



IntelliFill® i.v. Aseptic Enclosure



INTRODUCTION

Studies even in well-controlled environments show that contamination associated with manual processes may reach a rate of 5% (one dose in 20), primarily due to human touch or breath contamination.

IntelliFill i.v. is a pharmacy compounding device intended to automate the production of small volume parenteral (SVP) doses that would otherwise be prepared by hand. Hand preparation of such doses typically occurs on a Laminar Air Flow Bench (“hood”) within a hospital pharmacy IV room under, at best, ISO Class 5 particulate conditions. Although recent standards mandate otherwise, surveys of pharmacy practice indicate that compliance with proper cleaning and garb standards is very poor.

By contrast, IntelliFill i.v. performs these functions within an aggressively cleaned aseptic environment that operates within a clean air environment that demonstrates ISO Class 4 particulate levels at rest and ISO Class 5 conditions under use, except when both front doors are opened.

Maintenance of the aseptic environment is the responsibility of IntelliFill i.v. operators using techniques and materials taught by Baxa and/or developed and validated by the users.

ENVIRONMENTAL CONTROL

A state of control is maintained for the IntelliFill i.v. aseptic environment with the following techniques:

DOOR INTERLOCK CONTROL

IntelliFill i.v. performs aseptic transfer on an automation deck that is completely enclosed when it operates; humans do not manipulate doses as they are being prepared.

HEPA-FILTERED AIR

The air for the automation deck is passed through a HEPA (high-efficiency particulate absorbing) filter. The filter unit moves 100 ft/min (0.51 m/s) [=537 ft³/min] air when the doors are closed and 150 ft/min (0.76 m/s) [=805 ft³/min] air when the doors are opened. The volume of the aseptic environment is approximately 53 ft³, resulting in closed and opened air exchange rates of 10.1 exchanges/min and 15.2 exchanges/min, respectively.

IntelliFill i.v. users are instructed both by training and in published manuals that they may not operate the device until at least 30 minutes has elapsed since the HEPA filter blower was turned on.

The intent of the HEPA filter is to provide a clean-air environment for the aseptic fluid transfer process. Laminar air flow is not demanded nor maintained, although the flow of air across the

critical surfaces (the surface of the dial around which syringes are processed) is unobstructed and flows from the center of the dial outward to the exhaust vents in the side of the cabinet.

DAILY CLEANING

The IntelliFill i.v. automation deck must be cleaned daily by an appropriately garbed operator using Class-100 rated, sterilized wipes and 70% isopropyl alcohol. Baxa recommends the use of sterilized (cold filtered) 70% isopropyl alcohol, although off-the-shelf 70% isopropyl alcohol has also demonstrated the ability to provide sufficient sanitization.

Critical areas on the operating dial may be additionally cleaned and disinfected with bleach (6% sodium hypochlorite) and/or 3% hydrogen peroxide. The dial has been shown to tolerate concentrations of hydrogen peroxide up to 30%.

If bleach or peroxide is used on the dial, the protocol requires continuous exposure to the cleaning agent for 30 minutes prior to washing off with 70% isopropyl alcohol.

At the conclusion of cleaning, the operator fogs the inside of the automation deck with sufficient 70% isopropyl alcohol to keep surfaces wet for a period of at least 10 minutes. The operator then closes the cabinet and allows the device to stand for that 10 minute exposure period.

In addition to the daily cleaning, cleaning is required in response to drug spills or breaks in garb or other aseptic technique protocols.

USER GARB REQUIREMENTS

Users operating the device must be appropriately garbed whenever they enter the automation deck:

- Gown
- Gloves (unpowdered, latex-free)
- Mask
- Hair covering (including covering for facial hair where applicable)
- Individual site policies regarding makeup and jewelry must also be observed; it is recommended that operators not wear makeup or jewelry

ENVIRONMENTAL MONITORING/PROCESS CONTROL

AIR SUPPLY

The HEPA filter is inspected on the same schedule as laminar air flow hoods in the pharmacy (usually semi-annually). The filter must be free of breaks and/or tears and must have a throughput of at least 100 ft/min.

The same inspection measures particulate counts on the device while it is at rest. Particulate counts must conform to at least ISO Class 5; the device is expected to conform to ISO Class 4.

A sensor detects the presence of air flow through the filter and will not permit the IntelliFill i.v. to be operated if air flow cannot be detected. This can be demonstrated by temporarily obscuring the sensor, which will cause the device to report an error and cease operation.

TRAINING

Users are trained on cleaning, proper garb and operation of the device upon installation. Baxa provides Web-based training and testing for ongoing annual training recertification by the customer.

MEDIA CHALLENGES

The software prompts users to perform weekly media challenges of the device using the same equipment and techniques used to prepare actual doses. The media is trypticase soy broth certified by its manufacturer to be sterile and able to grow a wide variety of organisms (letter from manufacturer [see Appendix] attached). Challenges are run immediately after cleaning and again after 24 hours, just before the next day's cleaning is scheduled to occur. Media challenge syringes are incubated for 7 days at 30° C and observed for turbidity.

This method was validated with over 800 syringes during initial system testing. Independent laboratory analysis confirmed that contamination was always revealed by visually evident turbidity. The pharmacy may, at its discretion, have turbid samples speciated for more information regarding possible sources of contamination if it occurs.

ENVIRONMENTAL MONITORING

In addition to media challenges, IntelliFill i.v. users assess the bioburden in the automation deck with weekly assessments of air and surface contamination using agar paddles designed for the purpose of assessing laminar air flow hood bioburden.

These paddles were used during validation and were shown to always present visual contamination (in the form of distinct colonies) when they were contaminated, and not show evidence of contamination when they were not.

Air paddles are typically expected to have no contamination, as are contact paddles that are applied to the critical surfaces of the dial. Contact paddles on doors and other more frequently manipulated surfaces typically show no contamination, although some customers permit as many as five colony-forming units (CFU) on those paddles without taking remedial action.

END-PRODUCT TESTING

Some customers elect to perform end-product testing on batches of syringes intended for prolonged storage. Typically, end-product tests are performed by a hospital laboratory or referral laboratory.

IntelliFill i.v. is manufactured for Baxa Corporation by FHT, Inc.

Q.I.medical, inc

Growth of Selected Organisms in GroMed™ TSB Effective 1/1/05

The following list of organisms have been shown by investigators to grow successfully in our formulation of TSB:

Acinetobacter calcoaceticus
Bacillus species
Candida albicans
Corynebacterium species
Enterobacter aerogenes
Enterobacter cloacae
Enterococcus
Escherichia coli
Flavobacterium meningosepticum
Gram-negative rods
Klebsiella pneumoniae
Proteus mirabilis
Proteus vulgaris
Pseudomonas aeruginosa
Pseudomonas paucimobilis
Serratia marcescens
Staphylococcus aureus
Staphylococcus epidermidis
Streptococcus faecalis
Streptococcus pyogenes
Torulopsis glabrata

This list is by no means complete. These test organisms were picked to represent a broad variety of possible contaminants.

TSB is universally considered to be the media of choice for detecting the widest range of microbial contaminants in sterile drug products. It is the standard growth media because of its ability to support the growth of aerobic bacteria, facultative bacteria, yeasts, and fungi.

TSB is the growth media specified by The United States Pharmacopeial Convention for detecting the presence of aerobic microbial contamination in sterile drug products.

Sincerely,



Hilary Hedman
President

11/8/97

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