Non-Sterile Hybrid Isolator

Abstract

In 2011, Flow Sciences, Inc. was commissioned with providing an isolator for a large pharmaceutical company that was capable of protecting its employees by reducing their exposure below the occupational exposure level (OEL) of highly potent active pharmaceutical ingredients (APIs) in an isolator.. Here we describe the unit designed and constructed and the in-house testing results.

Background

In the ongoing search for new therapeutic treatments, pharmaceutical companies are developing a new class of active ingredients known as High Performance Active Pharmaceutical Ingredients (HPAPI). As the name suggests, these compounds are highly potent and therefore it is critical that exposure to the pure material is minimal. More commonly associated with oncology drugs, an 'explosion' of HPAPIs is predicted over the next 5 years due to the high levels of research currently being conducted in this area.

Clearly, with the advent of this phenomenon, containment of these compounds from the scientists tasked with working with them is of major concern. One reason for this is the high expense often associated with new equipment designed to handle the task. In order to combat these potentially high capital outlays, many companies are looking at alternative methods of containment, including modification of existing equipment. The Non-Sterile Hybrid Isolator, offered by Flow Sciences, Inc., is one such method of reducing the cost of containment (Figure 1).

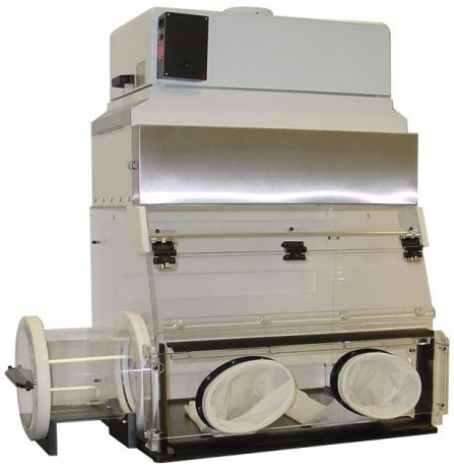

Figure 1. Non-Sterile Hybrid Isolator with bag in/bag out and main chamber.

The isolator is designed to protect personnel from exposure to chemicals including HPAPIs by fully encompassing equipment used by scientists during processes such as weighing, crushing and bag in/bag out procedures. The isolator has been developed using Flow Sciences' expertise in fluid dynamics and can be designed and manufactured to fit the customer's needs.

Case Study

In 2011, Flow Sciences, Inc. was tasked by a major pharmaceutical company with the design, construction and installation of a non-sterile hybrid isolator for use by its employees during powder handling operations. The design of the isolator included a bag in/bag out (BIBO) annex and a main enclosure.

After installation of the isolator, a third party industrial hygiene consulting company. , IES engineers, was contracted to perform Site Acceptance Testing (SAT) and determine the effectiveness of the

isolator. Using industry accepted testing methods; IES performed sampling of the air, surface and the testing area environment to evaluate the containment performance of the isolator using a surrogate powder (naproxen sodium) during typical operator procedures. The design containment performance target (CPT) for the VBE air samples was set at 75 nanograms of surrogate powder per cubic meter (ng/m^3) of air. This value was chosen to provide an additional margin of safety compared to the OEL for an API of 150 ng/m^3. Surface samples were collected and used for reference purposes. All of the containment verification testing activities were performed using industry accepted practices.[1-3]

Procedure

Prior to the containment verification assessment, the sampling strategy developed by IES was approved by the client and included typical and maximum use scenarios. The procedures, using naproxen sodium as an API surrogate, were: (1) reference standard development, comprising of: (a) dispensing approximately 500 mg of naproxen sodium into volumetric flasks; (b) development of a buffer capacity, which included dispensing of approximately 1 g of naproxen sodium into 50 mL water, followed by 5 minutes of mixing; (2) minor cleaning procedures of the VBE interior, including a wipe down of the floor surfaces and gloves with methanol and removal of equipment and materials used during the procedures. Each procedure was performed three times establish a greater level of confidence in the containment verification data.

Airborne samples were collected from personal, source and area locations. Personal samples were collected within the breathing zones of the operators. Source samples were collected at 200 mm from the potential emission source and area samples were collected at distances no closer than 1.5 m from the process or equipment and at a height of 1.5 m. These samples were then analyzed and exposures quantified.

Baseline samples were collected for all locations prior to performing the operations.

Results

Sample Description	**Run 1 (ng/m^3)**	**Run 2 (ng/m^3)**	**Run 3 (ng/m^3)**	**Average (ng/m^3)**
Powder Handling and Minor Cleaning				
Personal Breathing Zone	<5	<5	<5	<5
Area Sample – approx 1.5 m from isolator	<5	<5	<5	<5
Source Sample – approx 200 mm between both glove ports	<5	<5	<5	<5
Source Sample – Approx 200 mm above disposal port	<5	<5	<5	<5
Source sample – approx 200 mm from exhaust discharge	<5	<5	<5	<5
Continuous Area Sample During All Powder Handling Activities				
Area Sample – approx 3 m from isolator	<1			

As can be seen from the table above, all samples collected for the various zones were well below the CPT of 75 ng/m^3 air

Summary

In summary, FlowSciences designed, constructed and installed a non-sterile hybrid isolator for a large pharmaceutical company to limit exposure of employees to APIs during powder handling operations. Containment Verification Testing of the isolator, using a surrogate powder, was performed at the pharmaceutical company by IES, a third party industrial hygiene consulting company. The test results demonstrated that the isolator provided effective containment of powders to the CPT of 75 ng/m^3 for the tasks performed.

References

1) American Society of Heating, Refrigerating and Air-Conditioning Engineers, "Method of Testing Performance of Laboratory Fume Hoods, ANSI/ASHRAE 110-1995" Atlanta, GA, 1995.

2) International Society for Pharmaceutical Engineering, "ISPE Good Practice Guide: Assessing the Particulate Containment Performance of Pharmaceutical Equipment," Second Edition, 2012.

3) Section II: Sampling Measurements and Instruments of the OSHA Technical Manual

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