Recommendations & Rationale for Recommendations
The most effective way to deal with interruptions in power supply to air handling systems is to prevent them from happening in the first place. Production loses from power outages can be minimized or eliminated by supplying critical equipment with power from generators, automatic transfer switches, and uninterruptible power supplies (UPS).

However, in situations where such equipment is not installed, a contingency plan for handling power outages to air handling systems is needed. It is important to consider three questions when developing a procedure to deal with power interruptions to air handling equipment.

- **What should be done during the interruption?**

Most importantly APA personnel should act to minimize movement, especially into or around Grade A areas. It is also important to avoid opening of doors to areas of lower classification. Further, it is critical that APA personnel be trained in these procedures so there is no need to leave the APA.

- **What length interruption will require re-sterilization of product contact parts, unused closures, and unused containers?**

This question requires generation of data to answer. Setting a time limit without supporting data will risk product contamination or the unnecessary destruction of sterile product.

Determination of a time limit consists of extensive environmental monitoring after the APA power has been interrupted and the critical air handling systems ceases to function. This may also includes interruptions to the air handling systems of areas adjacent to the APA that would be affected by the interruption.

The essential monitors to include in the determination are total airborne non-viable particulates, viable quantitative (active) air and/or viable passive air (settling plates), and pressure differentials. Additional parameters such as temperature and humidity should be tested if they are critical to the process.

The Non-viable monitors and pressure differential monitors are the most sensitive indicators for detecting any changes in the quality of the APA environment. The state of microbiological control in an APA can be directly correlated from these monitors.

Although the viable monitors (active and passive) are not as precise a tool for this study, these measurements are also essential to provide a complete understanding of the total APA environment After testing, the monitor(s) that reached the predetermined acceptance criteria in the shortest time will define your power interruption time interval. After the power interruption time limit has been established, it should be integrated into process simulations (i.e. media fills) for an added level of assurance.

A power interruption time interval study should also reflect “in use” APA conditions according to procedures that define the actions of personnel present during a power interruption. For example, the power interruption study should take into account the

Further assurance can be achieved in controlled environments with numerous openings via the use of smoke studies. Careful analysis of smoke patterns around doors and openings can ensure that air does not flow from an adjacent area of lower classification into the area being tested.

- **Temperature and humidity**

If temperature and humidity in the controlled area are critical process parameters (e.g. lyophilization), and then these should also be included in determining the time limit during a power interruption. Testing can be performed concurrently with air quality tests or continuously throughout the outage period and the acceptance criteria should be no higher than the action levels employed during routine production. A conservative approach would be to assign lower acceptance criteria in order to provide a margin of safety.

- **Process simulations (Media Fills)**

After the power interruption time limit has been established, it can be qualified by incorporation into process simulations. Like the other tests mentioned above, it would be appropriate to incorporate power outages into process simulations only during qualification or requalification of the cleanroom (i.e. after major changes). As is the case with routine production, processing should be completed for units exposed to the environment during the power interruption with subsequent segregation of these units from the rest of the batch. Positive units from the segregated portion of the batch do not indicate failure of the entire media fill provided that written procedures and batch documentation are adequate to describe the associated clearance during routine production. It does however, indicate a need to revisit the data generated during the power interruption time limit determination and potentially perform this work again with more stringent acceptance criteria. It may also indicate a need for retraining of personnel. It should also be noted that releasing the portion of a product batch segregated during a routine production power outage would be extremely difficult to justify until the time limit has been qualified successfully with process simulations.

- **Revalidation**

A minimum of one validation study should be performed for the initial determination of a power interruption time limit. A revalidation should be conducted if significant changes are made to the HVAC system that may effect the initial validation.

- **How long will it take to return the APA to a controlled state?**

This is another question that requires data to answer. The Recovery Test is the standard method for determining the time interval for a controlled environment to return to its specified cleanliness class after being exposed to a source of airborne particulates[6]. It is essential that a recovery test be performed after the power outage study unless recovery time data was generated during the initial qualification of the APA. In the recovery test, a particulate source (smoke or aerosol) is generated from the center of a predefined grid area in the room until the particle count is above the controlled environment's at-rest level.

After the particle generator is shut off, the particle concentration should be allowed to decrease to a point (e.g., 1 minute) where the counter will not be saturated with smoke or aerosol. Particle measurements are subsequently taken until the original at-rest air particulate level is reestablished. The recovery time is defined as the time interval

