



LOUI J. SILVESTRI, PhD

AccuReg, Inc.

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SELECTED HIGHLIGHTS OF PROFESSIONAL EXPERIENCE:

- Consultant to developer and manufacturer of prescription pharmaceuticals (solid and liquid dosage forms), over-the-counter drugs (solid dosage), and medical devices (ocular products). Responsible for auditing clinical software systems (data management and analysis) for compliance to Quality System regulations and conformance to FDA requirements for software and computer system validations. Result: Recommendations for validating and utilizing existing software systems with improved processes to increase efficiency and efficacy.
- Consultant to developer and manufacturer of generic pharmaceutical cream, liquid, and solid dosage forms. Contracted to perform validity assessments on 10 products as a result of FDA inspection. Coordinated and worked “hands on” with team to review all available manufacturing and clinical data, and prepare detailed written report for each product, including analysis of supporting data. Final reports for all products were submitted to the sponsor and the FDA. Result: Products were assessed as acceptable and permitted to remain on the market.
- Consultant to a manufacturer of solid dosage generic pharmaceuticals. Audited contract manufacturing sites to assess GMP compliance, and audited contract testing laboratories to assess GLP (pharmacokinetic analysis) compliance. Result: Affirmation of most facilities as appropriate sites for contract manufacture and testing, but identification of one laboratory that was removed from the roster due to compliance deficiencies as revealed by the audit.
- Auditing consultant for pharmaceutical manufacturer who was performing a due diligence evaluation of a large pharmaceutical division the Client-firm was interested in acquiring. Critically reviewed batch records and other documentation, equipment qualification, process validations. Result: Discovery of several untoward practices that ultimately resulted in the Client-firm’s disengagement from the purchase.
- Auditing consultant for start-up pharmaceutical manufacturer who utilized a crystalline active ingredient in the preparation of their novel therapeutic. Performed a comprehensive mock-PAI audit of the foreign facility that manufactured the active ingredient. Result: The Client-firm received a detailed evaluation of the contractor’s strengths and weaknesses, and is currently addressing gap items in preparation for an actual FDA PAI.
- Consultant of record to contract manufacturer of generic pharmaceuticals and over-the-counter drugs. Coordinated and worked “hands on” with team of 3 responsible for development and implementation of comprehensive Quality System implementation program resulting from an FDA inspection. Program included establishment of Standard Operating Procedures, Standard Test Procedures, Master Batch Records, and other Quality System/manufacturing documentation; development of microbiology and environmental monitoring programs; development and execution of process and method validations; training in cGMPs and new procedures; establishment of record-keeping processes; and development of internal audit program. Result: Facility passed subsequent re-inspection by FDA with no 483.
- Auditing consultant to medical device manufacturer of bone drills and dissecting burrs. Responsible for semi-annual GMP inspection of assembly, testing, inspection, and packaging facilities since the client firm’s inception (1991). Result: Firm has implemented progressive Quality System improvements based on the results of auditor’s recommendations; most recent FDA inspection resulted in no 483.

Curriculum Vitae: Loui J. Silvestri, PhD, AccuReg Inc.

- Consultant to developer of surgical adhesive for repair of aortic dissections. Responsible for HE-IDE Clinical Protocol development, including study design, conduct procedures and methodology, eligibility criteria, evaluation and statistical analysis, management and recording procedures, randomization scheme and Informed Consent. Result: Approval to proceed with the HE treatment of patients who experience this otherwise fatal affliction.
- Consultant to developer and manufacturer of chemical medical devices. Responsible for GMP training and auditing, facility qualification, cleaning validation, and development of environmental monitoring programs. Prepared multiple U.S. and European regulatory submissions. Result: Facility passed most recent inspection with no 483. All submissions have been accepted by the governing regulatory bodies.
- Consultant of record to multi-facility developer and manufacturer of nuclear imaging devices, radiation therapy devices, radiation treatment planning devices, and standalone software medical devices. Responsible for preparation of regulatory submissions and development of comprehensive Quality System implementation programs, including evaluation and development manufacturing, testing, record-keeping, and other Quality System processes, development and review of complaint handling and MDR procedures, development and review of software and system validation programs, and preparation of FDA correspondence. Result: Ongoing Quality System improvements across all divisions.
- Consultant to developer and manufacturer of implantable ACL replacement prosthesis. Responsible for review of IDE submission, development of serological testing methodologies, assay validation protocol development and review, review of genotoxicity testing methods and data, development and review of sensitivity test methods, and FDA correspondence and liaison activities as expert immunologist. Result: Approval to proceed with IDE clinical study.
- Consultant to developer of an *ex vivo* filtration medical device used as a cancer therapeutic. Responsible for auditing for compliance to Protocol and GCPs, and for writing and reviewing Annual IDE/IRB Reports. Result: FDA support for initiation of pivotal clinical trials. Actively participating in preparation of PMA for the device.
- Consultant to developer and manufacturer of radiolabeled monoclonal antibody and gamma-detecting probe. Responsible for clinical protocol development and review, FDA correspondence and liaison activities, GMP/QSR compliance audits, technical support on microbiology issues, 510(k), IDE and IND reviews, and regulatory strategy. Result: Approval to proceed with Phase III clinical studies.
- Consultant to developer and manufacturer of antibodies and cell lines. Responsible for all aspects of technological process development and transfer, including QC microbiology program development, sterile fill testing and operations, raw material handling procedures, stability program development, specifications development, bioreactor operations discipline, equipment/process validations, regulatory and compliance strategies, and FDA correspondence/liaison activities. Result: Successful transfer of technology.
- Consultant of record for multi-facility medical device manufacturer under Consent Decree. Responsible for development of comprehensive Quality Systems Improvement Plan, team oversight and monitoring, FDA liaison activities, reporting to upper management and counsel, interim audits and preparatory “mock” inspections, and FDA Escort Team leader and coordinator. Coordinated team of over 30 consultants to implement 10-month plan addressing issues such as:
 - ⇒ Microbiology and environmental monitoring programs
 - ⇒ Pyrogen and LAL testing
 - ⇒ Analytical methods development and validation
 - ⇒ Raw material and component specifications
 - ⇒ Water system validation
 - ⇒ Complaint and failure investigations
 - ⇒ Plant upgrades and repairs
 - ⇒ QC laboratory improvements
 - ⇒ IQ/OQ/PQ, calibration and maintenance of facility and laboratory equipment.

Result: All facilities passed subsequent re-inspection by FDA. Manufacturing permitted to resume.

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QUALIFICATIONS:

- Over 8 years of doctoral and post-doctoral education in the field of immunochemistry, clinical immunology, microbiology and cell science.
- Founder and past-president of Allergen Products Manufacturers' Association (APMA).
- More than 18 years of progressive technical, clinical, and administrative experience in biotechnology and pharmaceutical environments.
- Extensive working knowledge of the scientific, regulatory, QA/QC, and business requirements necessary for the commercialization of biological, ethical and OTC pharmaceutical, medical device and diagnostic products.
- Seasoned auditor of a wide range of manufacturers, vendors, and contract research and testing organizations.
- Demonstrated expertise in regulatory strategy and compliance for, ethical and OTC pharmaceuticals, medical devices, *in vitro* diagnostics, and biologics including facility inspections, inspection and installation of documentation systems, process and analytical validations, etc.
- Highly experienced in the preparation of regulatory submissions for pharmaceuticals (INDs, ANDAs, NDAs, DMFs, etc.) and medical devices [e.g., IDEs, 510(k)s, PMAs, etc.]
- Expert in the preparation of regulatory submissions for medical devices containing software.
- Highly familiar with Quality System Regulations, cGMP, GLP, and GCP requirements for medical device, pharmaceutical and biological products.
- Industry-recognized expert in the design and execution of medical device software/computer system validations.
- Extensive experience in the development of microbiology programs and sterile/aseptic processing techniques.
- Highly experienced with biofacility design and operation, including the development and implementation of environmental monitoring programs.
- Expert in the design and execution of analytical method validations.
- Expert in the design and execution of process validations.
- Working knowledge of protein purification techniques.
- Hands-on experience with various standard and recombinant manufacturing techniques, including both prokaryotic and eukaryotic expression systems.
- Hands-on experience with the preparation and evaluation of business plans and business development packages.

PROFESSIONAL EXPERIENCE AND ACCOMPLISHMENTS:

AccuReg Inc., Plantation, Florida
President

(1987-present)

- Co-founded AccuReg Inc., a regulatory, compliance and product development group with scientific and regulatory expertise in the health-care industry.
- Responsible for the overall scientific and technical services provided to clients. Co-responsible for the clinical services provided to client firms.
- Responsible for the overall administrative and fiscal management of the company.
- Routinely prepares and submits appropriate documentation for medical product registrations/applications such as NDAs, ANDAs, DMFs, INDs, IDEs, 510(k)s, BLAs, etc.
- Routinely conducts Quality System Regulation audits, cGMP audits and validity assessments for client firms with recommendations for establishing and/or maintaining compliance.
- Supervises, coordinates and participates in design and execution of software/computer systems for client firms.
- Oversees, coordinates and participates in design and execution of analytical method and process validations.
- Routinely performs due diligence analyses and project feasibility analyses for new medical products, including regulatory, marketing, technical, and business proposals.
- Frequently conducts evaluations of environmental monitoring programs, design and lay-out of controlled environments (and other aspects of biofacility design), and development and implementation of procedures.

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Schering Research, Miami Division (Florida) (1984-1987)
Director, Department of Allergy and Immunology

- Responsible for the overall technical, clinical, and administrative function of the Department.
- Designed and successfully executed, in conjunction with clinical staff, numerous multi-site clinical trials of novel immunotherapeutic agents.
- Effectively coordinated responses to technical inquiries (lot-to-lot consistency, product biocharacterization, etc.) from the FDA-CBER.
- Directed technical staff to design and successfully execute toxicological, mutagenicity, and biodistribution pre-clinical studies.
- Established a national network of clinical sites to perform bioassay potency analyses on immunotherapeutics.

Key Pharmaceuticals, Miami, Florida (1981-1984)
Manager, Department of Allergy and Immunology

- Initiated the formation of the Department of Allergy and Immunology, Key Pharmaceuticals.
- Successfully developed the first scale-up processes for immunotherapeutics under development by Key.
- Successfully developed the initial Quality Control methodologies for release of Key's immunotherapeutics.
- Implemented process improvements that decreased manufacturing time by more than 25% and increased the reproducibility of the final products.
- Regularly and effectively made presentations to the FDA, professional colleagues, marketing groups, and other distinguished forums.

POST DOCTORAL EXPERIENCE:

Research Associate under L. Roden, MD (1979-1981)
Connective Tissue Research Labs, University of Alabama, Birmingham
and

Post-Doctoral Fellow under R. Stroud, MD (1977-1979)
and C. Bennett, MD
Department of Clinical Immunology and Rheumatology, University of Alabama, Birmingham

- Preparation of monoclonal antibodies to biological modifiers (complement inhibitors).
- Development of solid-phase ELISA for detecting sera-associated proteins expressed during inflammatory responses.
- Isolation, purification, and identification of complement components, and complement-inhibiting glycosaminoglycans (heparin-like molecules) from human sera.
- Participation in the clinical evaluation and therapeutic intervention in patients with allergic rhinitis.
- Development of a colorimetric and an HPLC assay for the accurate quantitation of sulfate in the glycosaminoglycans of connective tissue.
- Teaching experience in microbiology, pathogens, and immunology.

EDUCATIONAL CREDENTIALS:

- PhD (Accelerated Program), 1973-1977
University of Florida, Department of Immunology and Cell Science, Gainesville, FL
- BSG (Major: Biology and General Science; Minor: Biochemistry and Psychology), 1969-1973
Villanova University, Villanova, PA

PROFESSIONAL ORGANIZATIONS:

Regulatory Affairs Professionals Society (RAPS)
Parenteral Drug Association
Allergen Products Manufacturers' Association (Past President)