CriticalPoint's Pearls of Knowledge
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Unexpected Power Loss and Shutdown Procedures in a Sterile Compounding Facility

Stuff happens! It's true and it's unavoidable. We all know that if things can go wrong they will. Working in a sterile compounding facility creates an environment where planning for the unexpected is essential. What steps should be taken when there is a sudden and unexpected power outage? What about when an air handler belt breaks and airflow is suspended in the cleanroom? What if during routine environmental monitoring (EM) there is a serious excursion that necessitates a shutdown for cleaning and maintenance? Or, maybe it's time for routine maintenance on cleanroom air handlers. These are only a few of the instances where sound planning and thorough procedures can prevent significant gaps in quality control.

In this edition of CriticalPoint's Pearls, a few of the more critical principles will be discussed. Of course, it each facility must consider all aspects of unplanned or planned shutdowns that could affect their operation and develop detailed, sound Standard Operating Procedures (SOPs) to guide staff.

Airflow and Heating/Ventilation and Air Conditioning (HVAC)

Air supply and air conditioning to the cleanroom HEPA filters and primary engineering controls (PECs) is critical and must be maintained at all times. The best way to prevent unexpected airflow interruptions due to a power loss is by developing a system of UPSs for smaller equipment (e.g., automated compounding devices, incubators, etc.) and tying in a backup generator that supplies power, at a minimum, to the cleanroom air handlers and primary engineering controls. Backup generators require monthly testing and regular maintenance which must be memorialized in SOPs and documented in writing. This type of complex system is not commonly in place in pharmacies and may not be necessary at all facilities.

So, what happens if the facility does not have backup power or if a shutdown must be planned? The list below contains some items that may be considered when developing planned or unplanned shutdown procedures:

- When a planned or unplanned shutdown happens, it is best practice (a requirement in cGMP) to have previously established baseline and excursion level for temperature, humidity, and non-viable particle (NVP) count. These are predetermined levels at which point certain actions can be taken. These qualification studies are conducted to define a time after which the controlled environments exceed acceptable limits for particles, temperature, humidity and pressure differential.
- If your pharmacy experiences a planned or unplanned shutdown, you can use the experience to understand the effect the interrupted airflow and HVAC shutdown has upon the cleanroom environment over time.
- Of course, the longer the air handler(s) and HVAC system are shut down, the greater the chance of temperature and humidity changes and uncontrolled air to backflow into the controlled cleanroom environment, creating potential contamination.

- Knowing how long airflow and HVAC systems can be interrupted before established EM criteria are exceeded is facility dependent and must be tested to establish procedures for the facility.
- One possible way to perform this test is to perform particle sampling at predetermined locations at the beginning of a shutdown and at predetermined intervals during the shutdown. Keep in mind that unless your facility has continuous particle monitoring equipment in place, that personnel that may enter the room to place and program the particle counters will provide an additional source of contamination that cannot be completely controlled for. If a person must enter the controlled environment to place a particle counter, they must be properly garbed with no visible skin showing.
- Temperature and humidity should also be monitored initially and at the predetermined levels as well.
- It will not be necessary to monitor pressure differential if the HVAC is powered down since there will be no measurable pressure differential between rooms.
- When the particle counts exceed ISO limits or facility-specific criteria, an excursion level can be established. The amount of time it takes to reach this excursion level may be used to establish the maximum time the air handlers can be in shutdown mode before certain cleaning, disinfection and other procedures are initiated.

At the very least if your pharmacy experiences an unplanned shut down and the "excursion limit" has not been identified through qualification studies, consider the following:

1. Note the time of the power loss (shut down).
2. Any personnel inside the ISO controlled environments must exit immediately stopping any work in progress and leaving it in place.
3. Take any completed CSPs/batches and any completed or in process compounding worksheets or batch records out of the room with you so the time of the work was halted can be documented outside the room.
4. If work is taking place in a nonhazardous sterile compounding environment, exit the buffer room and the anteroom and doff garb in the non-controlled area.
5. If work is taking place in a hazardous drug sterile compounding environment, doff outer gloves, outer shoe covers, outer back closing and inner gloves before leaving the C-SEC, then leave the anteroom, doff the remainder of garb in the non-controlled area and perform hand hygiene.
6. Once personnel are outside of the room affected, place a "NO Admittance" sign on the entrance to the affected area.
7. Document the temperature, humidity and particle counts (if particle counter is in place) at the time of the shutdown. Continue to monitor these values regularly (based on your facility's SOP…maybe every 10 minutes). The more often these values are monitored, the finer your ability to identify the "excursion" time.
8. Systematically evaluate the equipment that is affected by this shut down beginning with the controlled environments working through the facility (autoclaves, incubators, refrigerators, freezers, telephones, office/warehouse HVAC, etc.).

9. Document the cause of the shutdown (if known) and whether this is a facility wide issue, compounding area issue or larger geographical area issue.
10. In the absence of "excursion data" ***and*** if the power is restored in less than 1 hour (this is not supported by data only by tradition), then do the following:
    a. Note the time power was restored
    b. Verify that the HVAC is fully restored to buffer rooms and anterooms.
    c. One person must enter each buffer room after performing hand hygiene and garbing according to SOPs.
    d. If PECs were not on a backup power source, manually check that every PEC has successfully turned itself back on. In some cases, it may be necessary to manually turn on the PECs. Check all gauges and verify proper function.
    e. Leave the controlled environment immediately.
    f. Depending on the size of the air handlers and number of PECs in each room, the room's particulate count should return to acceptable levels within 10 minutes but determine your own facility wait time by working with your cleanroom builder, designer and/or certifier. Remember Chapter <797> requires buffer rooms to have at least 30 ACPH which means the air is changing out in the room every 2 minutes. If all personnel immediately exited the room and no further activity took place during the power outage, particulate counts should return to acceptable levels quickly.
    g. Monitor room air pressure differentials which also should return to normal within 10 minutes but monitor their levels every 5 minutes.
    h. Also monitor temperature and humidity. Both temperature and humidity usually increase during power outages and will increase more depending on the temperature and humidity of adjacent areas.
    i. When temperature, humidity and pressure differentials return to normal for your facility, properly garbed personnel may reenter the controlled rooms. If possible, the workers who exited the room and were working on a batch or CSP in a particular PEC, should be the ones returning to that area with the batch record or compounding worksheet.
    j. Discard any hanging bags or vials that are accessed with transfer or other tubing.
    k. Remove all items from the PEC. Perform daily cleaning activities for that PEC (clean with a sporicidal agent followed by application of sterile 70% IPA after appropriate sporicidal dwell). If a C-PEC then perform appropriate decontamination, cleaning and disinfection, again cleaning with a sporicidal agent.
    l. Perform daily cleaning activities (easily cleanable horizontal surfaces and high touch surfaces then floors).
    m. Resume compounding.
    n. Perform dynamic air and surface sampling near the conclusion of the compounding day.

11. In the absence of "excursion data" ***and*** if the power is restored in greater than 1 hour (this is not supported by data but by tradition), then do the following:

a. Follow steps 10 a to k.

b. Perform a triple clean which is all activities in the monthly clean performed three separate and distinct times using a germicidal detergent the first application followed by a sporicidal for the last two applications. PECs as always will be cleaned with the germicidal detergent or sporicidal followed by sterile 70% IPA. Rooms and furniture cleaned with the EPA registered, one step cleaner/disinfectant.

c. Perform dynamic air and surface sampling near the conclusion of the compounding day.

- If emergency compounding must be performed, then it must be performed in a PEC that has been cleaned and disinfected (either once or three times depending on the conditions described above) and all room cleaning must cease while compounding occurs for the emergency only. BUDs assigned to CSPs compounded under these conditions will be limited to 12 hours.
- Since many facilities do not operate 24/7 and unplanned shutdowns may occur when personnel are not in the facility therefore if possible the installation of continuous monitoring systems in all critical areas and devices should be considered. This may include the cleanroom (temperature, humidity, NVP, differential pressures) and climate controlled devices, such as drug storage refrigerators/freezers and lab equipment such as incubators.
- If it a shutdown occurs during unstaffed hours, a procedure should be established to determine steps to be taken. If continuous monitoring is not installed, a conservative approach should be taken and the assumption made that excursion levels have been exceeded.

Climate Controlled Devices and Equipment (refrigerators, freezers, incubators)

Critical drug storage areas and laboratory equipment, such as refrigerators, freezers, and incubators, should also be monitored over time during a planned or unplanned shutdown. Ideally, refrigerators and freezers should be monitored with glycol-based temperature measuring devices to avoid errant monitoring. Glycol-based devices more accurately reflect temperature changes within a refrigerator or freezer than the non-glycol based devices and can be programmed to show maximum and minimum temperatures for specific time periods (24 hours, etc.). Obviously, these devices should be maintained according to the manufacturer's specifications, be calibrated and tested to NIST traceable standards annually, and operate on battery power with regular battery replacement. As discussed above, certain steps should be taken during a planned or unplanned shutdown:

1. Record the time of the shutdown.

2. Record the temperature of the device when the shutdown occurred.

3. Monitor the device on a regular basis (e.g. every 10 minutes, etc.) and document temperature changes over time.

4. The established minimum and maximum temperatures should be documented.

5. Establish procedures to employ to maintain product at required temperatures (e.g., move to a temporary storage location, etc.) should the established minimum/maximum temperatures be breached.
6. Establish measures to be taken if products (drug components or CSPs) were kept at unacceptable temperature ranges. These procedures must be specific in terms of product rejection, acceptance or testing based upon time and temperature conditions.
7. If incubators are effected and are being used to incubate surface, air or personnel touch plates, notify the pharmacy manager and/or personnel responsible for environmental sampling. These personnel must decide (with the help of knowledgeable microbiological experts) whether these samples must be rejected and resampled.

If possible, implement technology to facilitate continuous monitoring on all critical devices. Doing so will eliminate questions regarding drug product safety, will help during shutdown investigations and will help establish greater control over the facility.

Other items to consider during an unplanned shutdown:

- Was any other critical equipment in operation (autoclaves, dry heat ovens, filling lines)? If so, the Pharmacy Manager and/or persons responsible for quality must be notified and accept/reject criteria applied to the situation.
- Were any hazardous drug operations in process and was containment effected?
- Were electronic storage devices (narcotic storage) and/or documents affected and is a proper backup installed?
- Are facility security cameras and alarms on backup power?

These are a few of the most critical elements to address while preparing SOPs for planned and unplanned facility shutdowns. Consider conducting a walkthrough of the facility during normal operations, noting all the equipment, devices, and control systems that will be effected during a shutdown and ranking them in order based on how critical they are to your operation. Establish a priority list, the most critical items first. This is a process is like the checklists that are used when pilots experience a problem in flight. Checklists enhance the pilot's ability to efficiently and correctly diagnose and correct issues in a most to least critical fashion.