CAROLINE P. BELL, PHD

Preclinical Safety Assessment Scientist and Project Manager with 30+ years of Medical University and Global Pharmaceutical industry experience. Specializing in Toxicology and Core Safety Pharmacology studies, IND-enabling Services, Proof of Concept and Candidate Selection, Strategic Program Management, Investigative and Regulatory Cardiovascular and Renal Safety Pharmacology, CRO Selection, Audit and Monitoring, Preclinical Safety Assessment, Market Analysis, Business Opportunity Assessment and Safety Pharmacology Training Workshops. Expert in strategic planning of preclinical drug development programs, protocol design to provide a mechanistic understanding of potential drug toxicity, study oversight and proper study conduct to GLP, accuracy of data and reports, extrapolation of findings to risk/benefit assessment, expert reports for regulatory submissions and CTD documents, white papers and non-clinical representation at FDA meetings and Advisory Committee proceedings, preparation of papers for publication, analysis of preclinical outsourcing markets, CRO services and contracts. Can provide innovative and visionary solutions for process improvement, is a team player, with integrity and concern for personnel, has leadership skills to promote acceptance and implementation of new ideas and knowledge of new technologies in a changing environment. Over 50 peer reviewed publications and abstracts.

- Project Manager and Team Member on Multi-million $$$ Drug Development Programs (Multiple therapeutic areas)
- Cardiovascular Risk Assessment
- Scientific and Regulatory Submissions
- Non-GLP and GLP Toxicology Studies
- Core and Advanced GLP Safety Pharmacology Studies
- Mechanistic Toxicology and Safety Pharmacology
- Preclinical Compound Development
- Pharmacodynamics/Pharmacokinetics/Metabolism
- Strategic and Technical Laboratory Management
- CRO Study Management and Integration
- Oversight of Academic Alliance
- Discovery Models and Proof of Concept Studies
- In vitro Screening and Candidate Selection
- Discovery Experimental Models and Systems Design (Conscious Animal Cardiovascular Integrated Telemetry, Cardiovascular Physiology and Pharmacology, ECG interpretation, Orthostatic Hypotension, Renal Clearance Models, Blood Distribution and Volume, Ultrasonic Flow Probe, Echo Ultrasonography and Bioimpedence Methods)
- Safety Pharmacology Workshops to Pharmaceutical Industry
- Preclinical Safety Package Due Diligence
- Outsourcing Market Analyses
- Business Opportunity Focus Group - Bioavailability
- Business Problem Resolution and Process Improvement
- Personnel supervision/career development

PROFESSIONAL EXPERIENCE

PHARMAFACTS (Previously doing business as Strategic Safety Pharmacology consulting Consortium, Inc)

President and CEO 2001 – present

- Independent consultant to Pharmaceutical and Biotech industry on pre/non-clinical development programs
- Cardiovascular risk assessment
- Unique case-by-case mechanistic preclinical investigative programs for safety in parallel with clinical programs with safety concerns, determination of clinical biomarkers
- Strategic management of IND-enabling packages, compilation and submission (multiple therapeutic areas, routes of administration, small molecule and biologicals), medical writing of non-clinical CTD documents in parallel with clinical program to NDA stage and representation for questions at FDA Advisory Committee review
- Strategic development of Alternative Indications and Lead Backup Programs
- Management and oversight of outsourced studies - toxicology, safety pharmacology, analytical-bioanalytical chemistry, discovery and proof of concept models, candidate selection, protocol design, data assessment and analysis and report integration and review
- Post-drug approval mechanistic safety assessment programs
- CRO selection, facility audit for Discovery and Preclinical Development Outsourcing
- Assessment of current methodologies, GAP analysis and recommendations to meet GLP regulatory requirements for conduct of Safety Pharmacology Studies
- Summary documents on current basic and medical research and preparation of scientific position papers in response to regulatory questions
- Market analysis reports on outsourcing service providers and safety pharmacology software solutions
- Course Director; Workshops to Pharmaceutical Industry
- Global Harmonization Programs and Facilitator of Process Improvement Activities

GLAXOSMITHKLINE PHARMACEUTICALS, King of Prussia, PA

Assistant Director, Safety Pharmacology, Department of Preclinical Safety Assessment 1999 – 2001
Senior Investigator, Safety Pharmacology, Department of Preclinical Safety Assessment 1994 – 1999

- Project Leader (Safety Assessment) and member of international, multidisciplinary teams responsible for entire drug development programs, e.g. Angiotensin and Endothelin Antagonists, Insulin Sensitizers, Erythropoietin Agonists, GPIIb/IIIa Receptor
- Responsible for the oversight of preclinical toxicological/safety issues, regulatory reports
- Executive management of operations and resources
- Recognized for scientific excellence and investigative contributions to allay regulatory concerns resulting in the successful outcome of NDA files and support of drug development decisions
- Manage (in-house and CRO) generation and interpretation of Safety Pharmacology data (subspecialty cardiovascular and renal) to support assessment of risk/safety profile of all development compounds for IND/NDA submissions
- Study Director
- Devise and direct introduction of new methods and state-of-the-art technologies to ensure efficient, rapid, high quality core Safety Pharmacology screening.
- Conduct investigative toxicology and mechanistic pharmacology studies for preclinical programs and cardiorenal studies for compounds in Phase II-IV of development
- Interface with Discovery and create liaisons with Safety Assessment Department
- Establish alliances with academic institutions for drug-specific investigative studies

NEW YORK MEDICAL COLLEGE, Valhalla, NY

Adjunct Clinical Assistant Professor, Department of Pharmacology 1995 – 2000
Assistant Professor, Department of Pharmacology 1986 – 1994

- NIH, AHA and NY State Funded Investigator
- Direct basic research on renal and vascular mechanisms of hypertension principally in renin-angiotensin and eicosanoid fields.
- Teach pharmacology courses and mentor graduate/medical students and research fellows.
- Over 50 abstracts and peer reviewed publications (see Addendum).

UNIVERSITY OF TENNESSEE, Memphis, TN

Laboratory Supervisor, Department of Pharmacology 1978 – 1979

BURROUGHS WELLCOME, Beckenham. Kent, UK

Intramural Student Technician, Sir JR Vane (Nobel Laureate) Prostaglandin Research Group 1974 – 1975

EDUCATION

Postdoctoral Fellow 1984 – 1986

Department of Pharmacology, Cornell University Medical College, New York, NY, 10012

Cardiovascular Implications of Eicosanoids, relationship to cytochrome P450 and TCDD/PCB toxicity.

Ph.D. Thesis 1979 – 1984

Department of Pharmacology, New York Medical College, Valhalla, NY 10595

Thesis Title: Antihypertensive action of captopril, an angiotensin converting enzyme inhibitor; relationship to prostaglandins

B.Sc. Hons. 1973 – 1977

Department of Pharmacology and Pharmacy, Bath University of Science and Technology, Bath, Avon, England

HONORS AND AWARDS

Board of Directors and founding member of Safety Pharmacology Society
Invited speaker Safety Pharmacology Society, 2001. Renal Safety Pharmacology: The Fourth Core. Invited lecturer FDA, 1998. Perspectives on Renal Safety Pharmacology
Principal Investigator, American Heart Association, NY Affiliate, 1994-97
(relinquished) Principal Investigator, American Heart Association, NY Affiliate, 1991-94
Co-Investigator NIH-LBH Ro1, 1988-1994
Co-Investigator, USPHS Biomedical Support, 1985
Deans Faculty Award for Dedication and Service, 1993
Norman and Rosita Winston Fellowship, 1984-86

Graduate Student Forum, NY Medical College, First Place 1980 and 1981,

MEMBERSHIPS

American Association for the Advancement of Science
American Heart Association, High Blood Pressure Council
American Society Pharmacology &Experimental Therapeutics
New York Academy of Sciences
Pharmaceutical Consulting Consortium, Inc.
Round Table of Toxicology Consultants
Safety Pharmacology Society (Board of Directors)
Society of Toxicology
American College of Toxicology

ADDENDUM (publications also under names of Quilley and Bell-Quilley)

Armstrong, J.M., **Bell, C**., Lattimer, N., McGiff, J.C. and Mullane, K.M.: Contribution of prostaglandins to the renal vascular supersensitivity to vasoconstrictor agents exhibited by New Zealand genetic hypertensive rats. Clin. Sci. Mol. Med., 51:275s-278s, 1976.

Quilley, C.P., Wong, P.Y-K. and McGiff, J.C.: Hypotensive and renovascular actions of 6-keto-prostaglandin E_1, a metabolite of prostacyclin. Eur. J. Pharmacol., 57:273-276, 1979.

Quilley, C.P., McGiff, J.C., Lee, W.H., Sun, F.F. and Wong, P.Y-K: 6-Keto PGE_1: a possible metabolite of prostacyclin having platelet anti-aggregatory effects. Hypertension, 2:524-528, 1980.

McGiff, J.C. and **Quilley, C P**.: The rat with spontaneous hypertension is not a suitable model of human essential hypertension. Circ. Res., 48:445-463, 1981.

Wong, P.Y-K., Lee, W.H., Quilley, C.P. and McGiff, J.C.: Metabolism of prostacyclin: formation of an active metabolite in the liver. Fed. Proc., 40:2001-2004, 1981.

Chiba, S., **Quilley, C.P**., Quilley. J. and McGiff, J.C.: Captopril decreases vascular reactivity independently of changes in prostaglandin release in the rat isolated kidney. Eur. J. Pharmacol., 83:243-252, 1982.

Chiba, S., **Quilley, C.P**. and McGiff, J.C.: Decreased vascular responsiveness produced by angiotensin-converting enzyme inhibitors in the rat isolated kidney. Hypertension Suppl. II, 4:80-85, 1982.

Rifkind, A.B., Hattori, Y., Levi, R., Hughes, M. J., **Quilley, C.** and Alonso, D.R.: The chick embryo as a model for PGB and dioxin toxicity: Evidence of cardiotoxicity and increased prostaglandin synthesis. In: Banbury Report 18. Biological Mechanisms of Dioxin Action, A. Poland and R. Kimbrough, eds.,Cold Spring Harbor Press, 1984, pp. 255-266.

Quilley, C.P. and Rifkind, A.B.: Prostaglandin release by the chick embryo heart is increased by 2, 3, 7, 8-tetrachlorodibenzo-p-dioxin and by other cytochrome P-448 inducers. Biochem. Biophys. Res. Commun., 136:582-589, 1986.

Quilley, C.P., McGiff, .J.C. and Quilley, J.: Failure of chronic aspirin treatment to inhibit urinary prostaglandin excretion in spontaneously hypertensive rats: comparison with indomethacin and flurbiprofen. J. Pharmacol. Exp. Ther., 240:916-921, 1987.

Quilley, C.P., Chiba, S., Quilley, J. and McGiff, J.C.: Enhancement of the antihypertensive effect of captopril by aspirin in spontaneously hypertensive rats. Hypertension, 10:294-302, 1987.

McGiff, J.C. and **Quilley, C.P.**: Participation of prostaglandins in the regulation of the renal circulation. J. Cardiovas. Pharmacol., 10:(Suppl. 5):S24-S27, 1987.

Sullivan, J.M., Quilley, C.P. and McGiff, J.C.: Prostaglandins and Hypertension. In: Arterial Hypertension, Vol. 2, edited by A. Chobanian and J. Rosenthal, Springer-Verlag, 1988.

McGiff, J.C. and **Quilley, C.P.**: Interaction of nonsteroidal anti-inflammatory drugs.and antihypertensives. JAMA, 260:850-851, 1989

Quilley, J., **Quilley, C.P.** and McGiff, J.C.: Eicosanoids and Hypertension. In Pathophysiology, Diagnosis, and Management. eds. J.H Laragh and B.M. Brenner, Raven Press, Ltd, New York, pp 829-840,1990

Quilley, C.P. and McGiff, J.C.: Isomers of 12-hydroxy-5.8,10,14-eicosatetraenoic acid reduce renin activity and increase water and electrolyte excretion. J. Pharmacol. Exp. Ther., 254:774-780, 1990.

Carroll, M.A., **Quilley, C.P.** and McGiff, J.C.: Novel arachidonate metabolites generated by cytochrome P450-dependent monooxygenases, Pharmacol. Res., 23:309-318, 1991.

Stier, C.T., Jr., **Quilley, C.P.** and McGiff, J.C.: Endothelin-3 effect on a renal function and prostanoid release in the isolated kidney. J. Pharmacol. Exp. Ther., 262:252-256, 1992.

Quilley, C.P., Lin, Y.-S, and McGiff, J.C.: Chloride anion concentration as a determinant of renal vascular responsiveness to vasoconstrictor agents. Brit. J. Pharmacol., 108:106-110, 1993.

McGiff, J.C, and **Quilley, C.P.**: Thromboxane A2 and Prostaglandin Mediators in Hypertension. In: Thromboxane A2 and Other Vasoconstrictors in Clinical Conditions. eds. G.G. Neri Serneri, G.F. Gensini, E. Pozzi and D. Prisco, 1993.

McGiff, J.C., **Quilley, C.P.**, and Carroll, M.A.: The contribution of cytochrome P450-dependent arachidonate metabolites to integrated renal function. Steroids, 58:573-579, 1993.

Bell-Quilley, C.P., Lin, Y.-S., Hilchey, S.D., Drugge, E.D. and McGiff, J.C.: Renovascular actions of angiotensin II in the isolated kidney of the rat: relationship to lipoxygenases. J. Pharmacol. Exp. Ther., 267:676-682, 1993.

Jorgensen, P.E., Hilchey, S.D,, Nexo E., Poulsen S S., and **Quilley, C.P.**: Urinary epidermal growth factor is excreted from the rat isolated perfused kidney in the absence of plasma. J. Endocrinol., 139:227-234, 1993

Dellipizzi, A., Hilchey, S.D., **Bell-Quilley, C.P.**: Natriuretic action of angiotensin-(1-7), Brit. J. Pharmacol., 111:1-3, 1994

Quilley, J., **Bell-Quilley, C.P.** and McGiff, J. C.: Eicosanoids and hypertension. In Hypertension: Pathophysiology, Diagnosis, and Management. eds. J.H. Laragh and B.M. Brenner, Raven Press, Ltd, New York, pp 963-982,1994

Yin, K., McGiff, J.C. and **Bell-Quilley, C.P.**: Role of chloride in the variable response of the kidney to cyclooxygenase inhibition. Am. J. Physiol. 268:F561-F568, 1995

Hilchey, S.D and **Bell-Quilley, C.P.**: Association between the natriuretic action of angiotensin (1-7) and selective stimulation of renal prostaglandin I_2 release. Hypertension, 25:1238-1244, 1995

Askari, B. **Bell-Quilley, C.P.**, Fulton, D. Quilley, J. and McGiff, J.C.: Analysis of eicosanoid mediation of the renal functional effects of hyperchloremia. J. Pharmacol. Exper. Ther., 282:101-107, 1997

Hilchey, S.D., Quilley, J. and **Bell-Quilley, C.P.:** Vascular and Excretory Effects of Angiotensin II in the Rat Isolated Perfused Kidney: Influence of Angiotensin Receptor Antagonists. Pharmacology, 57:196-205, 1998

Sehgal, C.M., Arger, P.H., Silver, A.C., Patton, J.A., Saunders, H.M., Bhattacharyya, A., **Bell C.P.**: Renal Blood Flow Changes Induced with Endothelin-1 and Fenoldopam Mesylate using Quantitative Doppler US: Initial Results in a Canine Study. Radiology, 219: 419-426, 2001

Kurman MR, Sager P, Rudoltz MS, Eisner J, Goodman D, Heyman E, Salvail D, **Bell C**, Moore WR. Cardiovascular safety profile of VT-464 in patients with castrate-resistant prostate cancer (CRPC). Presented at the annual ASCO Genitourinary Cancer Symposium, San Francisco, January, 2016.

INVITED PRESENTATIONS

Angiotensin and Lipoxygenase Interactions in the Kidney. Gordon Conference, California 1992

Renal effects of Angiotensin (1-7). Pfizer Pharmaceuticals, Sandwich, Kent, UK, 1993

Ibid. Leaderly Pharmaceuticals, Pearl River, NJ, 1994

Interrelationships between angiotensins and eicosanoids in the kidney. St Louis University Medical School, St Louis MO, 1994

Ibid. Monsanto Pharmaceutical Co., St Louis MO, 1994

Ibid. University of Georgia Medical School, Savanna, GA, 1994

Perspectives on Renal Safety Pharmacology. Invited lecturer FDA, 1998.

Renal Safety Pharmacology: The Fourth Core. Safety Pharmacology Society, Chicago, 2001

ABSTRACTS

Quilley, C.P., Wong, P Y-K., Lee, W.H. and McGiff, J.C Hypotensive and renovascular actions of 6-keto-prostaglandin E_1, a stable circulating metabolite of prostacyclin. Presented at 33rd Ann. Conference of the Council for High blood Pressure Research, American Heart Association, 1979.

Chiba, S., **Qullley, C.P.**, Quilley, J. and McGiff, J.C.: Effect of captopril on norepinephrine-induced vasoconstriction and prostaglandin release in the rat kidney. Fed. Proc., 40:703, 1981.

Quilley, C.P., Chiba, S., Quilley, J., Palmeri, F. and McGiff, J.C : Captopril enhances prostaglandin synthesis in SHR rats but aspirin potentiates its antihypertensive actions. Fed. Proc., 40:681, 1981.

Yin, K., McGiff, J.C, and **Quilley, C.P.**: Cyclooxgenase mediated effects of chloride on renal function. VIII Int. Conf. Prostaglandins and Related Compounds. 651, 1992.

Quilley, C.P. and McGiff, J.C.: Aspirin enhances the blood pressure lowering action of captopril in spontaneously hypertensive rats. Eastern Hypertension Society, May, 1984

Quilley, C.P. and Rifkind, A.B.: TCDD and other cytochrome P-448 inducers increase prostaglandin release by chick embryo heart. Fed. Proc., 45:639, 1986

Quilley, C.P., McGiff, J.C. and Quilley, J.: Dissimilar effects of chronic treatment with aspirin, flubiprofen and indomethacin on renal prostaglandins, Fed. Proc., 45:659, 1986

Quilley, C.P. and Rifkind, A.B.: Increased cardiac prostaglandin release after in ovo exposure of chick embryos to dioxin and other cytochrome P-448 inducers. 6th Int, Conf. on Prostaglandins and Related Compounds, Florence, Italy, 1986

Quilley, C.P. and McGiff,J.C.: Renal effects of 12 R-HETE: a corneal metabolite of arachidonic acid. Brit. J. Pharmacol., 96:59P, 1989.

Quilley, C.P.: Stereochemical dependence of the renal effects of 12-HETE. Eastern Hypertension Society, Mar., 1989

Quilley, C.P. and McGiff, J.C.: A novel eicosanoid affects renal function. Hypertension, 14:338, 1989.

Lin, Y.-S., McGiff, J.C. and **Quilley, C.P.**: An inhibitor of lipoxygenase, BW755c, blunts the renal effects of angiotensin II. FASEB J., 4:a993, 1990.

Quilley, C.P., Lin, Y.-S and McGiff, J.C.: Renal actions angiotensin II are modified by lipoxygenase inhibitor, BW755C. Hypertension, 16:328, 1990.

Quilley, C.P., Lin, Y.-S. and Mcgiff, J.C.: Renal actions of angiotensin II are modified by an inhibitor of cytochrome P450-dependent arachidonic acid metabolism. Brit. J. Pharmacol., 102:40P, 1991.

Quilley, C.P.: Participation of non-cyclooxygenase-dependent pathways of arachidonic acid metabolism in the renal actions of angiotensin II. Gordon Conference on Angiotensins, 1991.

Quilley, C.P., Lin. Y.-S. and McGiff, J.C.: Inhibitors of cytochrome P450-dependent arachidonic acid metabolism modify the renal actions of angiotensin II. Hypertension, 18:380, 1991

Quilley, C.P., Lin, Y.-S. and McGiff, J.C.: Chloride anion concentration as a determinant of renal vascular responsiveness to vasoconstrictor agents. Brit. J. Pharmacol., 105:193P, 1992.

DelliPizzi, A.M., Hilchey, S.D., McGiff, J.C. and **Quilley, C.P.**: Renal actions of angiotensin-(1-7): Comparison with

angiotensin II. Pharmacologist , 34, 326, 1992.

Quilley, C.P., Hilchey, S.D.: Indomethacin blockade of angiotensin-(1-7) stimulated prostaglandin release attenuates the natriuretic response of the rat, isolated kidney. Brit. J. Pharmacol., 10:36P, 1993.

Hilchey, S.D. and **Quilley, C.P.**, Indomethacin blunts angiotensin-(l-7)-induced natriuresis. American Heart Association, 66th Scientific Sessions. 1993.

Jorgensen, P.E., Hilchey, S.D., Nexo, E., Poulsen, S.S., **Quilley, C.P.** EGF is released into the urine after proteolytic cleavage of the renal EGF-precursor by an aprotinin sensitive enzyme. Danish Society of Clinical Chemistry. 1993.

Askari, B., McGiff, J.C. and **Bell-Quilley, C.P.**: Evidence against thromboxane as a mediator of renal responses to high chloride. XIIth International Congress of Pharmacology, 1994.

Askari, B., McGiff, J.C. and **Bell-Quilley, C.P.**: Evidence for subclasses of thromboxane A_2/endoperoxide receptor in the kidney. 48th Session of the Council for High Blood Pressure. Oral presentation.

Bell-Quilley, C.P., Quilley, J. and Hilchey, S.: Functional evidence for heterogeneity of renal angiotensin receptors. Brit J. Pharmacol. 1996, P2

Ezratty, J.M., Schoenebeck, J.J. Gossett, K.A. and **Bell-Quilley, C.P.**: Renal and cardiovascular responses to prolonged endothelin-1(ET-1) infusion in conscious dogs. Society of Toxicology, 753, 1997

Ezratty J.M., Mumaw, J Silver, A.C., Gunning, M.A., Gossett, K.A. and **Bell-Quilley, C.P.**: Method for 24 hour continuous, quantitative urine collection in ambulatory, conscious dogs. Society of Toxicology, 1875, 1998

Pritchett, S.L., Gossett, K.A. and **Bell-Quilley, C.P.**: Surgical implantation and long-term maintenance of ultrasound transit-time flow probe for the measurement of mesenteric blood flow in the conscious rat. Society of Toxicology, 990, 1998

Sehgal, C.M., Arger, P.H., Silver, A.C., Patton, J.A., Saunders, M.H. and **Bell, C.P.**: Quantitative Doppler Imaging: A surrogate for Evaluating Renal Blood Flow Changes Induced by Endothelin-1 and Fenoldopam in Conscious Dogs. 1999