Cambridge Major Laboratories - US

Equipment List - Mini Plant Suites:

SUITE 1 CONTAINS:

- **1 x 50 Gallon GLR (DeDeitrich)**
- **1 x 100 Gallon GLR (DeDeitrich)**
- **1 x 100 Gallon Stainless Steel (Apache)**
- **1 x 50 Gallon Stainless Steel Receiver**
- **Various Stainless Steel Nutsche Filtration Units**

SUITE 2 CONTAINS:

- **1 x 50 Gallon GLR (DeDeitrich)**
- **1 x 100 Gallon GLR (DeDeitrich)**
- **1 x 25 Gallon Stainless Steel (Apache)**
- **1 x 50 Gallon Stainless Steel Receiver**
- **Various Stainless Steel Nutsche Filtration Units**

Our facilities house 2 mini plant suites with reactors up to 100 gallons. Each suite uses ASHRAE filtered air, and is fully isolated to ensure no cross contamination during API production runs.

FILTRATION /DRYING:

Supporting each suite are a variety of enclosed stainless steel Nutsche filters, centrifuges and tray dryers which are located in HEPA-filtered drying suites.

CONTROL SYSTEMS:

Heating and chilling is accomplished via a computer-controlled series of hot, ambient, and cold loops allowing for a temperature range of -20°C to 165°C. Vacuum is controlled via the computer system using water-ring or high-vacuum Bush oil pumps. A full scrubber system is also employed. Each suite has a control room with an Allen Bradley control system with graphical user interface.

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Equipment List - Pilot Plant Bays:

REACTOR BAY 1:

- **1 x 50 Gallon GLR (DeDeitrich)**
- **1 x 100 Gallon GLR (DeDeitrich)**
- **1 x 300 Gallon GLR (DeDeitrich)**
- **1 x 500 Gallon GLR (DeDeitrich)**
- **1 x 200 Gallon GL Receiver**
- **1 x 40" Centrifuge**
- **Various enclosed Stainless Steel Nutsche Filtration Units**

REACTOR BAY 2:

- **1 x 75 Gallon, 250 psi Hydrogenator (Apache Stainless) in Separate Building**
- **1 x 500 Gallon GLR (DeDeitrich)**
- **2 x 300 Gallon GLR (DeDeitrich)**
- **1 x 75 Gallon Cryogenic (-90˚C) Reactor (Apache Stainless)**
- **2 x 100 Gallon GLR (DeDeitrich)**
- **1 x 50 Gallon GLR (DeDeitrich)**
- **1 x 200 Gallon GL Receiver**
- **Various Stainless Steel Nutsche Filtration Units**
- **1 x 26" Centrifuge**
- **1 x 40" Centrifuge**
- **1 x 80L Agitated Cone Dryer**

The Washington Drive facility houses 2 main plant bays with reactors up to 500 gallons. Each bay contains several reactors and utilizes ASHRAE 95 filtered air.

FILTRATION/DRYING:

HEPA-filtered drying rooms and accommodating tray dryers are also available to both plant bays. Filtration is accomplished using portable, enclosed Nutsche filters, centrifuges, or agitated cone dryer with continuous liner to insure containment.

CONTROL SYSTEMS:

Heating and chilling is accomplished via a computer-controlled series of hot, ambient and cold loops allowing for a temperature range of -20˚C to 165˚C. Vacuum is controlled via the computer system using water-ring or high-vacuum Bush oil pumps. A full scrubber system is also employed. A cryogenic reactor system is computer controlled using a liquid nitrogen loop system with control down to -80˚C.

Each bay has a control room with an Allen Bradley control system with graphical user interface.

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SOLVENT TANK FARM:

- 5 X 8000 Gallon Bulk Solvent Tanks
- 2 x 6000 Gallon Organic Waste Storage Tanks
- 2 x 6000 Gallon Aqueous Waste Storage Tanks

REACTOR BAY 1 – CRYOGENIC REACTIONS:

- 1 x 500 Gallon 316L SS Reaction Vessel
- 1 x 1000 Gallon 316L SS Work-up Vessel

REACTOR BAY 2 – HYDROGENATION:

- 1 x 300 Gallon 316L Hydrogenation Vessel
- Enclosed Catalyst Removal Filter
- 1 x 500 Gallon Hastelloy C-276 Multi-phase Reactor (Cryo/Hydro)

Equipment List - Large Scale API Plant

REACTOR BAY 3:

- 2 x 2000 Gallon GLS Reactor (DeDietrich Optimix)
- 1 x 1000 Gallon GLS Reactor (DeDietrich Optimix)
- 800 mm Horizontal Peeler Centrifuge (Kraus-Maffei)
- 800 liter Helix Conical Dryers (Kraus-Maffei)

REACTOR BAY 4:

- 2 x 2000 Gallon GLS Reactor (DeDietrich Optimix)
- 1 x 1000 Gallon GLS Reactor (DeDietrich Optimix)
- 800 mm Horizontal Peeler Centrifuge (Kraus-Maffei)
- 800 liter Helix Conical Dryers (Kraus-Maffei)

REACTOR BAY 5:

- 1 x 1000 Gallon GLS Reactor (DeDietrich Optimix)
- 1 x 1000 Gallon 316L SS Reactor
- 1 x 500 Gallon 316L SS Reactor
- Plate Filters
- Tray Dryer
- 0.4 M^2 Filter/Dryer with Glove Box

REACTOR BAY 6:

- 1 x 1000 Gallon GLS Reactor (DeDietrich Optimix)
- 1 x 1000 Gallon 316L SS Reactor
- 1 x 500 Gallon GLS Reactor (DeDietrich Optimix)
- Plate Filters

CML's Grant Drive facility is located adjacent to the existing Washington Drive development facility which provides a seamless technical transfer during scale-up of large scale manufacturing processes. The facility incorporates the latest in cGMP manufacturing design, adhering to the Q7A guidelines.

The facility is a multi-story structure which features multiple reactor bays with separate HVAC and product isolation suites to minimize the possibility of cross-contamination. Each bay provides a different mix of vessel sizes and/or metallurgies in order to address the variety of process requirements for multi-purpose facility. The facility also houses separate bays for hydrogenation and cryogenics.

Process control is accomplished through the combination of a single fluid system (Therminol) and a PLC-based automated control system. The system not only provides control of both process and safety limits, but is also the primary means for process data acquisition. The reactors are capable of being controlled between -20°C to 160°C. The cryogenic system is capable of controlling to temperatures as low as -100°C. The vessels have high vacuum capability via Busch dry seal pumps or utility vacuum via liquid ring pumps. Process gases are vented through local scrubbers before going to the on site Thermal Oxidizer to ensure complete destruction of any hazardous or flammable vapors.

Product isolation and drying is a critical design consideration in CML's large scale API manufacturing facility. Separation trains feature identical horizontal peeler centrifuges with a direct connection to agitated Helix conical dryers, capable of extremely low vacuum and precise temperature control. CML also employs filter/dryer technology, as well as a range of pressure filters in the facility. All incoming air into the areas where final product is exposed and packaged are provided by HEPA filtered air from separate air handling systems. Product containers are then transferred to the appropriate storage rooms located nearby.

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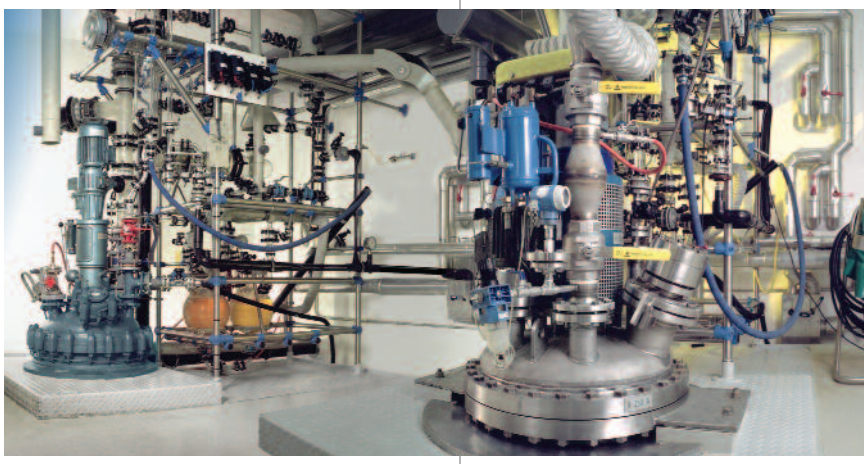
Equipment List - Pilot Plant:



GMP:

- 1 x 250 L GL
- 2 X 450 L GL
- 1 x 300 L Hastelloy C22
- 1 x 1,000 L GL
- All multi-purpose reactors
- Minimum stirring volume: 10 L
- Receiver vessels: 4 x 200 L glass, 250 L GL, 100 and 200 L stainless steel

ISOLATION EQUIPMENT:

- Pressure filters; 2 x 30 L Seitz (stainless steel), 60 L (stainless steel) Seitz 100L (stainless steel) and 2 x 200 L (stainless steel and GL)
- Vacuum filters; 4 x 200 L
- Centrifuge; 5 kg and 90 kg
- Hast-C Filter/dryer; 380 liter
- Separating funnels; 4 x 200 L glass
- Rotavapors; 1 x 10 L, 3 x 20 L 1 x 50 L
- Freeze dryer; 12 L
- Wiped film evaporator (WFE)

DRYING EQUIPMENT:

- Vacuum drying chambers (kilogram quantities)
- Filter dryer (50 kg)

HEATING:

- Steam; up to 9 bar (170°C)
- Oil heating up to 300 °C

CHILLERS:

- Chillers 5°C and -25°C
- Cryogenic cooling on Hastelloy C22 350 L Reactor (-100°C)

PRESSURE:

- -1 up to 6 bar at pilot plant scale
- Pressure reactors: 2 and 4 L; 40 bar, 20 L; 10 bar, 350 L; 6 bar

Our facility houses reactors in separate suites to accommodate the most challenging projects at the multi-kilogram scale. The facility is designed with isolation and containment in mind, and we routinely provide rapid scale up from early development batches in the lab, to plant scale under GMP conditions. Our plant has been designed to maximize flexibility, not only in reactor parameters (temperature, pressure, materials of construction), but flexibility to rapidly move from project to project, thus speeding overall development time.

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