# MURTY PHARMACEUTICALS, INC. (MPI)

---

## CAPABILITIES STATEMENT


---

**518 CODELL DRIVE, LEXINGTON, KY 40509**
**Email: info@mpirx.com**
**Tel: (859) 266-2446, Fax: (859) 266-6976**

# BACKGROUND AND FACILITIES

## BACKGROUND

President and Scientific Director, Dr. Ram Murty founded Murty Pharmaceuticals, Inc. (MPI) in 1995. Helping to establish and implement Good Manufacturing Practices Regulations (GMPs) since their inception in 1970s and through the 1980s, Dr. Murty has continued research, technology, and commercial based objectives for the NIH as well as the pharmaceutical industry. As a result, during the past decade, MPI was established with the defined goals to undertake high quality research projects covering New Chemical Entities from formulation through clinical supply phases as well as devising innovative delivery systems. Furthermore, the organization has recently established commercial scale manufacturing for solid oral dosage forms. This will provide MPI's clients and partners the option for a single source stop for research and development phases through commercialization.

## FACILITIES

MPI's 27,000 square foot facility is located in Lexington, Kentucky, USA. The facility is FDA approved for commercial scale manufacturing and maintains appropriate licenses with the DEA and the State Pharmacy Board. The facility comes equipped with a state-of-the-art laboratory containing a variety of elaborate and sophisticated instrumentation, two processing and manufacturing suites, secure and non-secure warehouse space, office space, and a fully automated packaging line.

## SERVICES

MPI offers a wide spectrum of services and expertise in scientific, professional, technical, manufacturing, quality control, and regulatory fields in compliance with applicable cGMP/GLP regulations. Services include formulation development, drug delivery design, analytical method development/ validation, drug stability assessment, clinical and commercial scale manufacturing, labeling, packaging, and shipping. The company also possesses state-of-the-art supercritical fluid (SCF) units for small-scale isolation, extraction, and purification of drug moieties. Finally, MPI provides documentation and regulatory support for DMF preparations and IND, NDA, and ANDA submissions.

### Testing of Active Pharmaceutical Ingredients (API's) and Excipients

Comprehensive testing consists of chromatographic, spectral, thermogravimetric, differential scanning calorimetric, and LC/MS techniques.

### Pre-formulation Studies

To develop dosage forms to achieve enhanced solubility, sustained delivery, enhanced stability, targeted delivery, improved bioavailability, acceptability for specialized use, and administration for alternate routes, systematic pre-formulation studies are conducted at MPI facilities. Listed below are some of the critical tests that MPI scientists can perform:

| | | | |
|---|---|---|---|
| Solubility profile | Partition coefficient | pH rate profile | Bulk density |
| Polymorphism | Particle size distribution | Flow properties | Stability |
| Dissolution | Drug-excipient interaction | Log pKa | TGA/DSC |

### Development of Dosage Forms

Oral dosage forms (conventional and extended release) - Tablets, Capsules, Liquids
Parenterals - Liquid and Lyophilized
Semi-solids - Gels, Ointments, Creams
Rectal/Vaginal - Suppositories, Solutions, Ointments

### Drug Delivery Systems

MPI developed proprietary, patented platforms for specific clients and partners, including the following:

| | | | |
|---|---|---|---|
| Microencapsulation | Controlled release | Sublingual | Transdermal Gels |

**Analytical Methods**

LC/MS
High performance liquid chromatography (HPLC)
Gas chromatography
UV/Visible spectrophotometry
Log pKa/Log P Determination
Supercritical Fluid Separations

**Analytical Method Development**

Raw material testing
Packaging material testing
Stability indicating assay
Dissolution testing
Cleaning residues - swab and rinse samples
Residual organic volatiles

**Analytical Method Validation**

Recovery
Accuracy
Precision
Repeatability
System suitability
Specificity- forced degradation studies
Solution stability
Ruggedness
Robustness

**Stability Assessment**

Stability protocols follow current practices incorporating ICH guidelines, which are implemented to determine the stability of the finished product in the proposed container-closure system. MPI's facility is equipped to conduct stability studies under the following storage conditions, but can meet other, more specialized conditions upon customer request.

Stability Conditions:
Long-term: 25° ± 2°C, 60% ± 5% RH for 3, 6, 9, 12, 18, 24, and 36 months
Intermediate: 30° ± 2°C, 60% ± 5% RH / 65% ± 5% RH for 1, 2, 3, and 6 months
Accelerated: 40° ± 2°C, 75% ± 5% RH for 1, 2, 3, and 6 months
Accelerated: 50° ± 2°C, 75% ± 5% RH for 1, 2, 3 months
A reference sample will be stored under ambient conditions unless specified otherwise
Freeze-thaw (-20°C to ambient)
Photostability

**Manufacturing Process Development and Validation**

Liquid orals
Tablets
Capsules
Semi-solids (gels, lotions, creams)
Solid dosage forms (suppositories)
Parenteral (both liquid and lyophilized)

**Clinical & Commercial Manufacturing and Re-packaging**

Solid Oral Dosage Forms: The firm has all necessary equipment for manufacturing solid oral dosage forms, including tablets and capsules of various sizes. Additionally, MPI has the necessary infrastructure and experience for the storage, distribution, and documentation for clinical supplies intended for all phases of NDA. Dedicated employees monitor all activities for clinical supplies and commercial batches.

For other dosage forms, including parenterals and semi-solids, the firm has capabilities to manufacture pilot batches. For production batches, outside sources with demonstrated compliance profiles and cost effective budgets are selected. MPI coordinates scale-up and technology transfer activities to maintain continuity as well as to provide overall assurance for meeting delivery schedules.

**Documentation and Regulatory Submission Support**

The firm has extensive experience in DMF and CMC preparation, for providing regulatory support for IND, NDA, and ANDA submissions.

**Consultation**

Product/process development
Facility design, development, and validation
Evaluation of pharmaceutical systems and equipment
Scale-up and technology transfer

## INSTRUMENTATION AND EQUIPMENT

### Laboratory Instruments

**LC/MS**
LC-MS Agilent 1100 HPLC with 1100 LC/MSD VL System

**High Pressure Liquid Chromatography**
HP 1050 with DAD and Autosampler
HP 1100 with DAD and Autosampler (4)
HP 1100 with VWD and Autosampler (3)
Waters Alliance 2690 with-
PDA/ECD/ fluorescence
Waters Alliance 2695 with PDA 2996 (with automated analytical method development capability)

**Semi-Preparatory HPLC (FPLC)**
Dionex Auto Summit System with DAD

**Spectrophotometry**
Perkin-Elmer Spectrophotometer 1000 FTIR
Beckman DU 64 UV/VIS
Beckman DU 520 UV/VIS

**Elemental-Metal Analysis**
Perkin-Elmer 3300 Atomic Absorption

**Dissolution**
Vankel -6 flasks
Hanson-Research-6 Biodis
Hanson-Research-6 flasks
Hanson-Research-8 flasks
Hanson Research Autosampler

Diffusion/Permeation System
Franz (vertical) skin diffusion (6 cells)
Valia-Chin lateral skin permeation (9 cells)

**Friabilator**
Pharmatest single drum
Electrolab Tablet Friabilator

**Stability/Storage Chambers**
Photostability chamber (ICH)
Long-term storage (25°C / 60% RH)
Intermediate storage (30°C / 60% RH)
Intermediate storage (30°C / 65% RH)
Accelerated storage (40°C / 75% RH)
Accelerated storage (50°C / 75% RH)
Refrigerators (8) [2-8°C]
Incubator (8-15°C)
Walk-in-Cooler (2-8°C), 630 Cu. Ft. (2)
Freezers (10) [-10 and –70°C]

**Classical and Wet Chemistry**
Melting point apparatus
Analytical balance (3)
Microbalance
Centrifuge: desktop and ultracentrifuge
pH meter (2)
Oxygen meter
Refractometer
Brookfield Viscometer
Muffle Furnace
Kruss P1000 Polarimeter

**Gas Chromatography**
HP 6890 with FID/TCD and Autosampler
HP 5890 with FID and Autosampler

**Calorimetry / Gravimetry / PQ / pKa**
Perkin-Elmer DSC-6
Perkin-Elmer TGA-6
PCA-200 with D-PAS

**Moisture Analysis**
Karl-Fischer DL-38 titrimeter
Denver IR 200

**Particle Size Analysis**
Malvern 2C autosizer
Hiac Royco counter
Bausch and Lomb microscope
Olympus SZX60 Stereo Microscope with-Camera

**Disintegration**
Vankel single bath (2)
Electrolab Tablet Disintegration Tester - Model -D-2AL

**Specialized Storage Facility**
DEA-Licensed Secure Controlled Substance Storage

**Miscellaneous**
NANO-pure water unit
Solid phase extraction unit
Sonicator bath (2)
Digital Torque Tester

**Automatic Titrator**
Mettler Toledo DL 53

# Pharmaceutical Processing Equipment

**Tabletting/Capsules**

Tablet press – 16
Tablet press – 27 stations (2)
Tablet hardness tester (2)
Tablet de-burring/de-dusting machine
Dust extractor machine
Semi-automatic capsule filling machine
Manual capsule filling machine (3)
Tablet tool cleaning maintenance kit
Vanguard Friability Tester
Logan HDT-300 Hardness Tester
Vanguard Tablet Hardness Tester
Vanguard Disintegration Tester
Vanguard Capsules Polishing and Sorting Machine
Single Roller Band Sealing Machine

**Liquid Mixing**
Agitator (0.5 HP)
Homogenizer
Colloidal Mill

**Drying**
Tray Drier (1)
Fluid bed drier – 10 Kg
Oven (2)
Gansons Fluid Bed Drier – 60kg

**Extractor**
Supercritical Fluid Extractor, 1L
Supercritical Fluid Extractor, 2X5 L

**Distillation**
Brinkmann R220, 20L Rotary Evaporator

**Mixing & Blending**
Double cone - 5 kg
PK blender (5 $ft^3$)
Drum blender – 20L
V-blender – 20L
Kitchen Aid Mixer 5L (2)
Hobart – 30, 40 qt and 60 qt
Ribbon (Mass) mixer
Octogonal Blender – 400L
Gansons Planetary Mixer – 100L

**Milling**
Centrifugal mill (Retsch)
Fitz mill (2)
Multimill (3)

**Pelletization**
Spherodizer
Marumerizer

**Sifting**
Sifter (30")
Sieves
Sieve Shaker

**Coating**
Coating Blower
48" Coating pan (2)
12" Coating pan
Coating spray system
Ganscoater GAC 250
Ganscoater GAC 600
Ganscoater GAC 1200

**Packaging**
Blister-packing machine
Pharmapack counting machine
Hispack Counters (2)
CVC Bottle Packaging Line

**Ointment Filling Machine**
Ointment/tube filling machine
Ointment/tube crimping machine

**Granulator**
Rotary granulator
Rapid mixing granulator, HSMG5, 5L
Rapid mixing granulator, HSMG50, 50L

**Parenteral Filling**
Vial filling machine
Ampule filling and sealing machine (2)
Manual ampule sealing machine
Lyophilizer
Masterflex peristaltic pump
Dry heat sterilizer
Power washer
NANO-pure water unit
Laminar airflow cabinets
Steam sterilizer

**Miscellaneous**
Balance (7)
Air Compressors (3)
Platform balance (2)
Refrigerated incubator
Reposograph
Bulk density tester
Culligan – USP Purified Water System

# QA / QC PROCEDURES

## Compliance with GMP Requirements

The firm is committed to maintaining a compliance profile with all applicable regulations including cGMPs, GLPs, State Board of Pharmacy requirements, and DEA regulations.

## Equipment Maintenance

All major processing equipment and laboratory instrumentation are maintained and calibrated by in-house personnel and, where necessary, by authorized representatives under appropriate service contracts.

## Inventory Controls

The bulk drug substances and excipients received at MPI are assigned a lot number, quarantined, sampled, tested, and released after verifying conformance with established specifications. An inventory control system is maintained to determine the traceability, rotation of stock, and reassay schedules, etc. Similarly, distribution records are retained with appropriate documentation in accordance with cGMP regulations.

## Validation Commitments

An integrated validation approach for various processes and procedures has been established. In addition, particular attention is focused on cleaning procedures to minimize cross contamination potentials during the processing, handling, and packaging of drug products.

## Packaging and Labeling

MPI complies with applicable cGMPs found in 21 CFR Parts 210 and 211 for packaging and labeling. All packaging components are received from selected vendors and assigned a lot number for each shipment to ensure traceability. For each shipment/component, inventory and usage logs, together with pertinent certification documents, are reviewed and retained.

MPI clients send label copies for review and approval. After approval, the labels are printed and controlled in a manner consistent with cGMP requirements. An inventory is maintained and reconciliation is performed.

## Shipments

After completing all quality control testing and conformance verifications, the products are released for distribution to clinical or client specified sites. Upon completion of a project, a production report is forwarded for review. The report includes a description of the manufacturing procedures, quality control test methods, results, and batch accountability measures employed. After receiving release authorization and shipping instructions, shipments are arranged through an insured, 24-hour delivery service. Accurate inventory, distribution records, and receipts for shipment are retained in files to ensure complete traceability.

**Quality Control Testing**

In-process quality control tests include materials at various stages of manufacturing. Finished product testing is formalized in conjunction with the project officers identified by MPI's clients. Quality control tests include integrity, appearance, weight variation, disintegration, dissolution, moisture content, potency, limit impurities, and other tests designed to evaluate conformance with product specifications. When necessary, qualified laboratories are utilized to undertake sterility, endotoxin, and other specialized tests as required pursuant to compendial procedures. All data is reviewed to verify conformance with product specifications prior to release. Any unexplained deviations are investigated, and the results are documented in master batch records.

**Documentation**

MPI has implemented a documentation system, which enables complete traceability. Manufacturing and control data are devised as per cGMP regulations and retained in a manner which renders easy retrieval. Complete details of master formula instructions and test results are formalized in a batch record system, which covers batch yields, accountability, and distribution. Representative samples are retained from each batch and documented. Any complaints/inquires pertaining to a specific lot are documented and thoroughly investigated. Results and summaries of all investigations are retained in appropriate files.

**Confidentiality and Security**

The organization is aware of the confidential nature of research investigations. All personnel engaged in the proposed investigations are instructed to support the firm's policies and the confidential nature of the work. All employees, prior to entering employment, execute a confidentiality agreement. The firm monitors the overall effectiveness of this pursuit.

An outside security firm monitors the entire facility and access to the facility is controlled. Unauthorized personnel are restricted from entering the premises in view of the highly selective and classified information that is being handled for various clients including Federal Government contracts. Dedicated rooms with electronic monitors are built within the facility for the storage and control of drug substances. In addition, the firm has provided storage space for highly classified information to prevent unauthorized distribution, and to maintain confidentiality. The firm always ensures that it has no conflicts with other commitments and/or projects.