Jon L. Ruckle, MD
Curriculum Vitae

EXPERTISE:

- Product Development Strategy from preclinical through proof of concept
- Phase I protocol design, writing and supervision of study conduct:
    - First-Time-In-Humans
    - Biologics and small molecules
    - Safety, Tolerability, and Pharmacokinetic profiling with Single Ascending Dose, Multiple Ascending Dose, and combination/accelerated study designs
    - "Bridging" studies under ICH E5 Guidelines for registration in Japan or other foreign jurisdictions
    - Ethnic comparison studies
    - Bioavailability/Bioequivalence, food effect, drug interaction, ECG intensive QT/QTc studies
    - Pharmacodynamic and genomic markers
    - Healthy normal males and females, and special populations including healthy elderly, pediatrics, obese, postmenopausal, and patient populations including Diabetes, Hypertension, Hyperlipidemia, Osteoporosis, Renal impaired, Hepatic impaired, Osteoarthritis, Asthma, Psoriasis, etc.
    - Routes of administration including PO, IV, SQ, SL, Inhaled, Topical/transdermal, Intranasal, and Intraocular
    - AME/^{14}C mass balance studies
    - "PET" Imaging
- "Microdose" protocol design
    - "Phase 0" under an exploratory IND for candidate selection
    - Explore and confirm tissues and compartments of distribution
    - Enhanced Phase I studies for absolute bioavailability, mass balance, or characterization of unique human metabolites
- Phase Ib/II "Proof of Concept" study design
    - Safety, Tolerability, and Efficacy in the target patient population

- Active comparator vs. placebo controlled study designs

- Informed Consent writing
- Medical Monitoring
- Data Safety Board participation

EDUCATION:

- Internal Medicine Residency: Mayo Clinic, Rochester, MN (1984)
- Medical School: Loma Linda University School of Medicine, Loma Linda, CA (1980)
- BA: Pacific Union College, Angwin, CA (1973)

EXPERIENCE

Current Positions, Jul 2008 to present:

Principal
Pacific Pharma Group, LLC
1220 Akipohe St. #1C
Kailua, HI 96734
808-349-9812
jon.ruckle@pacificpharmagroup.com

Senior Investigator
Hawaii Clinical Research Center
1286 Queen Emma St.
Honolulu, HI 96813
808-538-2828
jon.ruckle@hawaiiclinicalresearch.com

May 2006-Jul 2008 Medical Director, Covance Clinical Research Unit, Honolulu, HI
Aug 2000-May 2006 Associate Medical Director and Medical Director, Radiant Research Unit, Honolulu, HI

- Served as the Principal Investigator for numerous Phase I clinical trials, and managed sub investigators and the clinical research team.
- Introduced Phase I systems to Radiant Research Honolulu and led ongoing system development.
- Assisted the Radiant management team in development of Phase I systems and capabilities at other sites, leading to 8 Radiant Research sites being acquired by Covance in May 2006.
- Expanded the scope of studies, as summarized in the "expertise" list above; highlights include completion of nearly 50 "Bridging" studies for Japanese registration, introduction and development of "microdose" studies (Jun 2005), Chinese and "pan-

Asian" ethnic comparison studies, a PET study, introduction of ^{14}C AME studies to Honolulu, and first-time-in humans studies including 6 with biologics in the post-TeGenero era and the industry's first Japanese "bridging" study which was also first-time-in humans.
- Led expansion of the range of clinical domains and patient populations.
- Led expansion of client relationships in the US, Japan, EU, and Korea, ranging from multi-national large Pharma to small companies with a single product.
- Incorporated extensive interaction with clients to provide consultation re: protocol design and product development strategies.
- Assisted the Business Development team in the US and Japan with conferences and presentations.
- Worked closely with the operations team to achieve an approximately 6 fold increase in productivity and over 8 fold increase in profitability.

Sep 1995-Jul 2000 Medical Director, Northwest Kinetics LLC, Tacoma WA

- Served as the founding Medical Director of NWK, a dedicated Phase I research facility, and pioneered general Phase I capabilities for the pharmaceutical industry in the Pacific Northwest region.
- Developed systems, training programs, and successfully led the unit from the initial start up through stable, profitable operations. Accomplishments include building a core clinical team, a recruitment database for reliable subjects, and a diverse panel of satisfied industry clients who returned for repeat studies. NWK continued to develop on this foundation, and was acquired by Charles River Laboratories in Oct 2006.
- Provided consultation with clients for study design and product development strategies.
- Study highlights include the first Japanese Bridging study in the US under E5 guidelines (July 1998), special population studies including pediatrics, healthy elderly, diabetes, asthma, hypertension and psoriasis, ethnic comparison studies with genotype markers, and first-time-in humans studies with both biologics and small molecules.
- Served on the IRB for MultiCare Medical Center and the Western Institutional Review Board.

1987-1995 Primary care medical practice, teaching, and research, Tacoma WA

- Primary care medical practice as an Internist, with Western Clinic (1987-1991) and MultiCare Internal Medicine (1991-1995), including a faculty appointment as Assistant Clinical Professor of Family Medicine, University of Washington.
- Western Clinic responsibilities included service as Internal Medicine Chairman, Medical Director, and President, during transitions including design and construction of an entire new clinic facility, multiple managed care contract negotiations, and a computer system conversion.
- Extensive involvement with development of computerized patient medical records, including membership in the American Medical Informatics Association 1991-1995, with utilization of a prototype system in my own practice.
- Participated in multiple committees for MultiCare Medical Center and the Washington State Medical Associations regarding Quality Assurance and the development of clinical outcomes studies.
- Began research career, serving as Principal Investigator for 13 Phase II-III trials from 1989 to 1995.

1986-1987 Primary care medical practice and teaching, San Jose, CA.

Primary care medical practice as an Internist, including a faculty appointment as Associate Chief, Primary Care Division, Department of Internal Medicine, Santa Clara County Valley Medical Center, a Stanford University affiliated residency program.

1984-1986 Primary care medical practice, Bunn, NC

Primary care medical practice and appointment as Medical Director, Bunn Community Health Center in Bunn, NC, a small rural town. This was in fulfillment of a National Public Health System scholarship obligation.

CERTIFICATIONS:

Diplomate in Internal Medicine, American Board of Internal Medicine, # 097022, 1984
Diplomate of the National Board of Medical Examiners, # 241738, 1982
DEA, Number available upon request, 1982

MEDICAL LICENSURE

Hawaii, #MD11129, 2000
Washington (Inactive), #24572, 1987
California (Inactive), #G56984, 1986
North Carolina (Inactive), #27971, 1984
Minnesota (Inactive), #26791, 1982

PUBLICATIONS

1. Scott D, **Ruckle J**, Dar M, Baker S, Kondoh H, Lockhard S. "Phase I trial of 13-valent pneumococcal conjugate vaccine in Japanese adults." Pediatr Int. 2008 Jun; 50(3):295-9.

2. Vuong LT, **Ruckle JL**, Blood AB, Reid MJ, Wasnich RD, Synal HA, Dueker SR. "Use of accelerator mass spectrometry to measure the pharmacokinetics and peripheral blood mononuclear cell concentrations of zidovudine." J Pharm Sci. 2007 Sep 13

3. **J. Ruckle**, M. Jacobs, W. Kramer, R. Kumar, K. Underwood, R.S. Pearsall, A.E. Pearsall, J. Seehra, C. Condon, M.L. Sherman. "A Single Dose of ACE-011 is Associated with Increases in Bone Formation and Decreases in Bone Resorption Markers in Healthy, Postmenopausal Women." Abstracts of the 29th annual meeting of American Society for Bone and Mineral Research, Sep 2007

4. Nigel H. Grieg, **Jon Ruckle**, Patrick Comer, Lidia Brownell, et al, "Anticholinesterase and Pharmacokinetic Profile of Phenserine in Healthy Elderly Human Subjects." Current Alzheimer Research, 2005, 2, 483-492.

5. Poon, Terri, Nelson Patric, Shen Larry, et al., "Exenatide Improves Glycemic Control and Reduces Body Weight in Subjects with Type 2 Diabetes: A Dose-Ranging Study." Diabetes Technology & Therapeutics, Jun 2005, Vol 7, No. 3:467-477.

6. Labellarte, Michael M.D.; Biederman, Joseph M.D., PH.D.; Emslie, Graham M.D.; Ferguson, James M.D.; Khan, Arifulla M.D.; **Ruckle, Jon M.D.;** Sallee, Randy M.D., PH.D.; Riddle, Mark M.D., "Multiple-dose pharmacokinetics of fluvoxamine in children and adolescents." J Am Acad Child Adolesc Psychiatry. 2004 Dec; 43(12):1497-505.

7. Richard Wasnich, **Jon Ruckle**. "High Fructose Diet Induces Hepatic Dysfunction in Healthy Men." Medicine On Line January 1, 2003.

8. Eiznhamer DA, Creagh T, **Ruckle JL**, Tolbert DT, Giltner J, Dutta B, Flavin MT, Jenta T, Xu Z-Q, "Safety and pharmacokinetic profile of multiple escalating doses of (+)-Calanalide A, a naturally occurring nonnucleoside reverse transcriptase inhibitor, in healthy HIV-negative volunteers." HIV Clinical Trials 2002; 3(6):435-450.

9. Richard Wasnich, Lily Li, Xiaoming Lin, **Jon Ruckle**, Christopher TenHoor, Daniel Freedman. "The Pharmacokinetic Properties of Alefacept Are Similar Among Caucasian and Japanese Healthy Volunteers." P850, 63rd Annual Meeting of the Society for Investigative Dermatology, May 15-18, 2002.

10. Creagh T, **Ruckle JL**, Tolbert DT, Giltner J, Eiznhamer DA, Dutta B. "Safety and pharmacokinetics of single doses of (+)- Calanalide A, a naturally occurring nonnucleoside reverse transcriptase inhibitor in healthy, human immunodeficiency virus-negative human subjects." Antimicrob Agents Chemother 2001 May;45(5):1379-1386.

11. Sperof, Leon, Symons, James, Kempfert, Nona, et al., "The effect of varying low-dose combinations of norethindrone acetate and ethinyl estradiol (femhrt(R)) on the frequency and intensity of vasomotor symptoms." Menopause. 7 (6):383-390, November 2000.

12. Clemmons DR, Moses AC, McKay MJ, Sommer A, Rosen DM, **Ruckle J**. "The Combination of Insulin-like Growth Factor-1 and Insulin-like Growth Factor Binding Protein-3 Reduces Insulin Requirements in Insulin-dependent Type 1 Diabetes: Evidence for *In Vivo* Biological Activity." J Clin Endocrinol Metab 85 [4], 1518-1524. 2000

13. Marbury TC; **Ruckle JL**; Hatorp V; Andersen MP; Nielsen KK; Huange WC; Strange P, "Pharmacokinetics of Repaglinide in subjects with renal impairment," Clin Pharmacol Ther 2000 Jan;67 (1):7-15.

14. D.S. Tolbert, A. Karim, J. Nasafi, **J.L. Ruckle**, and J. Qian, "Effect of Double Strength Grapefruit Juice on the Pharmacokinetics of Eplerenone," AAPS poster, November, 2000.

15. G. He, J. Massarella, **J.L. Ruckle**, Y. Ninomiya, A. Dorr, C. Woodruffe-Peacock, P. Ward, and A. Brown, "The Comparative Pharmacokinetics and Safety of the Oral Neuraminidase Inhibitor Oseltamivir when Given in Multiple Doses to Healthy Japanese and Caucasian Subjects," Jpn J Clin Pharmacol Ther 31(2) Mar 2000.

16. Dixon R; Engleman K; Kemp J; **Ruckle JL**, "A comparison of the pharmacokinetics and tolerability of the novel antimigraine compound zolmitriptan in adolescents and adults," J Child Adolesc Psychopharmacol 1999; 9(1):35-42.

17. Glenn F. Carlson MD, A. Benjamin Suttle PH.D, **Jon L. Ruckle** MD, Bruce K. Birmingham PhD, "Lack of Interaction between Zafirlukast and Theophylline in Children," ACAAI, November, 1999.

18. **J. Ruckle**, T. Creagh, D. Tolbert, J. Giltner, B. Dutta, C. Thomas, T. Wright, Z.-Q. XU, "Clinical Safety and Pharmacokinetic Profile of Single and Multiple Escalating Doses of (+)-Calanalide A, A Naturally Occurring NNRTI, in Healthy HIV-Negative Volunteers," 39th ICAAC, September, 1999

19. **J. Ruckle**, J. Giltner, T. Creagh, B. Dutta, D. Tolbert, Z-Q Xu, "Clinical Safety and Pharmacokinetics of (+)-Calanalide A, A Naturally Occurring NNRTI, in Normal Healthy and HIV-Infected Volunteers." 6th. Conference on Retroviruses and Opportunistic Infections, January, 1999.

20. **Ruckle, J.L.** and Hatorp, V. "Repaglinide Pharmacokinetics in Patients with Renal Impairment Versus Healthy Volunteers." Diabetologia (1998) 41: [Suppl 1]/Issue 8

21. Creagh, T.; Xu, Ze-Qi; Ray, L.; Giltner, J.; Nayer, T.; **Ruckle, J.** "Preliminary Clinical Safety Profile of (+)-Calanolide A- A New Novel NNRTI." (poster for 5th Conference on Retroviruses and Infecious Diseases, February 1998, Chicago).

22. Xu, Ze-Qi; Creagh, T.,; Giltner, J.; **Ruckle, J**.; Frank, P.; Tolbert, D.; Flavin, M.T. "Preliminary Clinical Safety and Pharmacokinetics Profile of (+)-Calanalide A- A Naturally Occurring NNRTI." (poster for 12th. Annual World AIDS Conference, July 1998, Geneva).

23. Stimpel, Michael, Koch, Brigitte, Jansen, Thomas et al. "Moexipril Versus Captopril in Patients with Mild to Moderate Hypertension." Journal of Cardiovascular Pharmacology. 28(6):769-773, December 1996.

24. "Computerized Patient Records, An Essential Technology," in Health Information: Management of a Strategic Resource, Ed. by Abdelhak, Mervat, et. al. W. B. Saunders Co., 1996.

25. Silver FW, **Ruckle JL**. "Depression: Management techniques in primary care. Postgraduate Medicine" Mar;85(4):359-66.

26. **Ruckle, JL** "IMIS: Use of object oriented programming techniques for physician workstations and computerized medical records." Proceedings of the Raima Technology Conference, September 28-30, 1992, Seattle WA.

RESEARCH EXPERIENCE SUMMARY

283 total studies through Aug 2008; detailed list available upon request

Type of Phase I Studies/Therapeutic Domain	# of Studies
Japanese Bridging	48
Ethnic Comparison (non-Japanese)	9
Large Molecule/Biologic	40
First Time In Human	12
Microdose	3
AME ^{14}C	3
PET scan	1
Medical Device	9
Diabetes	38
Osteoporosis	28
Hypertension/Cardiovascular	16
Elderly	13
Pediatrics	9
Asthma	9
Obesity/Weight Loss	8
Hyperlipidemia/Hypercholesterolemia	7
Osteoarthritis	7
Gastroenterology/Hepatic	6
Renal Insufficiency	6

Dermatology	5
Oncology	4
Vaccine	5
Women's Health	5
QTc intense	3