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Ministry of higher education and scientific research

Abdelhafid Boussouf university center – Mila

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Module: Pharmaceutical Processes

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Content of the material:

Chapter 4: Manufacturing Environment

01/ Production of pharmaceutical water

The fabrication of pharmaceutical water involves several key processes to ensure that the water meets the stringent quality standards required for pharmaceutical use:

1. Source Water Selection
   - Quality Assessment: The source water (e.g., municipal water, well water) must be assessed for impurities, including microorganisms, heavy metals, and organic compounds.
   - Regulatory Compliance: Ensure the source complies with local and international regulations.
2. Pre-Treatment
   - Filtration: Remove larger particulates using sand filters or cartridge filters.
   - Activated Carbon Treatment: Remove chlorine, chloramines, and organic impurities.
   - Softening: If necessary, use ion exchange to reduce hardness (calcium and magnesium).
3. Purification Processes
   - Reverse Osmosis (RO):
     - Water is forced through a semi-permeable membrane, removing dissolved solids and impurities.
     - Typically used as a primary purification step.
   - Distillation:
     - Water is boiled, and the steam is collected and condensed.
     - This process removes most impurities, including volatile organics and pathogens.
   - Electrodeionization (EDI):
     - Combines ion exchange and electrodialysis to further purify water.
     - Effective in reducing ionic contaminants.
4. Post-Treatment
   - Filtration: Utilize 0.2-micron filters to remove any remaining microorganisms.
   - UV Treatment: Expose water to ultraviolet light to further disinfect and kill bacteria and viruses.
5. Storage and Distribution
   - Storage Tanks: Use stainless steel or glass tanks to store purified water.
   - Controlled Environment: Maintain a controlled environment to prevent contamination (e.g., temperature, cleanliness).
   - Piping System: Use sanitary piping materials to distribute water without contamination.
6. Quality Control
   - Microbial Testing: Regularly test for bacterial contamination using techniques such as membrane filtration or multiple-tube fermentation.
   - Chemical Testing: Regularly analyze for residual chemicals, conductivity, and total organic carbon (TOC).
   - Documentation: Maintain detailed records of water quality, testing, and maintenance.
7. Regulatory Compliance
   - Standards: Ensure compliance with pharmacopeial standards (e.g., USP, EP) for Water for Injection (WFI), Purified Water (PW), etc.

- Validation: Validate processes and equipment to ensure consistent quality.

The fabrication of pharmaceutical water is a critical process that requires meticulous attention to detail. Each step must be carefully controlled and monitored to ensure that the final product meets regulatory standards and is safe for use in pharmaceutical applications. Regular maintenance and quality control are essential to uphold the integrity of the water throughout its lifecycle.

02/ Air treatment

Air treatment in the pharmaceutical industry is critical to ensure a contamination-free environment, which is essential for the production of safe and effective products. Here's a detailed overview of the air treatment processes specific to this industry:

1. Air Filtration

- Pre-Filters: Coarse filters capture larger particles (dust, pollen) before air enters more sensitive areas.
- HEPA Filters: High-Efficiency Particulate Air (HEPA) filters remove at least 99.97% of airborne particles down to 0.3 microns, including bacteria and fungal spores.
- ULPA Filters: Ultra-Low Penetration Air (ULPA) filters provide even higher efficiency (99.999% of particles) for critical areas.

2. Air Change Rates

- Controlled Air Changes: Facilities are designed with specific air change rates (e.g., 20-60 air changes per hour) to maintain air quality and control contamination levels.
- Positive Pressure: Critical areas, such as cleanrooms, are maintained at positive pressure to prevent the ingress of contaminated air.

3. Disinfection Methods

- UV-C Light: Ultraviolet light is used to disinfect air by inactivating microorganisms without chemical residues.
- Ozone Treatment: In some cases, ozone is used to sterilize air; however, it must be carefully managed due to potential toxicity.

4. Humidity Control

- Dehumidification: Maintaining optimal humidity levels (typically 30-60%) is crucial to prevent microbial growth and maintain product stability.
- Humidity Sensors: Continuous monitoring ensures that humidity levels remain within specified ranges.

5. Ventilation Systems

- HVAC Systems: Heating, ventilation, and air conditioning systems are designed to filter and condition air throughout the facility.

- Dedicated Supply and Exhaust: Separate air supply and exhaust systems prevent cross-contamination between different areas.

6. Monitoring and Control

- Real-Time Monitoring: Systems continuously monitor air quality parameters, including particulate count, temperature, humidity, and airflow velocity.
- Building Management Systems (BMS): Automate HVAC and air treatment processes based on real-time data, ensuring compliance with regulatory standards.

7. Regulatory Compliance

- Standards Adherence: Compliance with regulatory bodies (e.g., FDA, EMA) and industry standards (e.g., ISO 14644 for cleanrooms) is mandatory.
- Validation and Documentation: Air treatment systems undergo validation to ensure they operate effectively, and detailed records are maintained for audits.

8. Regular Maintenance

- Routine Inspections: Regular checks of filters, HVAC systems, and monitoring equipment are essential to ensure optimal performance.
- Filter Replacement: Scheduled replacement of filters to maintain efficiency and prevent system overload.

Air treatment in the pharmaceutical industry involves a combination of advanced filtration, disinfection, humidity control, and stringent monitoring systems. These processes are essential to maintain a clean and controlled environment, ensuring product safety and compliance with regulatory standards. Regular maintenance and validation further enhance the reliability of air treatment systems in pharmaceutical manufacturing.

05/ Regulating Active Pharmaceutical Ingredients

The safety and effectiveness of drug products are directly impacted by the caliber of its active components and are ensured through process optimization. In numerous cases over the past few decades, subpar API Process Development and production as well as tainted active components have been linked to adverse health effects, including death. Because of this, regulatory procedures and approvals of active ingredients have been made more stringent in most of the countries across the globe.

The regulation of active components will strengthen the pharmaceutical drug supply chain, improve the quality and safety of medications for patients, and align a company with global regulatory practices.

Active pharmaceutical ingredients (APIs) are prequalified by an independent process that determines those that are high-quality and produced in accordance with WHO Good Manufacturing Practices (GMP). Prequalification of a Finished Pharmaceutical Product (FPP) for which prequalification is sought is significantly easier if an API that has already received prequalification is employed in its production.

06/ Pharmaceutical Industry in Algeria: cooperation with USA

After years of restricted market access and uncertainty for American pharmaceutical companies, 2021 is finally a year of positive change. Last year, the Algerian Government established the Ministry of Pharmaceutical Industry (MOPI) and the National Agency for Pharmaceutical Products (ANPP) to help modernize Algeria's pharmaceutical industry. Since their inception, both organizations have made significant progress in several critical areas identified by industry, including drug pricing procedures, overly burdensome regulations, and a dysfunctional process for establishing and maintaining marketing operations.

American pharmaceutical exporters should take note of the following market developments when considering entering or expanding in Algeria:

⇨ In December 2020, MOPI issued new regulations to decrease the wait times for registering new drugs dramatically. What used to take up to five years could now take as little as five months for proprietary drugs (four months for technical analysis and one month for pricing) and as little as three months for generic medicines.

⇨ At the end of February 2021, MOPI issued regulations that resolved the longstanding issue of representative offices for foreign pharmaceutical companies operating in Algeria. The new regulation permits foreign pharmaceutical companies to market their products locally and establishes clear rules for establishing local pharmaceutical entities. MOPI also allowed for temporary authorizations of up to one year for medicines prescribed to treat serious diseases when there is no equal treatment in the market and when approved by another regulatory body (such as the U.S. Food and Drug Administration).

These positive changes demonstrate MOPI's desire to improve Algeria's pharmaceutical industry, and the Commercial Service in Algeria will monitor how these changes impact U.S pharmaceutical companies during the rest of 2021.