Maintaining a Hospital Pharmacy Compounding Program

Michael J. Freudiger, PharmD, APh, BCPS, BCGP
Disclosure Information

Maintaining a Hospital Compounding Program
Michael J. Freudiger, PharmD, APh, BCPS, BCGP

• I have no financial relationships to disclose. AND

• I will not discuss off-label use and/or investigational use in my presentation.
Learning Objectives

At the completion of this activity, you will be able to:

- Identify appropriate beyond use dates to compounded sterile products.
- Describe an environmental cleaning, sampling, and monitoring plan for the sterile compounding area.
- Identify an optimal employee’s compounding education modules.
Compounding Program Elements

- Employee Education
- Quality Assurance
- Employee Safety
- Compounding Process
- Regulatory Compliance

Patient Safety
Compounding Program Elements

- Employee Education
- Employee Safety
- Quality Assurance
- Compound Process
- Regulatory Compliance

Patient Safety

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### Table 10. Summary of Terms

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
<th>Applicability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beyond-Use Date</td>
<td>Either the date or hour and date after which a CSP must not be used or administration must not begin. The BUD is determined from the date/time that preparation of the CSP is initiated.</td>
<td>Applies to all CSPs</td>
</tr>
<tr>
<td>Expiration Date</td>
<td>The time during which a product can be expected to meet the requirements of the compendial monograph, if one exists, provided it is kept under the prescribed storage conditions.</td>
<td>Applies to all conventionally manufactured products, APIs, and excipients</td>
</tr>
</tbody>
</table>
The BUDs for CSPs in Table 11 and Table 12 are based primarily on factors that affect the achievement and maintenance of sterility, which include, but are not limited to, the following:

- Environment in which the CSP is prepared (e.g., PEC in a cleanroom suite or SCA)
- Aseptic preparation and sterilization method
- Components and ingredients (e.g., sterile or nonsterile starting ingredients)
- Whether or not sterility testing is performed
- Storage conditions (e.g., packaging and temperature)
A shorter BUD is required when the stability of the CSP or its components is less than the hours or days stated in Table 11 or Table 12. Additionally, the BUD must not exceed the shortest remaining expiration date or BUD of any of the starting components, regardless of the source.

Table 11 establishes the longest permitted BUDs for Category 1 CSPs. Category 1 CSPs may be prepared in an SCA or cleanroom suite (see 4.2 Facility Design and Environmental Controls).

Table 11. BUDs for Category 1 CSPs

<table>
<thead>
<tr>
<th>Storage Conditions</th>
<th>Controlled Room Temperature (20°–25°)</th>
<th>Refrigerator (2°–8°)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BUD</td>
<td>≤12 hours</td>
<td>≤24 hours</td>
</tr>
</tbody>
</table>
Table 12. BUDs for Category 2 CSPs

<table>
<thead>
<tr>
<th>Sterilization Method</th>
<th>Sterility Testing Performed and Passed</th>
<th>Controlled Room Temperature (20°–25°)</th>
<th>Refrigerator (2°–8°)</th>
<th>Freezer (−25° to −10°)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aseptically prepared CSPs</td>
<td>No</td>
<td>Prepared from one or more nonsterile starting component(s): 1 day</td>
<td>Prepared from one or more nonsterile starting component(s): 4 days</td>
<td>Prepared from one or more nonsterile starting component(s): 45 days</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Prepared from only sterile starting components: 4 days</td>
<td>Prepared from only sterile starting components: 9 days</td>
<td>Prepared from only sterile starting components: 45 days</td>
</tr>
<tr>
<td>Yes</td>
<td>30 days</td>
<td>45 days</td>
<td>90 days</td>
<td></td>
</tr>
</tbody>
</table>

Proposed USP 797 draft as of 7/27/2018
CURRENT USP 797

- **Low Risk**: 48 hours RT, 14 days FR, 45 days FZ
- **Medium Risk**: 30 hours RT, 9 days FR, 45 days FZ
- **High Risk**: 24 hours RT, 3 days FR, 45 days FZ
- **Immediate Use**: 1 hour

**RT** = room temperature  
**FR** = refrigerated  
**FZ** = frozen
CURRENT USP 797

- **Low Risk**: 48 hours RT, 14 days FR, 45 days FZ
- **Medium Risk**: 30 hours RT, 9 days FR, 45 days FZ
- **High Risk**: 24 hours RT, 3 days FR, 45 days FZ
- **Immediate Use**: 1 hour

PROPOSED USP 797 UPDATE (as of 7/27/2018)

- **Category 1**: 12 hours RT, 24 hours FR
- **Category 2** (no sterility testing): 4 days RT, 9 days FR, 45 days FZ
- **Category 2** (sterility testing): 28 days RT, 42 days FR, 45 days FZ

RT = room temperature
FR = refrigerated
FZ = frozen
USP 797: Assigning Beyond Use Use Dates

**BEYOND USE DATE**

- **Microbial sterility** (USP 797 limits, air quality during compounding)

**EXPIRATION DATE**

- **Chemical stability**
- **Type of container** (PVC, non-PVC, glass)
- **Type of solution** (D5W, NS, LR, SWFI, etc.)
- **Final concentration of drug in solution**
- **Storage conditions** (room temperature, refrigerated, frozen)
- **Light exposure** (sunlight, UV light, total light protection)
Labelling: How to Reduce Confusion?

• Need to review each drug for shortest date → **Standardize**!
  - Need to discuss with staff what is least confusing and standardize language on labels.

Must start by: (date @ time)
Discard by: (date @ time)
BUD Assessment: Continuous Infusion

- Compounded drug stability = 7 days RT (RT only)
- Batched USP 797 BUD^{2017} = 30 hr RT
- Hospital policy maximum hang time = 96 hr RT

TIME (hours)

Freudiger 2018

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Compounded drug stability = 48 hr RT (RT only)
Batched USP 797 BUD$^{2017}$ = 30 hr RT
Hospital policy maximum hang time = 96 hr RT

RT = room temp
FR = fridge temp
BUD Assessment: Continuous Infusion

- Compounded drug stability = 48 hr RT (RT only)
- Batched USP 797 BUD$^{2017}$ = 30 hr RT
- Hospital policy maximum hang time = 24 hr RT

RT = room temp
FR = fridge temp

24 hr hang time (limited by policy)

18 hr hang time (limited by drug stability)
BUD Assessment: Continuous Infusion

- Compounded drug stability = 24 hr FR, 24 hr RT
- Batched USP 797 BUD\textsuperscript{2017} = (limited by drug stability)
- Hospital policy maximum hang time = 24 hr RT

RT = room temp
FR = fridge temp

TIME (hours)

Freudiger 2018
• Compounded drug stability = 72 hr FR, 8 hr RT
• Batched USP 797 BUD\textsuperscript{2017} = (limited by drug stability)
• Hospital policy maximum hang time = 24 hr RT

RT = room temp
FR = fridge temp

30 min infusion

TIME (hours)

Freudiger 2018
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Master Formula: Equipment & Environmental BUD Limitations

- Maximum BUD as listed above are applicable only if the sterile product is compounded in an ISO-5 environment within an ISO-7 area.
- A 12 hour maximum BUD limitation is applied when sterile products are compounded in ISO-5 environments within a segregated compounding area (not meeting ISO-7 air quality or 30 air changes per hour) or when the compounding area is undergoing environmental remediation. (or 24 HR in draft 797)
- A 1 hour maximum BUD limitation is applied when the compounding area does not meet the minimum USP 797 environmental standards.

### Ceftazidime 22.5 mg/1 mL Intravitreal Injection Syringe

**Compounded with Preservative Free Ingredients & Solutions.**

<table>
<thead>
<tr>
<th>Compounding Ingredients (Active + Inactive) &amp; Supplies</th>
<th>Sample Label</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ceftazidime in the available dosage form(s): 1 Gram vial</td>
<td></td>
</tr>
<tr>
<td>Sterile water for injection (SWFI) preservative free (PF): 20 mL vial</td>
<td></td>
</tr>
<tr>
<td>Sodium chloride (NS) for injection preservative free (PF): 10 mL vial</td>
<td></td>
</tr>
<tr>
<td>Sterile empty container (10 mL or greater)</td>
<td></td>
</tr>
<tr>
<td>Syringes of appropriate size: 1 mL, 10 mL</td>
<td></td>
</tr>
<tr>
<td>Filter needle(s) (5-micron), regular needles of appropriate size</td>
<td></td>
</tr>
<tr>
<td>Syringe caps (snap or luer lock)</td>
<td></td>
</tr>
</tbody>
</table>

**USP 797 Beyond Use Date (BUD)**

<table>
<thead>
<tr>
<th>Drug Physical/Chemical Stability</th>
<th>Hazardous Classification</th>
<th>Maximum BUD</th>
</tr>
</thead>
<tbody>
<tr>
<td>45 days frozen</td>
<td>Non-Hazardous</td>
<td>1 hour</td>
</tr>
<tr>
<td>168 days refrigerated</td>
<td></td>
<td>1 hour</td>
</tr>
<tr>
<td>168 days frozen</td>
<td></td>
<td>1 hour</td>
</tr>
<tr>
<td>7 area.</td>
<td></td>
<td>1 hour</td>
</tr>
</tbody>
</table>

### Equipment & Environmental BUD Limitations // Hazardous Drug Compounding Requirements

#### Non-Hazardous Drug:
- CAI (compounding aseptic isolator), CACI, or laminar flow hood

#### Hazardous Drug:
- CACI (compounding aseptic containment isolator) – “glove-box hood”

**Beyond the Date Limit:** Maximum BUD as listed above are applicable only if the sterile product is compounded in an ISO-5 environment within an ISO-7 area. A 12 hour maximum BUD limitation is applied when sterile products are compounded in ISO-5 environments within a segregated compounding area (not meeting ISO-7 air quality or 30 air changes per hour) or when the compounding area is undergoing environmental remediation. A 1 hour maximum BUD limitation is applied when the compounding area does not meet the minimum USP 797 environmental standards.

### Compounding Procedure

1. Dilute a ceftazidime 1 gram powder vial with 20.6 mL of *NS* (conc. = 50 mg/mL), vial has overfill.
2. Withdraw 20 mL (conc. 50 mg/mL) ceftazidime and add 24.4 mL of *NS* (new conc. = 1000 mg/44.4 mL, 22.5 mg/mL) or to make 2 syringes, withdraw 1 mL (conc. 50 mg/mL) ceftazidime and add 1.22 mL of *NS* (new conc. = 22.5 mg/mL).
3. Inject the dilution through a 5-micron filter-needle into a sterile empty container.
4. Attach the appropriate connector or pin to the sterile container and withdraw 1 mL (= 22.5 mg) volume into a 1 mL syringe and seal with a syringe cap.
5. This makes 44 x 1 mL syringes (or 2 syringes), label as indicated and store in freezer; thaw before use.

### Observations & Logistical Notes

Freeze after preparation, store in main pharmacy freezer until delivered to ophthalmic surgical centers.

1.5 hours for 44 syringes
10 min for 2 syringes

### Quality Reviews During Compounding & Final Dispensing

1. SOURCE: No evidence of contamination, foreign bodies, bacterial endotoxins, precipitation, appropriate size & needle length
2. COMPONENTS: Container divided at cap, neck, crimps, post sleeve, container trim components, leaks, or other visible damage
3. PRODUCT: Final compounded meets the ordered components, required initial and final diluents, final volume and final concentration.
4. STORAGE & BUD: Storage components were stored correctly, final compounded product labeled for correct storage conditions and BUD
5. LABELS: Labels are clear, barcodes are clear, compounding lot or included, storage conditions and BUD/expiration dates are visible
6. PRODUCT APPROVALS: Confirmation of compounding personnel involved in the process with final approval by the pharmacist.

### References for Compounding, Drug Stabilty, BUD Classifications

1. Micromedex 2018
2. United States Pharmacopeia General Chapter <797> [USP39/NF34]
3. Micromedex 2019
6. CACI (compounding aseptic containment isolator) – “glove-box hood”

USP-NF General Chapter <797> [USP39/NF34] www.ivpsymposium.org
# USP 797: Assigning Beyond Use Dates

<table>
<thead>
<tr>
<th>PRODUCT</th>
<th>BUD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single dose vials (SDV)</td>
<td>6 hours</td>
</tr>
<tr>
<td>Multi-dose vials (MDV)</td>
<td>28 days</td>
</tr>
<tr>
<td>Ampule of medication</td>
<td>1 hour</td>
</tr>
<tr>
<td>Baxter Viaflex bag of IV fluid = 50 mL after overwrap removed</td>
<td>15 days</td>
</tr>
<tr>
<td>Baxter Viaflex bag of IV fluid ≥ 100 mL after overwrap removed</td>
<td>30 days</td>
</tr>
<tr>
<td>Mini-bag of 50 mL volume after overwrap removed</td>
<td>15 days</td>
</tr>
<tr>
<td>Mini-bag of 100 mL volume after overwrap removed</td>
<td>30 days</td>
</tr>
<tr>
<td>Mini-bag of 50 mL volume with ANY drug vial attached</td>
<td>15 days</td>
</tr>
<tr>
<td>Mini-bag of 100 mL volume with MOST drug vials attached</td>
<td>15 days</td>
</tr>
<tr>
<td>Mini-bag of 100 mL volume with SPECIFIC* drug vials attached</td>
<td>30 days*</td>
</tr>
</tbody>
</table>

*cefazolin, cefuroxime, ceftriaxone, aztreonam, zosyn

Reference: Manufacture Package Inserts
In the absence of stability information that is applicable to a specific drug and preparation, the following table presents maximum BUDs recommended for non-sterile compounded drug preparations that are packaged in tight, light-resistant containers and stored at controlled room temperature, unless otherwise indicated.

<table>
<thead>
<tr>
<th>Non-Sterile Formulation Type</th>
<th>Beyond Use Date (BUD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Aqueous Formulation</td>
<td>The BUD is not later than the time remaining until the earliest expiration date of any API or 6 months, whichever is earlier.</td>
</tr>
<tr>
<td>Water-Containing Oral Formulations</td>
<td>The BUD is not later than 14 days when stored at controlled cold temperatures.</td>
</tr>
<tr>
<td>Water-Containing Topical/Dermal and Mucosal Liquid and Semisolid Formulations</td>
<td>The BUD is not later than 30 days.</td>
</tr>
</tbody>
</table>
Non-Sterile Formulation Type | Beyond Use Date (BUD)
--- | ---
Solid dosage forms | BUD 180 days controlled room temperature
**Preserved** aqueous dosage forms | BUD 30 days controlled room temperature
**Non-preserved** aqueous dosage forms | BUD 14 days refrigerated
Non-aqueous dosage forms | BUD 90 days controlled room temperature

- **Solid dosage forms**: Capsules, tablets, granules, powders.
- **Preserved aqueous dosage forms**: An aqueous preparation is one that has a water activity (Aw) of > 0.6 (e.g., emulsions, gels, creams, solutions, sprays, or suspensions).
- **Non-preserved aqueous dosage forms**: Any preparation other than solid dosage forms that have a reduced Aw of ≤ 0.6 (e.g., suppositories, ointments, fixed oils, or waxes).
Compounding & Stability References

Trissel, Handbook on Injectable Drugs. 20th Edition
- ISBN: 978-1585286157
- Drug compatibility in solution, with additives
- Drugs in syringe compatibility
- Y-site injection compatibility (1:1 mixture)

<table>
<thead>
<tr>
<th>Monograph drug name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Solution</td>
</tr>
<tr>
<td>(1)</td>
</tr>
</tbody>
</table>

- Solution in which the test was conducted.
- Manufacturer of the solution.
- Manufacturer of the drug about which the monograph is written.
- Concentration of the drug about which the monograph is written.
- Description of the results of the test.
- Reference to the original source of the information.
- Designation of the compatibility (C) or incompatibility (I) of the test result according to conventional guidelines.
Bing and Nowobilski-Vasilios, Extended Stability for Parenteral Drugs, 6th Edition

- Covers all aspects of determining stability, including the changing elastomeric landscape and the ongoing variability in stability data.
- Nearly all 165 stability monographs completely updated
- Updated chapters on applying stability data in patient care and parenteral nutrition
- Previously unpublished data for specific types of infusion devices and containers Direct communications from drug and device manufacturers, and a focused review of previously published data from practitioners.

https://store.ashp.org/Store/ProductListing/ProductDetails.aspx?productId=597629135
Trissel’s Stability of Compounded Formulations, 6th Edition

• ISBN: 978-1582122960

• Compiles all currently available stability information on drugs in compounded oral, enteral, topical, ophthalmic, and other specialized preparations. It includes monographs on 571 products, including 61 new monographs and 163 monographs

• Each monograph organized categories: Properties, General Stability Considerations, Stability Reports of Compounded Preparations, including repackaging information, Compatibility with Other Drugs and Compatibility with Common Beverages and Foods

• Summaries from 2,043 published articles and books, including 329 new to this edition

• Index of nonproprietary and brand names

https://ebusiness.pharmacist.com/PersonifyEbusiness/Shop-APhA/Product-Details/productId/286040071
Lexi-Comp Drug Information Handbook (and phone app)

• ISBN: 978-1-59195-370-8

• This handbook follows a dictionary-like format, with drug products organized alphabetically and cross-referenced by U.S. and Canadian brand names and index terms.

• Contains 1600 drug monographs, each offering up to 45 fields of information specific to a particular medication.

• Appendix offering helpful treatment guidelines and therapy recommendations, and a Pharmacologic Category Index.

• 1696 Drug Monographs, with up to 45 fields of information

• More than 50 Pages of Appendix Information
AHFS Drug Information Handbook


- Information is evidence-based, reviewed by subject matter experts, and supported by nearly 90,000 references. Every year’s edition is updated with an expanded number of monographs:
  - Interactions, adverse reactions, and cautions, including ongoing revisions addressing opiate safety issues and their role in pain management.
  - Extensive dosage and administration information.
  - Pharmacology and pharmacokinetics.
  - Prescription, OTC, ophthalmic, and dermatologic drugs.
  - Extensive off-label uses and related dosing options.

http://www.ahfsdruginformation.com/ahfs-drug-information/
Review Everything: Standardize, Simplify, Educate

- Manufacturer’s product labeling and data
- Micromedex, Clinical Pharmacology, Lexi-Comp
- AHFS Drug Information
- Trissel’s Stability of Compounded Formulations
- Trissel’s Handbook on Injectable Drugs
- Trissel’s Clinical Pharmaceutics Database
- King Guide to Parenteral Admixtures
- Bing’s Extended Stability of Parenteral Drugs
- USP <797> for appropriate beyond use dates
- Published drug studies and data
- Institute for Safe Medication Practice (ISMP)
- Published stability studies and journal articles
Open Dates & Expiration Dates on MDV
Open Dates & Expiration Dates on PO Bottles
QA & Expiration Dates of Assembled Products
Routine Checking of IV Push Kits
Compounding Program Elements

- Employee Education
- Employee Safety
- Compounding Process
- Quality Assurance
- Regulatory Compliance

Patient Safety
Quality Assurance: Overview

• **End Product Sampling**
  • Sterility Testing
  • Potency Testing

• **Environmental Sampling**
  • Viable Air and Surface Sampling
  • Hazardous Drug Wipe Testing

• **Facility & Equipment Monitoring**
  • Temperatures, Air Pressures, Humidity, Daily & Weekly Cleanings, Eye Wash
  • Compounding Hood Certifications with Non-Viable Air Particle Testing
  • Smoke Pattern Testing of Hoods, Calibration of Equipment

• **Employee Sampling**
  • Media Fill and Fingertip Testing
Quality Assurance: CSP Sterility Testing

• End Product Sampling
  • Sterility Testing

• Take immediate corrective action for “out-of-limit” results

• Document all corrective actions
Quality Assurance: CSP Potency Testing

• End Product Sampling
  • Potency Testing

• Take immediate corrective action for “out-of-limit” results

• Document all corrective actions
Quality Assurance: **Cleaning Chemicals**

- Do you have the appropriate cleaning agents?
  - Sporicidal? Fungicidal? Bactericidal?
  - Sanitizing? Sterilizing?
  - Chemo decontamination?
  - Safe for compounding work surface?
- Are they being used correctly?
- Are they being used in the correct order?
- Are they being used at the appropriate frequency?

See all manufacturer directions and best practice documents. www.ivpnsymposium.org
Quality Assurance: Employee Sampling

- Media-Fill Test
- Gloved Fingertip Test
- Separate tests for each compounding environment
- Take immediate corrective action for “out-of-limit” results
- Document all corrective actions
Quality Assurance: **Employee Sampling**

- Positive controls
- Education for those reviewing the media results
Quality Assurance: Viable Air Sampling

(+) Pressure
ISO-7
30 ACPH

AIR FLOW

CLEAN SIDE OF ANTE ROOM

ISO-5 HLFW
Non-HD CLEAN ROOM

Sink
BENCH
Sterile-LOD
DIRTY SIDE OF ANTE ROOM

AIR FLOW

(-) Pressure
ISO-7
30 ACPH

AIR FLOW

HAZARDOUS CLEAN ROOM

CHEMO DRUG STORAGE
ISO-5 Glovebox

CHEMO Fridge
SUPPLY STORAGE

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Quality Assurance: Viable Air Sampling

1. ISO-5 HLF
2. Non-HD CLEAN ROOM
3. Sterile-LOD
4. CLEAN SIDE OF ANTE ROOM
5. (+) Pressure ISO-7 30 ACPH
6. BENCH
7. HD-LOD
8. HAZARDOUS CLEAN ROOM
9. ISO-5 Glovebox

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Quality Assurance: Viable Air Sampling

- Volumetric air sampler
- Samples taken under dynamic conditions (while compounding)
- 500 liters (current USP 797)
- 1000 liters (draft USP 797/29/18)

USP-NF General Chapter <797> [USP39/NF34]
Quality Assurance: Viable Air Sampling (bacterial)

- **Test:** Bacterial
- **Agar:** TSA
- **Incubator:**
  - $30^\circ - 35^\circ C \times 48$ hr (then)
  - $20^\circ - 25^\circ C \times 5$ days

Proposed USP 797 draft as of 7/27/2018
Quality Assurance: **Viable Air Sampling (fungal)**

- **Test:** Fungal
- **Agar:** Malt Extract
- **Incubator:**
  - $26^\circ - 30^\circ C \times 5 - 7$ days

**USP-NF General Chapter <797> [USP39/NF34]**

www.ivpnsymposium.org
Quality Assurance: **Viable Surface Sampling**
Quality Assurance: Viable Surface Sampling

1. Non-HD CLEAN ROOM
2. ISO-5 HLFW
3. ISO-5 HLFW
4. (+) Pressure ISO-7 30 ACPH
5. CLEAN SIDE OF ANTE ROOM
6. Sink
7. (+) Pressure ISO-7 30 ACPH
8. CHEMO DRUG STORAGE
9. SUPPLY STORAGE
10. ISO-5 Glovebox
11. HD-LOD
12. Sterile-LOD
13. DIRTY SIDE OF ANTE ROOM
14. BENCH
15. (+) Pressure ISO-7 30 ACPH
16. AIR FLOW
17. AIR FLOW
18. AIR FLOW
19. HAZARDOUS CLEAN ROOM

www.ivpnsymposium.org
Quality Assurance: **Viable Surface Sampling**

- **Test:** Bacterial
- **Agar:** TSA
- **Incubator:**
  - $30^\circ - 35^\circ C \times 48$ hr
  - (then)
  - $20^\circ - 25^\circ C \times 5$ days

Proposed USP 797 draft as of 7/27/2018
Quality Assurance: **Viable Surface Sampling**

- **Test:** Fungal
- **Agar:** Malt Extract
- **Incubator:**
- **26° – 30°C x 5 – 7 days**
Quality Assurance: Viable Surface Sampling
### Viable AIR Sampling

<table>
<thead>
<tr>
<th>Type of Air</th>
<th>Alert Level</th>
<th>Action Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>ISO Class 5 Air</td>
<td>1 CFU per plate</td>
<td>&gt; 1 CFU per plate</td>
</tr>
<tr>
<td>ISO Class 7 Air</td>
<td>&gt; 5 CFUs per plate</td>
<td>&gt; 10 CFUs per plate</td>
</tr>
<tr>
<td>ISO Class 8 Air</td>
<td>&gt; 50 CFUs per plate</td>
<td>&gt; 100 CFUs per plate</td>
</tr>
</tbody>
</table>

### Viable SURFACE Sampling

<table>
<thead>
<tr>
<th>Type of Air</th>
<th>Alert Level</th>
<th>Action Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>ISO Class 5 Air</td>
<td>&gt; 1 CFU per plate</td>
<td>&gt; 3 CFU per plate</td>
</tr>
<tr>
<td>ISO Class 7 Air</td>
<td>&gt; 2 CFUs per plate</td>
<td>&gt; 5 CFUs per plate</td>
</tr>
<tr>
<td>ISO Class 8 Air</td>
<td>&gt; 50 CFUs per plate</td>
<td>&gt; 50 CFUs per plate</td>
</tr>
</tbody>
</table>

- Take immediate corrective action for “out-of-limit” results
- Document all corrective actions

Proposed USP 797 draft as of 7/27/2018
Sampling is performed before weekly or monthly full clean, or more frequently depending on sample growth trends.

<table>
<thead>
<tr>
<th>Day</th>
<th>Swab</th>
<th>Plate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sunday</td>
<td>S1</td>
<td>P1</td>
</tr>
<tr>
<td>Monday</td>
<td>S2</td>
<td>P6</td>
</tr>
<tr>
<td>Tuesday</td>
<td>S3</td>
<td>P2</td>
</tr>
<tr>
<td>Wednesday</td>
<td>S4</td>
<td>P3</td>
</tr>
<tr>
<td>Thursday</td>
<td>S5, S6</td>
<td>--</td>
</tr>
<tr>
<td>Friday</td>
<td>S7</td>
<td>P4</td>
</tr>
<tr>
<td>Saturday</td>
<td>S8</td>
<td>P5</td>
</tr>
</tbody>
</table>
Quality Assurance: Sample Failures

- Surfaces samples failed!
- Bacterial samples = 8 CFU
- What do I do?
Quality Assurance: Sample Failures

• Surfaces samples failed!
• Bacterial samples = 8 CFU
• What do I do?
  • Clean the area thoroughly
  • Review sources of contamination
  • Resample locations
Review Sources of Contamination

- **Sources of Contamination**: Cardboard, clothes, clean room shoes, mouse pads, non-cleanroom cloth chairs, etc.
- **Bring Only Necessary Items in the Cleanroom**: Only bring items needed for your process should be in the room, and they should be cleanable.
- **Other Factors**: Improper, missing or used/old gowning materials, controlling access to the area, a need for increased cleaning frequency and/or improved cleaning method.
- **Review Cleaning Process**: Terminal cleaning includes the cleaning out of storage bins, cleaning on top of door frame, top of equipment, and underneath shelving.
Quality Assurance: Re-Sampling Plan

Environmental Surface Sampling: **BACTERIAL** Location: **ONCOLOGY** - (Air-Lock Sampling)

Collected by: ________________ Reviewed by: ________________

QUARTER: __________; Test Date: __________

Media Type: TSA (w/ Lecithin and Polysorbate 80)

Incubation: 30 - 35°C x (48 - 72 hours)

Media Manufacturer: QI Medical; Lot #: __________; Expiration: __________

<table>
<thead>
<tr>
<th>S#</th>
<th>Description</th>
<th>bCFU Result</th>
<th>Alert Level</th>
<th>Action Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Airlock 1 - Sample B1</td>
<td>0</td>
<td>&gt; 2 CFU</td>
<td>&gt; 5 CFU</td>
</tr>
<tr>
<td>2</td>
<td>Airlock 1 - Sample B2</td>
<td>0</td>
<td>&gt; 2 CFU</td>
<td>&gt; 5 CFU</td>
</tr>
<tr>
<td>3</td>
<td>Airlock 2 - Sample B3</td>
<td>0</td>
<td>&gt; 2 CFU</td>
<td>&gt; 5 CFU</td>
</tr>
<tr>
<td>4</td>
<td>Airlock 2 - Sample B4</td>
<td>0</td>
<td>&gt; 2 CFU</td>
<td>&gt; 5 CFU</td>
</tr>
</tbody>
</table>
Quality Assurance: HD Wipe Testing

Non-HD CLEAN ROOM

ISO-5 HLFW

(+) Pressure
ISO-7
30 ACPH

Air Flow

Sink

Bench

Sterile-LOD

DIRTY SIDE OF ANTE ROOM

Air Flow

HD-LOD

CHEMO Fridge

Supplies Storage

CHEMO DRUG STORAGE

HAZARDOUS CLEAN ROOM

(+/-) Pressure
ISO-7
30 ACPH

ISO-5 Glovebox

1

Air Flow

Air Flow

IRIS-5 HLFW

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Quality Assurance: HD Wipe Testing

• **Testing Locations**: all areas where HD drugs
  • Hoods, floors, pass-throughs, counters, carts, storage, shelves
  • Workstations in pharmacy, keyboards, chairs, etc.
  • Workstations outside of pharmacy (nursing, offices)
  • Areas near disposal areas, or waste holding areas

• **Frequency**: quarterly (per sampling policy)

• **When**: before decontamination of the work surfaces

• **Recordkeeping**: document all sample sites, results, follow trends

• **Review**: pharmacy, nursing, other dept. representatives

Kienle PC, Fortier CR, Kastango ES. The need for wipe analysis to address hazardous drug surface contamination. BD Publication 2018
Quality Assurance: HD Wipe Testing

- Sampling kits test for many common drugs:
  - Busulfan
  - Cyclophosphamide
  - Cytarabine
  - Daunorubicin
  - Docetaxel
  - Doxorubicin
  - Etoposide
  - Fluorouracil
  - Ifosfamide
  - Methotrexate
  - Paclitaxel
  - Platinum Analogues
  - Vincristine
Quality Assurance: **HD Wipe Testing**

- Handheld device
- Results within 10 min
- Tests for 2 common drugs:
  1. Methotrexate
  2. Doxorubicin
- Logs results to track trends
- Allows for routine testing

### Quality Assurance: Temperature Monitoring

<table>
<thead>
<tr>
<th>EQUIPMENT</th>
<th>ISO CLASS</th>
<th>TEMPERATURE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incubator (calibrated)</td>
<td>--</td>
<td>30° to 50° C (86° to 122° F)</td>
</tr>
<tr>
<td>TSA Media (bacterial)</td>
<td>--</td>
<td>30° to 35° C (86° to 95° F)</td>
</tr>
<tr>
<td>Malt Extract (fungal)</td>
<td>--</td>
<td>26° to 30° C (78° to 86° F)</td>
</tr>
<tr>
<td>Refrigerator</td>
<td>--</td>
<td>2° to 8° C (36° to 46° F)</td>
</tr>
<tr>
<td>Freezer (per USP 797)</td>
<td>--</td>
<td>-25° to -10° C (-13° to 14° F)</td>
</tr>
<tr>
<td>Freezer (Baxter products)</td>
<td>--</td>
<td>-30° to -20° C (-22° to -4° F)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ENVIRONMENTS</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Clean/Buffer Room</td>
<td>ISO 7</td>
<td>18° to 20° C (65° to 68° F)</td>
</tr>
<tr>
<td>Ante Room</td>
<td>ISO 8</td>
<td>18° to 20° C (65° to 68° F)</td>
</tr>
<tr>
<td>Storage Room (general environment)</td>
<td>ISO &gt; 8</td>
<td>20° to 25° C (68° to 77° F)</td>
</tr>
<tr>
<td>Outtake Room</td>
<td>ISO &gt; 8</td>
<td>18° to 20° C (65° to 68° F)</td>
</tr>
</tbody>
</table>
Quality Assurance: **Air Pressure Monitoring**

Air pressure of at least (+) 0.02 inches water column to each space
Quality Assurance: Air Pressure Monitoring

• Non-Hazardous Compounding Area
  • 0.02 (+) iwc related to other spaces
  • 12 to 30 air changes per hour

• Hazardous Compounding Area
  • 0.01 to 0.03 (-) iwc
  • 12 to 30 air changes per hour

• Monitoring of Compounding Hoods
Quality Assurance: **Humidity Monitoring**

- No humidity requirements in current USP 797 (as of 2018).
- Draft USP 797 (for 2019) specifies humidity less than 60% for the compounding suite.
- Specifications need a range:
  - Selected 30 – 60% in SOP
Record Keeping & Review

• How are you organizing and storing your quality assurance records?
  • Electronic only?
  • Paper only?
  • Both?

• Are you reviewing the reports that are generated or do they just get filed away?
• Who else is reviewing the reports?
Record Keeping & Review
Compounding Program Elements

Employee Education

Patient Safety

Employee Safety

Quality Assurance

Compounding Process

Regulatory Compliance
Employee Education: *Training Program*

- Gowning and garbing (PPE)
- General compounding education
- Advanced training for advanced processes
- Training on all compounding equipment
- Correct cleaning procedures
- Direct hands-on, didactic instruction
- Readings on compounding (with video)
- Reading of regulations and hospital’s policy and procedure

USP-NF General Chapter <797> [USP39/NF34]  www.ivpnsymposium.org
Employee Education: Validation & Documentation

- Does the training match your operation?
- Is the training high quality?
- **Written exam**, verbal question & answer
- Direct observation of competency
- Regular evaluations of each compounder’s competency
- Is the training performed routinely and documented?
- Are the training records readily available?
- Testing of employee with media-fill and fingertip tests (also part of QA monitoring) and **positive controls performed/recorded**
Employee Education: Sample Topics

- Basic syringe technique; negative pressure technique
- Needle/syringe dead space
- Priming infusion lines for chemotherapy bags
- Breaking and using ampules
- First air, arrangement of items in the hood
- Equipment calibrations
- Calculations
- Cleaning the hood and appropriate use of chemicals
Employee Education: **PPE and HD Containment**

- Correct order of hazardous PPE placement and removal
- Understanding non-HD and HD lines of demarcation
- Safe handling of hazardous drugs
- Using chemo deactivating agents
- Hazardous spill kit
- Hazardous vapor respirators
- Appropriate use of CSTDs
Employee Education: **Compounding Equipment**

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[Image of compounding equipment]
Davis, Karen. Sterile Processing for Pharmacy Technicians. 2014

- ISBN: 9781455711277
- Facilities, Equipment, and Supplies
- Routes of Administration
- Types of Compounded Sterile Preparations
- Calculations for Sterile Compounding
- Sterile Compounding Process
- Compatibility, Stability, and Beyond-Use Dating
- Quality Assurance
- Total Parenteral Nutrition (TPN)
- Chemotherapy and Hazardous Drugs

- ISBN: 978-1-58255-837-0
- Very comprehensive topic list
- Fundamentals of pharmaceutical calculations
- International system of units, pharmaceutical measurements
- Density, specific gravity, specific volume
- Percentage, ratio strength, expressions of concentrations
- General dose calculations
- Dose calculations with patient parameters (pediatrics, geriatrics)
- Clinical calculations (heparin, CRCL based renal doses)
- Electrolytes (millequivalents, millimoles, osmolarity), etc.
Sakai J, Kasun L. Pharmacy Calculations: An Introduction for Pharmacy Technicians. ASHP 2012

- Basic numbers (introductory)
- Metric system, apothecary, time, temperatures
- Reading prescriptions
- Using critical thinking skills and solving problems
- Ratios, proportions, dose calculation
- Percent strength and dilutions, formulas and compounding
- Infusion and injections
- Business math
Pickar GD, Pickar-Abernethy A. Dosage Calculations. 9e (2015)

- ISBN: 978-1439058473
- Comprehensive math review
- Full color drug labels
- Critical thinking assessments
- Basic and advanced calculations
- Intravenous adult and pediatric calculation examples
- Unique three-step teaching layouts (Convert, Think, Calculate)
- Teaches logic in calculating to reduce medication errors
- Clinical simulations and reasoning skill scenarios
- Test questions are formatted like graduate licensure exams

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Calculations Study Books


- Concentrations, dilutions, dose calculations
- Density, specific gravity, significant figures
- Infusion rates, concentrations (minor mention only)
- Primarily uses proportions to present math problems and the steps to solve them throughout the book
- Practice questions throughout the book
- Book references British Pharmacopeia and BNF
- Provides access to online videos
- Critique: good reference, needs more hospital topics

- ISBN: 978-0853696025
- For students and pharmacists needing a math refresher
- Simple numbers, ratios, metric conversions, dilutions, formulations, dosing, density, displacement, molecular weights, parenteral solutions
- Does NOT include Cockcroft-Gault, Henderson-Hasselbalch, and other advanced or formula-based calculations
MCQs in Pharmaceutical Calculations. Pharmaceutical Press 2009

- ISBN: 978-0-85369-836-4
- For **students** and pharmacists needing a math refresher
- Basic formulas for manipulation, dilutions, dosing
- Pharmacokinetics, pharmaceutical chemistry
- Book is mostly a collection of practice questions and helpful steps in solving them
- Questions relevant to community and hospital practice
- The authors describe this as a practice question book and NOT a reference book
Critical Point

- [https://www.criticalpoint.info/](https://www.criticalpoint.info/)
- Sterile Compounding Training
- Compliance Tools
  - Standard operating procedures
  - Forms
  - Resources
- Custom Training
- Blogs and newsletters
- Webinars

“Our mission is to increase patient safety by delivering engaging educational programming that results in a measurable change in performance in the work setting, facilitating achievement of desired patient and business outcomes.”
Intravenous and Parenteral Nutrition (IVPN) Academy: Cleveland Clinic Abu Dhabi

• Facilitated by experienced sterile compounding specialists
• Teaches current sterile compounding and best practice through presentations, e-learning in collaboration with Critical Point, didactic lectures, hands-on training in a state-of-the-art sterile preparation center

• Trainees learn:
  • Cleanroom physical design and layout
  • Engineering controls and airflow science
  • Personnel media fill testing
  • Principles associated with workflow, cleaning, environmental sampling, validation, staff training, documentation, policy/procedure

• Application: https://fs10.formsite.com/CCADclinicaltraining/form96/index.html
Employee Education: Working Speed

• Haste makes waste, and drug errors!
• Double check everything!
• Caution with high-alert medications!
Employee Education: High Alert Drug List

How are these handled in your hospital?

• Double signatures?

https://www.ismp.org/recommendations/high-alert-medications-acute-list
Employee Education: High Alert Drugs & Safety

READ LABELS CAREFULLY
Employee Education: Avoid Distractions

- Phone??
- Music??
- Video on phone??
Employee Education: Review Processes

- Regularly review current processes for needed improvements
- Review local errors
- Review published errors
- Inspect area for similar risks
- Summarize risk for staff
Conclusion

• Select appropriate BUDs and ensure staff (pharmacy, nursing, etc.) are educated on the meaning of BUD related terminology.

• Design a robust quality assurance plan to maintain patient safety.

• Review your staff’s education program to provide current and engaging information for overall improvement.

• Emphasize the goal of it all: **PATIENT SAFETY!**

• Share information and educate others.

• **Become the expert in your pharmacy!!!**
References: Books & Guidelines

• USP 797 – Pharmaceutical Compounding Sterile Preparations [USP 40 – NF35] 2017
• USP 795 – Pharmaceutical Compounding Non-Sterile Preparations [USP 40 – NF35] 2017
• USP 800 – Hazardous Drugs Handling in Healthcare Settings [USP 40 – NF35] 2017
• USP 1231 – Water for Pharmaceutical Purposes [USP 40 – NF35] 2017
• Trissel’s Handbook on Injectable Drugs
• Extended Stability of Parenteral Drugs (Bing)
• NIOSH List of Hazardous Drugs 2016
• ISMP Institute for Safe Medication Practice
• ASHP Guidelines on Compounding Sterile Preparations
• ASHP Guidelines on Quality Assurance for Pharmacy Sterile Products
• Kienle PC, Fortier CR, Kastango ES. The need for wipe analysis to address hazardous drug surface contamination. BD Publication 2018
Questions?

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