Applications Concept:

Use of an IMD-A® System for Personnel Training in Cleanroom and Aseptic Manufacturing Environments

Major Benefit:

Immediate Feedback to Trainees on Undesirable Cleanroom Behavior

Introduction

Many pharmaceutical, biotechnology, ophthalmology and food and beverage companies manufacture and package their products in cleanrooms or other highly controlled environments using operating procedures designed to minimize contamination of products with foreign materials. Microbial contamination, in particular, is a serious concern because of the potential danger to the health of recipients. A major source of microbial introduction into aseptic manufacturing environments is from the people that work in them[A] [B]. Billions of microbes occur naturally on human skin and an estimated 10^7 skin particles are shed per person per day[C]. Rigorous precautions must be taken to prevent human-borne contamination of drugs and other products. In addition to building controls and cleaning and sanitization routines, technicians must wear appropriate protective clothing and equipment such as gowns, gloves, and face masks. Guidelines are also given for appropriate behavior within cleanrooms, for example, to minimize movement and talking and avoid touching the face or hair while working in the room.

Developing good procedures for gowning and cleanroom behavior is an important part of maintaining good control. Equally critical to this process is ensuring that personnel are trained effectively and that they adhere to established procedures while working.

IMD-A Systems: Ideal Training Tools

Azbil BioVigilant's Instantaneous Microbial Detection™ systems detect and report the presence of airborne microbes and inert particles continuously and in real-time using an optically-based system that requires no culturing, staining or reagents. Both the IMD-A 300 (low flow) and IMD-A 350 (high flow) instruments are 21 CFR Part 11 compliant and validated to USP<1223> and EP 5.1.6.

IMD-A systems offer a unique opportunity to provide technicians with immediate feedback on microbial and particle levels, delivering a valuable tool for operator training programs and assessments. The IMD-A 350 system is particularly recommended because of the higher flow rate of 28.3 LPM which enables sampling larger volumes of air during training sessions[D].

IMD-A system features for personnel training include:

- Instantaneous detection of microbes and inert particles

- Simultaneous detection of particle number, size and biologic status

- Reporting of real-time results with the PharmaMaster® software interface

- Video camera and synchronized data playback functionality

- Marker function enabling activity tracking and display in data files and reports

IMD-A systems display results in real-time using the IMD-A PharmaMaster software (Figure 1). The display options include a graph that plots counts for biologics, particles ≥ 0.5 μm, and particles ≥ 5 μm every second while the air is sampled, as well as updating total and average counts for each particle type so changes in contamination levels are easily noted. In addition, each IMD-A system is supplied with a small video camera that can be used to record and display activity in the room during sampling. The software features a playback function that allows a review of videos for completed samples as they were collected, replayed in synchrony with the recorded data.

Corollary video is a powerful tool to enhance the depth and quality of data collected during gowning and cleanroom training[E].

[A] Whyte W. Sterility Assurance and Models for Assessing Airborne Bacterial Contamination. PDA J Pharm Sci and Tech. 1986; 40: 188-197.

[B] Tham KW, Zuraimi MS. Size Relationship Between Airborne Viable Bacteria and Particles in a Controlled Indoor Environment Study. Indoor Air. 2005; 15: 48-57.

[C] Noble WC. Dispersal of Skin Microorganisms. Br. J Dermatol. 1975; 93: 477-485.

[D] Azbil BioVigilant, Product Specifications: IMD-A Series, LI-005.

[E] Beer C. Gowning Training: The Use of Video Recording Together with Microbial Assessment. PDA J Pharm Sci and Tech. 1991; 45: 128-131.

BioVigilant®
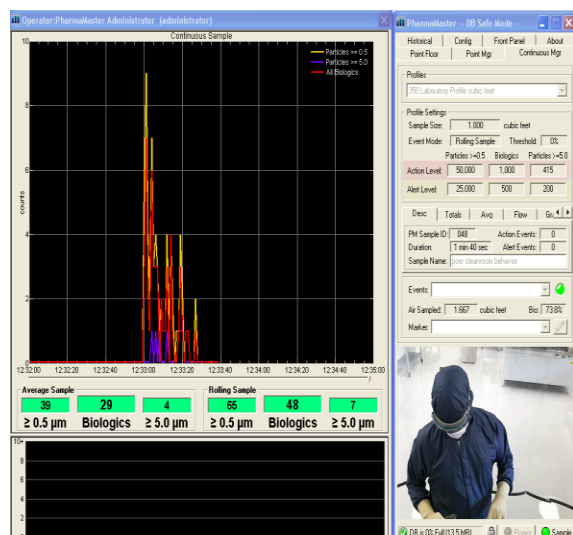Instantaneous Microbial Detection

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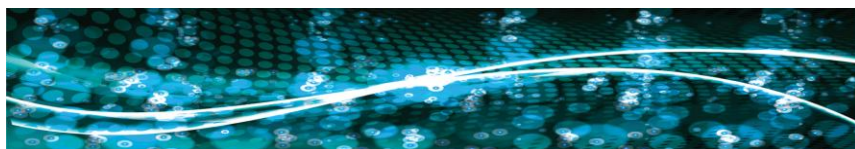
Figure 1: IMD-A System's PharmaMaster software interface provides immediate feedback to operator on improper technique.

Operators have the option of adding text markers during sampling to denote activities or events that occur. These markers are then displayed at the appropriate time within detailed data files and reports which can be useful for tracking the correlation of activities and behavior to the risk of microbial and particle contamination.

The immediate feedback and data review functions are powerful tools for personnel training by demonstrating the need for correct cleanroom attire and compliance to cleanroom procedures.

Example: Appropriate Cleanroom Behavior Training

Cleanroom behavior training was demonstrated in collaboration with the staff of the North Carolina BioNetwork Capstone Center at the Golden Leaf Biomanufacturing Training and Education Center (BTEC).

The demonstration was performed in an ISO 5 area located within an ISO 7 room, separated by hanging softwall curtains. Operators dressed in cleanroom gowns performed a short demonstration of "good cleanroom behavior" during which they remained gowned, moved slowly and simulated normal operations for the area. This was followed by a demonstration of "poor cleanroom behavior" in which abnormal activities and gowning violations were performed. For example, operators moved rapidly, introduced non-sterile materials, touched their faces, removed gloves and masks, talked loudly and held

the curtain open to the ISO 7 room for an excessive amount of time.

The IMD-A system was used to collect a ten-minute (0.28 m^3) sample for each of the "good" and "poor" behavior demonstrations, and an M Air T air sieve sampler with TSA media plates was used concurrently to collect two four-minute (0.1 m^3) samples. Text markers were entered in the PharmaMaster software during sampling to indicate activities as they occurred and the video recording option was used to monitor activities.

Results and discussion

Total counts

Total counts for each particle classification and TSA plate are shown below:

Counts/ CFU	IMD-A 350			Air Sampler	
Sample	≥ 0.5	Bio	≥5	Plate 1	Plate 2
Good cleanroom behavior	9	4	1	0	0
Poor cleanroom behavior	235	104	47	0	0

IMD-A counts for the poor cleanroom behavior sample were markedly higher than the good behavior sample, clearly demonstrating the need to comply with cleanroom procedures. No colonies, however, were grown for either sample using a traditional air sampler.

Traditional growth-based methods have limited utility for this application because of the reduced sensitivity as compared to the IMD-A system, and their inability to detect viable but non-culturable organisms. Higher sensitivity and lower variability with IMD-A systems, as compared to air samplers, were shown during USP<1223> and EP 5.1.6 validation testing[F].

[F] Azbil BioVigilant, USP<1223> and EP 5.1.6 Validation Testing of IMD-A 300/350 Systems, LI-007.
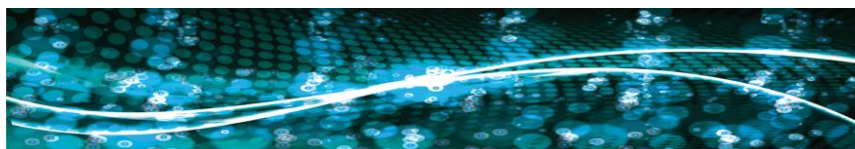
Correlating activities with contamination using text markers

Analysis of the markers displayed in the detailed IMD-A data files showed that certain activities caused large spikes in biological and inert particles. Graphs showing counts over time for each sample are shown with selected markers in Figures 2 and 3.

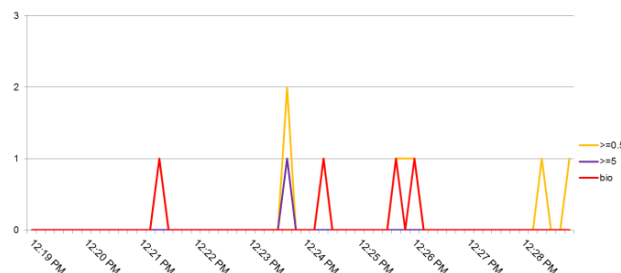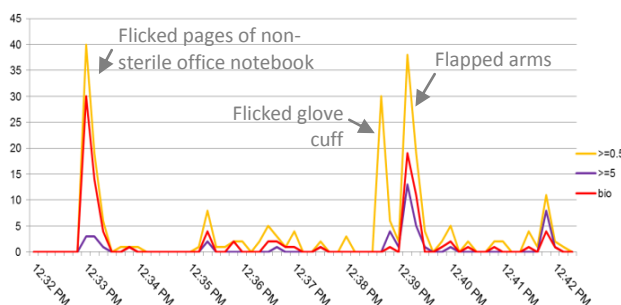**Figure 2: Good cleanroom behavior**

Figure 3: Poor cleanroom behavior

Synchronized video and data playback

Use of the video and data playback function provided more detailed analysis of the effect of various behaviors on contamination levels. For example, it was noted that removing eye protection and touching the face had a minor effect on microbial and particle counts. When operators flapped their arms, however, air was forced out from inside the cleanroom garments and a large amount of contamination was introduced. Other activities that caused spikes in biologic and inert particles included when operators flicked the cuffs of their gloves and when a non-sterile, non-cleanroom paper notebook from a nearby office was brought in and the pages flicked rapidly near the sample inlet (Figures 1, 3 and 4).
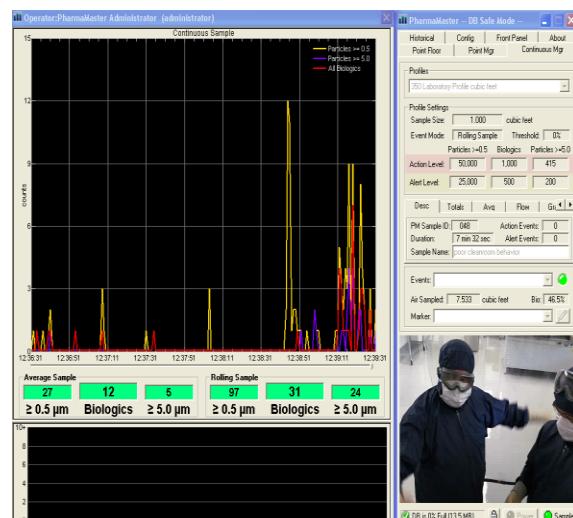

Figure 4: The video and playback option provides direct feedback to operators on the effect of certain cleanroom behaviors.

Conclusions

- Poor cleanroom behavior resulted in higher counts than good cleanroom behavior.

- Use of markers and video function demonstrated why certain activities are not recommended in cleanrooms.

- Real-time reporting gave operators immediate feedback during testing, and use of the video and data review function enabled detailed analysis of activities posing the greatest contamination risk.

The demonstration of appropriate and inappropriate cleanroom behavior shows that the IMD-A 350 system can provide an immediate and visually powerful tool to illustrate why following cleanroom procedures is important for minimizing microbial and particle contamination. Use of the IMD-A system can greatly enhance personnel training programs and operator assessment and qualification to increase overall compliance.

Additionally, the IMD-A system is an ideal tool for analysis of site procedures and cleanroom materials to identify areas of contamination risk and improve overall quality in pharmaceutical manufacturing operations.

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Instantaneous Microbial Detection
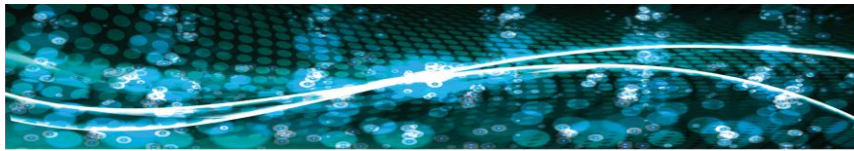
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Support

Please contact Azbil BioVigilant's Applications team or your sales executive for additional assistance.

We can assist with:

- On-site and remote support by our Field Applications Scientist team

- Complete evaluation protocols and data analysis tools

- Custom protocol development including a sample training protocol

Azbil BioVigilant thanks the staff of the North Carolina BioNetwork Capstone Center at the Golden Leaf Biomanufacturing Training and Education Center (BTEC) in Raleigh for collaborating on the development of this applications concept.

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