Curriculum Vitae

INGRID STUIVER, Ph.D.
Director, Clinical Research
Tri-City Medical Center

Professional Profile

More than twenty years experience in research, development and clinical research at academic and biotechnology institutions.

- *Clinical Expertise:* Established an institutional/hospital clinical research department and internal institutional project review committee; liaised with external IRB, Sponsors, CRO's and clinical research sites. Ensured that institution and ancillary groups such as pharmacy, laboratory and imaging were compliant with all FDA, OHRP, GCP rules, regulations and guidance's and federal, state and local laws. Wrote all policies and procedures pertaining to clinical research. Ensured that institutional and site staff and personnel were trained and/or credentialed in GCP, HSP and hospital policies and procedures. Established CMS compliant registration, invoicing and billing workflow. Developed contract negotiation guidelines and led all clinical research-related contract, agreement and budget negotiations. Developed all department specific policies and procedures. Participated in regulatory planning and led the execution of studies and study report preparation needed to meet FDA CMC requirements for a Xenotransplantable biological product. Managed Phase I/IIa and Phase II Clinical trial sites in the US and Europe for cervical dysplasia treatment; Directed, liaised with and ensured compliance of clinical CROs and core laboratories. Developed and wrote clinical protocols, IB, presentations and clinical study reports for FDA submission. Managed clinical materials manufacture and ensured that deliverables were received on time in US and EU. ADMET Certified.
- *GLP and GMP Experience:* Designed, wrote, edited, finalized SOPs for a GLP Facs Sorting Facility and Xenotransplantation cGMP facility; trained and monitored cGMP operators onsite and at cGMP facility for Xenotransplantation product manufacture.
- *Team Building:* An effective and articulate communicator with excellent, respectful, team-building and interpersonal skills; contributes significantly to the overall direction and focus of projects as they align with corporate objectives; works well with individuals at all levels and disciplines; believe that the basis of leadership is to assist others in their journey to success; led successful teams consisting of 2-6 people in the areas testing biologicals, GLP assay development/qualification and validation studies, cGMP process implementation and Clinical Research; enjoy taking on responsibility for challenging projects, finding solutions in a team-oriented fashion and collaborating with outside leaders in the field; excellent drive and work ethic; outstanding ability to multitask.
- *Technical Writing Consultancy:* Outstanding track record as a successful grant, patent, technical and medical writer; founder and owner of a successful scientific and technical writing/review consultancy (9 manuscripts published, 1 in preparation; numerous grant proposals written). Wrote, received and managed as principal investigator, multiple NIH grants totaling ~ $2.8 MM; served on an NIH grant review committee.
- *Research Program and Project Management Experience:*
  Established, directed and was responsible for the execution of several successful research programs; met project deadlines and introduced new drug candidates; managed and led consortium/contract negotiations with grant collaborators; successful results in Xenotransplantion program provided a means to raise private and federal capital; successful transfer of licensed technology and R&D projects were completed on time and on budget; designed comprehensive *in vivo* (mouse, rat and non-human primate (NHP)) proof of concept studies for MicroIslet P™ (encapsulated porcine islets), with external collaborators/GLP labs; Study Monitor for GLP Mouse Safety and Toxicology porcine islet Xenotransplantation studies; Study Director for NHP research and GLP porcine islet Xenotransplantation studies; developed Master Files for sponsor SOPs; developed GLP CMC assays required by the FDA for cGMP runs, directed and managed cGMP facility qualification runs, was responsible for the management and execution of pre-clinical and non-clinical reports required for IND submission; was the scientific expert/liaison for the Clinical team.

Employment Experience/Accomplishments:

3/11-Present **Director of Clinical Research**
Tri-City Medical Center

- Established an institutional clinical research department and internal scientific review committee and designed efficient work flow; liaised with external IRB, Sponsors, CRO's and all external clinical trial sites.
- Ensured that institution and ancillary groups such as pharmacy, laboratory and imaging were compliant with all FDA, OHRP, GCP rules, regulations and guidance's and federal, state and local laws.
- Implemented an institutional research monitoring program for all departments and ancillary groups.
- Experience in managing corrective action for investigator-driven non-compliance issues.
- Established CMS compliant registration, invoicing and billing process, specific for hospitals. Utilizing a clinical research specific Access DB all research billing audited, split and invoices dropped to the correct payor of record.
- Ensured that institutional and site staff and personnel were trained and/or credentialed in GCP, HSP and hospital policies and procedures.
- Developed contract negotiation guidelines and led all clinical research-related contract, agreement and budget negotiations.
- Worked closely with Finance to ensure real institutional costs were covered and established clinical research charge rates.
- Developed all department specific policies and procedures.
- Assisted Pharmacy in development of IDS policies and procedures.
- Wrote 3 PCORI Pilot Grant proposals.
- Participated in Nursing, Stroke and Diabetes meetings.

4/07-Present **ISG Consulting**
www.isgconsult.com
Owner

- Pre-IND and IND Package Preparation, Clinical protocol (Phase I, II and III), IB, clinical presentation and medical writing experience.
- Successful scientific writing in academic and industrial settings.
    - Grant composition, review and editing. Experience with the following Grant types: R01, R29, P41, SBIR I and II, SIG and C06 awards. Funded awards included R01, R29, P41, 2 x SBIR I and 1x SBIR II;
    - Journal article composition, review and editing.
    - Patent development and writing.
    - Development, qualification and pharmacokinetic report writing.

06/08-02/09 **Sr. Director of Research and Development**
3/01-06/08 **Director of Research**
MicroIslet, Inc.

- Successfully managed the transfer of licensed/patented technology from Duke University to corporate setting, on time and on budget.
- Responsible for, established and directed the xenotransplantation research and development programs, which initially included 2 direct reports and 2 Directors. Identified and worked closely with multiple external collaborators, some of whom I recruited to the SAB. Subsequently, as Sr. Director of Research and Development, managed 6 direct reports in 3 departments. Also managed all GLP studies conducted at 2 CROs (below) and cGMP teams.
- Participated with Senior Management in strategic planning, presentation of development, preclinical and clinical project schedules and goals met, data presentation for corporate and board presentations as well as conducted a significant number of external technology assessments.
- Recruited all original members of the scientific advisory board (SAB). Coordinated SAB telephone conferences and annual meetings. Established and managed

several collaborative in vivo transplantation studies with members of the SAB.

- Established critical islet quantification and quality control assays (dose, viability and function) prior to *in vivo* studies. Participated in the development and optimization of novel device-related micro and macro-immuno-isolation strategies.
- The successful preclinical results of immuno-isolated porcine islets transplanted in mice, rats and non-human primates are summarized in final reports, publications, meeting abstracts and patent filings. Represented MicroIslet at National and International transplant meetings.
- Participated in Regulatory planning and directed the design and execution of *in vitro* and *in vivo* Non-Clinical studies needed to meet FDA CMC requirements for Xenotransplantation of encapsulated porcine islets.
- Study Director for Non-Human-Primate GLP Safety and Toxicology study investigating MicroIslet P™ as a transplantation solution for Type I Diabetes.
  - Designed study parameters and endpoints in collaboration with CRO and in line with clinical objectives.
  - Managed team oversight, CRO site and MI transplant coordination.
  - Final Study report composition, assembly and quality controlled data base generation and compilation.
- Study Monitor for GLP Mouse Safety and Toxicology study investigating MicroIslet P™ as a transplantation solution for Type I Diabetes.
  - Designed study parameters and endpoints in collaboration with CRO in line with clinical and FDA required objectives.
  - Managed CRO site and MI transplant coordination.
- Directed and managed GMP operator training and provided the GMP operators with technical and process oversight. Responsible for the scientific, technical and process transfer to GMP operators on location and its transfer of process technology to GMP laboratory facility. Summarized results of cGMP qualification runs for corporate review.
- Critically evaluated, analyzed and summarized *in vitro*, *in vivo* and pre (non)-clinical data. Responsible for the Research and Non-clinical study data collection and of scientific report compilation in preparation for IND submission.

1/98-3/01 **Assistant Director of Clinical Research**
Research Scientist II
MAXIA Pharmaceuticals, Inc. (Acquired by Incyte Corporation).

- As a CRA and later as Assistant Director of Clinical Research at Maxia Pharmaceuticals, Inc. (now Incyte Pharmaceuticals), managed all clinical trial sites involved in the Phase I/IIa Clinical Trial, testing the safety and efficacy of a retinoid-related small molecule on ablation of cervical dysplasia, a precancerous condition. This included:
  - GCP/ICH guidelines: Significant experience with GCP/ICH guidelines. Completed a clinical monitor training class receiving an A+.
  - *Project management:* CRO supervision, investigator recruitment, site selection, qualification, initiation and site closure; study coordination, source document development, on-site monitoring, site management in the US and Europe. Master file and SOP preparation.
  - *Data Management:* CRF monitoring and reconciliation with source documents; Data reconciliation and DB closure of Phase I/IIa study with CRO.
  - *Medical writing:* Protocol design and preparation for Phase II studies, SOP and CRF development; study presentations, data summary reports, final reports, IB, Annual Reports; in-depth scientific reports on current research related to our clinical trials.
  - *Materials Management:* Negotiated contracts and liaised with manufacturing facilities (GMP and other) to obtain sufficient clinical product for both US and EU clinical trial sites. Worked with the design team for the optimal package structure and the clinical team for optimal package labeling.
  - *Training and supervision:* Trained and supervised research associates and CRAs, CRO team members and trained new Directors coming on board.
- Responsible for the development of several cell based, *in-vitro* drug-screening assays for the discovery of novel retinoid-based nitric oxide synthase inhibitors for the treatment of osteoarthritis arthritis. Secondary screening of potential

compounds included comparisons to data from other disease models, analysis of *in vivo* pharmacological study results, and comparisons with chemical/structural databases and discussions with the chemistry team.
- Information Systems: Established the IT infrastructure at MAXIA including internet access, email, hard- and software purchases, and provided primary technical support and maintenance for the first 1-2 years of operation.

6/95-1/98 **Sr. Research Associate**

12/93-6/95 **Research Associate**

Scripps Clinic and Research Foundation

Projects:

1) The Role of $\alpha_{IIb}\beta_3$ in Early Platelet Adhesion Events and Other Hematological Conditions.

2) Analysis of Integrin-Ligand Mediated Adhesion Strength and Function Under Conditions of Flow.

3) The Influence of Divalent Cations on the Structure and Function of Integrin $\alpha_v\beta_3$ and $\alpha_{IIb}\beta_3$.

4) Exploration of Integrin Expression in Embryonic Neuronal Tissue.

- Project Director. One direct report.
- Principal Investigator: Five year NIH R01 grant entitled "Dynamic Regulation of Adhesive Forces Mediated by $\boldsymbol{\alpha_{IIb}\beta_3}$". This work has included:
  - Development of cell based assays analyzing the adhesive capacity of $\boldsymbol{\alpha_{IIb}\beta_3}$. Assays include static adhesion and shear dependent adhesion (flow).
  - Characterization of cation-dependent integrin function and structure using purified proteins, cell based assays and microscopy techniques (fluorescent and electron).
- In collaboration with G. Sosinsky (UCSD), obtained a second NIH (P41) grant supporting studies defining cation-induced structural changes within α_v integrins.
- Established confocal microscopy and histology experiments identifying integrins expressed by astrocytes and neurons.

8/96-1/02 **Consultant/Scientific Advisor**

Cytometry Research Services

- Advisor for tissue culture laboratory set-up.
- Designed and implemented sponsor-specific protocols and SOPs.
- Preparation of complete GLP guidelines/manual for submission to FDA.
- Scientific consultant for academic/industrial projects requiring flow cytometry.

1/95-1/96 **Consultant**

Stratagene, Inc.

- Obtained preliminary data on integrin expression profiles by hNT neurons.
- Provided documentation for integrin-related product ideas.

12/91-12/93 **Research Associate**

The Scripps Research Institute

Project: Structural and Functional Analysis of $\alpha_v\beta_3$ and $\alpha_v\beta_5$ Integrins: The role of integrins in cancer, arthritis and neurological disease models.

- Studied the effects of divalent ions on integrin mediated focal contact formation.
- Purified $\alpha_v\beta_3$ and $\alpha_v\beta_5$ integrins for use in antibody and assay development.
- Developed several monoclonal and polyclonal antibodies to $\alpha_v\beta_3$ and $\alpha_v\beta_5$ integrins, one of which is currently licensed to Chemicon, Inc (now part of Millipore, USA).
- Published a manuscript detailing the effects of divalent ion on integrin location within the cell membrane and its functional activation.

1985-1992 **Ph.D. Candidate in Molecular and Cellular Biology**

University of Arizona, Tucson, AZ

Dissertation: Differential Gene Expression in Tetradecanoylphorbol Acetate (TPA) Responsive and Non-Responsive Mouse Fibroblast Cells.

- Graduate studies focused on protein kinase C dependent-cell signaling pathways induced by the tumor promoter TPA, and consequential gene expression and

mechanisms of cell transformation and cancer.
- o Studied the TPA inducible PKC activation and its involvement in collagen gene expression in NIH 3T3 cells and variants thereof.
- o Role of collagen gene expression in tumor-promotion and cancer explored.
- o Significant familiarity with cellular signaling pathways such as PKC activation and downstream signaling.
- o Publication of results.

Invited Speaker:

JDRF/NIDDK/NCRR/NASA sponsored Cell Encapsulation Workshop – 2002 and 2004

Education:

2012	BIOSTATISTICS Certification; CHRC (Certified in Healthcare Research Compliance) in process.
2011	ADMET Certified.
1985-1992	University of Arizona, Tucson, AZ **Ph.D. in Molecular and Cellular Biology** Minor in Biochemistry
1982-1985	University of California, Revelle College, San Diego, CA **B.A. in Biochemistry and Cell Biology** Minor in Music Literature: Emphasis in Opera
1979-1981	University of Washington, Seattle, WA Pre-Med and Pre-Engineering course work

Publications and Manuscripts (most recent listed first):

1. **Stuiver, I.,** Volk, Hans-Dieter and von Herrath, M. (2011). Histocompatible human parthenogenic stem cells (pSC): General immunogenetics and discussion of viable stem cell transplant options. (In preparation).

2. **Stuiver, I.,** Szabo, A., Meissner, D., Evanoff, G., Miller, E. Salomon, D. R. (2011). Transplantation of Microencapsulated Adult Porcine Islets Render Diabetic NOD SCID and C57BL/6 Mice Normoglycemic (In preparation).

3. **Stuiver, I.** (2011) Encapsulated Single Porcine Islet Cells Confer Long-Term in vivo Function (In preparation).

4. **Stuiver, I.** (2011). Automated Microscopic Assessment of Islet Equivalence and Purity. (In preparation).

5. **Stuiver, I.,** Brassard, J., F.G. Klier, Ruggeri, Z.M., Sosinsky, G (2011). Conformation and Functional Changes Induced by Divalent Cations in β_3 Integrins (In preparation).

6. **Stuiver, I.,** O'Toole, T.E., Ginsberg, M.H., Thomas J. Kunicki and Ruggeri, Z.M. (2011). Selective Effects of Divalent Cations on Fibrinogen and von Willebrand Factor Interaction with $\alpha_{IIb}\beta_3$ in Different Functional States (In preparation).

7. **Stuiver, I.** and Von Herrath, M. (2007). Thompson Review: Clinically Significant Immunomodulatory Therapies. Thompson Scientific, July, 2007

8. **Stuiver, I.** and Von Herrath, M. (2007). At Long Last: Clinically Significant Immunomodulatory Therapies. Expert Rev. Clin. Immunology 3(5): 667-670.

5. Tagaya, M., Haring, H.P., **Stuiver, I.,** Wagner, S., Abumiya, T., Lucero, J., Lee, P., Copeland, B.R., Sieffert, D., del Zoppo, G.J. (2001). Rapid Loss of Microvascular Integrin Expression During Focal Brain Ischemia. Reflects Neuron Injury. J. Cerebral Blood Flow and Metabolism 21:835-846.

6. **Stuiver, I.**, and Smith, J.W. (1996). Divalent Cations Regulate the Organization of Integrins $\alpha_v\beta_3$ and $\alpha_v\beta_5$ on the Cell Surface. J. Cell.Phys. 168:521-531.

7. **Stuiver, I.**, M.J.C. Hendrix, Y. Shimizu and N. Shimizu. (1996). The Phorbol Ester TPA Regulates Collagen Gene Expression at the Transcriptional Level. Cell Struct. Funct. 4:259-269.

8. **Stuiver, I.**, and Smith, J.W. (1995). Characterization of a Panel of Monoclonal Antibodies Specific for Integrin $\alpha_v\beta_5$. Hybridoma 14:545-549.

9. Stuiver, I. and O'Toole, T.E. (1995). Regulation of Integrin Function and Cellular Adhesion. Stem Cells 13:250-262.

10. Stuiver, I., Shimizu, Y., and Shimizu, N. (1991). Phorbol Ester Induced Expression of the Collagen Type I-Pro-A2 Gene in Mouse 3T3-L1 Cells and Its Absence in a TPA-Nonresponsive Variant. Bioch. J. 278:369-373.

11. Reizer, J., Novotny, J.N., Stuiver, I., and Saier, M.H. Jr. (1984). Regulation of Glycerol Uptake by the Phosphoenolpyruvate-Sugar Phosphotransferase System in Bacillus subtilis. J. Bact. 159:243-250.

Abstracts:

1. **Stuiver, I.** (2008) Encapsulated Single Porcine Islet Cells Confer Long-Term in vivo Function. Transplantation 86 (2S):558

2. Ricks, L, SooHoo, W, Patel, M., LaFontaine, N., Basu, A. and **Stuiver, I** (2008). Reduced insulin Requirements in Transiently Immunosuppressed Non-Human Primates Transplanted with MicroIslet P™ (Alginate Encapsulated Porcine Islets): A Non-Clinical Safety Study. Transplantation 86 (2S): 28

3. **Stuiver, I** (2008). Encapsulated Single Porcine Islet Cells Confer Long-Term in vivo Function. Abstract 2714: XXII International Congress of The Transplantation Society, August, 2008

4. Bartel, R.L., Ospina, H., **Stuiver, I.,** Salomon, D. (2005). Encapsulated Porcine Islets Treated with a Cocktail of Survival Factors Function Long-Term in Diabetic Lewis rats. Rachmel Levine Symposium, November, 2005

5. Bartel, R.L., Ospina, H., **Stuiver, I.,** Salomon, D. (2005). Encapsulated Porcine Islets Treated with a Cocktail of Survival Factors Function Long-Term in Diabetic Lewis rats. Xenotransplantation Congress, Goteborg, September.

6. Szabo, A., **Stuiver, I.** Meissner, D., Evanoff, G. Miller, E., Salomon, D. (2004). Successful Function of Microencapsulated Porcine Islets in Streptozotocin Diabetic Immuncompetent Mice. ATC Conference, Boston May 14-18, 2004.

7. Meissner, D., **Stuiver, I,** Szabo, A., Evanoff, G. Miller, E., Salomon, D. (2004). Microencapsulated Adult Porcine Islets Using MicroIslet's Proprietary Formulation MPF2. NIH Encapsulation workshop Mar 28-29.

8. **Stuiver, I**. Meissner, D., Szabo, A., Evanoff, G. Miller, E., Salomon, D. (2004). Naked and Encapsulated Adult Porcine Islets Render NOD/SCID Mice Normoglycemic. NIH Encapsulation workshop Mar 28-29. Invited speaker.

9. **Stuiver, I** (2003). Automated Microscopic Assessment of Islet Equivalence and Purity. Seventh International Xenotransplantation Congress, Sept. 29-Oct 4, 2003.

10. **Stuiver, I**, Szabo, A., Meissner, D., Evanoff, G. Miller, E., Salomon, D. (2003). Microencapsulated Adult Porcine Islets Render Streptozotocin-Diabetic Immunoincompetent and Immunocompetent Mouse Strains Normoglycemic. Seventh International Xenotransplantation Congress, Sept. 29-Oct 4, 2003.

11. **Stuiver, I**, Szabo, A., Meissner, D., Evanoff, G. Miller, E., Salomon, D. (2003). Microencapsulated Adult Porcine Islets Render Streptozotocin-Diabetic Immunoincompetent Mouse Strains Normoglycemic. Levine Symposium. Nov. 4-7, 2003.

Note: 9 abstracts dated from 1989-1999 not listed, but available upon request.

Patents:

1. **I. Stuiver**: Automated Microscopic Assessment of Islet Quantity, Quality, Equivalence and Purity. (2006). Patent application publication number WO 2005/033665.

2. Meissner, D. and **Stuiver, I.** Bead embedded cells. (2006). Patent application # 20050147595.

3. **Stuiver, I.** Single Cells Derived from Islets Perform Optimally In Vivo. (2008). Submitted for review.

Grants/Awards:

2008-2009 **Principal Investigator:** NIH SBIR Phase I to test effects of LSF on porcine islet survival in NOD mice. Funding for 1 year. $243,000.

2005-2008 **Principal Investigator:** NIH SBIR Phase II entitled: Encapsulated Porcine Islets into Rhesus Macaques" to study the safety and efficacy of encapsulated porcine islet transplantation in non-human primates. Funding for 3 years. $1,700,000

2003-2004 **Principal Investigator:** NIH SBIR Phase I entitled "Optimization & Automation of Pancreatic Islet Isolation" to study porcine islet isolation processes. Funding for 6 months. $150,000

1999-2004 **Principal Investigator:** NIH P41 through UCSD. The funded equipment is used for further integrin structural studies. Funding for 5 years.

1998-2003 **Principal Investigator:** NIH R01 entitled "Dynamic Regulation of Adhesive Forces Mediated by $\alpha_v\beta_3$". Funding for 5 years. $750,000

Societies:

1988-2003/ 2006-2010 Member of the American Society for Cell Biology

2002-2009 Member of International Society of Xenotransplantation

2002-2009 Member of International Society of Transplantation

2001-2009 Member of the American Diabetes Society

1999-2003 Member of the American Society for Biochemistry and Molecular Biology

1998-2001 Member of the OsteoArthritis Research Society International

1992-1993 Vice President for The Society of Fellows-The Scripps Research Institute

1993 Program Director-Chair: The Society of Fellows-The Scripps Research Institute

1988-1991 Member of Sigma Delta Epsilon

Languages:

English, Dutch, French and German.

References:

Available upon request.