HVAC Design for Pharmaceutical Facilities (GMP's)

An Online Continuing Education Course for Engineers

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HVAC DESIGN
FOR
PHARMACEUTICAL FACILITIES

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HVAC Design for Pharmaceutical Facilities

In pharmaceutical manufacturing, how space conditions impact the product being made is of primary importance. The pharmaceutical facilities are closely supervised by the U.S. food and drug administration (FDA), which requires manufacturing companies to conform to cGMP (current Good Manufacturing Practices). These regulations, which have the force of law, require that manufacturers, processors, and packagers of drugs to take proactive steps to ensure that their products are safe, pure, and effective. GMP regulations require a quality approach to manufacturing, enabling companies to minimize or eliminate instances of contamination, mix ups, and errors.

The GMP for HVAC services embraces number of issues starting with the selection of building materials and finishes, the flow of equipment, personnel and products, determination of key parameters like temperature, humidity, pressures, filtration, airflow parameters and classification of cleanrooms. It also governs the level of control of various parameters for quality assurance, regulating the acceptance criteria, validation of the facility, and documentation for operation and maintenance.

Various countries have formulated their own GMPs. In the United States, it is regulated by several documents such as Federal Standard 209, code of Federal regulations CFR 210 & 211 etc, which are revised and updated from time to time. The European Community has a "Guide to Good Manufacturing Practice for Medicinal Products" and in the United Kingdom it is BS 5295. The World Health Organization (WHO) version of GMP is used by pharmaceutical regulators and the pharmaceutical industry in over one hundred countries worldwide, primarily in the developing world. In some countries, the GMP follows largely the country of the principal technology provider. All GMP's have one common theme……

"CLEANLINESS, CLEANLINESS and CLEANLINESS"

What can HVAC do?

HVAC system performs four basic functions:

1. Control airborne particles, dust and micro-organisms – Thru air filtration using high efficiency particulate air (HEPA) filters.

2. Maintain room pressure (delta P) – Areas that must remain “cleaner” than surrounding areas must be kept under a “positive” pressurization, meaning that air flow must be from the “cleaner” area **towards** the adjoining space (through doors or other openings) to reduce the chance of airborne contamination. This is achieved by the HVAC system providing more air into the “cleaner” space than is mechanically removed from that same space.

3. Maintain space moisture (Relative Humidity) – Humidity is controlled by cooling air to dew point temperatures or by using desiccant dehumidifiers. Humidity can affect the efficacy and stability of drugs and is sometimes important to effectively mould the tablets.

4. Maintain space temperature - Temperature can affect production directly or indirectly by fostering the growth of microbial contaminants on workers.

Each of above parameter is controlled and evaluated in light of its potential to impact product quality.

What HVAC can’t do?

1. HVAC can not clean up the surfaces of a contaminated surfaces, room or equipment

2. HVAC can not compensate for workers who do not follow procedures

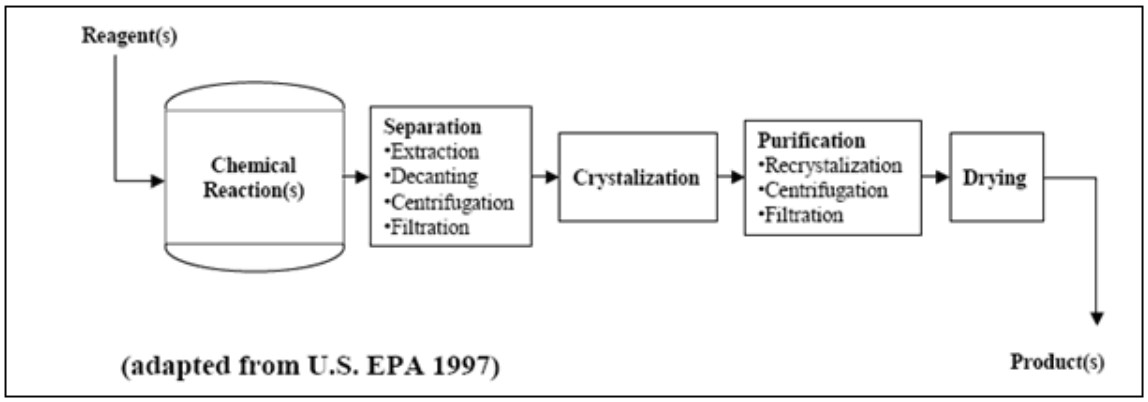
We will learn about the specific design aspects later in this course, but first we will briefly discuss the generic pharmaceutical process.

Pharmaceutical Process

The task of the pharmaceutical manufacturer is to combine the medicinally active agents provided by a fine chemicals plant, or by extraction from vegetable, animal or other source, with suitable inactive ingredients so that the end product may be used in the correct dosage to produce the effect needed.

Simplified Process

Figure below illustrates a simplified diagram of the chemical synthesis process for pharmaceuticals. There are five primary stages in chemical synthesis: (1) reaction, (2) separation, (3) crystallization, (4) purification, and (5) drying. Each of these five stages is described below.



Reaction(s) –

In the reaction process, raw materials are fed into a reactor vessel, where reactions such as alkylations, hydrogenations, or brominations are performed. The most common type of reactor vessel is the kettle-type reactor generally made of stainless steel or glass-lined carbon steel, range from 50 to several thousand gallons in capacity. The reactors may be heated or cooled, and reactions may be performed at atmospheric pressure, at elevated pressure, or in a vacuum. Generally, both reaction temperature and pressure are monitored and controlled. Nitrogen may be required for purging the reactor, and some intermediates may be recycled back into the feed. Some reactions are aided via mixing action provided by an agitator. A condenser system may be required to control vent losses. Reactors are often attached to pollution control devices to remove volatile organics or other compounds from vented gases.

Separation –

The main types of separation processes are extraction, decanting, centrifugation, and filtration. The extraction process is used to separate liquid mixtures.

- Extraction process is used to separate liquid mixtures. It takes advantage of the differences in the solubility of mixture components i.e. a solvent that preferentially combines with only one of the mixture components is added to the mixture. Two

streams result from this process: the extract, which is the solvent-rich solution containing the desired mixture component, and the raffinate, which is the residual feed solution containing the non-desired mixture component(s).

- Decanting is a simple process that removes liquids from insoluble solids that have settled to the bottom of a reactor or settling vessel. The liquid is either pumped out of the vessel or poured from the vessel. Leaving the solid and a small amount of liquid in the ves

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Purifica

Purification follows separation, and typically uses the separation methods described above. Several steps are often required to achieve the desired purity level.

Re-crystallization is a common technique employed in purification. Another common approach is washing with additional solvents, followed by filtration.