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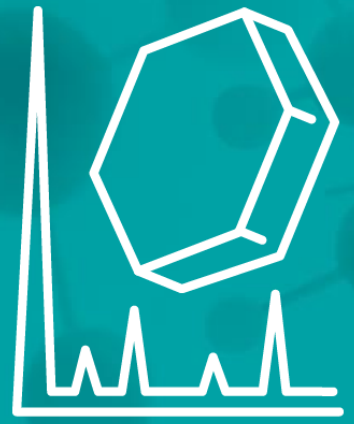

# Analytical & Solid State Services

June 2017

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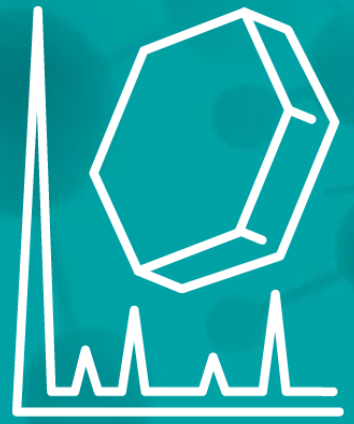

# Analytical & Solid State Services

***Through our global network of laboratories, we serve clients with GMP and non-GMP requirements. FDA and EMEA registered. DEA I-V capabilities. Potent compound capabilities. ISO 17025, ISTA certifications.***

# Industry-Leading Analytical Services

## One source for global end-to-end solutions

| | DISCOVERY | DEVELOPMENT | COMMERCIAL |
|---|---|---|---|
| Early Candidate Support | | | |
| Analytical Testing Services | | | |
| Method Development, Validation, Batch Release and Stability Lot Testing | | | |
| Solid-State Chemistry | | | |
| Package and Device Testing | | | |

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# Early Candidate Support Services

## *In vitro* analysis, stability, solubility, dissolution and excipient compatibility

### Discovery

Our comprehensive discovery biology, synthetic and medicinal chemistry, DMPK and bioanalytical services span the continuum from hit-to-lead identification through candidate selection. World-class high-throughput screening capabilities include:

- Compound and sample management
- High-throughput robotic screening platform
- Advanced data informatics

Innovative instrumentation delivers speed and efficiency in for screening novel targets.

### Physical and chemical properties evaluation

- pKa, logP/logD determination
- Determining equilibrium solubility
- Establishing pH solubility profiles
- Dissolution testing
  - Aqueous, organic and biorelevant media
  - Intrinsic, powder, tablet and capsule
  - USP or fit-for-purpose material sparing methods

### Monitoring chemical and physical stability

### Preclinical formulation screening and selection

- Excipient compatibility to support drug product formulation design
- Amorphous, solid dispersions, supersaturated solutions

### Problem solving and research studies to investigate:

- Processing issues
- Dissolution inconsistencies
- Content uniformity issues
- Formulation difficulties
- API and drug product performance issues

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# Analytical Testing Services

## Comprehensive Menu of cGMP Analytical Technologies

### X-ray Diffraction
- Standard, VT and RH
- Indexing
- Single crystal structure solution

### Thermal Analyses
- DSC: standard, modulated, nanoDSC
- TGA, TG-IR
- Hot bench
- Microcalorimetry: solution and isothermal
- Melting point

### Chromatography
- Reversed-phase HPLC
- Ion exchange HPLC
- Size exclusion w/ MALS and RID
- UPLC
- GC

### Spectroscopy
- IR: FT and mapping
- NIR imaging
- Raman: FT and mapping, solution probe
- NMR: solids and liquids
- UV-Vis: cuvette and plate reader
- Fluorescence
- Mass: QTrap LC-MS/MS, MALDI-TOF, Q-TOF

### Microscopy
- Polarized light
- SEM: standard / environmental / EDX
- Hot / cold stage microscopy
- Vibrational

### ICP-MS
- Heavy Metals Testing

### Volatiles Content Determination
- Karl Fischer
- TGA

### Vapor Sorption

### Micromeritics
- Particle size: laser light scattering
- Surface area: BET
- Porosity, bulk and tap density
- Sonic sieve

### Biochemical Services
- Isolation and purification
- Identification and authentication
- Protein crystallization
- Electrophoresis
- Light scattering
- Protein sequence & composition
- LAL Endotoxin

**Using standard, compendial or compound-specific validated methods.**

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# Analytical Testing Services

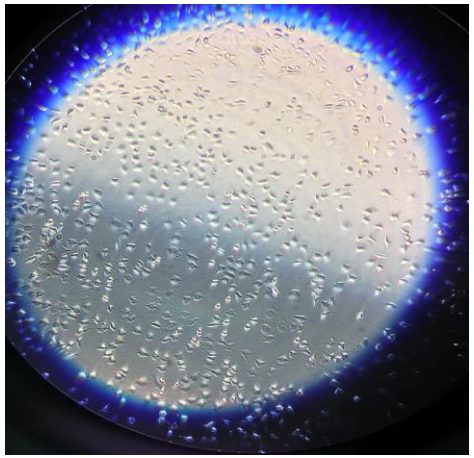
## Microbiological and Biological Testing

### Microbiology

- Water and in-process bioburden and pathogen testing
- Microbial Limits of Non-Sterile Products
  - Enumeration
  - Specified / Objectionable organism
- Antimicrobial / Preservative Effectiveness testing
  - Stability / Formulation / R&D Support
- Environmental Monitoring
  - Process / System Validation
  - Program Design
  - Compressed Air
  - Cleanroom / Controlled Environments
- Biological Indicators
  - Processing
  - Population Verification
- Method Development / Suitability / Validation
- Purified Water System Validation
- Cleaning Validation
- Disinfectant Studies

### Biology

- Bacterial Endotoxin Testing
  - LAL
  - Method Development / Suitability / Validation
- Biological Reactivity
  - Tests *In Vitro*
    - ISO and USP
  - Tests *In Vivo*



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# Analytical Testing Services

## Extractables & Leachables and Impurities

Leading expertise in **Extractables/Leachables Study** designed to satisfy Industry & Regulatory requirements

- **Meeting FDA Expectations** for
  - Containers & Packaging
  - Mfg Systems/Processes, SUS
  - Devices, Combo Products, etc.

- Compliance to **USP <661.2>**
  *plus alignment to future <665>*

- Adherence to **USP <1663>**
- Adherence to **USP <1664>**
- Alignment to future **USP <1031>**

- Compliance to **ISO 10993**
  - Chemical Characterization
  - Tox Risk Assessment (TRA)

- **PQRI** Best Practices
- **BPOG** Alignment
- **BPSA** Recommendations
- **ICH** Requirements on Impurities

- Impurities
  - Unknown Impurities Identification
  - Trace Organic Analysis
  - Impurity Profiling

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# Analytical Testing Services

## Toxicology Risk Assessment

Quality Risk Assessment is recommended by regulatory body.  AMRI has the technical expertise and resource to guide customer to navigate through the complex assessment process.

- Extractable/Leachable Profile Tox Risk Assessment (TRA)
- Genotoxic Impurity Risk Assessment and Management ICH(M7)
- Elemental Impurity Risk Assessment ICH(Q3D)
- Establishment of Allowable Leachable Substances (ISO 10993-17)

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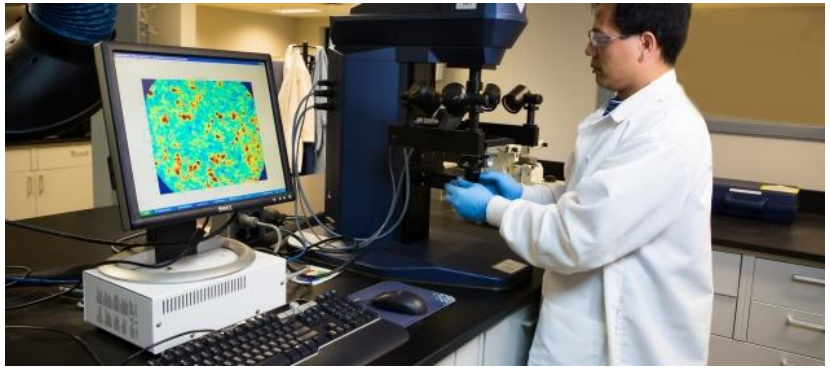
# Method Development, Validation, Batch Release and Stability Lot Testing

## Method development with a phase-appropriate approach

- Identification test methods to ensure the desired solid form is present
- Limit test methods to determine if one or more minor solid forms are present
- Quantitative methods to accurately determine the amount of forms

## Batch release and stability lot testing with issued certificate of analysis (CoA) for API and drug product



## Troubleshooting and consulting services

- Assessment of materials to help determine the origin of issues in API, drug product, and delivery devices
  - Batch-to-batch variability
  - Performance:
    - Dissolution, bioavailability and flow properties
  - Content uniformity
  - Presence of unknown materials

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# Solid State Chemistry Services

## Solid form screening, purposeful design of crystallization processes

### Solid form screening and selection

- Crystallization of hard-to-crystallize materials
- Polymorphs, hydrates and solvates
- Multicomponent crystalline forms, salts / cocrystals
- Single crystal growth and structure determination
- Comprehensive physical properties investigation
- Establishing thermodynamic and kinetic relationships
- IP protection strategy of APIs

### Problem-solving capabilities

- Supramolecular property modulation
- Batch-to-batch variability

### Proprietary software

- Pattern matching
- Structure solution from X-ray powder diffraction (XRPD) data
- TRIADS XRPD indexing algorithm

### Purposeful design and optimization of crystallization processes

- Targeting API with desired purity, crystal form and particle characteristics
- Troubleshooting of existing processes for the final API or key intermediates
- Optimization of crystallization method for late stage candidates
- Chiral resolution via diastereomeric salt formation or cocrystallization

### Key differentiators

- Fit-for-purpose approach for each development stage
- Deliver reproducible downstream processes
- Ability to identify critical performance attributes of API for use in formulations

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# Package and Device Testing

The leader in container qualification testing, Whitehouse Laboratories can assist with all required USP, EP and JP testing for all container systems. Our experienced and dedicated staff is available to advise and consult to ensure complete compliance to FDA requirements.

**Container tests routinely performed include:**

- USP glass testing
- USP plastic containers
- USP container performance testing
- USP elastomeric closure testing
- USP biological reactivity
- Comprehensive EP and JP container testing

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# Package and Device Testing

Offering expertise in parenteral primary package leak testing pursuant to the revisions to USP <1207>, effective August 1, 2016.

- ASTM F 2391-05: Helium Mass Spectrometry
- ASTM F 2338-09: Vacuum Decay
- High voltage leak detection (HVLD)
- Laser-based headspace analysis
- Mass extraction

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# Package and Device Testing

Our cGMP and ISO 17025 laboratory offers physical package testing to meet your R&D needs through package validation, quality control testing and product performance tests, whether for the Container Closure System (CCS) as a whole or its components.

Core capabilities include:

- **Physical Package Component Testing**
- **Physical Package (CCS) Testing**
- **Simulated distribution testing per ASTM D4169, D7386 and the ISTA Series of Standards (ISTA Certified Laboratory)**
- **Pre-conditioning and/or simulating an environmental condition**
- **Pre and post-test inspection and testing**
- **Environmental Cycling and Shelf Life Studies**

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# Package and Device Testing

ISO 11608 specifies requirements and test methods for needle-based injection systems intended to be used with needles and with replaceable or nonreplaceable containers. ISO 11608 comprises seven parts, under the general title: Needle-Based Injection Systems for Medical Use — Requirements and Test Methods.

Whitehouse currently provides testing including:

**Part 1:** Needle-based injection systems
**Part 2:** Needles
**Part 3:** Finished containers
**Part 4:** Requirements and test methods for electronic and electromechanical pen-injectors
**Part 5:** Automated functions

# Package and Device Testing

## Medical Device Package Validation - ISO 11607

- **ISO 11607 Stability Testing:** Real-time aging and accelerated aging (ASTM F1980) to demonstrate that the sterile barrier system maintains integrity over time for the anticipated shelf life of the product
- **ISO 11607 Performance Testing:** ISTA and ASTM distribution simulation to demonstrate that the packaging system provides protection though the hazards of handling, distribution and storage
- **ISO 11607 Package Strength Testing:** Physical tests to demonstrate the mechanical performance of the sterile barrier system
- **ISO 11607 Package Integrity Testing:** Physical tests to demonstrate the sterility and integrity of the sterile barrier system

**For more information contact:**
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