Learning Objectives

After attending this discussion, the participants will be able to:
1. Appreciate the differences between an isolator and a BSC
2. Consider issues related to work practices between an isolator and a BSC
3. Identify relevant references and tools for incorporating cabinet(s) into work processes

Sterile Compounding in Pharmacy

- Sterile compounding in hospital and ambulatory care settings is undergoing changes
  - Laminar flow technology has been around for >20 years
  - Recently barrier-isolation technology is becoming available

- Recent guidelines
  - ASHP Guidelines on Handling Hazardous Drugs
  - ISOPP Standards of Practice. Safe Handling of Cytotoxics
    - Pre-publication

Barrier Isolator Technology

- History of use in pharmacy
  - 1980s First available in Europe
  - Early 1990s Preferred ‘enclosure’ in UK and Ireland
  - Mid 1990s Introduced/Used in USA
  - Late 1990s Introduced/Used in Singapore
  - 2000s Introduced/Used in Thailand & Malaysia

- It was developed to remove operator from the environment in which products are prepared, eliminating source of contamination
- Enclosed, ventilated controlled environment (vertical laminar or turbulent airflow)
- Access is through transfer hatch/chamber; operation conducted through fixed-glove access
- Good aseptic technique and support materials are required
Design – main characteristics

- Protection of products
  - Physical barrier
  - Permanent enclosure
  - Transfer devices (interlocking door)
  - HEPA filters (Grade A)

- Protection of operators
  - Physical barrier
  - Permanent enclosure
  - Transfer devices (interlocking door)
  - Evacuation of air outside building

Air-flow in Isolator

Specification for a barrier isolators should include:

- Physical Structure
- Internal environment
- Transfer and Interaction technologies
- Monitoring system

Physical Structure

- Hard shell
  - Hard Plastic
  - Plexiglass
  - Stainless Steel

- Soft shell
  - Soft Plastic Film

- Best construction is stainless steel type 316L

Internal Environment

- Typical specs
  - All interior surfaces of the isolator are to be smooth and cleanable, including welds
  - Easy access for maintenance
  - Both entering and existing air is to be HEPA filtered. Filters protected during cleaning
  - Air introduced will have directional flow. Per Federal Std 209E, system is capable of maintaining at least class 100 environment
  - Capable of maintaining required pressure (0.25-1.0 inches of water pressure)

Transfer technologies

- Offers means of introducing materials into work areas without compromising internal integrity of system

- Selected based on the level of protection needed
  - Simple transfer hatches
  - Laminar-airflow interfaces
  - Timed air lock
Interaction technologies
- Allows operator to interact with the process or equipment contained in barrier system
  - Gloves ports
  - Half-suits

Interaction technologies - Gloves ports
- Sleeves-and-gloves arrangement
- One piece system
  - Higher integrity but more expensive
- Two-piece system
  - Better fit for gloves
  - Less expensive

Interaction technologies - Half suits
- Were developed to increase lifting capabilities and expand areas of reach within work areas.
- Disadvantages:
  - Difficulty in cleaning
  - Difficulty in entering and exiting
  - Hygiene issues with multiple users

Monitoring system
- Used to determine that workstation is operating within the design parameters
  - Gauges with visual readouts
  - Alarm/Alert system

The many 'looks' of ISOLATORS...

Optional Features...
- Inner doors released by foot switches
- Sliding transfer chamber tray
- Adjustable height
- CCTV monitoring system
- Easy Change Cuff Ring System
Important things to consider in selecting barrier isolator:
- **Vendor support**
  - Servicing and maintenance
  - Installation without disruption in existing areas
- **Durability**
  - Materials of construction
- **Functionality**
  - Size
  - Ergonomics
  - Movement of materials in/out of workstations
  - Heat load and noise level
  - Lighting
  - Ease of cleaning and disinfecting work areas
  - Ability to change system to meet future needs
- **Cost**
  - Capital cost/Cost of setup
  - Operating cost (disposable items and maintenance)
  - Productivity

Remember to ask for a list of references and follow up with calls or site visits.

Biological Safety Cabinets
- Biological safety cabinets (BSC) are designed to provide three types of protection:
  - Personnel protection from material inside the cabinet
  - Protection for the material inside of the cabinet
  - Protection for the environment from the material inside of the cabinet
- There are three types of BSCs, Class I, II, and III

Biological Safety Cabinets
- **Class I Cabinets**
  - are designed to provide personnel and environmental protection only.
  - product inside the cabinet is not protected and thus subject to contamination.

Biological Safety Cabinets
- **Class II Cabinets**
  - Class II, Type A Cabinets
    - Not vented
  - Class II, type B1 Cabinets
    - must be vented; 30% of the air is exhausted from the cabinet while 70% is recirculated back into the room.
  - Class II, type B2 Cabinets
    - must be totally exhausted; 100% of the air from the cabinet is exhausted through a dedicated duct.
  - Class II, type B3 Cabinets
    - must be vented; 70% of the air is exhausted from the cabinet while 30% is recirculated.
Biological Safety Cabinets

- **Class III Cabinets**
  - are designed to provide maximum protection to the worker and the environment.
  - Sometimes called Class III glove boxes, these units are gas-tight enclosures with a non-opening view window.
  - Intake air is filtered through a HEPA filter, and exhaust air passes through two HEPA filters before being exhausted to the outdoors.

**Recommendations:**
- National Institute for Occupational Safety and Health (NIOSH)
- American Society of Health-System Pharmacists (ASHP)
- International Society of Oncology Pharmacy Practitioners (ISOPP)
  - When sterile hazardous drugs are being compounded, use one of the following ventilated cabinets:
    - Class II BSC (Type B2 is preferred)
    - Class III BSC
    - Isolators intended for asepsis and containment (aseptic containment isolators) [NSF/ANSI 2002; PDA 2001]

**Practice Issues**

- **Safety (personnel)**

**Comparison of Definitions for the BSC III and Isolator**

- Class III BSC is a unidirectional laminar airflow cabinet where the front is “closed” by a window fitted with sleeves and gloves to allow the manipulation inside the cabinet.
- Operates usually in a negative air pressure.
- Pass through hatches are used. One hatch is used for entry and one for the exit of the finished product and waste.
- A manual decontamination process (different from sterilisation) is usually performed in the pass through before materials enter the cabinet. The cabinet is NOT sterile and is NOT sterilized. For cleaning and decontamination of the cabinet, the window of the cabinet may be opened periodically.

**Comparison of Definitions for the BSC III and Isolator**

- Isolator, on the other hand, is a totally enclosed system running usually in positive air pressure with turbulent airflow and which is sterilized by gas sterilization.
- Products and preparation devices are introduced into the isolator using pass throughs which are always sterilized.

**Safety Issues - BSC**

- Schub, Heidi; Bigelow, Susan; Dobish, Roxanne1; Chambers, Carole R. Antineoplastic agent workplace contamination study: the Alberta Cancer Board Pharmacy perspective. Journal of Oncology Pharmacy Practice. 2005; 11(3): 102-9
Safety in BSC - Conclusions

Studies of surface contamination have discovered deposits of hazardous drugs within the cabinets, outside cabinets on the floor in front of the Class, and workplace counter tops.

Workers must understand that BSC does not prevent the generation of contamination within the cabinet and that the effectiveness of BSCs in containing hazardous drug contamination depends on:

• operators' use of proper technique
• operators' work practices
• operators' housekeeping practices

Safety Issues - Isolators


"Measurable amounts of cytotoxic drugs were detected on the floors of both units and on the disposable gloves worn by staff preparing the drugs. There was also evidence in both units of some very low-level drug absorption from urine measurements, using the most sensitive analytical technique of platinum analysis."


"Contamination was routinely found inside the isolators but rarely outside the isolators, indicating that the isolator technology is offering good protection of the cytotoxic drug handlers as well as the environment during preparation. On the other hand, contamination was found on the surfaces of infusion bags and gloves in contact with infusion bags filled with cytotoxic drugs. Consequently, personal protective equipment is still recommended during the manipulation and administration of the drugs because of potentially contaminated drug vials and final products."

Safety in Isolators - Conclusions

Isolators, like Class II BSCs, do not prevent the generation of contamination within the cabinet workspace, and their effectiveness in containing contamination depends on:

• operators' use of proper technique
• operators' work practices
• operators' housekeeping practices

The potential for the spread of hazardous drug contamination from the pass-through and main chamber of the isolator to the workroom may be reduced by surface decontamination, but no wipe-down procedures have been studied.

Appendix E—Recommendations for working in BSCs and isolators.

The use of a Class II or III BSC or isolator must be accompanied by a stringent program of work practices, including operator training and demonstrated competence, contamination reduction, and decontamination.

• Do you place unnecessary items in the work area?
• Do you over-crowd work zone?
• Do you plan work (needed supplies) ahead?
• Do you spray or wipe critical sites?
• Do you practice wipe down before placing items in cabinet?
• Do you place transport bags in cabinet?
• Do you do surface decontaminated for final preparation?

Section 7: Special Devices

ISOPP Standards of Practice. Safe Handling of Cytotoxics

To prevent or minimize the possible contamination during reconstitution and administration of cytotoxic drugs

These special devices may be considered in 3 categories:

a) Devices to protect the handler of the vial/ampoule
b) Devices to protect the operator during preparation
c) Devices to protect the administrator during administration of the cytotoxic drug to the patient

Appendix E—Recommendations for working in BSCs and isolators.

Do you decontaminate work surface before and after compounding?
Do you decontaminate all surfaces of cabinet at the end of the batch, day, or shift?
Do you wipe down the outside of BSC front opening and the floor in front of the BSC daily?
Do you seal and then decontaminate surfaces of waste and sharps containers before removing from cabinet?
Do you decontaminate after each spill in cabinet?
Do you seal all contaminated materials (e.g. gauze, wipes, towels, wash or rinse water) in bags or plastic containers and discard as contaminated waste?
Practice Issues

- Safety (personnel)

  Staff training > technique > housekeeping > facility & Equipment

Practice Issues

- Safety (personnel)

- Work flow

Facility - BSC

Grade B (EC GMP) environment

Facility - Isolator

Grade C or D environment

Workflow Issues - Preparation

<table>
<thead>
<tr>
<th>PPE</th>
<th>BSC</th>
<th>Isolator</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPE</td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Restricted Access</td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Personnel</td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Items (pre &amp; post)</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Restricted hand movement</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Efficiency</td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Work area in cabinet</td>
<td>+</td>
<td></td>
</tr>
</tbody>
</table>

PPE

<table>
<thead>
<tr>
<th>Class of Room</th>
<th>Requirements for PPE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class D</td>
<td>Hair / Beard Covering</td>
</tr>
<tr>
<td></td>
<td>Normal Protective Clothing</td>
</tr>
<tr>
<td>Class C</td>
<td>Hair / Beard Covering</td>
</tr>
<tr>
<td></td>
<td>Clothes gripped at wrist with raised collar</td>
</tr>
<tr>
<td></td>
<td>Clothing must not shed fibres or particles</td>
</tr>
<tr>
<td>Class A / B</td>
<td>Hood or other head covering</td>
</tr>
<tr>
<td></td>
<td>Mask</td>
</tr>
<tr>
<td></td>
<td>Sterile, Non-powdered gloves</td>
</tr>
<tr>
<td></td>
<td>Sterile or disinfected boots or overshoes</td>
</tr>
<tr>
<td></td>
<td>Sterile clothing which must not shed fibres or particles</td>
</tr>
<tr>
<td></td>
<td>Sterile clothing must be capable of retaining particles shed by operator</td>
</tr>
</tbody>
</table>
Workflow Issues - Preparation

<table>
<thead>
<tr>
<th></th>
<th>BSC</th>
<th>Isolator</th>
</tr>
</thead>
<tbody>
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<td>Efficiency</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Work area in cabinet</td>
<td>+</td>
<td></td>
</tr>
</tbody>
</table>

Practice Issues
- Safety (personnel)
- Work flow
- Monitoring
  - Physical
  - Microbiological

Monitoring - Physical
- Aim is to monitor whether the cabinet is performing to specification.

<table>
<thead>
<tr>
<th></th>
<th>BSC</th>
<th>Isolator</th>
</tr>
</thead>
<tbody>
<tr>
<td>Integrity of the HEPA filters</td>
<td>6-12 mth</td>
<td>6-12 mth</td>
</tr>
<tr>
<td>Airflow velocity</td>
<td>3 mthly</td>
<td>3 mthly</td>
</tr>
<tr>
<td>Air circulation (smoke test)</td>
<td>monthly</td>
<td>monthly</td>
</tr>
<tr>
<td>Leak test</td>
<td>----</td>
<td>continuous</td>
</tr>
<tr>
<td>Airflow retention (smoke test)</td>
<td>3 mthly</td>
<td>----</td>
</tr>
<tr>
<td>Pressure differential</td>
<td>3 mthly</td>
<td>3 mthly</td>
</tr>
<tr>
<td>Particulate</td>
<td>3 mthly</td>
<td>3 mthly</td>
</tr>
<tr>
<td>Noise</td>
<td>3-6 mthly</td>
<td>3-6 mthly</td>
</tr>
<tr>
<td>Light</td>
<td>3-6 mthly</td>
<td>3-6 mthly</td>
</tr>
</tbody>
</table>

Monitoring - Microbiology
- Aim is to ensure quality of environment the product is exposed during manipulation.

<table>
<thead>
<tr>
<th></th>
<th>BSC</th>
<th>Isolator</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Passive (settle plates)</td>
<td>Daily</td>
<td>Daily</td>
</tr>
<tr>
<td>Active (air sampler)</td>
<td>Monthly</td>
<td>Monthly</td>
</tr>
</tbody>
</table>

Practice Issues
- Safety (personnel)
- Work flow
- Monitoring
  - Physical
  - Microbiological

It is recommended that the cabinets be left running 24 hours a day, 7 days a week in order to help prevent microbiological and chemical contamination.

Balancing... COST, SAFETY, EFFICIENCY
### Costing & Budget...

<table>
<thead>
<tr>
<th>Set up</th>
<th>BSC</th>
<th>Isolator</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capital Room</td>
<td>+++</td>
<td>++</td>
</tr>
<tr>
<td>Cabinet</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Consumables</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Maintenance Room</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Cabinet</td>
<td>+</td>
<td>++</td>
</tr>
</tbody>
</table>

**10+ 9+**

More expensive

### Safety & Efficiency...

<table>
<thead>
<tr>
<th>Set up</th>
<th>BSC</th>
<th>Isolator</th>
</tr>
</thead>
<tbody>
<tr>
<td>Safety</td>
<td>++</td>
<td>+++</td>
</tr>
</tbody>
</table>

More desirable

<table>
<thead>
<tr>
<th>Efficiency (speed)</th>
<th>BSC</th>
<th>Isolator</th>
</tr>
</thead>
<tbody>
<tr>
<td>workflow</td>
<td>++</td>
<td>+</td>
</tr>
</tbody>
</table>

More desirable

### Unresolved issues related to current compounding practice

- Exposure risks
  - needle stick injuries
  - Surface contamination
  - Cumulative strain disorders
- Prep errors in dosage
- Prep errors in drug
- Recruitment & Training

### Alternative to BSC and Isolators

- State-of-the-art technology coupling **robotic**, software design and automated waste handling system

### The Automated Solution

- CYTOCARE
- VDO
THANK YOU