The GMP facility situated in Woburn, Massachusetts may be readily used for the manufacture of commercial and clinical drug substance and drug product.

The facility comprises several areas where defined manufacturing operations are performed. The facility currently includes the following areas, totaling 60,000 ft^2 ±:

Cell Bank Storage, Virus Seed Stock Storage, Inoculum Preparation, Cell Culture, Purification and Final Formulation, Media and Buffer Preparation, Utility areas, and Drug Product Operations (Filling, Visual Inspection and Controlled Rate Freezing), along with several ancillary support rooms. Access to production areas is controlled by a card key system and limited to authorized personnel.

The building design provides a controlled environment for the manufacturing of bulk pharmaceutical product, along with support areas, and warehousing. Each room within the facility has a surface finish and HVAC consistent with the intended function of the area. The qualified utilities provide support for the equipment and the process operations performed within each defined area.

Environmental controls and product protection elements were analyzed and incorporated in the facility design. Flow of components, products and personnel are regulated to ensure product quality. Room pressurization, airlocks and gown rooms facilitate product/process separation and containment. Additionally, the facilities are designed for durability and ease of cleaning.

Two warehouses, totaling approximately 2,000 ft^2, include Control Room Temperature (CRT) storage areas, and includes a cold storage room (2 °C to 8 °C). A reject cage is also available, to temporarily store rejected material.

The site offers ample parking, with nearby connections to I-93 and I-95. In addition, the area is served by regional MBTA bus routes, and a commuter rail service hub.

Heating, ventilation, and air conditioning (HVAC) systems:

The HVAC system is comprised of one to dedicated subsystem to support cleanroom areas, and a further two subsystems support laboratories, manufacturing support and office areas. HVAC systems include heat transfer coil ERV systems for energy recovery.

The cleanroom HVAC system supplies the manufacturing process areas with conditioned air to maintain the environment in a pre-determined state of control. The cleanroom HVAC system is comprised of three rooftop air handling units (AHUs), seven recirculating fan units, two exhaust fan systems and components for control of airflow, room temperature, and relative humidity. The HVAC system is controlled and monitored by the building management system (BMS). The three rooftop air handling units supply external air that has been filtered, dehumidified and temperature adjusted and operate with 100% make-up air (no conditioned air from the processing areas is returned to the rooftop AHUs). Final temperature control is performed via local reheat coils for the various cleanroom areas. The drug product filling room is equipped with a humidification system to control humidity. Air is delivered to the production spaces through ceiling mounted terminal high efficiency particulate air (HEPA) filters.

Area classification is established and maintained through HEPA filtration and air changes. A defined pressurization cascade is maintained in the GMP area through a monitored pressure control system. The CMS (Critical Monitoring System) monitors, generates and records

operational and pressurization data to assure the systems are maintained within specifications. The building management system (BMS) controls, monitors, generates alerts/alarms and records utility systems operational values.

Water systems:

Purified Water (PW)

The PW System is designed to produce purified water to supply pure steam and Water for Injection (WFI), process area use, and a satellite system for laboratory use. The PW System has been designed to filter and remove impurities from the incoming water supply in order to produce pure water that is suitable for use in the facility. With the exception of grade 7 areas, which are cleaned with sterile WFI, the PW is used in the manufacturing suites to formulate room sanitizing solutions and for general cleaning. A dedicated instrumentation and control package monitors critical parameters. The system is monitored by the CMS for distribution loop operating pressure, TOC, Conductivity, and a general fault alarm. The PW System is composed of the following sub-systems:

- Pretreatment System - consists of the pre-filters, carbon filter and reverse osmosis process
- Polishing System - consists of the TOC/UV unit, deionization, UV unit and final filtration.
- Distribution Loop - consists of a distribution pump, storage tank, vent filter, level controls, and on-line monitoring of TOC and Conductivity.

Pure Steam Generator and Water-For-Injection (WFI) Condenser

The Pure Steam Generator system is designed to produce pure steam and water for pharmaceutical applications that meets WFI quality water. The water supply is from the Purified Water system. The Pure Steam distribution system delivers Pure Steam to the autoclaves.

Water for Injection (WFI) Storage and Distribution System

The WFI system receives condensed pure steam from the Pure Steam generator then maintains and distributes the WFI to the use points. A pump is used to distribute WFI through 316L stainless steel sanitary distribution tubing consisting of a 1 ½" main loop and a ½" sub-loop. The main loop recirculates continuously at >80ºC. The sub-loop is maintained hot until there is a need for WFI in manufacturing, at which time the WFI entering the sub-loop is cooled to process requirements using a heat exchanger.

Other relevant utilities:

Compressed Air System

The compressed air system supplies dry, oil-free compressed air for use throughout the facility. The system consists of two oil-less compressors, two desiccant dryers and a 120-gallon receiver. Prior to distribution, the air is filtered using 0.2 µm rated final filters. The distribution piping delivers compressed air for manufacturing use, HVAC system control use and non-manufacturing use.

Compressed air for manufacturing is used for filter integrity testing, equipment use and instrument control use and is monitored by the BMS. The compressed air system is tested quarterly.

CO_2 Distribution Systems

The manufacturing facility is equipped with four CO_2 gas distribution systems: two nominal five percent (5%) CO_2 systems and two nominal >99% CO_2 systems. One of each system supplies the manufacturing cleanroom area and one of each system supplies the general lab areas (QC, Process Development). The CO_2 systems provide nominal five percent (5%) CO_2 / 95% air mixed gas to some of the facility biosafety cabinets for use in cell growth vessels. The >99% CO_2 systems provide >99% CO_2 gas for use in cell culture operations. The carbon dioxide gas cylinders (5% and >99 %) are sampled and tested prior to release for use. The facility BMS control system monitors the CO_2 distribution systems' operating pressure. The mixed CO_2 system is tested quarterly.