

## **1 Purpose**

The purpose of this Guideline is to provide guidance on the design and specification of utilities associated with the manufacture, quality control and storage of API, intermediates and investigational products within an R&D facility.

## **2 Scope and Applicability**

This Guideline applies to the manufacture, testing and storage of investigational medicinal products for human use or for stability studies intended to be filed with the NDA/MAA submissions within R&D.

## **3 Definitions**

### **3.1 Potable Water (Non-Compendial Water)**

Water, that as a minimum, meets national standards for water intended for human consumption that have been documented as at least equivalent to World Health Organization (WHO) guidelines.

The national standards for the USA, Europe and Japan meet or exceed the WHO guidelines. Potable Water is also known as Drinking Water.

### **3.2 Purified Water**

Water produced by a suitable method (e.g., deionization, reverse osmosis, distillation, etc.) from Potable Water to meet specifications as defined by a compendial monograph.

### **3.3 Water for Injection (WFI)**

Water produced by a suitable method (e.g. distillation) from Potable Water, usually with an intermediate purification step(s), to meet specifications as defined by a compendial monograph.

### **3.4 Building Management System (BMS)**

System management hardware and software systems that allow computerized automation or microprocessor controlled operation, data collection and management of HVAC systems.

### **3.5 Classified Areas**

Pharmaceutical facility areas that require validated and controlled environmental air systems.

### **3.6 Clean (Pure) Steam**

High quality steam produced from purified water (or better) with a distribution system constructed of non-rusting materials and used in applications that may

## **5.1 HVAC**

### **5.1.1 General GMP Requirements**

The HVAC system must be designed appropriate to the products (APIs, intermediates, investigational products) handled and operations performed. Manufacturing area HVAC systems must prevent the infiltration of contaminants from external sources including recycled exhaust air, and cross contamination between HVAC systems must be avoided. Additionally these systems require qualification/validation and change control procedures.

For warehousing and product storage areas temperature monitoring and where appropriate temperature control is required.

Building Management or Monitoring Systems used in the control and monitoring of critical HVAC data in classified areas must be validated.

### **5.1.2 Air Quality**

The quality of air needed in classified areas is based on the products handled and operations performed.

Air quality and air classifications for non-sterile operations must be designed to follow appropriate regulatory requirements and industry practices. For APIs the level of product exposure and the point in the manufacturing process should be considered when defining the air quality required.

Additional restrictions must be defined when handling, processing and storing highly potent materials such as antibiotics, hormones, radioactive materials or cytotoxic compounds. In addition, products that could cause potential allergic reactions such as penicillin and cephalosporins must be effectively controlled via the use of dedicated and separate facilities. HVAC systems serving microbiological laboratories must be separate from HVAC systems serving production areas.

### **5.1.3 Air Quantity/Air Flow Patterns/Room Pressurization**

The requirements for the HVAC system to deliver the appropriate quantity of air for defined purposes for a room or work area must follow available international standards.

### **5.1.4 Temperature and Humidity**

Requirements for temperature and humidity must take into account the needs of the product, process and employees.

## **5.2 Water**

Electrical systems in use throughout R&D vary greatly from site to site and system to system, but there are some minimum parameters that should be reviewed. The system must meet specification requirements for frequency, phase and voltage stability during periods of use. There must be schematics and documentation of all system components and use points.

For critical systems back up supplies or un-interruptible power supplies should be considered.

## **5.5 Compressed Air Systems**

The installation and operation of compressed air systems within the cGMP areas of each facility must be defined and monitored. Requirements for air contacting product include validation of the system, and as a minimum absence of moisture, limit for hydrocarbons/oil and instructions for filtration according to international standards and compendial monographs.

## **5.6 Other Gas Systems**

All gas systems, for product contact, including nitrogen, oxygen or other gases must meet minimum purity and quality specifications as defined by the process requirements. Gas supplies must be tested or certified to meet all quality and purity requirements as appropriate according to international standards and compendial monographs.