine specimens." AAPS Seventh Annual Meeting, San Antonio, TX, November 15-19, 1992.

109. J.P. Zhong, Y.F. Wang and R.J. Sawchuk. "Absorption of three antiviral nucleosides from different anatomic regions of rabbit intestine." AAPS Seventh Annual Meeting, San Antonio, TX, November 15-19, 1992.

110. Y.F. Wang, S.L. Wong, and R.J. Sawchuk. "On-line microdialysis calibration using retrodialysis and the zero-net flux method: application to a study of the distribution of AZT to rabbit CSF and thalamus." AAPS Seventh Annual Meeting, San Antonio, TX, November 15-19, 1992.

111. R.J. Sawchuk. "Comparative distribution of AZT into brain tissue extracellular fluid during intravenous and intraventricular infusion using microdialysis." 26th Annual Higuchi Research Seminar, Lake of the Ozarks, MO, March 14-17, 1993.

112. Y. Wang and R.J. Sawchuk, "Comparison of renal clearance of AZdU following IV bolus and constant-rate Infusion." 8th Annual Meeting, American Association of Pharmaceutical Scientists, Orlando, FL, November 14-18, 1993.

113. Y. Wang and R.J. Sawchuk. "Assessment of oral absorption of AZT and AZdU in the rabbit using deconvolution." 8th Annual Meeting, American Association of Pharmaceutical Scientists, Orlando, FL, November 14-18, 1993.

114. Y. Wang, Y. Wei and R.J. Sawchuk. "Microdialysis studies of carrier-mediated transport of AZT from brain to plasma during intracerebroventricular infusion." 8th Annual Meeting, American Association of Pharmaceutical Scientists, Orlando, FL, November 14-18, 1993.

115. B.K. Malhotra, M. Lemaire, and R.J. Sawchuk. "Investigation of the CNS distribution of EAB 515 in freely moving rats by microdialysis." 8th Annual Meeting, American Association of Pharmaceutical Scientists, Orlando, FL, November 14-18, 1993.

116. A.K. Shah, R.C. Brundage, K.D. Lake and R.J. Sawchuk. "Estimation of plasma free fraction (fu) of cyclosporine (CYA) in the rabbit and heart transplant (HT) patients by NONMEM using a physiological model of renal clearance (CLr)." 8th Annual Meeting, American Association of Pharmaceutical Scientists, Orlando, FL, November 14-18, 1993.

117. B.K. Malhotra, R.C. Brundage, M. Lemaire, and R.J. Sawchuk. "Modeling of the CNS distribution of EAB 515 following IV and ICV administration." 5th Symposium: Frontiers of Pharmacokinetics and Pharmacodynamics, Baltimore, MD, April 18-20, 1994.

118. R.C. Brundage, B.K. Malhotra, J.A. Maloney and R.J. Sawchuk. "Brain distribution of tacrine and the 1-hydroxy and 2-hydroxy tacrine metabolites determined by microdialysis in freely-moving rats." 5th Symposium: Frontiers of Pharmacokinetics and Pharmacodynamics, Baltimore, MD, April 18-20, 1994.

119. Y. Wang and R.J. Sawchuk. "CNS Distribution of inulin-[^{14}C]-carboxylic acid in rabbits." 9th Annual Meeting, American Association of Pharmaceutical Scientists, San Diego, CA, November 6-10, 1994.

120. B.K. Malhotra, R.C. Brundage and R.J. Sawchuk. "Simultaneous microdialysis of portal and jugular blood following IV bolus and oral lavage in freely-moving rats." 9th Annual Meeting, American Association of Pharmaceutical Scientists, San Diego, CA, November 6-10, 1994.

121. R.C. Brundage, B.K. Malhotra, J.A. Maloney and R.J. Sawchuk. "Brain distribution of tacrine and its 1- and 2-hydroxylated metabolites determined by microdialysis in freely-moving rats." 9th Annual Meeting, American Association of Pharmaceutical Scientists, San Diego, CA, November 6-10, 1994.

122. B.K. Malhotra, R.C. Brundage, Y. Wang and R.J. Sawchuk. "Dialysis membrane-limited and aqueous boundary layer-limited *in vitro* microdialysis recovery." 9th Annual Meeting, American Association of Pharmaceutical Scientists, San Diego, CA, November 6-10, 1994.

123. B.W.Y. Cheung, Y. Wang and R.J. Sawchuk. "Preliminary studies of effects of hydroxy-propyl-beta-cyclodextrin on carbamazepine distribution into rabbit brain." 9th Annual Meeting, American Association of Pharmaceutical Scientists, San Diego, CA, November 6-10, 1994.

124. R.J. Sawchuk, J.A. Maloney, L.L. Cartier, R.J. Rackley, K.K.H. Chan and H.S.H. Lau. "Analysis of diclofenac and four of its metabolites in human urine by HPLC." 9th Annual Meeting, American Association of Pharmaceutical Scientists, San Diego, CA, November 6-10, 1994.

125. R.C. Brundage, M. Lemaire and R.J. Sawchuk. "Modeling of the CNS distribution of EAB 515 following IV and ICV administration." 9th Annual Meeting, American Association of Pharmaceutical Scientists, San Diego, CA, November 6-10, 1994.

126. B.K. Malhotra, M. Lemaire, J.F. Brouillard and R.J. Sawchuk. "High-performance liquid chromatographic (HPLC) analysis of EAB 515 in brain and blood microdialysate (on-line) and in plasma ultrafiltrate of freely-moving rats." 10th Annual Meeting, American Association of Pharmaceutical Scientists, Miami Beach, FL, November 5-9, 1995.

127. R.J. Sawchuk, R.C. Brundage, E.D. Kharasch and M.D. Karol. "Physiological-based pharmacokinetic (PBPK) modeling of sevoflurane, a volatile anesthetic." 10th Annual Meeting, American Association of Pharmaceutical Scientists, Miami Beach, FL, November 5-9, 1995.

128. R.C. Brundage, S. Thomas Forgue and R.J. Sawchuk. "Comparative distribution of a series of aminoacridines of varying polarities into rat cortex using microdialysis." 10th Annual Meeting, American Association of Pharmaceutical Scientists, Miami Beach, FL, November 5-9, 1995.

129. Z. Yang, R.C. Brundage, L.L. Cartier, J.A. Maloney and R.J. Sawchuk. "Development of a microdialysis method to study brain distribution of stavudine (d4t) in freely-moving rats." 10th Annual Meeting, American Association of Pharmaceutical Scientists, Miami Beach, FL, November 5-9, 1995.

130. B.K. Malhotra, R.C. Brundage and R.J. Sawchuk. "Estimation of presystemic disposition of drugs based upon combination of area ratios and deconvolution." 10th Annual Meeting, American Association of Pharmaceutical Scientists, Miami Beach, FL, November 5-9, 1995.

131. M.A. Osman, R. J. Sawchuk, and M.K. Youssef. "In Situ Absorption of the Antiviral drug, stavudine, from the rabbit intestine." European Symposium on Formulation of Poorly Available Drugs for Oral Administration, Paris, February 5- 6, 1996.

132. M.A. Osman, R.J. Sawchuk, and M.K. Youssef. "Ganciclovir (DHPG), an antiviral nucleoside that exhibits high absorptive clearance in the rabbit colon *in situ*." European Symposium on Formulation of Poorly-available Drugs for Oral Administration, Paris, February 5- 6, 1996.

133. B. K. Malhotra, M. Lemaire, J.F. Brouillard, and R.J. Sawchuk. "High-performance liquid chromatographic (HPLC) analysis of EAB 515 in brain and blood microdialysate (on-line) and in plasma ultrafiltrate of freely-moving rats." 11th Annual Meeting, American Association of Pharmaceutical Scientists, Miami Beach, FL, October 29-31, 1996.

134. R.J. Sawchuk, R.C. Brundage, E.D. Kharasch, and M.D. Karol. "Physiologically-based pharmacokinetic (PBPK) modeling of sevoflurane, a volatile anesthetic." 11th Annual Meeting, American Association of Pharmaceutical Scientists, Miami Beach, FL, October 29-31, 1996.

135. R.C. Brundage, S.T. Forgue, and R.J. Sawchuk. "Comparative distribution of a series of aminoacridines of varying polarities into rat cortex using microdialysis." 11th Annual Meeting, American Association of Pharmaceutical Scientists, Miami Beach, FL, October 29-31, 1996.

136. Z. Yang, R.C. Brundage, L.L. Cartier, J.A. Maloney, and R.J. Sawchuk. "Development of a microdialysis method to study brain distribution of stavudine (d4T) in freely-moving rats." 11th Annual Meeting, American Association of Pharmaceutical Scientists, Miami Beach, FL, October 29-31, 1996.

137. B.K. Malhotra, R. C. Brundage, and R. J. Sawchuk. "Estimation of presystemic disposition of drugs based upon combination of area ratios and deconvolution." 11th Annual Meeting, American Association of Pharmaceutical Scientists, Miami Beach, FL, October 29-31, 1996.

138. Z. Yang and R.J. Sawchuk. "A modified solvent drag model and its application in studying intestinal absorption of polar drugs." 12th Annual Meeting, American Association of Pharmaceutical Scientists, Boston, MA, November 2-6, 1997.

139. Z. Yang and R.J. Sawchuk. "Estimating the intestinal absorptive clearance of drugs: consideration of water absorption during in situ single-pass perfusion studies." 12th Annual Meeting, American Association of Pharmaceutical Scientists, Boston, MA, November 2-6, 1997.

140. Z. Yang, P. Manitpisitkul, F.P. LaCreta, C.K. Knupp, R.H. Barbhaiya, and R.J. Sawchuk. "*In situ* studies of the regional absorption of lobucavir and ganciclovir from rabbit intestine." American Association of Pharmaceutical Scientists Annual Meeting, San Francisco, CA, November 15-19, 1998.

141. Z. Yang, Y. Huang, G. Gan, and R.J. Sawchuk. "Microdialysis evaluation of the brain distribution of stavudine following intranasal administration." American Association of Pharmaceutical Scientists Annual Meeting, San Francisco, CA, November 15-19, 1998.

142. Z Yuan, P. Ji, S. Giebink, and R.J. Sawchuk. "Antibiotic Middle Ear Pharmacokinetics by Microdialysis." American Association of Pharmaceutical Scientists Annual Meeting, San Francisco, CA, November 15-19, 1998.

143. R.J. Sawchuk, P. Ji, Y. Huang. "Distribution of Amoxicillin to Middle Ear Fluid Using Microdialysis Sampling." Higuchi Research Seminar, Lake of the Ozarks, MO, March 14-17, 1999.

144. Y. Huang, and R.J. Sawchuk. "Antibiotic Pharmacokinetics in Chinchilla Middle Ear using Microdialysis." Association of Pharmaceutical Scientists Midwest Regional Meeting, Chicago, IL, May 17, 1999

145. R.J. Sawchuk, P. Ji, Y. Huang, and S. Giebink. "Kinetics of Transport of Antibiotics to Middle Ear Fluid Using Microdialysis Sampling." Seventh International Symposium on Recent Advances in Otitis Media, Fort Lauderdale, FL, June 1-5, 1999.

146. G. Gan, and R.J. Sawchuk. "Intestinal Absorption and Pre-Systemic First Pass Elimination of Minocycline and Propranolol in Rabbits" *American Association of Pharmaceutical Scientists Annual Meeting*, New Orleans, LA, November 14-18, 1999.

147. B.W.Y. Cheung, L.L. Cartier, H. Q. Russlie, and R.J. Sawchuk. "Using Sample Pooling Methods in the Determination of AUC and AUMC in Pharmacokinetic Studies" *American Association of Pharmaceutical Scientists Annual Meeting*, New Orleans, LA, November 14-18, 1999.

148. Y. Huang, L.L. Cartier, and R.J. Sawchuk. "Analysis of Clarithromycin by Chemiluminescence: In Vitro/InVivo Microdialysis Studies" *American Association of Pharmaceutical Scientists Annual Meeting*, New Orleans, LA, November 14-18, 1999.

149. P. Guo, P. Ji, B.W.Y. Cheung, J.B. McCarthy, and R.J. Sawchuk. "Fibronectin Peptide (FN C/H V-Y) Assay and Stability in Human and Rat Plasma" *American Association of Pharmaceutical Scientists Annual Meeting*, New Orleans, LA, November 14-18, 1999.

150. R. J. Sawchuk, B. W. Y. Cheung, L. L. Cartier, H. Q. Russlie, T. Zhu, Y. Huang, G. S. Giebink, D. Mulford and M. Mayer. "Kinetics of Cefditoren Distribution to Middle Ear Fluid in The Unanesthetized Chinchilla" *40th Interscience Conference on Antimicrobial Agents and Chemotherapy.* Toronto, ON, September 17-20, 2000

151. G.S. Giebink, T.M. Sheehy, M. Quartey, R.J. Sawchuk, M. Mayer Cefditoren Pharmacodynamics for Streptococcus Pneumoniae (Pnc) Acute Otitis Media (AOM) in the Chinchilla Model" *40th Interscience Conference on Antimicrobial Agents and Chemotherapy.* Toronto, ON, September 17-20, 2000.

152. Y. Huang, R. J. Sawchuk. "Studies of the Middle Ear Distribution Kinetics of Amoxicillin in the Awake Chinchilla Using Microdialysis". *American Association of Pharmaceutical Scientists Annual Meeting*, Indianapolis, IN, October 29- November 2, 2000.

153. J.Z. Peng, R.C. Brundage, and R.J. Sawchuk. "Study of Presystemic Elimination of 4-mono-methylamino-antipyrine (MAAP) after Consecutive Doses in Freely Moving Rats Using On-line Microdialysis". *American Association of Pharmaceutical Scientists Annual Meeting*, Indianapolis, IN, October 29- November 2, 2000.

154. T. Zhu, Y. Huang, L.L. Cartier, R. J. Sawchuk "In Vitro Microdialysis and Protein Binding Studies of Cefditoren" *American Association of Pharmaceutical Scientists Annual Meeting*, Indianapolis, IN, October 29- November 2, 2000.

155. G. Gan, L. L. Cartier, Y. Huang, Z. Yang, R. J. Sawchuk "Intestinal Absorption and Presystemic Elimination of the Prokinetic Agent, EM574, in Rabbits" *American Association of Pharmaceutical Scientists Annual Meeting*, Indianapolis, IN, October 29- November 2, 2000.

156. L. C. Musib, J. C. Cloyd, A.K. Birnbaum, T. J. Hietpas, R. J. Sawchuk, I. E. Leppik, T. R. Browne, S. F. Holloway, G. S. Holden, J. O. Rarig. "Preliminary Report on Phenytoin Bioavailability in the Elderly Using an Intravenous Stable-Labeled Isotope". *American Association of Pharmaceutical Scientists Annual Meeting*, Indianapolis, IN, October 29- November 2, 2000.

157. Z. Yang, L. M. Zadjura, C. J. D'Arienzo, D. B. Wang-Iverson, R. J. Sawchuk "Use of Sample Pooling in Drug Discovery to Screen for Pharmacokinetic Properties of Compounds in Rats" *American Association of Pharmaceutical Scientists Annual Meeting*, Indianapolis, IN, October 29- November 2, 2000.

158. R.J. Sawchuk, Y. Huang, P. Ji, M. Quartey, G.S. Giebink. "Influx/Eflux Penetration Clearance of Amoxicillin between Plasma and Middle Ear Fluid in Freely Moving Chinchillas using Microdialysis" *4th Extraordinary International Symposium on Recent Advances in Otitis Media,* Sendai, Japan, April 16-20, 2001.

159. T. Zhu, B. W. Cheung, L.L. Cartier, G. S. Giebink, D.J. Mulford, M.D. Mayer, R.J. Sawchuk. "Study of Cefditoren Distribution Kinetics to Middle Ear Fluid in Freely-moving Chinchillas Using Microdialysis." *American Association of Pharmaceutical Scientists Annual Meeting*, Denver, CO, October 21-25, 2001.

160. W. Liu, B.W. Cheung, L.L. Cartier, T. Zhu, M.M. Paris, R.J. Sawchuk. "In vitro/In vivo Microdialysis and Protein Binding Studies of the ketolide antibiotic, ABT-773." *American Association of Pharmaceutical Scientists Annual Meeting*, Denver, CO, October 21-25, 2001.

161. Y. Huang, R.J. Sawchuk. "Estimation of Amoxicillin Influx and Efflux Clearance between Plasma and Middle Ear Fluid Following Simultaneous Systemic and Local Ear Doses in Awake Chinchilla Using Microdialysis." *American Association of Pharmaceutical Scientists Annual Meeting*, Denver, CO, October 21-25, 2001.

162. J.Z. Peng, R.C. Brundage, R.J. Sawchuk. "The Influence of Drug Pre-exposure on First-pass Metabolism of Tacrine in Rats." *American Association of Pharmaceutical Scientists Annual Meeting*, Denver, CO, October 21-25, 2001.

163. J.Peng, R.J.Sawchuk, and R.P.Remmel "Mechanism-based inactivation of CYP1A2 by tacrine" *11th North American Meeting of the International Society for the Study of Xenobiotics*, Orlando, FL. October 27-31, 2002.

164. Y. Song, L.L.Cartier, B.W Cheung, R J Sawchuk. "An Animal Model for Multi-site CSF Disposition Studies of Intrathecally Administered Agents". *American Association of Pharmaceutical Scientists Annual Meeting*, Toronto, Ontario, Canada. November 10-14, 2002.

165. J.Z. Peng, R.Remmel, R.J.Sawchuk. "Modeling And Simulation Of In Vivo PK Profiles Based On Mechanism-based Inhibition From In Vitro Studies: Inactivation Of CYP1A2 by Tacrine" *American Association of Pharmaceutical Scientists Annual Meeting*, Toronto, Ontario, Canada. November 10-14, 2002.

166. Y. Song, L.L.Cartier, B. Cheung, R.J. Sawchuk. "Multi-site CSF Disposition Studies of Intrathecally Administered Antiviral Nucleosides in a Novel Animal Model". *8th International Meeting of the International Society for the Study of Xenobiotics*, Dijon France. April 27-31, 2003

167. W. Liu, B. W. Y. Cheung, R. J. Sawchuk. "Distribution Kinetics of Cethromycin in the Chinchilla Middle Ear". *8th International Symposium on Recent Advances in Otitis Media*. Fort Lauderdale, FL. June 3 - 7, 2003

168. P. Ji, L. Cartier, B. W. Y. Cheung, R. J. Sawchuk. "Distribution Kinetics of Cefdinir Between Plasma And Middle Ear Fluid In The Freely Moving Chinchillas". *American Association of Pharmaceutical Scientists Annual Meeting*, Salt Lake City, UT. October 26-30, 2003.

169. W. Liu, B. W. Y. Cheung, R J Sawchuk. "Efflux Transport Of Cethromycin Following Direct Intra-bulla Dosing In The Chinchilla Middle Ear". *American Association of Pharmaceutical Scientists Annual Meeting*, Salt Lake City, UT. October 26-30, 2003.

170. Y. Song and R. J. Sawchuk. "Pharmacokinetics of Zidovudine and Stavudine in the Cerebrospinal Fluid after Intrathecal Administration in a Novel Rabbit Model". *American Association of Pharmaceutical Scientists Annual Meeting*, Baltimore, MD. November 8, 2004.

171. N. Mostafa and R. J. Sawchuk. "Determination of Ofloxacin Clearance from the Middle Ear Fluid using Microdialysis". *American Association of Pharmaceutical Scientists Annual Meeting*, Nashville, TN. November 7, 2005.

172. Z. Li, B. W. Y. Cheung, L. Cartier, and R. J. Sawchuk. "The Possible Role of P-glycoprotein in the Distribution of Clarithromycin to the Middle Ear". *American Association of Pharmaceutical Scientists Annual Meeting*, Nashville, TN. November 7, 2005.

173. R. J. Sawchuk, L. M. Page, and R. L. Rauck. "Pharmacokinetics of Gabapentin Injection in Cerebrospinal Fluid and Plasma with Intrathecal Administration". FDA Science Forum, Washington, DC. April 18, 2006.

174. R. J. Sawchuk. "Bugs and Drugs: Does the Anti-infective Agent get to the Target Site?" *American Pharmacists Association Annual Meeting*, Atlanta, GA. March 18, 2007.

175. R. J. Sawchuk. "Future Perspectives on the Contributions of Microdialysis in Drug Research and Development" Fifth International Symposium on Microdialysis in Drug Research and Development. Leiden, NE. April 25, 2007.

176. R.J. Sawchuk. "Drug Delivery to the Middle Ear across the Tympanic Membrane for Therapy of Acute Otitis Media". Global Gators 6th Symposium on Clinical Pharmacy and Clinical Pharmacology. Munich, Germany. June 9, 2007.

177. T. Wang, R. J. Sawchuk and W. F. Elmquist. "Modeling Distributional Kinetics: Comparison of Two Methods Based on a Partial-Areas Analysis". *American Association of Pharmaceutical Scientists Annual Meeting*, San Diego, CA, November 13, 2007.

178. L. Laksiri, C. Dahyot-Fizelier, S. Lefeuvre, S. Marchand, O. Mimoz, R. J. Sawchuk, and W. Couet. "Microdialysis Study of Imipenem Distribution in the Peritoneal Fluid of Patients with Peritonitis". *Interscience Conference on Antimicrobial Agents and Chemotherapy*, Washington, DC. October 26, 2008.

179. R. J. Sawchuk, G. M. Wall, B. W. Y. Cheung, L. L. Cartier, and D. B. Madhura. "Trans-tympanic Membrane Delivery of an Antibiotic into Chinchilla Middle Ear: a Model for the Treatment of Otitis Media". *European Society for Pediatric Infectious Diseases Meeting 2010*, Nice, FR, May 4-8, 2010.

180. R. J. Sawchuk, B. W. Y. Cheung, L. L. Cartier, D. B. Madhura, and L. Maertens. "An Acute Otitis Middle Ear Model in the Chinchilla with Implanted Tympanostomy Tubes". *European Society for Pediatric Infectious Diseases Meeting 2012*, Thessaloniki, GR, May 8-11, 2012.

EXHIBIT B: MATERIALS CONSIDERED LIST

Exhibit	Description
1002	File History For U.S. Patent No. 8,329,680, at 250-258 ("Dec. 21, 2010 Office Action"); at 278-294 ("June 20, 2011 Amendment"); at 334-356 ("Jan. 17, 2012 Amendment"); at 357-383 ("Jan. 17, 2012 Declaration")
1027	DeFriend et al., *Investigation of a New Pure Antiestrogen (ICI 182780) in Women with Primary Breast Cancer*, 54 Cancer Research 408 (1994) ("DeFriend")
2080	Mark A. Longer et al., *Sustained-Release Drug Delivery Systems*, *in* Remington's Pharmaceutical Sciences 1676 (Alphonso R. Gennaro ed., 18th ed. 1990) ("Remington's")
2132	Dec. 3, 2002 Office Action, File History for U.S. Patent No. 6,774,122 ("Dec. 3, 2002 Office Action")
2133	Aug. 21, 2008 Amendment and Response, File History for U.S. Patent No. 7,456,160 ("Aug. 21, 2008 Amendment")
2134	Nicholas G. Lordi, *Sustained Release Dosage Forms*, *in* The Theory and Practice of Industrial Pharmacy 430 (Leon Lachman et al. eds., 3d ed. 1986) ("Lachman's")
2135	Aug. 21, 2008 Declaration, File History for U.S. Patent No. 7,456,160 ("Aug. 21, 2008 Declaration")