BioSpectra

Regulatory & Quality Program

BioSpectra Quality Management

- Quality Manual
- Training/Personnel Qualification
- Validated Systems
- Qualified Equipment and Utilities
- Analytical Method Validation
- Data Integrity
- Document Management
- Facility/Systems Management
- Change Control

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What is “Full GMP”?

Validation – process, testing, annual review

Impurities – characterization, profiles, degradation

Stability – Long and short term

Cleaning – Protocols, validation

Supply Chain – Qualification, inspections

Equipment – Qualification, IQ, OQ, PQ, real-time maintenance

Product Dlvp. – Full GMP workup under IPEC and ICH Q7

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Comprehensive Quality & Regulatory Program

- Validation of all GMP Manufacturing Systems
- Rigorous Preventive Maintenance Program
- Qualification of all Equipment
- Stringent Cleaning Protocols
- Environmental Monitoring
- Change Control Process
- Equipment IQ-OQ-PQ
- Document Control

Regulatory Control & Support

- Creation and Submission of Drug Master Files for APIs and Excipients
- Creation and Control of all Critical Documentation
- Management of all External Audits and Certifications

Quality Control

- Fully staffed, on-site Quality Control Laboratories
- Validation and Verification of all Test Methods
- Qualification of all Instrumentation including ICP-MS, GC-MS, HPLC, UV/Vis, TOC, Ion Chromatographer, Conductivity Meter, Microcount UATR, Polarimeter, Karl-Fisher Titrator & more

Quality Management

- Registered with US FDA as API Manufacturer
- ICH Q7 Compliant Quality System
  - Quality Manual
  - Training/Personnel Qualification
  - Validated Systems
    - Cleaning Validation
    - Process Validation
  - Qualified Equipment and Utilities
  - Analytical Method Validation
  - Document Management
  - Data Integrity
  - Facility/Systems Management
  - Change Control

Quality Management

- Material Management
  - Supplier Approval Program
    - Questionnaires/Auditing
    - Product Statements
    - Approved Raw Material and Components
      - Receipt
      - Quarantine / Analysis
      - Approval
  - Approved/Traceable Batch Records
    - Manufacturing
    - In Process Testing
    - Packaging
  - Finished Good Testing
  - Release Criteria and Inspection

Quality Management

- Product Care
  - Gowning
    - Uniforms
    - PPE
  - Handling
    - Personnel Training
    - Production Traceability
  - Inspection
    - Equipment and Product
  - Storage
    - Specific Conditions and Packaging
    - Stability
- Continuous Inspection
  - Internal Audit
  - Quality/Safety Walkthrough
  - Pre-Process Room Inspection

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Quality Management

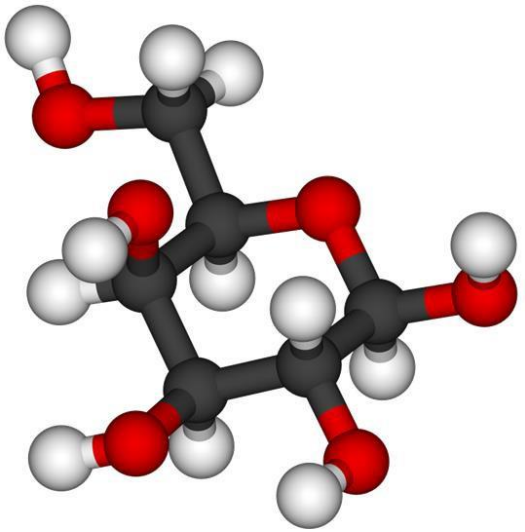
- Management of Non-Conformance
  - Discrepancies
  - Laboratory Investigations
  - Complaints
  - For-Cause Training
  - CAPA
  - Supplier Corrective Action
- Quality Trending
  - Quarterly Senior Management Review
  - Annual Product Review

Regulatory Support

- Product Support
  - Drug Master File/Veterinary Master File
  - Regulatory Packets
  - Questionnaires
  - Product Statements
  - Technically Unavoidable Particle Profile
  - REACH
  - Global Regulatory
  - Audit/Inspection Hosting
  - Additional Support Materials as Needed

Technical Review-Supply Chain

- Supplier Management
  - Approved Supplier
    - Testing
    - Questionnaire
    - Product Statement
    - Audit
  - Raw Material Testing
    - Specifications
    - Expectations



D-Galactose

Technical Review-PD/PV

- Product Development
  - Process Design
  - Development Batches
    - Critical Process Parameters (CPP)
      - Based on Specification
    - Impurity and Degradation tested by UPLC
- Process Validation
  - Equipment Qualification
  - Validation Batches
    - In-Process Testing
    - CPP/CQA Evaluation
    - Stringent Product Testing from Raw Material through Finished Product
    - Continued Process Verification – Quality Trending / Annual Product Review
  - Bacterial Endotoxin Testing
    - Raw Material through Finished Product

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Technical Review-QC

- Finished Good Test Methods
  - Harmonized with USP/EP/JP
  - In Review
- Characterization
  - UATR
  - Specific/Optical Rotation
- Trace metals
  - ICP
- Solvents
  - Approved Service Provider
- Stability Indicating
  - ICH Q1
- Degradation and Impurity Profile
  - ICH Q3

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BioSpectra Regulatory Inspection History

FDA U.S. FOOD & DRUG ADMINISTRATION

BioSpectra's Bangor, PA facility
January 2016 and August 2017 with no findings.

BioSpectra's Stroudsburg, PA facility
August 2010 with no findings.

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Audit Topics: Quality System

Details	ICH Q7 Good Manufacturing Guide Reference	BioSpectra Documents Provided During Audit
Assures overall compliance with cGMPs and internal procedures and specifications	• Section 2, Quality Management • Section 3, Personnel • Section 6, Documentation and Records • Section 13, Change Control • Section 14, Rejection and Reuse of Materials • Section 15, Complaints and Recalls • Section 16, Contract Manufacturers (including laboratories)	• Deviation Procedure and list • CAPAs (corrective and preventative action) • OOS issued list • Investigation Procedure • Change Control Procedure and List • Equipment • Customer Notification • Compliant/Recalls • Quality Manual • Annual Product review Training • Internal/External Audit Schedule • Organizational Chart • Job Description • Documentation- SOPs • GMP Manufacturing • SOP Index • Stability data/Reports • FDA Registration/Inspection Report • Supplier Approval Program • Service Provider Approval Program • Instrument Calibration • Method Validation

Audit Topics: Facilities & Equipment

Details	ICH Q7 Good Manufacturing Guide Reference	BioSpectra Documents Provided During Audit
Includes activities which provide an appropriate physical environment and resources used in production	● Section 3, Personnel ● Section 4, Buildings and Facilities ● Section 5, Process Equipment ● Section 6, Documentation and Records	● Master Validation Plan ● Equipment Preventative Maintenance ● Equipment Calibration ● Equipment Cleaning ● Equipment Qualification ● Building/Facility Management ● HVAC System ● Air/Water ● Pest Control ● Environmental Monitoring ● Subcontracting Policy ● Facility Tour ● Waste Handling

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Audit Topics: Materials

Details	ICH Q7 Good Manufacturing Guide Reference	BioSpectra Documents Provided During Audit
Includes measures and activities to control starting materials, intermediates, and containers. It includes validation of computerized and inventory control processes, storage and distribution controls	● Section 3, Personnel ● Section 4.3, Water ● Section 6, Documentation and Records ● Section 7, Materials Management ● Section 10, Storage and Distribution	● Materials Management and Material control ● Raw Material Receipt and Approval ● BSE/TSE ● Rejected Material ● Cross Contamination ● Material flow/personnel ● Animal Origin/ Use of derived materials ● Shelf Life Validation ● Inventory management

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Audit Topics: Production

Details	ICH Q7 Good Manufacturing Guide Reference	BioSpectra Documents Provided During Audit
Includes measures and activities to control the manufacture of materials, including in-process sampling and testing, and process validation.	● Section 3, Personnel ● Section 6, Documentation and Records ● Section 8, Production and In-process Controls ● Section 12, Validation	● Batch Records (Issue/review/release) ● Process Logbooks ● Packaging and labeling ● Cleaning Procedures ● Gowning Requirements ● Equipment Calibration ● Process Validation for specific product

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Additional Audit Topics to Discuss

System	Details	ICH Q7 Good Manufacturing Guide Reference
Packaging and Labeling	Includes measures and activities that control the packaging and labeling of intermediates and API's	● Section 3, Personnel ● Section 6, Documentation and Records ● Section 9, Packaging and Identification Labeling of APIs and Intermediates ● Section 17, Agents, Brokers, Traders, Distributors, Re-packers, and Re-Labelers
Laboratory Control	Includes measures and activities related to laboratory procedures, testing, analytical methods development and methods validation or verification, and the stability program.	● Section 3, Personnel ● Section 6, Documentation and Records ● Section 11, Laboratory Controls ● Section 12, Validation