

**ORIT**

***Oral Generic Pharmaceuticals Development and Commercialization***

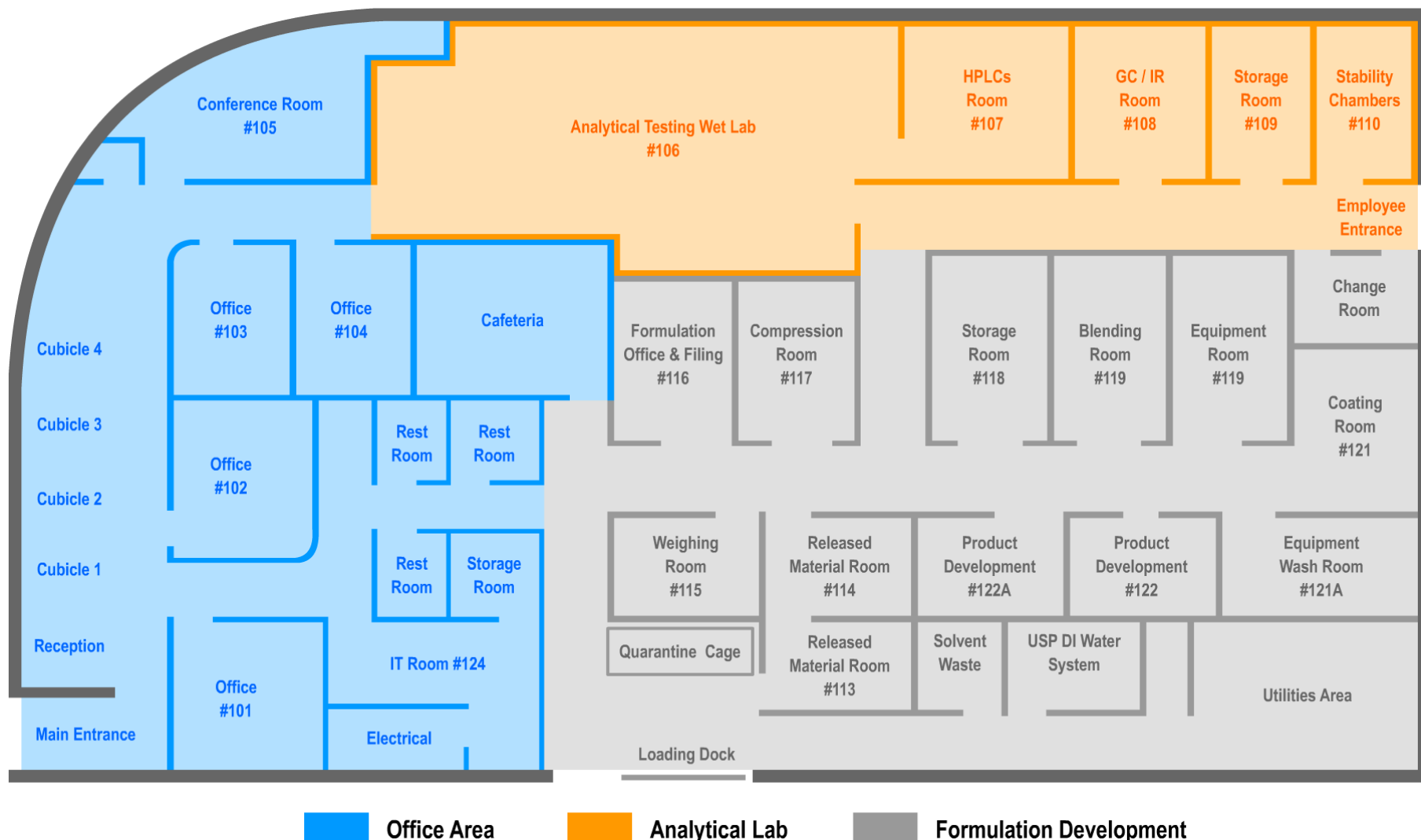
## 2 Overview

- **Founded and Established in Aug. 2005 by Dr. Satish Patel, President & CEO**
- **R&D Focused on Oral Rx Generic Pharmaceuticals including:**
  - **Tablets (IR, CR, XR, DR)**
  - **Soft Gelatin Capsules (Liquid Filled)**
  - **Hard Gelatin Capsules (Powders and Pellets)**
  - **Oral Solutions and Suspensions (IR)**
  - **Oral Dry Powders / Granules for Reconstitution (i.e. Solutions, Suspensions)**
- **Collaborative Business Model (Manufacturers and Marketers)**
- **“Tech. Transfer” to Manufacturing Party and Licensing to Marketing Party**
- **Small Batch Manufacturing (i.e. R&D Scale and Pilot Bio-Studies Batches)**
- **Analytical Capabilities (i.e. Methods Validation and Transfer, ICH Stability Testing, Commercial Release Testing)**
- **Regulatory Affairs including In-House Capabilities for ANDA Compilation and Submission in eCTD format through ESG (FDA Gateway)**
- **4 ANDAs Approved Under Orit’s Ownership (Listed in FDA Orange Book)**
- **6 ANDAs Filed and Under FDA Review**

### **3 Facilities and Compliance**

- FDA Registered Facility (FEI Number, DUNS Number, NDC Labeler Code) and Compliant with Annual FDA Establishment Registration**
- Compliant with Annual GDUFA Requirements (Self-Identification as “Analytical Testing Laboratory”)**
- Compliant with cGLP and cGMP (required due to Commercial Release Testing, Stability Testing, and Pilot Bio-Studies Batch Manufacturing)**
- FDA Inspection Sept. 2013 (No 483s Issued)**
- Approx. 10,000 sq. ft. incorporating:**
  - **Administrative Offices – Regulatory and Executive**
  - **Analytical Lab (cGLP) – QA/QC, Commercial Testing, Stability Testing, R&D Testing**
  - **Pilot Production Area (cGMP) – Small-Scale R&D Trial Batches and Pilot Bio-Studies Batches**

# Building Layout



## **5 Analytical Laboratory Area**

- Large Open Area Wet Lab with Various Analytical Equipment and Separate DI Water System**
- Distek Dissolution Apparatus (Evolution and Symphony) with Auto Sampler**
- Dedicated Rooms for HPLCs and UPLCs with Waters Empower 3 Software**
- Separate Network Environment (Waters Server and LAC/E Systems)**
- Dedicated Low UV-Light Room for Light Sensitive Compounds**
- HPLC System with Auto-Sampler (Waters Transfer Module) directly transfers samples from Distek Dissolution Apparatus (Located in Low UV-Light Room)**
- GC System with Headspace on Empower 3 Software (Located in Low UV-Light Room)**
- Dedicated Stability Room with Stability Chambers (CRT and ACC with Chart Recording)--- INT Chamber to be added, INT currently outsourced**
- Retained Samples Storage Area**

- **12 Separate Rooms / Suites Dedicated for Production Operations including:**
  - **Warehousing (Released, Under Test, and Quarantine Areas)**
  - **Weighing Room (Various Scale Balances, Standard Weights)**
  - **Blending (V-Blenders of Various Sizes)**
  - **RMG High Shear Mixing and Low Shear Mixing**
  - **Milling, Roller Compaction, Paste Kettle, Jacketed Solution Tank**
  - **Fluid Bed Spray Granulation and Pellets Coating (Wurster Column)**
  - **Fluid Bed Drying and Tray Drying**
  - **Tablet Compression and Tablet Coating**
  - **Hard Gelatin Encapsulation (Powders and Pellets)**
  - **R&D Bench Top Work Space (Various Miniature Equipment)**
  - **Materials and Equipment Storage (Homogenizers, Pumps, Change Parts)**
  - **Separate Equipment Washing Room**

## 7 Equipment Considerations

- ❑ All Analytical, Product Development, and Facility Equipment are “Qualified” (IQ, OQ, PQ) and routinely calibrated as per SOP
- ❑ Project specific equipment should be similar to manufacturer site equipment for ease in early process identification, “tech transfer”, and scale up batches
- ❑ Special equipment purchases based on unique product development requirements can be evaluated based on manufacturing site setup and feasibility
- ❑ Technical evaluation of manufacturing site equipment and transfer “compatibility”
- ❑ Future plan to expand pilot production area capacity with additional equipment for multiple project runs
  
- ❑ For Current List for Orit Labs Equipment, please click below:
  - [Analytical Equipment List \(click here\)](#)
  - [Formulation Equipment List \(click here\)](#)

## Oral Dosage Forms Capabilities

- Immediate Release**
  - High Solubility, Poor Solubility, Small Molecule, Large Molecule, Nano-Particle Matching
- Controlled Release**
  - Delayed, Extended, Bi-modal, Pulsatile, Osmotic, Polymer Matrix, Functional Coating
- Orally Disintegrating**
  - Fast Dissolve, Taste Masking, Fast Disintegration (upon swallowing)
- Pelletized Forms**
  - IR, CR, XR, DR, Micro-Granules, Non-Pareil Seeds
- Soft Gelatin Capsules**
  - Fill Development such as Solutions, Suspensions, Micro-Emulsions, Semi-Solids Emulsion Pastes
- Oral Liquids**
  - Solutions, Syrups, Suspensions, Powders for Reconstitution



## 9 Drug Delivery Technologies

- Orit uniquely “adapts” a formulation and process for a particular product
- Different molecules behave differently in same technology platforms (i.e. one CR formulation platform may not work for all molecules)
- Allows for customization, flexibility, and, ultimately, ruggedness for both formulation and process

Technology	Description
<i>Controlled / Extended / Sustained Release</i>	Once or Twice Daily Dosing
<i>Biphasic Release</i>	Immediate Release combined with Sustained Release (rapid onset followed by sustained duration)
<i>Pulsatile Release</i>	Multiple pulses of drug release at intervals with periods of no release
<i>Time Release</i>	Drug Release at a Specific Time
<i>Delayed Release</i>	Drug Release to Lower GI Tract (pH dependent release)
<i>Colonic Release</i>	Drug Release to Colon
<i>Optimized Bio-Availability</i>	Improved Absorption of Low Solubility Drugs (Nano-particles)
<i>Micro-emulsions</i>	Improved Bioavailability of Poorly Soluble Drugs using oils and surfactants
<i>Orally Disintegrating (ODT)</i>	Rapid Dissolve in Mouth for Improved Patient Compliance

## 10 QbD Product Development

- **Based on ICH Guidances - Q8(R2), Q9, Q10**
- **Essentially, Quality Risk Management Approach to Product Development which Links Raw Materials Attributes and Manufacturing Process Steps to the CQAs of the Drug Product**
- **Determine QTPP (Quality Target Product Profile) and CQAs (Critical Quality Attributes) for Drug Product**
  - Based on RLD Characterization, Drug Substance (API) Properties
- **Perform Risk Assessment (Initial Risk > Update Risk) -- Linking Material Attributes and Process Parameters to Drug Product CQAs.**
  - Drug Substance (API) Attributes effects on Drug Product CQAs
  - Drug Product Formulation Variables (Excipients) effects on Drug Product CQAs
  - Manufacturing Process Steps effects on Drug Product CQAs
- **Formulation Development and Manufacturing Process Development**
  - Excipient Compatibility Studies, Excipient Selection, Process Selection
  - Scale-Up from Lab Scale > Exhibit Batches (update risk assessment during scale-up)
- **Determine Control Strategy**
  - Raw Material Attributes (API and Excipients)
  - Manufacturing Process Steps (In-Process Materials, Critical Process Parameters)
  - Finished Product Specification
- **Lifecycle Management (Validation and Commercial Batches)**
  - Continuous Monitoring and Improvements Post Approval (i.e. Trend Analysis)

# 11 Services and Capabilities

## □ Analytical Services

- Analytical Method Development and Validation
- ICH Stability CRT, ACC, INT (In-house Stability Chambers)
- Commercial Release Testing and Ongoing Commercial Stability Testing as per ICH
- QA / QC for Commercial Analytical Testing

## □ Formulation Development and Small Batch Manufacturing

- R&D trial batches manufactured onsite (small-scale) and cGMP batch manufacturing for Pilot Bio-Studies

## □ Site Transfers

- On Premises Consultation with Manufacturing Sites
- Analytical Method Transfers and Verification
- Scale-Up at Manufacturing Sites (Exhibit Batches, Validation)

## □ eCTD ANDA Compilation and Submission

- In-house eCTD software and FDA ESG (Gateway) for Modules m1, m2, m3, m5
- eCTD Documents Preparation, Review, and Submission as per latest FDA Guidance / Requirements (as per most current ANDA Checklist)
- Amendments Lifecycle Operations (New, Replace, Delete) (i.e. FDA Deficiency Responses)
- Rapid turn around for adapting to FDA's latest requirements

## □ Regulatory

- Responses to FDA Deficiencies (Responding to FDA Complete Response Letters)
- ANDA Submission and Reviews, Annual Reporting (via ESG), Complaint Handling, FDA Adverse Event Reporting (AERS), Inspections and Auditing (Consultants)
- CBE-30 and PAS (ANDA Supplements)

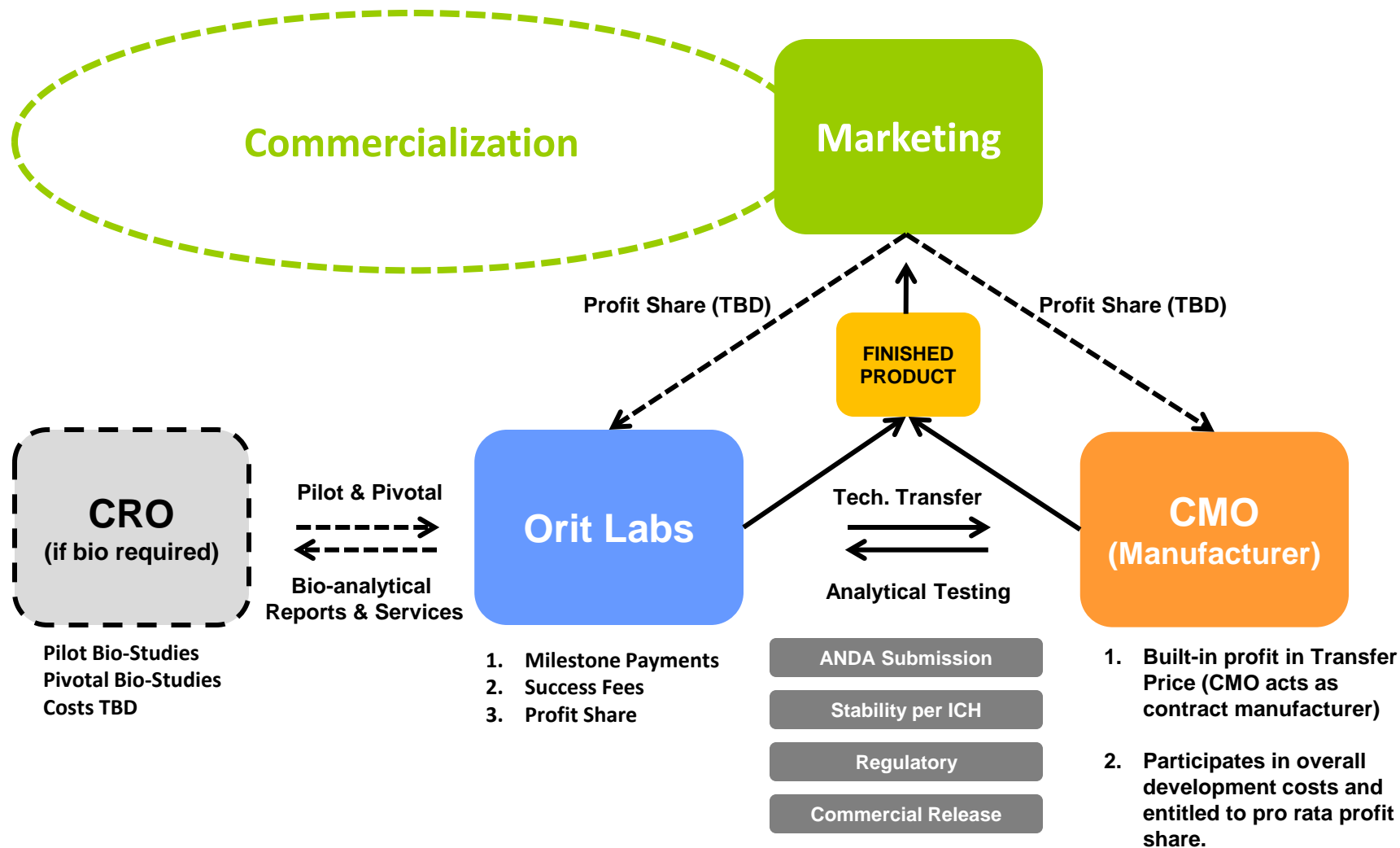
- **ANDA Submission > ANDA Acceptance > ANDA Amendments > ANDA Approval > ANDA Maintenance > ANDA Lifecycle**

## 12 Products and Status

Product	Dosage Form	TE	Strengths	ANDA Owner	Current Status
Ergocalciferol	IR Softgel Capsules	AA	1.25 mg (50,000 Units)	Orit	FDA Approved
Benzonatate	IR Softgel Capsules	AA	100 mg, 200 mg	Orit	FDA Approved
Cyclobenzaprine	IR Tablets	AB	5 mg, 10 mg	Orit	FDA Approved
Levetiracetam	IR Solution	AA	100 mg/mL	Orit	FDA Approved
Levetiracetam	IR Tablets	AB	250, 500, 750, 1000 mg	Customer	FDA Approved
ORIT-004	IR Tablets	AA	Two strengths	Orit	Under FDA Review
ORIT-006	IR Tablets	AA	Two strengths	Orit	Under FDA Review
ORIT-011	IR Solution	AA	One strength	Orit	Under FDA Review
ORIT-012	IR Powder, Reconstituted	AA	One strength	Orit	Under FDA Review
CUST-002	IR Tablets	AB	Two strengths	Customer	Under FDA Review
ORIT-014	IR Tablets	AB	Two strengths	Orit	Under FDA Review
ORIT-007	IR Tablets	AB	Two strengths	Orit	Pivotal Bio-Studies
ORIT-008	IR Tablets	AA	Three strengths	Orit	Tech Transfer Ready
ORIT-009	IR Tablets	AA	Four strengths	Orit	Tech Transfer Ready
ORIT-010	IR Softgel Capsules	AB	Two strengths	Orit	In Development
ORIT-013	XR Tablets	AB	Three strengths	Orit	Pilot Bio-Studies
ORIT-015	IR Tablets	AA	One strength	Orit	Tech Transfer Ready

- Development Fees, Milestone Based Payments:**
  - Contract Sign-Off and Project Initiation
  - Analytical Methods and Formulation / Process Development
  - Tech. Transfer to CMO (Methods Validation/Verification and Product Transfer)
  - Successful Scale-Up of 3 Exhibit Batches at CMO
  - Successful Completion of Pilot and/or Pivotal Bio Studies (if required)
  - ANDA Preparation and Submission in eCTD format
  - ANDA Filed and Accepted For Review (US FDA)
  - ANDA Approval (US FDA)
- Pilot and Pivotal Bio-Studies (CRO Outsourced)**
- Manufacturing and Transfer Prices (CMO Outsourced)**
- Ongoing Commercial ICH Stability Testing (Orit or CMO)**
- Commercial Analytical Testing (Orit or CMO)**
- Consultants (Regulatory, Audits, Inspections)**
- ANDA Ownership (TBD) and Regulatory Agent (Orit or Customer)**
- ANDA Licensing Fees and Profit Sharing Considerations**

# 14 Business Model Flowchart



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## Appendix 1 - Analytical Equipment

Type	Manufacturer/ Model (Qty)	Specifications
<b>Chromatographic</b>		
HPLC Separations Modules	Waters Alliance 2695D (3), e2695D (1)	Empower 3
HPLC UV Detectors	Waters 2487 Dual $\lambda$ Absorbance (3)	Empower 3
HPLC PDA Detector	Waters 2996, 2998 Photodiode Array	Empower 3
HPLC Data Acquisition Servers	Waters LAC/E <sup>32</sup> (3)	Empower 3
HPLC Auto Sampler	Waters Transfer Module	Empower 3
UPLC	Waters Acquity H-Class	Empower 3
GC System	Agilent 7890A	Empower 3, FID
GC Headspace	Agilent G1888 Network Headspace	Auto-sampler
GC Injector	Agilent 7683B	NA
<b>Spectrometric</b>		
UV Spectrophotometer	Perkin Elmer Lambda 20	w/ Auto-sampler, Printer
FT-IR Spectrometer	Perkin Elmer Spectrum One	w/ PC, Spectrum ES, Printer
UV View Sys	Spectroline CC-80	Long Wave 365nm, Short Wave 254nm
<b>Dissolution</b>		
Dissolution Apparatus	Distek Evolution 6300 (2)	6 Vessel, Apparatus I & II
Dissolution Apparatus	Distek Symphony 7100 (1)	6 Vessel, Variable Speed and Media Control
Dissolution Water Bath Temp	Distek Evolution TLS-0200C (2)	NA
Dissolution Medium Degasser	Distek MD-1	500ml, 900ml, 1000ml
<b>Titrimetry</b>		
Potentiometric Titrino	Metrohm 794 Basic Titrino	w/ Printer
Karl Fisher Titrino	Metrohm 795 KFT	w/ Printer
Titrino Stirrer	Metrohm 728 Stirrer	NA
Titrino Stand	703 Ti Stand	NA
pH Meter	Thermo Electron 720A+	NA
<b>Weighing</b>		
Electronic Balance	Mettler Toledo XS 204	4 digit, max. 220g
Electronic Balance	Mettler Toledo XS 205 Dual Range	5 digit, max. 220g,
Electronic Balance	Mettler Toledo AB 204-S	4 digit, max. 220g
Electronic Balance	Sartorius PT120	2 digit, max. 120g
Electronic Micro Balance	Mettler Toledo XP26	4 digit, max. 22g (ie. 0.001 mg)
<b>Mixing</b>		
Sonic Shifter	ATM L3P	NA
Sonicator	Branson 8510	NA
Mechanical Shaker	Eberbach 6000	NA
Multi-Wrist Shaker	Barnstead / Lab-Line	16 wrists
Electromagnetic Sieve Shaker	Electropharma LMS-8	NA
Centrifuge	Fisher Scientific 225A	NA
<b>Temperature</b>		
Laboratory Thermometers (5)	Fisher Scientific ISO9001 /ISO17025	Digital
Melting Point Apparatus	Fisher Scientific V-116	NA
Vacuum Oven	Fisher Scientific Isotemp 280A	NA
Muffle Furnace	Fisher Scientific 650.14	NA
Water Bath	Thermo Electron Precision 280	NA
Laboratory Refrigerator	Revco 0633	25 cu. ft.
Auto DSC Cabinet	Bel-Art	w/ Humidity Meter
Stability Chambers (2)	Hotpack 1750 (417522, 417532)	ACC and CRT, w/ Chart Recorders
<b>Miscellaneous</b>		
Polarimeter / Optical Rotation	Polyscience / Jenoptik SR6	NA
Viscometer	Brookfield LVDV-II +Pro	NA
De-ionized / Distilled Water System	Millipore Direct Q	30 Litre
Washer	Miele Professional G7804	NA
Chemical Fume Hoods (2)	Labconco	NA



## Appendix 2 – Formulation Equipment

Type	Manufacturer/ Model	Specifications
<b>Weighing</b>		
Electronic Balance	Acculab ALC-110.4	4 digit, max. cap. 110g
Electronic Balance	A&D FX-200	3 digit, max. cap. 290g
Electronic Balance	Sartorius GP-5202	2 digit, max. cap. 5.2kg
Electronic Balance	GSE 4518SS	2 digit, max. cap. 200lb
Electronic Balance	Adam CFW-660a	2 digit, max. cap. 300kg
Physical Balance	Toledo 2020	NA, max.cap. 50kg
<b>Mixing/Granulation</b>		
Low Shear Mixer	Kitchen Aid	6 Quart, Variable Speed
Low Shear Mixer	Hobart 600D	55 Litre, Variable Speed
High Shear Mixer, RMG	Bectochem GMP	6 Litre
<b>Drying / Coating</b>		
Mini Fluid Bed Processor / Flow Coater	Freund/ Okawara	Mini, Drying/ Coating, with micro pump
Fluid Bed Processor / FBD	Bectochem	1.5kg, Drying/ Coating, Worcester Column
Tray Dryer (Bench Oven)	Quincy Lab 21-250ERS	25kg
<b>Milling</b>		
Multi-mill	Bectochem	Multiple Sieves, Variable Speed, Lab Scale
Oscillating Mill	Mendel MRC-5M <sup>1</sup>	Multiple Sieves, Lab Scale
Cadmil	Cadmach	Multiple Sieves, Variable Speed
<b>Blending</b>		
V-Blender	Bectochem GMP	1,2,4,8,12,16 Quarts, Variable Speed
V-Blender	Bush Tank	1 cu. Ft., Variable Speed
<b>Compression</b>		
Roller Compactor	Mendel MRC-5	Lab Scale
Rotary Tablet Press	Bectochem PE16DDSR	16 Station, D-Tooling, Single Layer
Rotary Tablet Press	Cadmach CMB-4-D27	27 Station, D-Tooling, Bi-Layer
Dedusters	Cadmach	Vibro –Dedusters (2)
<b>Tablet Coating</b>		
Coating Pan	Bectochem	15” Digital Control Interface
Coating Pan	Vector/Freund	48cm/ 60cm Interchangeable Pans
Dust Collector	Torit	NA
<b>Hard Gelatin Encapsulation</b>		
Manual Encapsulation Machine (benchtop)	NA	Capsule Sizes 00, 0, 1, 2, 3, 4
Automatic Encapsulation Machine (R&D)	Kambert SMART-1	Capsule Sizes 00, 0, 1, 2, 3, 4
<b>Miscellaneous</b>		
Homogenizer	Ross	Variable Speed
Electric Stirrers	Arrow	Variable Speed
Paste Kettle	Bectochem	7 Litre
Peristaltic Pump	Electrolab	Variable Speed
Micro Tube Pump	Eyela	Variable Speed
SS Jacketed Liquid Mixing Tank	Rosemount	40 Litre
Hand Filled Capsule Machine	ACG/PAM	300 manual hand filled
Various Sieves (Pharma grade)	Various	Various Sieves Sizes
<b>Physical Parameters</b>		
Electronic Moisture Analyzer	Sartorius MA 45	NA
Tap Density Tester	Electrolab ETD-1020	USP I and II
Electromagnetic Sieve Shaker	Electropharma EMS-8	NA
Electronic Digital Caliper	Fisher Scientific	English / Metric
Hardness Tester	Schleuniger Pharmatron 6D	N, kp, Sc, R, lb
Friability Tester	Distek DF-3	USP
Disintegration System	Distek 3106	NA