

Analytical Laboratory Outsourcing with  
Quality: Pharmaceuticals, Medical  
Devices & Combination Products

Life Sciences Alley Presentation  
March 5, 2009

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# Overview

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- ◆ Outsourcing Strategies
- ◆ Advantages/Challenges of Outsourcing
- ◆ Best Practices of Outsourcing
- ◆ Compliance Expectations of a Contract Laboratory - Audit Expectations
- ◆ Development/Validation of Analytical Methods

# Outsourcing Strategies

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## ◆ Strategic

- Outsourcing Part of Business Strategy
  - \* Virtual Companies
  - \* Outsourcing Non-Core Competency
  - \* Internal Labs Not cGMP
  - \* Cost - Outsource in Lieu of Capital or Human Resource Investment
- Organization Aligned
  - \* Buy-In At All Levels
  - \* Investment in Internal Resources to Manage Outsourcing

# Outsourcing Strategies

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## ◆ Tactical

- Designed or Implemented To Gain a Temporary Limited Advantage.
  - \* Back-up Capacity
  - \* Short-Term Support
  - \* Outsourcing During Capacity Build-Up
- Not a Core Strategy
  - \* Challenges at Operational Levels
  - \* Limited Investment in Internal Resources

# Outsourcing Strategies

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- ◆ Contract Labs Must Manage Both Types of Outsourcing Strategies
  - Strategic – Typically More Collaborative
    - Status/Project Meetings More Common
    - More Client Involvement
  - Tactical – Requires More Proactive Communication from Contract Lab
    - Self Reporting

# Advantages of Outsourcing

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## ◆ Cost

### – Non-routine – One Time Activities

- \* Registrational Stability Storage and Testing
- \* Process/Facility Validation Work
- \* Cleaning Validations
- \* Investigation Work Involving Expensive Equipment
- \* Method Development/Validation
- \* Comparitor Studies
- \* Method Updates/Remediation

# Advantages of Outsourcing

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## ◆ Cost

- Routine Activities - Ability of Contract Lab to Leverage Costs
  - \* Excipients/Raw Materials
  - \* Costs of cGMP
  - \* Validation (IQ/OQ/PQ) of Analytical Equipment
  - \* Cost of Stability Chambers
  - \* Cost of Monitoring and Back-Up Generator Systems
  - \* Residual Solvent and Sterilant Analysis

# Advantages of Outsourcing

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## ◆ Cost

### – Variables to Consider When Comparing Costs:

- \* Personnel (Salaries, Benefits)
  - \* Equipment Costs (Purchase, Validation, Maintenance)
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- \* Data Review Time
  - \* Quality Assurance Time
  - \* Occupancy, Utilities, Consumables, Waste Disposal
  - \* Cost of Learning Disciplines Beyond Core Competency of Organization
  - \* “Lost Opportunity” Costs

# Advantages of Outsourcing

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- ◆ Regulatory/Compliance
  - Multiple Clients with Different Procedures & **Different Regulatory Experiences** and Interpretations
  - Frequent Audits
  - Provides Advise Based on Experiences (Free Consulting)



# Advantages of Outsourcing

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- ◆ Increased Productivity/Efficiency
  - Client Can Focus on Core Competencies
    - \* Focus on Development and Validation
    - \* Third Party Support - Contract Manufacturers
  - Ability to Keep More Projects Moving Forward Simultaneously
    - \* Divert Flow of “Routine” to Concentrate on “New”
    - \* Capitalize on Contract Laboratory’s Flexible Workforce and Diverse Expertise

# Advantages of Outsourcing

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## ◆ Capacity

### – Building of Internal Capacity Not Keeping Pace with Projects

- \* Temporary and Long-Term Approaches

### – Personnel

- \* Desire to “Rebuild” After Economic Conditions?
- \* On Site and Off Site “FTE” Programs
- \* Co-Employment Laws

# Challenges of Outsourcing

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- ◆ Project Management - Client Perspective
  - “Project Management” versus “Throwing it Over the Fence” – Managing the Tactical Clients
  - Identify Project Manager Capable and Empowered to Make Quality Decisions
  - Funneling Communication Through a Single Point of Contact
    - Ability to Answer Questions and Follow-up Questions

# Challenges of Outsourcing

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- ◆ Project Management - Lab Perspective
  - Ability to Obtain Information “Up Front” To Do The Job Right the First Time!
  - Understanding Multiple Clients with Different Requirements and Procedures
  - Limited Access to Information
    - \* Full Product Documentation/History
    - \* Development and Validation Data
  - Technical Limitations of Primary Contact

# Challenges of Outsourcing

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## ◆ Contract Laboratory Options

- Use of Niche Providers Versus Broad Based Service Laboratories
  - \* Sub-Contracting
- Need to Balance Capability, Capacity, Quality, and Cost of Services
- Geographical Location
  - \* Impact on Ability to Deliver Samples
  - \* Impact on Ability to Troubleshoot
  - \* International Challenges

# Best Practices of Outsourcing

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- ◆ Prepare for Challenges In Advance
  - Discuss Limitations or Nuances of Methods or Samples
  - Identify Channels and Levels of Communication – Especially for Out of Spec
- ◆ Conduct “Kick-Off” Meetings for Each New Project
  - Not As Critical for Routine Compendial Work

# Best Practices of Outsourcing

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- ◆ Align Technical to Technical Contacts Early in the Process
- ◆ Encourage and Support Initial Training/Feasibility
  - Training at “Expert Laboratory” Site
    - \* No Substitute for Directly Observing Method
    - \* Nuances of Method Can Be Addressed/Discussed
  - Support Running “Feasibility” or Practice Samples

# Best Practices of Outsourcing

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- ◆ Make an Effort to Understand Contract Laboratory's Organization and Procedures
  - Not All Contract Laboratories Operate the Same Way
  - Increases Effectiveness of Communication
  - Increases Awareness of Impact of Requests
  - “Clients Who Understand How We Work Have Projects That Go Much Smoother”

# Best Practices of Outsourcing

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- ◆ Follow Contract Laboratory's Procedures
  - Suitability of Contract Lab's Procedures Assessed During Quality Audits
  - Allows Contract Lab Most Efficiency
- ◆ Provide Single Point of Contact
  - Empowered to Address or Facilitate Technical and Quality Issues
  - Avoids Communication of Conflicting Information

# Best Practices of Outsourcing

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- ◆ Define Clear Cycle Time Expectations
  - Establish “Standard Turn Around Times”
  - Establish Process for Requesting “Rush”
- ◆ Clearly Define Specification Requirements Up Front
  - Compendial Specifications Versus In-House
  - Alert/Action Limits Versus Regulatory Specifications

# Best Practices of Outsourcing

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- ◆ Define Payment Methods Up-Front
  - Provide Purchase Order Numbers Assigned with Appropriate Dollar Amounts
    - \* Avoids Delays in Delivery of Data
    - \* Avoids Wasted Energy on Past Due Invoices for Both Parties
  - Clearly Define How Additional Charges Beyond the Quote Will Be Handled
    - \* Change Orders

# Best Practices of Outsourcing

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- ◆ Establish Regularly Scheduled Business Review Meetings
  - Integrate All Levels Between Organizations
  - Review Contract Laboratory Metrics
    - \* Cycle Time
    - \* Quality Metrics
  - Review Current and Future Project Load
    - \* Give Contract Laboratory Opportunity to Plan and Forecast

# Compliance Expectations of a Contract Lab (Audit Tips)

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- ◆ Organization/Personnel
- ◆ Facilities
- ◆ Equipment
- ◆ Laboratory Controls - Building Quality Into Operations
- ◆ Laboratory Records and Documentation

# Organization/Personnel

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- ◆ Organization of Personnel
  - Can Differ by Functional Department
    - \* Excipients/Raw Materials
    - \* Finished Product/Stability
    - \* APIs
    - \* Specific Techniques
  - Supervisor/Analyst Ratio
  - Independent Peer Review
  - Quality Unit/Operational Employee Ratio

# Personnel Training/Analyst Qualification

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- ◆ Training Modules
  - Technique Based
  - Core Modules
  - Electives Based on Job Duties
  - Proficiency Assessments
- ◆ Method Specific Modules
  - Technique Dependant Methods
  - Client Required

# Building and Facilities

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## ◆ Security

- Controlled/Limited Access
- Employee/Visitor Identification

## ◆ Disaster Recovery Plan

- Disaster Recovery Team with Predefined Plans For:
  - \* Electrical Failures
  - \* Fire
  - \* HVAC Failures
  - \* Computer Failures
  - \* Injury
  - \* HAZ/MAT Spills

## ◆ Water Systems

- USP/EP Grade Water Supply
- Tested/Monitored Weekly

# Building and Facilities

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- ◆ Cleaning/Housekeeping
  - Procedures and Controls in Place
- ◆ Insect/Rodent Control
  - Routine and Ongoing Monitoring
- ◆ Emergency Power
  - Short Term - Example UPS Used for Critical Operations
  - Long Term - Diesel/Natural Gas Generators

# Building and Facilities

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- ◆ Environmental Monitoring for Micro Labs
- ◆ Temperature & Humidity Control/Monitoring of Laboratory and Sample Storage Areas
  - System Capable of Alerting on Excursions
  - System Must Provide an Ongoing Record/Trace of Temperature/Humidity Conditions
- ◆ Change Control - Facilities
  - Assess Impact of Change on Overall Operations

# Equipment

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- ◆ Validation for New Instruments/Equipment
  - Validation Plan
  - Vendor Evaluation
  - User Functional Requirements
  - IQ/OQ/PQ - Test Plans and Documentation
  - Validation Summary
  - System Acceptance and QA Approval
  - System Maintenance
    - \* Re-qualification, Change Control, SOPs

# Equipment

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- ◆ Legacy Systems - Retrospective Validation Project Plans
  - Validation Plan
  - Gather Historical Data to Support Past Operation and to Justify Continued Use
  - Validation Summary
  - System Acceptance and QA Approval
  - System Maintenance



# Equipment

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- ◆ Instrument/Equipment Calibration & Maintenance
  - M&C Program - Metrology Group
  - Operation/Maintenance/Calibration/Qualification Procedures
  - Intervals Established Based on Use, Internal Requirements, and Vendor Recommendations
  - Calibration Traceable to National Standards (NIST) Whenever Possible
  - Detailed Documentation in M&C Logbooks

# Equipment

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- ◆ Effective “Tag Out” System
  - Insure Non-Validated/Maintained Instruments Not Used
- ◆ Change Control - Equipment
  - Assess Validation Impact
  - Equipment Moves - PQ to IQ/PQ Approach
  - Retirement Plans - Close Out PQ

# Building Quality Into Operations

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- ◆ Quality Policy
  - Based on Overall Business and Management Philosophies, Mission, and Goals
  - Detailed Overview of Quality Systems
  - Provides Employees Clear Guidance for Production of Analytical Data

# Building Quality Into Operations

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## ◆ Document Control

- SOPs/Methods/Specifications Readily Accessible
- “Expiration” of Printed SOPs/Methods/Specifications if Using LIMs
- Contract Lab Specific Challenges
  - \* Additional Instructions Not Included in Method
  - \* Lab Needs Mechanism to Capture this Information

## ◆ Control of Samples

- Assigned to Controlled Location
- Tracked by Individual (Chain of Custody)

# Building Quality Into Operations

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- ◆ Routine Quality Control Checks
  - Key to Building Quality Into Operations
  - Helps to Prevent Need for Historical Evaluation of Data
  - Need to Balance Cost vs. Benefit/Risk



# Routine QC Checks - Examples

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- ◆ Balance Qualification/Daily Checks
  - Yearly Service by Vendor
  - Bi-Annual “USP Accurate Weight” Qualification
  - Daily “S Class” Weight Check
- ◆ FTIR Daily Quality Control Check
  - Daily Scan of NIST Traceable Polystyrene
- ◆ pH Meters and Auto-pipettes
  - Calibrated at Each Point of Use

# Routine QC Checks - Examples

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- ◆ Chromatographic Analysis - Beyond System Suitability
  - Blanks - Filtered Sample and Standard Solvents
  - Check Standards
  - Continuing System Suitability (Every 6 Hrs.)
  - Impurity Markers/Resolution Solutions
    - \* Injected Every 24 Hours for Extended Runs
  - Dosage Forms Weighed Prior to Testing
  - Ability to Query Data Based on Instrument, Column, Method, Client, and Analyst

# Laboratory Records/Documentation

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- ◆ Recording Laboratory Data
  - Establish Standards for Free Form Documentation
  - Advantages of Pre-formatted Worksheets
  - Documentation Error Codes
- ◆ Electronic Records
  - Audit Trail and Ability to “Lock Down”
  - Back-up
  - Archival and Restore

# Laboratory Records/Documentation

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- ◆ Clearly Define “Raw Data” in Procedures
  - First Electronic Signal Captured by the Data Acquisition System
  - Printout from Karl Fischer Titrator
  - Sample Weight Documented in Analyst Notebook.
- ◆ Unused Data - Needs to be Explained and Documented in Detail
  - Failed QC
  - Analyst Error

# Method Development

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- ◆ Contract Labs Leverage Overall Experience
  - Experience with Similar Projects and/or Technologies
  - Diversity of Regulatory Issues
  - Focused on Analytical Solutions as Core Business – Offer Creative Solutions
- ◆ Balance Experiences with Confidentiality
  - Organizational Culture to Include Strict Confidentiality

# Method Validation

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- ◆ Contract Labs Leverage Overall Experience
  - Diversity of Client Base – Refine Standard Protocols Based on Client Feedback
  - Validation Approaches Under Constant Scrutiny
  - Challenged by Client Approval Process
  - Develop “Library” of Protocols
- ◆ Diversity of Techniques
  - Validation of Many Different Techniques (e.g. Dissolution/Elution, ICP, AA, FTIR, IC)