LOUI J. SILVESTRI, PhD

AccuReg, Inc.
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SUMMARY OF QUALIFICATIONS:

Loui Silvestri, PhD, has over 8 years of doctoral and post-doctoral education in the field of immunochemistry, clinical immunology, microbiology and cell science, and more than 25 years of progressive technical, clinical and administrative experience in the commercial healthcare industry. He has extensive working knowledge of the scientific, regulatory, QA/QC, and business requirements necessary for the commercialization and ongoing compliance of ethical and OTC pharmaceutical, medical device, diagnostic, and biological products. An industry-recognized professional in the Quality Systems Regulation, cGMP, GLP, and GCP requirements for medical device, pharmaceutical and biological products, Dr. Silvestri specializes in the development, management and "hands on" direction of comprehensive compliance plans for companies operating under Consent Decree and Critical-Level Warning Letters. He also holds extensive experience in the evaluation of analytical assays, review of bioequivalence studies, clinical study design and auditing to ensure compliance to overall Good Clinical Practices and regulatory requirements applicable to the governing bodies. He is a member of PDA, RAPS and FDLI, and a founder and past-president of Allergen Products Manufacturers' Association (APMA).

SKILLS:

Quality Assurance / Compliance for OTC Drug, Pharmaceutical, Medical Device, Diagnostic, and Biological Products	Development and Auditing of Medical Device Quality Systems for compliance to 21 CFR 820 and ISO 9001/13485
Clinical Study Design and Auditing (including pre-BIMO)	cGMP, GLP, and GCP Audits and Implementation Plans
Regulatory Submissions for OTC, Pharmaceutical, Medical Device, Diagnostic, and Biological Products	Remediation of Consent Decrees and Critical-Level Warning Letters
Comprehensive Audits, pre-PAIs, and Remediation Plans for OTC, Pharmaceutical, Medical Device, Diagnostic, and Biological Products	Review of Bioequivalence Studies
Audits and Assessments of Analytical Assays	Expert Witness for Scientific, Regulatory, QA/QC, and Business Requirements Pertaining to Medical Products
Formal Training: Immunochemistry; Microbiology and Cell Science; Clinical Immunology	Software/Computer Systems Compliance with 21 CFR 11

SELECTED HIGHLIGHTS OF RECENT PROFESSIONAL EXPERIENCE:

Implementation Director for 18-month Consent Decree compliance remediation project for Abbott Diagnostics Division, a major medical diagnostics manufacturer. Managed a team of over 60 consultants and hundreds of client personnel. Result: FDA inspection found the client in substantial compliance with the Quality Systems Regulation.

Consultant to three separate investment groups who required technical, regulatory and quality-compliance evaluation of potential pharmaceutical generic drug acquisition targets. Particular focus was on the regulatory status of the ANDAs and the acceptability of the bioequivalence studies. Result: Per Dr Silvestri's recommendation, two of the investment firms successfully invested in and merged the target generic firms, and the third investment group declined investment per Dr. Silvestri's recommendation based on unacceptable bioequivalence data. This third target firm latter experienced significant regulatory action.

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

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.

PROFESSIONAL EXPERIENCE AND ACCOMPLISHMENTS:

AccuReg Inc., Plantation, Florida *(1987-present)*

President

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.

Extensive quality systems experience in the Quality System Regulations for medical devices (21 CFR Sec. 820) and ISO 9001/ISO 13485 quality systems. Twenty (20) years' experience as a Lead Auditor for Quality Systems compliance.

Extensive experience in cGMP (21 CFR 210/211) audits and validity assessments for client firms with recommendations for establishing and/or maintaining compliance.

Conducts audits of commercial off-the-shelf (COTS) and proprietary software systems for 21 CFR Part 11 and validation compliance.

Conducts Lead Auditor compliance audits of bioequivalence studies used to support ANDA market applications for generic drugs.

Oversees all activities of the Clinical Services Division.

- Directs and serves as lead auditor for AccuReg's mock bioresearch monitoring (BIMO) and Good Clinical Practices (GCP) auditing teams. Activities include bioresearch audits of clinical research studies, clinical sites and clinical research organizations (CROs) for compliance to protocol and to FDA, EU and other regulations as applicable, risk assessment and prioritization of findings, and preparation of corrective action recommendations.
- Directs the creation of clinical development plans for new products, including regulatory strategy, investigational protocol/study design, FDA/regulatory body interactions, study auditing and site qualification, and comprehensive "hands on" and management aspects of new product approval submissions.

Prepares and submits appropriate documentation for medical product registrations/applications such as NDAs, ANDAs, DMFs, INDs, IDEs, PMAs, 510(k) s, BLAs, etc.

Conducts Good Laboratory Practice (GLP) assessment, often in combination with Part 11 compliance evaluations.

Oversees, coordinates and participates in design and execution of analytical method and process validations.

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.

Seasoned auditor of a wide range of manufacturers, vendors, and contract research and testing organizations.

Extensive experience in the development of microbiology programs and sterile/aseptic processing techniques.

Working knowledge of protein purification techniques. Hands-on experience with various standard and recombinant manufacturing techniques, including both prokaryotic and eukaryotic expression systems.

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 *(198 1-1984)*

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 *(1979-198 1)*
Connective Tissue Research Labs, University of Alabama, Birmingham

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

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 colorometric and an HPLC assay for the accurate quantification of sulfate in the glycosaminoglycans of connective tissue.

Teaching experience in microbiology, pathogens and immunology.

Formal medical training.

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)

Food and Drug Law Institute (FDLI)