

Dr. William Irwin, DABT, ERT

Ex. 6

Email :

Ex. 6

Tel :

Skilled Interdisciplinary Scientist

Toxicologist--Biochemist/Molecular Biologist--Chemist--Physical Scientist

EXPERIENCE SUMMARY:

- Diplomat of the American Board of Toxicology (DABT Certification)
- European Registered Toxicologist (ERT Board Certification)
- Currently a GS-14 toxicologist as US EPA Structure Activity Team committee co-chair (detail)
- Chair of US EPA Hazard and Risk Assessment Tech Team committee
- Expert in analog identification, read across and structure-activity relationships (SAR)
- Member of the OPP SAR read across team for 6 years (Residues Of Concern Knowledge team)
- Regularly advise senior OPPT managers in read across and toxicology topics
- Developed tools for read across endeavours (dermal & GI absorption, surfactancy calculators)
- Developed and lead the Qualitative Risk Assessment Strategies team
- Given briefings to division directors, office director and the Assistant Administrator
- Given multiple presentations at public meetings representing the Agency (SOT, ACS)
- Written several Technical Directives for contracting work projects
- Worked on the team that developed 4 new Chemical Categories (Lung Effects Project)
- High Quality Work: Published in *Nature, PNAS, JBC, Arch. Tox., Book Chapters*
- My Independent Initiatives Vital to Project Successes
- Very Motivated and Very Innovative
- Very Independent, but Also a Team Player
- Work at the Leading Edge of Fields
- PhD in Biochemistry/Molecular Biology
- Experience at US EPA, Pfizer, Cerep, Lipton, GSK,
- Biotech Senior Scientist equivalent to a GS14
- Hazard Characterization, Exposure Models & Risk Assessment for Chemicals
- 4.5 Years Postdoctoral Research in BioPhysics lab: Muscular Dystrophy, Mitochondrial Disease
- BS in Chemistry, Physics, Mathematics --In vitro Assay Consultant
- U.S. Patent (1st Author) --Process and Product Design
- Mitochondrial Research Expert --Research in Italy, England, Croatia, USA
- Muscle Research Expert --Primary and Tumor Cell Assay Experience
- Research Has Led to Clinical Trials --Biotech Sales & Marketing
- Research in Pharmaceutical, Toxicology, Food, Photographic, Protein Folding Areas
- Research in Biotech, Purification and Environmental Areas
- High Content Screening (HCS) Microscopy Assay Expert
- HTS Assay Design Expert (Biological, Chemical, Physical)
- Teaching Experience in Biochemistry, Toxicology, Chemistry & Physics
- In vivo Tumor Models and Animal Surgery
- Toxicology Presentation with Professor Don Fox (C&D Toxicology Author)
- 4 Book Chapters (In vitro toxicology, endocrine-repro & development, protein folding)
- Toxicology Journal Editor & Scientific Integrity Experience
- QSAR and Risk Assessment Review Committee
- US EPA Innovation Award (Lung Toxicity Project toxicology lead)
- Policy Contributions, Risk Assessment Forum, OECD LLNA Sensitization Committee

Position Qualifications and Education:

I have sufficient college credits to qualify for Chemist, Biochemist, Physical Scientist, Biologist and Toxicologist. I am currently a co-chair of the read across Structure Activity Team, the perfect combination of skills for this SAR position. No other candidate may have degrees in all of the listed

categories (biology, toxicology, physical science, chemistry). I was on the OPP QSAR read across team (ROCKS) for 6 years and studied SAR for years in the pharmaceutical industry, thus I may be the most experience candidate for this SAR position. I have developed tools for read across in RAD, such as the dermal absorption project guidance, dermal absorption calculator and the surfactancy/solubility calculator. I developed and led the Qualitative Risk Assessment Strategies team and presented this project at the 2017 ACS meeting. I was the toxicology lead for Lung Effects Project, which developed four new Chemical Categories in OPPT and received an Innovation Award. I have written several Technical Directives for contracting work. I have given presentations on read across topics. I have briefed and advised senior management at the Director, Office Director and Assistant Administrator levels in the Agency. I worked for 4 years in the pharmaceutical industry with Pharmacology experience. I performed research on a muscular dystrophy therapy that later had successful clinical trials, so my combination of skills have been validated in the health sciences in practical terms.

Senior Scientist: I was a senior scientist toxicologist in industry with people reporting to me, equivalent to a GS-14 senior scientist. I have certified for multiple GS14 positions previously (i.e. certification scores up to 98). I am currently a GS-14 senior scientist as the SAT SAR co-chair in RAD in OPPT (detail).

Toxicology: >78 credit hours in biochemical toxicology research during PhD, 13 years professional experience as a toxicologist (Pfizer, GSK, Cellumen, US EPA), DABT board certification in toxicology, Book chapter on endocrine/developmental/reproductive toxicity of organotins, In Vitro and mitochondrial toxicology expert, Toxicology journal editor, seminars, etc. Applications of thermodynamics to toxicology SOT presentation with Dr. Don Fox (*C&D Toxicology* author). In vivo project on tumorigenesis of pesticide acetylaminofluorene (*PNAS* paper). I participated in a Scientific Advisory Panel on the pyrethroids. Toxicology assays patent. I gave 7 presentations to represent the US EPA at SOT meetings. Drug cumulative work in pharma. OECD LLNA sensitization validation committee, US EPA Risk Assessment Forum, designed 10 ToxCast assays, Co-chair of the US EPA Hazard and Risk Assessment Tech Team, Innovation Award for the US EPA Lung Toxicity Project as the toxicology lead, US EPA Focus committee member, US EPA Structure Activity committee

Toxicology Experience: Endocrine disruption, Immunotoxicity, Cancer models, Myotoxicity, Blood Cell Toxicity, In vitro models, Hepatotoxicity, Pharma models, Mitochondrial toxicity, Imaging toxicology, Dermal sensitization, Lung toxicology

Biochemistry-Biology-Health Sciences: PhD in biochemistry/molecular biology from the Sanford School of Medicine. Biochemistry is critical to Mechanism Of Action investigations. Animal surgery and physiology experience. My muscular dystrophy research was published in the prestigious journal *Nature*. The research led to a therapy with successful clinical trials which validated my health sciences qualifications.

Chemistry: BS degree in analytical chemistry, >40 credit hours, worked as a research chemist for ~9 years with duties such as product/process development, chemical testing, assay development and water treatment/testing roles. I developed products for the pharmaceutical, medical and food technology industries. I developed P-Chem models for dermal exposure of chemicals and environmental fate.

Physical Science: 35 credit hours in physics-engineering-electronics (24 credits needed for a major), taught electronics laboratory, performed physical testing methods in industry (viscosity, polarimetry hysteresis, solubility, Soxlet fat content, moisture content, etc). Physical-chemistry analysis for Quantitative Structural Activity Relationship modeling.

Mathematics-Computer Science: 29 credit hours, Integral and differential calculus, Statistical Design of Experiments training, graphical data analysis skills, computer programming and design of computer circuits.

Pharmacology: I worked in the pharmaceutical industry for ~4 years, thus I learned the pharmacology of many drugs and pesticides (equivalent experience to a degree) based on experiments both in vivo and in vitro. I tested hundreds of drugs and chemicals for on-target effects and adverse effects with in vitro toxicity assays.

Volunteer Work: SOT educational outreach program volunteer, Chemistry tutor, agricultural extension agent volunteer, volunteer farm worker for low income people, chemistry lab instructor, electronics lab instructor, biochemistry lab instructor, ROCKS committee, RARC committee, Scientific Integrity Committee, HED Tox Study Group presenter, RAD template committee, CAPHRA Pyrethroid Committee and Scientific Advisory Panel Committee, Overseas muscle disease project for 4 years (lead to a successful human clinical trial), COOP volunteer (EPA continuity of operations project)

Risk Assessment Factor	William Irwin, PhD, DABT, ERT Qualifications
Leadership	Co-Chair of the US EPA Hazard and Risk Assessment Committee, Currently a GS-14 co-chair of the US EPA Structure Activity Team committee (detail); Supervised & Mentored many associates at Lipton, US EPA (HED, RAD), Pfizer, GSK, Cellumen (Chem., Tox., Biochem.); Briefed Lipton General Manager, Assistant Administrator, Deputy Assistant Administrator, Office Director and R&D Director on projects; Toxicology lead for the Lung Toxicity Project (Innovation Award); First Author <i>Nature</i> Paper (12 authors team, only 3 years), Risk Assessor, Acting Branch Chief, Mentored & Taught Environmental Chemistry & Biochemistry & Physics Laboratory, Independent: Initiated Pivotal Projects with little Supervision, Developed P-Chem model for exposure; <u>Senior Scientist Toxicologist</u> in Biotech equivalent to a GS14 (>2 years): Designed main company product, Patents 1st Author, supervised staff; Designed 10 ToxCAST Assays; Participated in a Scientific Advisory Panel on the pyrethroids; Designed Tox Imaging Assays (12 authors team paper, widely used assays, only 3 years), Overseas Muscular Dystrophy Therapy Team-- Successful Clinical Trials, 1st author on Nature paper, First Pyrethroid Hazard Model to ToxSAC, Industry Meetings, Tox Study Group Instruction, First Protocol to ToxSAC, Seminar on Mitochondrial Toxicity, Two Seminars on In Vitro Toxicology, Represented EPA in 7 SOT and one ACS Presentations, Book chapter on pesticide endocrine disruption, Maturity, Risk Assessment Forum, OECD Dermal Sensitization Assay Validation Team, Qualitative risk assessment team leader
Policy Contributions	Pyrethroid Scientific Advisory Panel Committee Inhalation Policy Contributions Dermal Policy Contributions Gastro-Intestinal Policy Contributions Quantitative Structural Analysis Relationship Contributions Structural Alerts Policy Contributions Immunotoxicity Policy Contributions In Vitro Policy Contributions US EPA ToxCAST Assay Contributions Qualitative Risk Assessment Strategies
Teamwork	HazRATT and SAT Committees co-chair; ROCKS QSAR Committee, RARC risk assessment committee, ToxSAC every meeting, CAPHRA team, Pyrethroids/Inhalation, Tox21, COOP, Inerts, Defibrillator team, EOGRTS reproduction study, Assisted other branches, Mitochondrial Tox resource, Scientific Integrity Committee, Risk Assessment Forum, OECD LLNA Validation Team, Document review and QC

Interdisciplinary Analytical Research	<u>Designed Physical & Chemical Analytical Assays</u> as a research chemist (Process & Production Plant Experiments \$20,000/day at times), <u>Muscular Dystrophy Research</u> (Biochemistry, Toxicology, Pharmacology & Physiology), <u>Tox Assay Validation, ISO "9000" QC/QA, Imaging Tox Assays</u> (biochemistry, optics, toxicology)
Toxicology	<u>Toxicologist, DABT Board Certification</u> (peer status), Pharma, Biotech, <u>Regulatory Tox Experience</u> >78 Tox Research credits during PhD, Clinical Chemistry, Tested Pesticides in Pharma, In Vitro Tox (Pesticide & Invertebrate Tox Models: rotenone, antimycin & cyanide), Bradford-Hill Analysis
Chemistry	<u>Chemistry Degree</u> (44 Credits), <u>ROCKS Member</u> , Taught <u>Environmental Chemistry Lab</u> <u>Research Chemist</u> for ~9 years, Know <u>DEEM Software</u> , Water Treatment Expertise, QSAR
Physical Science	<u>Physics Degree</u> (35 Credits, with electronics research & engineering), Taught <u>Physics Laboratory</u>
Pharmacology	<u>Pharma Experience</u> at Pfizer & GSK pharmaceuticals, <u>Tox And App. Pharm. Journal Editing</u>
Exposure Modeling	Developed P-Chem model to explain pesticide transfer from collars to fur to hand to mouth based on physics, biochemistry & chemistry partitioning & experience as a research chemist (RD Award). Lived on Farm 22 years: <u>Used many herbicides, insecticides, fungicides, Physics & Chemistry degree</u> gives understanding of important exposure factors (vapor pressure, mp, bp, viscosity, surface tension, partition coefficients, pKa, solubility, diffusion, charge, etc)
Biochemistry/Molecular Biology-MOA Knowledge	<u>PhD in Biochemistry/Molecular Biology</u> , MOA at molecular level skills, Taught Biochem Lab, Regularly review pesticide biochemistry papers for senior staff
Physiology	<u>Muscular Dystrophy Research</u> , <u>Surgery in animals</u>
Mathematics, Data Analysis & Modeling	<u>Mathematics Minor</u> , Statistical Design of Experiments Course, "BMD" Calculations in pharma
Cancer Research	<u>Cancer Postdoc research</u> on herbicide Acetylaminofluorene in vivo published in <i>PNAS</i> , Cancer presentation at SOT
Writing & Presentation Skills	<u>Nature paper</u> (first author), papers in <i>PNAS</i> , <i>JBC</i> , <i>Arch. Tox</i> , <i>Repro. & Dev.</i> Toxicology Chapter, Two in vitro toxicology book chapters, protein folding book chapter, Papers cited over 1000 times, <u>Journal Editing</u> (<i>JBC</i> , <i>TAAP</i> , etc), Risk Assessments, <u>Over 52 Seminars</u> in 4 Countries (USA; London, Sandwich England; Zagreb, Vodice
In Vitro & Tox21 Skills	<u>Designed & Adapted Assays</u> >10 years, Patents, In Vitro toxicology review articles, <u>Assays implemented into ToxCAST</u>
Training	I have helped train and mentor the newer toxicologists at Cellumen, Pfizer, GSK, US EPA (HED, RAD). I have supervised multiple research associates over the years, such as when I was a senior scientist in industry. I also participated in the student mentoring programs at the SOT meetings. My <i>Nature</i> paper has been cited over 359 times and led to other disease investigations. My imaging toxicology paper has been cited over 423 times and widely implemented and copied.
Honors	<u>DABT Toxicology Certification</u> , European Registered Toxicologist (<u>ERT</u> board certification); <u>Physics Honor Society</u> , <u>Mathematics Honor Society</u> ; US EPA Innovation Award; US EPA Bronze Medal

Experience:

My mitochondrial research published in *Nature* led to successful clinical trials for a muscular dystrophy therapy. I have a very powerful skills set to be a versatile scientist with my toxicology background, research chemist work, and physics/mathematics degrees plus my direct experience with chemical exposure on a farm. Very few people possess my mix of skill. I have demonstrated teamwork, high productivity, quality assurance and customer service at several jobs, as demonstrated by my past bonus awards. I have skills in data analysis, developing new methods, teamwork and instruction on technical matters. I also have experience in hazard characterization, exposure and risk assessment of chemicals, plus quality control methods.

In my past experience, I have planned and performed scientific investigations, developed new methods or adapted existing methods and validated these models, then implemented them in practical applications. I have originated projects and led them in my previous experience. I have developed interdisciplinary analytical procedures in toxicology, physics and chemistry areas. I have performed environmental sampling and testing to determine the exposure to waste products of industry. I have excellent analysis and problem solving skills, from the most advanced toxicology models in pharma. Obviously, I have pharmacology experience from working at Pfizer and GSK pharmaceuticals in the Safety Sciences Department (Toxicology/Pharmacology). At Pfizer, my main focus was developing advanced in vitro toxicology assays similar to the Tox21 initiative. At GSK my focus was antimicrobial compound research. I have presented many toxicology seminars in scientific meetings

to various stakeholders in industry and the public, thus I appreciate the needs of various viewpoints. I have published my research in outstanding journals such as *Nature Genetics*, thus I have excellent communication skills. At Lipton, I was deeply involved in the ISO quality assurance (QA) implementation.

A versatile scientist absolutely needs degrees in the multiple disciplines to perform at the higher levels, which is an interdisciplinary endeavor, with a PhD degree preferred. My background in toxicology from pharma provides excellent experience in the most advanced toxicology models in the world, an exceptional education for hazard characterization and risk assessment of chemicals/pesticides. My DABT board certification confirms that I am at the top of my field in toxicology, as evaluated by my peer toxicologists. I have a BS degree in Chemistry and functioned at a high level as a research chemist for about 9 years for Lipton. Thus, I well comprehend the chemistry aspects of hazard identification, also supported by my work on the US EPA ROCKS QSAR and Risk Assessment committees. I lived on a farm for 22 years, so I well understand the exposure aspect (ORE) of occupational chemical use, having directly applied pesticides many times myself. I also have a degree in Physics, and interpreting the physical properties of chemicals is crucial to interpreting their exposure potential (solubility, viscosity, melting point, hydrophobicity, surface tension, etc) and I have performed many of these physical tests myself. My environmental testing and water purification experience also aids my understanding of exposure to hazardous materials from industry. I have a PhD in Biochemistry/Molecular Biology which is very valuable in determining the mechanism of toxicity of chemicals (i.e. MOA), often the result of enzymatic inhibition or receptor binding or damage at the molecular level. Biochemistry is a strong bridging discipline between toxicology and residue chemistry. My mathematics minor is very valuable in complex calculations, advanced modeling, and statistical analysis. My supervisor at Lipton was a statistical modeler and I was taught statistical design of experiments techniques. I have considerable experience in computer programming which can aid modeling projects.

I have >10 years experience developing in vitro toxicology assays and analysis. My experience with toxicology from pharma is very valuable, since some chemicals are also drugs or have the same mechanism of toxicity. Some pharma companies also make chemicals, so understanding their methods is important. I am continually seeking knowledge and science information, as demonstrated by my continued meeting attendance, presentations and publications. My memberships in the Physics Honor Society, Society of Toxicology, Diplomat of the American Board of Toxicology and Mathematics Honor Society demonstrate my consistent quest for excellence. I have taught in Chemistry, Biochemistry, Physics and Toxicology settings.

Introduction I have over 10 years experience with product and assay development, with over 10 years experience in the pharmaceutical-related industry. I have worked for the US EPA, Pfizer, Cerep, Lipton, and GSK in product and assay development (risk & toxicology/pharmacology departments). I have a BS in Analytical Chemistry, with other degrees in Physics and Mathematics. I also have a PhD in Biochemistry, with 4.5 years post-doctoral experience (mostly toxicology/pharmacology research). I am a Diplomat of the American Board of Toxicology, a certification confirming mastery of the specialty.

I strive for excellence and my recent evaluations have been “exceeds expectations” or “outstanding”. I am a very motivated person, with papers in excellent journals such as *Nature Genetics* (first author) and *PNAS*. My *Nature Genetics* paper was central to our laboratory getting a \$1.4 million grant subsequently and it was listed as one of the top research advances of the year by *Neurology Today*. This work was also a pivotal one in both the fields of mitochondrial and muscular dystrophy research that has led to successful human clinical trials. I am an expert in High Content Screening imaging and mitochondrial research.

My independent initiatives have been pivotal to make my previous projects successful. I work well in a team format, but I also work very well independently. I have demonstrated leadership roles. I have very good problem-solving skills and I have initiated new projects at previous pharmaceutical companies. I have excellent oral and written communications skills. I have presented my research at international meetings. I have good equipment repair skills. I have experience with HCS and HTS laboratory automation. I have supervisory skills experience. I have experience with patents, new product development and process development.

I have over 10 years work in product development and I have a great deal of experience in this area. I have provided a great deal of input into products for my past companies (technically and as a market viewpoint). I even supervised implementing new processes that I designed into the production facilities. I am extremely practical in business matters as they apply to research.

Research expenditures (time and money) need to be focused on products that will make profit for the company. Research decisions need to be market driven and based on what the customers will purchase, so that the company can prosper. As a manager, I am demanding, but fair. I have always met my goals and I often exceed them. I obtained the prestigious Highly Skilled Migrant Programme UK Visa while working for Pfizer.

Summary: Risk assessments for pesticides experience, Toxicologist, PhD in Biochemistry, Nature & PNAS publications, >10 years post-graduate experience as a scientist, 14 years industrial research experience, 4.5 years postdoctoral research experience, toxicology experience at US EPA, Pfizer, Cerep, and GSK (toxicology/pharmacology), BS degrees in Chemistry and Physics/Mathematics, experience with many different types of assays (chemical, biochemical and physical), product development and production plant implementation experience, fluorescence microscopy assay expertise, High Content Screening, Macrolide biochemistry, GSK work experience, Muscle Research experience, Mitochondria research experience, Statistically Designed Experiments, Computer Programming, US Patent as first author, Lipton experience, Interests/knowledge in Diabetes and Transplantation, Environmental testing, “ISO9000” skills, SDS-PAGE, Immuno-Assays, Graduate School GPA=3.9, EpiSuite QSAR Chemical Modeling Software, ICCVAM, Journal Editing experience, DABT Certification, PBPK, Process Chemist experience, Highly Skilled Migrant Programme UK Visa, Senior Scientist in biotech

Work Experience:

Toxicologist, US Environmental Protection Agency (US EPA): 8 Years August 2, 2009-Present. Work involved writing and reviewing hazard characterizations and risk assessments for herbicides, fungicides, insecticides, and toxic substances to protect the environment and the general public. Duties also involved critically reviewing tox studies or protocols, writing data evaluation records, presenting tox research at SOT meetings, interacting with the press, participating in QSAR evaluations and providing scientific guidance to in vitro tox assay development, as well as mitochondrial-based studies. I also am a member

of the ROCKS committee, which evaluates the structural properties of chemicals and residues in plants/animals. I was a co-author on a 20-page book chapter reviewing organotin toxicity and its reproduction/developmental/endocrine disruption effects. My farm experience with many chemicals, chemistry, toxicology and physics backgrounds provide unique insights into the needs of the consumers, public, wildlife and manufacturers. I received an award for developing a physical chemistry model of exposure. I am also on the Risk Assessment Review Committee (RARC) which has the final evaluation of EPA risk assessments. I participated in a Scientific Advisory Panel on the pyrethroids. Presented 6 times at SOT: mitochondrial toxins, organotin endocrine model, neurotoxicity signs, toxicology application of thermodynamics, organelle imaging toxicology, cancer biology models. Dermal, inhalation and gastro-intestinal policy work, as well as toxicity structural alerts and qualitative risk assessment strategies. OECD dermal sensitization assay validation team. Risk Assessment Forum. HazRATT committee co-chair. Lung Toxicity Project toxicology lead (Innovation Award). Focus risk assessment committee, Structure Activity QSAR committee, Mentoring and training new staff

Cellular Toxicologist-Senior Scientist Cellumen, Inc.: 2.5 Years Nov. 1, 2006-March, 2009, Research involved developing new test assays using advanced HCS imaging technology to assess drug toxicity and mechanism of action, representing company in booth at trade shows and overseeing collaborations with partner companies. Primary and tumor cell isolation/propagation for use in assay development. I developed and patented a panel of assays which was the major revenue producer for the company and was a senior level-researcher that contributed to major research decisions and policies in the company. I supervised my own research associate, as well as co-supervised several others. Research also yielded a publication on cellular systems biology and a US patent (first author). Trained and mentored staff, wrote SOPs, set policies, and QC of data. Laid off due to economic recession.

Toxicology Assay Consultant, GSK Pharmaceuticals 9 Months HTS Lab (Pliva Site, Zagreb, Croatia): Feb. 1, 2006-Oct. 15, 2006 Research involved developing new test assays to assess drug toxicity and cellular action (mostly antimicrobials and antibiotics) utilizing fluorescence plate readers, FACS and fluorescence microscopy. Research into alternate macrolide pharmaceutical applications, immunotoxicity assays, mitochondrial assays and effects on cells at the sub-cellular level were also performed. I supervised two research associates in the HTS laboratory. Research yielded two review articles on tox assay development guidance. I left when offered Cellumen position back in the USA.

Cellular and Biochemical Toxicologist, Pfizer Pharmaceuticals 3 Years, Sandwich Site (Kent England, Dec. 2002-Dec. 2005). Research involved developing new test assays to assess drug toxicity utilizing fluorescence microscopy and High Content Screening technology in the Safety Sciences/Pharmacology department and in collaboration with Cerep and the University of Padova, Italy. The first year of research was in Padova, Italy at the University developing muscle tox assays and the remaining two years were in Sandwich, England at the Pfizer Global Research Centre (supervised by SRG with Cerep funding). Research also involved optimizing High Content Screening microscopy technology for mechanism of action and toxicology studies for drug discovery. Supervision and training of 3 junior lab members was also involved. Research yielded a high-impact 25-page paper on HCS applications in toxicology with impressive concordance to human toxicity which has been highly cited (Arch. Tox. 2006, cited 423 times). Many types of compounds were evaluated on the system such as antibiotics, medications, pesticides, solvents, household chemicals, etc. The research was involved with animal reduction, refinement and replacement (the 3 R's and ICCVAM projects). I started this research while still in Italy during postdoctoral study (one year overlap period). Completed three full contracts and went to GSK.

Research Chemist, Lipton/Kind & Knox, Inc./DGF Stoess/Gelita 9 Years Chemist in research and development laboratory. Research involved test method development and experiments/troubleshooting in the production facilities. Other work involved developing new products and improving existing products derived from collagen for the pharmaceutical, photographic and food industries. Implementing new technology, up-scaling laboratory research into the production facilities, and supervising laboratory interns was also performed. Kind & Knox is a division of DGF Stoess, the largest producer of medical-grade collagen and collagen-derived protein products in the world (previously owned by Lipton/Unilever). I made presentations to the general manager.

I have "ISO9000" QA/QC skills, as well as statistical designed experiments experience. I have excellent skills of adapting quickly and determining which components of a process are critical and to find solutions to improve both efficiency and quality. I worked as a process scientist in a development laboratory, transferring laboratory models into practical implementation on a large scale. I also have extensive experience in water treatment, purification and testing. I left to complete a PhD program.

Post Doctoral Study, Paolo Bernardi Laboratory 2 Years (University of Padova, Italy, Department of Biochemistry and Pathology): June 15, 1999-June 2001. Supported by Telethon Fellowship/Grant #1141 ("**Mitochondria as Targets of Pharmaceutical Intervention in Muscle Disease**"). Research involved the study of anesthetics and extra-cellular matrix protein knockout on skeletal muscle as models of muscular dystrophy. The study of the mitochondrial permeability transition/apoptosis in intact muscle cells, fibroblasts and hepatocytes was performed. The calcein-release method and the cytochrome c release immunoassay were used to monitor the permeability transition in intact cells (normal vs cancerous), utilizing fluorescence microscopy and confocal microscopy, respectively. Calcium measurement techniques/signaling (cytosolic and mitochondrial) were also performed in collaboration with the Tullio Pozzan laboratory. Most of the research was in toxicology areas.

***Research yielded a *Proceedings of the National Academy of Sciences* article on an epigenetic carcinogen and a *Journal of Biological Chemistry* publication on anesthetic myotoxicity.

Post Doctoral Study, Paolo Bonaldo Laboratory 2 Years (Department of Histology, Microbiology and Medical Biotechnologies, University of Padova) June 2001-Dec. 2003. Supported by Telethon Grant #1201 ("**Study Of Bethlem Myopathy Using Collagen 6 Knockout Mice As An Animal Model**"). Research involved the study and histology of collagen VI knockout mice in as a model of Bethlem/Ullrich Muscular Dystrophies. The mitochondrial permeability transition in intact muscle cells was monitored using TMRM fluorescence assays by fluorescence microscopy and confocal microscopy. Calcium signal transduction and calcium measurement techniques were also performed. Also, started performing research for Pfizer while still in Italy during my postdoctoral study.

***Research yielded a *Nature Genetics* publication with myself as a first author and listed in *Neurology Today* as one of the top research advances of 2003. *This research led to successful human clinical trials for a muscular dystrophy therapy, methods replicated for other diseases and cited 359 times.*

Effluent Water Monitoring Consultant 4 Months (IBP Inc., Iowa, Kansas, Texas) Collected samples of production plant effluents at various locations and waste water lagoons and tested them in the laboratory for industrial waste products that could adversely affect the environment.

Skills: Toxicology risk assessment and data analysis, QSAR, ICCVAM, COOP disaster team, Fluorescence and confocal microscopy, High Content Screening microscopy, HPLC skills, Problem-solving skills, Calcium testing, Protein purification/chemistry, Polymer chemistry, Affinity and Ion exchange chromatography, A wide range of chemical and physical testing assays, Primary cell isolation and culture (hepatocytes, skeletal muscle, fibroblasts, cardiac myocytes, etc.), Electrophoresis, Western blotting, Electronic and mechanical equipment repair skills, Equipment modification skills, Mitochondrial and permeability transition expertise, Mitochondria isolation/testing (heart, liver, kidney, muscle, invertebrates, etc.), Metabolism biochemistry and biochemical assays, Enzyme kinetics, Interests in structure/function relationships of compounds on biological systems, Computer skills and programming, Statistical designed experiments, Animal surgery, Invertebrate tox models, Biochemistry laboratory teaching, Research intern supervision, Team project research, Excellent English language skills, "ISO9000" skills (QA/TQM), Macrolide biochemistry, Muscle research experience, New Product development, Process development, Computer skills (Excel, Word, PowerPoint, programming, etc.), Company Representative at trade show booth, Scored very high on PA Forensic Scientist exam and the Environmental position exam, Environmental Chemistry laboratory instructor, Defibrillator/First Aid, ToxSAC experience, Basic & Applied Myology Board Member, Highly Skilled Migrant Program UK Visa

Specialized Training:

High Content Screening Imaging Microscopy Training (3 weeks) Course covered in-depth the theory and practical applications of simultaneous, multi-probe fluorescence microscopy in research and medicine. Cellomics, Inc. Pittsburgh, Pennsylvania, 2003 (updated in 2005)

Ion Exchange Chromatography/Technology Course (3 Days) Course covered applications and theory of advanced ion exchange purification and separation methods in industry and research. The focus was on the purification of drinking water from hazardous materials. Illinois Water Treatment Co., Dearborn, Illinois

Membrane Separation/Purification and Filtration Technology Course (3 Days) Course covered applications and theory of advanced membrane separation/purification/filtration technology in industry and medicine. Chicago, Illinois.

Statistical Design of Experiments (T.J. Lipton, Inc.) Course covered the basics of designing statistically optimized experiments and data interpretation

ISO Quality Systems Covered the essentials of “ISO9000” type of quality systems implementation and auditing procedures

US Patents Workshop (MIC, 3 Days) Course covered the fundamentals of US patent concepts and applications

EpiSuite OSAR Chemical Modelling Course Structure analysis relationships software, US EPA, 2009

Toxicology Study Groups US EPA 2009-2010 and 2017

Physiologically Based Pharmacokinetic (PBPK) Models in Risk Assessment SOT Meeting, 2011

Grant Writing Workshop

Advanced Writing Training US EPA, 2011

Risk Assessment Training US EPA, 2011

Neurotoxicity Assessment Training US EPA 2012

NIST Standards Workshop NIST 2013

Alternative In Vitro Toxicology Testing for the 21st Century SOT Workshop, 2012

NIH Nanomaterials Workshop NIH, 2013

Practical Applications of Emerging Scientific Tools, ASCCT Symposium NIH, 2013

Adverse Outcome Pathways Workshop NIH 2014

Primary Mitochondrial Disorders Workshop NIH 2014

OECD QSAR Toolbox Training June 2017

Alternative Methods Toxicology Workshop IIVS July 2017

Education:

Bachelor of Science Degree (Morningside College)

Major: *Chemistry* Minors: *Physics, Mathematics*

Undergraduate Research involved interfacing normal laboratory equipment to computers. I was a laboratory instructor for an Environmental Chemistry class and an Electronics (Physics) class.

PhD Degree: Biochemistry and Molecular Biology (Sanford School of Medicine, GPA=3.9)

Doctoral research involved developing methods to protect vital tissues from hypoxia (i.e. transplantation conditions) or conditions of exposure to toxins. In particular, our laboratory sought to protect mitochondrial integrity and tissue/cell viability during conditions of hypoxia/transplantation, mitochondrial inhibition, toxic insults or stress. Most experiments involved toxicology, metabolism or pharmacology research (>78 credit hours in toxicology research). Other projects during the doctoral program involved invertebrate toxicity models, protein folding/chaperone/collagen synthesis enzyme biochemistry and ethanol metabolism enzyme kinetics (i.e. aldehyde dehydrogenase).

***Research yielded a *Biochemical Biophysical Research Communications* article on the toxicity of aldehydes and a book chapter publication *Prolyl Hydroxylase, Protein Disulfide Isomerase and Other Structurally Related Proteins*.



UNIVERSITY OF
SOUTH DAKOTA
SANFORD SCHOOL OF MEDICINE

October 16, 2012

Ms. Brittany J. Jones
Human Resources Specialist
U. S. Environmental Protection Agency
Human Resources Management Division—Branch A
Research Triangle Park, North Carolina 27711

Dear Ms. Jones:

RE: William A. Irwin, PhD, DABT

Dr. William Irwin has asked that I write regarding his application for a position with your organization. Will earned his Ph.D. in our Department of Biochemistry and Molecular Biology in 1999. I was chair of the department and a member of Will's dissertation committee. The title of Will's dissertation was the "An Investigation into the Protective Mechanisms of Fructose on Hepatocytes During Hypoxia". This work focused on the impact of a variety of mitochondrial toxins that induce hypoxia in mammalian hepatocytes. Cyanide, rotenone and antimycin A, all government-regulated pesticides, damage hepatocyte mitochondria which results in hepatocyte death and ultimately liver failure. Will demonstrated that fructose can protect hepatocyte mitochondria from toxin damage, thereby preventing hepatocyte death. Will's research approaches and methods were the tools of biochemical toxicology. The identification of fructose's protection from the toxic effects of these compounds is applied toxicology.

If I can provide additional information, please do not hesitate to contact me.

Sincerely yours,

A handwritten signature in black ink, appearing to read 'R. Lindahl'.

Ronald Lindahl, Ph.D.
Executive Dean

Patents: “Cellular Systems Biology Assays to Assess Human Toxicity Potential Utilizing Primary Rat Hepatocytes” (William Irwin, Larry Verneti, Kate Johnston), Filed in USA and Europe (pending)

Publications:

Irwin, W., Bergamin, N., Sabatelli, P., Merlini, L., Megighian, A., Reggiani, C., Braghetta, P., Columbaro, M., Volpin, D., Bressan, G.M., Bernardi, P., Bonaldo, P., “**Mitochondrial Dysfunction and Apoptosis in Myopathic Mice with Collagen VI Deficiency**” (2003) *Nature Genetics* Vol. 35 (No. 4): 367-371

See also commentaries about this article:

Rizzuto, R. **The Collagen-Mitochondria Connection** (2003) *Nature Genetics* Vol. 35 (No. 4): 300-301

From the Editor’s Desk (2004) *Matrix Biology* Vol. 22: 519-520

Editors’ Picks: Top Research Advances From 2003 (2004) *Neurology Today* Vol.4 (No. 1): 5-6

Hayworth, J. “**Mitochondria Play a Role in Disease (Biochemist William Irwin)**” *Sioux City Journal* (2003)

Hayworth, J. “**Scientist Irwin Takes Studies To Italy**” *Sioux City Journal* (2003)

Kloehn, P., Soriano, M., Irwin, W., Penzo, D., Scorrano, L., Bitsch, A., Neumann, H-G., Bernardi, P. “**Early Resistance to Cell Death and to Onset of the Mitochondrial Permeability Transition During Hepatocarcinogenesis With 2-Acetylaminofluorene**” (2003). *Proceedings of the National Academy of Sciences* Vol. 100 (No. 17): 10014-10019

Irwin, W., Jelic, D., Antolovic, R. “**Biomarkers for Drug Discovery: Important Aspects of *in vitro* Assay Design for HTS and HCS Bioassays**” (2006) *CROATICA CHEMICA ACTA 81 (1): 51-59*

Verneti, L., Irwin, W., Guiliano, K., Gough, A., Johnston, K., Taylor, D. “**Cellular Systems Biology Applied to Pre-Clinical Safety Testing**” *Drug Efficacy, Safety, and Biologics Discovery: Emerging Technologies and Tools* (Wiley & Sons, 2008)

Irwin, W., Jelic, D., Antolovic, R. “**Bio-Assays for Drug Safety and Mechanism Assessment: Design, Precautions and Integration**” (“Medicinal Chemistry in Drug Discovery”, July 2009)

Doherty, J., Irwin, W., “**Organo-Tins: Reproductive and Developmental Effects in Mammals**”, US EPA sponsored, Manuscript published in the book “Reproductive and Developmental Toxicology”, Elsevier, February 2011

Irwin, W., Fontaine, E., Penzo, D., Bernardi, P., “**Bupivacaine Myotoxicity Is Mediated By Mitochondria**” (2002). *Journal of Biological Chemistry* Vol. 277(No. 14): 12221-12227.

Irwin, W., Gaspers, L., Thomas, J., “**Inhibition of the Mitochondrial Permeability Transition by Aldehydes**” (2002). *Biochemical Biophysical Research Communications* Vol. 291 (No. 2): 215-219

Noiva, R., Onodera, S., Schwaller, M., Irwin, W. “**The Peptide Binding Site of Protein Disulfide Isomerase**” pp. 369-395. In *Prolyl Hydroxylase, Protein Disulfide Isomerase and Other Structurally Related Proteins* (1998), Editor Norberto Guzman, Marcel Dekker, Inc. New York

O’Brien, P., Irwin, W., Diaz, D., Howard-Cofield, E., Bernardi, P., et al “**High Concordance of Drug-Induced Human Hepatotoxicity With *in vitro* Cyto-Toxicity Measured in a Novel Cell-Based Model Using High Content Screening**” (2006). *Archives of Toxicology*: 2006 Sep;80(9):580-604

Slaughter, M., Hougham, C., Hitchcock, J., Potter, A., Brain, P., Irwin, W., “**A Medium-Throughput, Sensitive *in vitro* Screen for Chronic Cyto-Toxicity Assessment of Nucleoside Analogues**”, Manuscript in preparation

Irwin, W., Gaspers, L., Thomas, J., “**Fructose Protects Hepatocytes During Hypoxia or Toxin Exposure by Inhibition of the Mitochondrial Permeability Transition**”. Manuscript in preparation

Affiliations: *American Board of Toxicology (ABT), Society of Toxicology (SOT), Physics Honor Society, Mathematics Honor Society, American Chemical Society, ABT Standards of Knowledge Committee, SOT National Capital Area Chapter, SOT In Vitro Toxicology Specialty Section*

Languages: English (fluent), Italian (essential), Spanish (basic), Croatian (basic)

Invited Seminars:

American Chemical Society Annual Meeting (August, 2017), “**Qualitative Risk Assessment Strategies**”

US EPA (October, 2016), “**Critical Aspects of In Vitro Assay Design, Analysis and Integration**”

SOT Meeting (March, 2015), **Ask An Expert Program: “In Vitro Toxicology Assay Design”**

SOT Meeting (March, 2014), **Ask An Expert Program: “Mitochondrial Toxicology”**

US EPA (Oct. 2, 2012), “**Important Aspects of In Vitro Assay Design and Interpretation**”

US EPA (May 25, 2010), “**Mitochondrial Toxicities and Interactions With Other Organelles**”

Notre Dame School of Medicine (May 29, 2009) “**Organelle Pathologies in Disease States**”

Stem Cell Research Center, University of Pittsburgh (Feb. 9, 2009) “**Mitochondrial and SR Pathologies in Muscular Dystrophy**”

Croatian Society of Biochemistry Annual Meeting (Oct. 3, 2006, Vodice, Croatia), “**High Content Screening Imaging Applications in Toxicology and Pharmaceutical Discovery**”

Becton Dickinson (August, 2006) “**High Concordance of HCS-Based Toxicity Assays With Human Drug Toxicity**”

Cellumen, Inc. (August, 2006) “**High Content Screening Applications in Drug Discovery Programs**”

Cellomics, Inc. (August, 2006), “**Human Drug Toxicity Concordance With High Content Screening In Vitro Assays**”

University of Iowa Medical School (Aug. 10, 2006) “**Mitochondrial Research: Experimental Design, Assay Precautions and Data Interpretation**”

University of Iowa Medical School (Aug. 9, 2006) “**High Content Screening Fluorescence Microscopy Applications in Medical Research**”

University of Iowa Medical School (K. Campbell sponsor, Aug. 9, 2006) “**In Vivo and In Vitro Characterization of the Collagen VI Knockout Mouse Model of Muscular Dystrophy**”

Croatian Genetic Society, (May 17, 2006, Zagreb, Croatia) “**Use of Macrolides as Discovery Tools in Medical Research: Muscular Dystrophy Applications**”

Pfizer Pharmaceuticals, Safety Sciences (October 24, 2005, Sandwich, England) “**Organelle Pathologies in Muscle Disease**”

High Content Screening Conference (October 19, 2005, Le Meridien, London, England) “**Predicting Drug-Induced Hepatotoxicity With in vitro Cyto-Toxicity Assays: High Content Screening Methods**”

Croatian Society of Biochemistry and Molecular Biology (September 2005, Zagreb, Croatia) “**The Unexpected Organelle Pathology in Collagen VI Deficiency Muscular Dystrophies**”

Pfizer Pharmaceuticals (March 2005, Sandwich, Kent, England) “**The Role of Mitochondria in Carcinogenesis**”

Sanford School of Medicine (February 28, 2005) “**The Unexpected Organelle Pathologies in Collagen VI Deficiency Muscular Dystrophies**”

Pfizer Pharmaceuticals (May 2004, Sandwich, Kent, England) “**High Content Screening Multi-Channel Fluorescence Microscopy Applications in Toxicology**”

Pfizer Pharmaceuticals (March 2004, Sandwich, Kent, England) “**Important Biochemical and Metabolic Considerations in Muscle Diseases and Their Therapies**”

Pfizer Pharmaceuticals (November 2003, Sandwich, Kent, England) “**Mitochondrial Membrane Potential Measurement Applications in Toxicology, Techniques and Precautions**”

University of Padova, School of Medicine (October 2003, Padova, Italy) “**High-Content Screening Methods: Utilizing Coherent Multi-Probe Fluorescence Microscopy to Monitor Simultaneous Sub-cellular Events**”

Pfizer Pharmaceuticals (May 15, 2003, Sandwich, Kent, England) “**Anesthetic Toxicology: Calcium And Mitochondrial Roles In Muscle Pathology**”

Padova Foundation of Organ Transplantation (March 20, 2003, Padova, Italy) “**Organ Transplantation: Important Metabolic and Biochemical Considerations**”

Sanford School of Medicine (September 28, 2001): “**An Animal Model of Human Bethlem Myopathy: Muscle Characterization of Collagen VI Knockout Mice**”

NovaSite Pharmaceuticals (September 21, 2001, San Diego, California,): “**Muscle Characterization of Collagen VI Knockout Mice: An Animal Model of Human Bethlem Myopathy**”

University of Colorado, Health Sciences Center (December, 1999, Denver, Colorado): “**Fructose and Glycerol Protection of Hepatocytes During Hypoxia Is Mediated by Mitochondria**”

University of North Carolina (December 1999, Chapel Hill, North Carolina): “**Fructose Protects Hepatocytes During Hypoxia by Inhibition of the Mitochondrial Permeability Transition**”

-
DGF Stoess, Inc. (February, 1993, Sioux City, Iowa) “**The Biochemistry of Collagen Proteins and Implications in Various Pathologies**”

Sanford School of Medicine (January 1993): “**Collagen Biochemistry in Health and Disease**”

Seminars:

London School of Hygiene and Tropical Medicine (May 22, 2009) **“High Throughput Screening Assay Applications in Tropical Disease Research”**

Toxicology 2003 Conference (Dec. 9 2003, London, England) **Predicting Drug-Induced Human Hepatotoxicity With In Vitro Cytotoxicity Assays**

University of Padova, Department of Medical Biotechnology (May 2003, Padova, Italy): **“Collagen VI, Calcium and Mitochondrial Roles In Bethlem Myopathy”**

University of Padova, Department of Microbiology (December 2002, Padova, Italy): **“Important Metabolic Considerations in Muscle Diseases for Therapeutic Intervention”**

University of Padova, Department of Histology (May 2002, Padova, Italy): **“An Animal Model of Human Bethlem Myopathy: Characterization of the Pathological Defects in the Skeletal Muscles of Collagen VI Knockout Mice”**

University of Padova, Department of Biomedical Sciences (July 2001, Padova, Italy) **“Ullrich Muscular Dystrophy Is Caused By Mutations In The Collagen VI Genes”**

University of Padova, Department of Medical Biotechnology (May 2001, Padova, Italy): **“The Role of Mitochondria in Muscle Cell Death”**

University of Padova, Department of Biomedical Sciences (March 2000) **“HIV-1 Mediates Apoptosis By Its Proteins Inducing The Mitochondrial Permeability Transition”**

University of Padova, Department of Biomedical Sciences (September 1999, Padova, Italy): **“Fructose Protects Liver During Hypoxia By Its Metabolite Glyceraldehyde Protection of Mitochondrial Function”**

Sanford School of Medicine (June 1999): **“An Investigation Into the Protective Mechanisms of Fructose To The Liver During Hypoxia”**

Sanford Medical School, Department of Biochemistry and Molecular Biology (January 1998): **“Membrane Transporters That Lack Protein Components”**

Sanford School of Medicine (October 1997): **“Artificially-Gated Pores: Designer Pore Applications in Cancer Chemotherapy, Cryopreservation and Biosensors”**

Sanford School of Medicine (January 1997): **“Immunophilins: Protein Folding Roles in Signal Transduction, Vision, Secretion and AIDS”**

Sanford School of Medicine (December 1996): **“Prion Proteins and Disease”**

Sanford School of Medicine (March 1996): **“Gerontogenes, Diet, Free Radicals and Aging: Factors That Affect the Lifespan of an Organism”**

Sanford School of Medicine (October 1995): **“The Involvement of Mitochondria in Cell Life and Programmed Cell Death”**

Sanford School of Medicine (May 1995): **“How Does Fructose Protect Liver Tissue From Hypoxia?”**

Sanford School of Medicine (October 1994): **“The Role of Mitochondria in Ischemia-Reperfusion Injury”**

Sanford School of Medicine (April 1994): **"Investigation Into the Role of the Protein Disulfide Isomerase Subunits in Prolyl Hydroxylase Activity"**

Meetings Presentations:

American Chemical Society Annual Meeting (August 2017): **"Adverse outcome pathways- a mechanistic approach for future risk assessments"**

American Chemical Society Annual Meeting (August 2017): **"In vitro metabolomics as alternative testing strategy for predicting adverse outcome pathways of the exposome"**

Mitochondrial Health Meeting (June 2017, Arlington, VA) Poster Presented: **"Mitochondrial Involvement in Carcinogenesis"**

Society of Toxicology Meeting (March 2017, Baltimore MD) Poster Presented: **"Mitochondrial Roles in Tumorigenesis"**

Mitochondrial Biology Symposium (NIH, Bethesda, MD, May 19-20, 2016) Poster Presented: **"Organelle Imaging Toxicology: Utilizing Coherent Multi-Probe Fluorescence Microscopy to Monitor Mitochondrial Health and Other Simultaneous Sub-cellular Events"**

Future Tox III, Society of Toxicology Meeting (November 2015, Crystal City, VA) Poster Presented: **"Utilizing Coherent Multi-Probe Fluorescence Microscopy to Monitor Simultaneous Sub-cellular Events"**

Society of Toxicology Meeting (March 2015, San Diego, CA) Poster Presented: **"Organelle Imaging Toxicology"**

Society of Toxicology Meeting (March 2014, Phoenix, AZ) Poster Presented with Professor Don Fox: **"Compound-Induced Bioenergetics Alterations: Relevance to Pathophysiology"**

Society of Toxicology Meeting (March 2012, San Francisco, CA) Poster Presented: **"Functional Observational Battery in Perspective"**

Society of Toxicology Meeting (March 2011, Washington, DC) Poster Presented: **"Organotin Toxicology: A Novel Mitochondrial Nernst Model"**

Society of Toxicology Meeting (March 2010, Salt Lake City) Poster Presented: **"The Role of Mitochondria In Toxicology"**

World Pharmaceutical Congress (May 2008, Philadelphia) **Represented Cellumen, Inc at trade booth**

High Content Analysis 2007 (Jan. 2007, San Francisco) **Represented Cellumen, Inc. at trade booth**

Croatian Biophysics Congress (September 2006 Rovinj, Croatia) Poster Presented: **"Non-Radioactive Fluorescence-Based Cell Quantitation Assay Development"**

Society For Biomolecular Screening Meeting (September 2005, Geneva, Switzerland) Poster Presented: **"An In Vitro Oxidative Stress Biomarker Assay For Drug Toxicity Screening"**

Telethon Convention (2005, Salsomaggiore Terme, Italy) Poster Presented: **"Therapeutic Intervention in Muscular Dystrophy Targeting Mitochondria"** Bernardi, P., Irwin, W., Angelin, A., Bergamin, N., Sabatelli, P., Merlini, L., Megighian, A., Reggiani, C., Braghetta, P., Columbaro, M., Volpin, D., Bressan, G.M., Bonaldo, P.

New R&D Opportunities Forum (December 9, 2004, Sandwich, England) Poster Presented ***Poster Presented: Low-Dose Enhancement Drug Responses in In Vitro Toxicity Assays: Detecting and Modelling Hormesis Effects of Drugs***

Ethical Innovation in the Laboratory (Sept. 21, 2004, Sandwich, England) Poster Presented: ***Utilizing In Vitro, Human Tumor Cell Line-Based Fluorescence Microscopy Screening Assays (High Content Screening) to Reduce Animal Testing in Drug Safety Assessments.*** The intent was to refine, reduce and replace animal testing (the 3 R's) with advanced in vitro toxicology models and ICCVAM initiatives.

Biomarkers Forum (April 29, 2004, Sandwich, England) Poster Presented: ***Evaluation of Fluorescence Microscopy-Based In Vitro Safety Assays (High Content Screening) For Predicting Drug Toxicity in Humans***

Telethon Convention (2004, Italy) Poster Presented: ***“Mitochondrial Intervention in Muscle Disease”*** Bernardi, P., Irwin, W., Angelin, A., Bergamin, N., Sabatelli, P., Merlini, L., Megighian, A., Reggiani, C., Braghetta, P., Columbaro, M., Volpin, D., Bressan, G.M., Bonaldo, P.

Group Italian Bioenergetics Biophysics Congress (2003, San Daniele, Italy) Oral Presentation: ***“Lack Of Collagen VI Causes Mitochondrial Dysfunction And Calcium Dysregulation In Skeletal Muscle”*** Irwin, W., Bergamin, N., Sabatelli, P., Merlini, L., Megighian, A., Reggiani, C., Braghetta, P., Columbaro, M., Volpin, D., Bressan, G.M., Bernardi, P., Bonaldo, P.

Telethon Convention (2003, Italy) Poster Presented: ***“Study of the Mitochondrial Pathogenesis of Bethlem Myopathy Using COL6A1 Knockout Mice as an Animal Model”.*** Bernardi, P., Irwin, W., Angelin, A., Bergamin, N., Sabatelli, P., Merlini, L., Megighian, A., Reggiani, C., Braghetta, P., Columbaro, M., Volpin, D., Bressan, G.M., Bonaldo, P.

Group Italian Bioenergetics Biophysics Congress (2001, Ancona, Italy) Oral Presentation: ***“An Animal Model of Human Bethlem Myopathy: Characterization of the Pathological Defects in the Skeletal Muscles of COL6A1 Knockout Mice”*** Irwin, W., Bergamin, N., Sabatelli, P., Merlini, L., Megighian, A., Reggiani, C., Braghetta, P., Volpin, D., Bressan, G.M., Bernardi, P., Bonaldo, P.

Group Italian Bioenergetics Biophysics Congress (2000, Friuli, Italy) Oral Presentation: ***“Mitochondria in Muscle Cell Death by Bupivacaine”*** Irwin, W., Fontaine, E., Bernardi, P.

South Dakota Academy of Sciences Congress (1996, Rapid City, South Dakota) Oral Presentation: ***“Fructose and Its Metabolite D-Glyceraldehyde Protect Hepatocytes During Hypoxia”***

South Dakota Academy of Sciences Congress (1995, Madison, South Dakota) Oral Presentation: ***“Investigation Into the Protective Mechanism of Fructose During Hypoxia”***

Keystone Symposia: Mitochondria and Pathogenesis (2002, Keystone USA). Poster Presented: ***“Mitochondrial Dysfunction in Muscle Fibers From Collagen VI Null Mice”.*** Irwin, W., Bergamin, N., Sabatelli, P., Merlini, L., Megighian, A., Reggiani, C., Braghetta, P., Columbaro, M., Volpin, D., Bressan, G.M., Bernardi, P., Bonaldo, P.

Telethon Convention (2002, Riva del Garda, Italy) Poster Presented: ***“Study of the Pathogenesis of Bethlem Myopathy Using COL6A1 Knockout Mice as an Animal Model”.*** Irwin, W., Bergamin, N., Sabatelli, P., Merlini, L., Megighian, A., Reggiani, C., Braghetta, P., Columbaro, M., Volpin, D., Bressan, G.M., Bernardi, P., Bonaldo, P.

Group Italian Bioenergetics Biophysics Congress (2001, Ancona, Italy) Poster Presented: ***“Mitochondrial Changes During Chronic Feeding With the Hepatocarcinogen Acetylaminofluorene”.*** Klohn, P., Soriano, M., Irwin, W., Bitsch, A., Neumann, H-G., Bernardi, P.

Telethon Convention (2001, Riva del Garda, Italy) Poster Presented: **“Study of the Pathogenesis of Bethlem Myopathy Using COL6A1 Knockout Mice as an Animal Model”**. Irwin, W., Bergamin, N., Sabatelli, P., Merlini, L., Megighian, A., Reggiani, C., Braghetta, P., Volpin, D., Bressan, G.M., Bernardi, P., Bonaldo, P.

Telethon Convention (2001, Riva del Garda, Italy) Poster Presented: **“Mitochondria as Targets of Pharmaceutical Intervention in Muscle Cell Death”** Irwin, W., Fontaine, E., Penzo, D., Bernardi, P.

Group Italian Bioenergetics Biophysics Congress (2000, Friuli, Italy) Poster Presented: **“Modulation of the Mitochondrial Permeability Transition at the P Site”**. Kloehn, P., Soriano, M., Irwin, W., Bitsch, A., Neumann, H-G., Bernardi, P.

Frontiers of Mitochondrial Research Congress (2000, Albany, USA) Poster Presented: **“The Role of Mitochondria in Muscle Cell Death”** Irwin, W., Fontaine, E., Penzo, D., Bernardi, P.

Telethon Convention (2000, Rimini, Italy) Poster Presented: **“Study of the Pathogenesis of Bethlem Myopathy Using COL6A1 Knockout Mice as an Animal Model”**. Irwin, W., Bergamin, N., Sabatelli, P., Merlini, L., Megighian, A., Reggiani, C., Braghetta, P., Volpin, D., Bressan, G.M., Bernardi, P., Bonaldo, P.

Telethon Convention (2000, Rimini, Italy) Poster Presented: **“Therapeutic Intervention in Muscle Cell Death By Mitochondrial Modulation”** Irwin, W., Fontaine, E., Bernardi, P.

Telethon Convention (1999, Rimini, Italy) Poster Presented: **“Mitochondria as Targets of Pharmaceutical Intervention in Muscle Cell Death”** Irwin, W., Fontaine, E., Bernardi, P.

Frontiers of Mitochondrial Research Congress (September 1998, Albany, USA) Poster Presented: **“Fructose Protects Hepatocytes During Hypoxia by Inhibition of the Mitochondrial Permeability Transition”** Irwin, W., Thomas, J.

American Society of Biochemistry and Molecular Biology Meeting (August 1997, San Francisco, USA) Poster Presented: **“Fructose Protection of Hepatocytes During Hypoxia and the Mitochondrial Permeability Transition”** Irwin, W., Thomas, J.

American Society of Biochemistry and Molecular Biology Meeting (1996, New Orleans, USA) Poster Presented: **“Protection of Hepatocytes by Fructose During Hypoxia”** Irwin, W., Thomas, J.

Mary Manibusan, Senior Managing Toxicologist
1150 Connecticut Ave., NW
Washington, DC
20005
(202) 772-4926
mmanibusan@exponent.com

Dear Sir or Madam,

December 13, 2015

It is my great pleasure to recommend Dr. William Irwin for a position with your company. I had the honor of hiring Dr. Irwin into the USEPA Office of Pesticide Programs when I had served as the Chief of the Toxicology and Epidemiology Branch. As a new hire, I immediately recognized Dr. Irwin's potential as a key contributor and future leader of the Office of Pesticide Programs.

During the years that followed, Dr. Irwin has not only met my expectations, but exceeded them at many different levels. He has been a key contributor to the pyrethroid FIFRA Scientific Advisory Panel meetings due to his direct experience in Pharma with sodium channels; this is an important project for the Agency. As a technical reviewer, he has served as a member of the Residue Of Concern Knowledge based Subcommittee, Quantitative Structure Activity Relationship and Risk Assessment Review Committee and has performed the many functions of a highly skilled and experienced risk assessor.

The Office of Pesticide Programs has some challenging chemicals, including Chlorpyrifos, Amitraz, Dicamba and Dr. Irwin has contributed to these excellent assessments. In total, he has given six unique presentations at SOT representing HED, served as a representative on the Scientific Integrity Committee and wrote a chapter on organotin pesticide endocrine disruption in a development and reproduction book.

Dr. Irwin has a unique background that includes a PhD in Biochemistry and ideal experience for mode of action investigations. I highly recommend Dr. Irwin for a technical leadership position within your company and organization.

Sincerely,

Mary Manibusan, Former Director of the Endocrine Disruptor Screening Program

December 1, 2015

To Whom It May Concern:

I am writing this letter of reference for Dr. William Irwin. Dr. Irwin is currently employed by the Health Effects Division of EPA's Office of Chemical Safety and Pollution Prevention and works in the capacity of toxicologist. In his current position, Dr. Irwin has made many contributions to the agency. A few of his notable achievements are listed below:

- Mitochondrial toxicology expert (models validated in clinical trials)
- In vitro toxicology expert (assays implemented into ToxCAST)
- Editor of a toxicology journal -DABT board certification in toxicology
- Key contributor to the pyrethroid Science Advisory Panel due to experience with sodium channels, an important project for the agency
- Member of the several HED peer review committees
- Served as lead toxicologist on several complex pesticide active ingredients
- Gave 5 presentations at SOT representing HED
- Served as representative on the Scientific Integrity Committee
- Wrote a book chapter on organotin pesticide endocrine disruption

William is a valuable member of HED. Although I am not his first -line supervisor, I am aware of his contributions to the organization. As his Division Director, I see William as a highly intelligent individual with scientific expertise in toxicology. William is a dedicated and hard-working scientist who often put his personal life on hold to work on issues of scientific importance.

Dr. Irwin holds himself and those around him to high standards, and takes great care in his work. Perhaps most importantly, William is a curious and creative scientist who likes to investigate new approaches and methods. He is very proficient with technology and his cell biology training, specifically in mitochondrial function, was very valuable to much of his work in HED.

Based on all the above factors, I recommend Dr. Irwin for a scientific position.

Sincerely,

Dana Vogel,
Director, Health Effects Division, OPP/OCSP/USEPA
