

Clinical Pearls 2010

Thomas Johns, PharmD

Topics

- Antibiograms
- Compounded Sterile Products (CSPs)

Antibiogram

ANTIBIOTIC SUSCEPTIBILITY OF COMMON ORGANISMS

Data are percent Susceptible
January 2002 - June 2003

Organ Organism	No. of Isolates	Amikacin	Ampicillin	Ampicillin/Sulbactam	Aztreonam	Cefepime	Clindamycin	Colistin	Colistin/Imipenem	Colistin/Polymyxin B	Ceftazidime	Ceftazidime/Avopivoxin	Ceftriaxone	Ciprofloxacin	Meropenem	Vancomycin	Linezolid	Trimethoprim-Sulfamethoxazole	Tigecycline	Chloramphenicol
<i>Acinetobacter baumannii</i>	83	84				52	75		72	71			81	95	92	92	70	80	64	
<i>A. baumannii</i> (n=10)	27	10			0	11	50		15	15			4	81	72	78	50	4	78	
<i>Citrobacter freundii</i>	37	100	51	24	86	81	78	19	88	87	73	89	92	100	100	97	78	85	76	
<i>Citrobacter koseri</i>	42	100	0	93	93	95	88	88	83	100	79	98	95	100	100	96	80	88	88	
<i>Enterobacter aerogenes</i>	58	100	15	3	93	92	80	14	85	87	69	85	95	96	100	95	85	87	97	
<i>Enterobacter cloacae</i>	170	88	9	5	75	73	78	2	83	84	38	59	94	99	99	89	88	83	88	
<i>Escherichia coli</i>	1084	88	51	82	94	94	84	88	74	88	91	98	89	99	99	99	87	88	80	73
<i>Escherichia coli</i> (n=10)	53	100	11	92	92	94	86	49	88	88	87	98	96	100	100	96	84	88	96	
<i>Escherichia coli</i> (n=10)	401	88	4	93	93	93	83	80	83	84	88	98	94	99	99	96	83	84	89	
<i>Morganella morganii</i>	38	100	3	8	66	80	87	5	84	100	15	97	80	97	100	85	82	87	67	
<i>Providencia stuartii</i>	203	100	87	99	94	97	87	85	81	87	97	99	91	99	100	89	88	82	82	
<i>Pseudomonas aeruginosa</i>	442	85			76	22	80		78	87			83	69	82	85	87	80		
<i>Pseudomonas cepacia</i>	14		93						100											100
<i>Serratia marcescens</i>	82	100	9	4	87	85	83	0	88	85	0	98	95	96	100	73	83	85	94	
<i>Serratia marcescens</i> (n=10)	58						41										44		97	

Source: CDC, National Nosocomial Infection Survey (NNIS)

Antibiograms

- Summary of antimicrobial susceptibility in an institution for the purpose of trending resistance
- Acceptable for empiric use: $\geq 80\%$
- Often reported by ICU and general floor
- Do not include duplicate isolates
- Need to follow trends not just one report
- Formulary tool?
- May be used to define “drug of choice” for hospital
- How often should it be reported?

Typical clinical questions...

- What antibiotic should I use to treat Ms. Smith's UTI?
- I have a gram's stain result for 2+ GNR from a sputum culture. Which antibiotic should I prescribe?

Interpretation of results...

- “S” – Susceptible
 - ◆ Likely to achieve optimal therapeutic outcome with usual doses of antibiotic
- “I” – Intermediate
 - ◆ May achieve optimal therapeutic outcome with maximal doses or infections where drug concentrates at that site
- “R” – Resistant
 - ◆ Not likely to achieve optimal therapeutic outcome

Antibiotic Cost / Day (2009)

Antibiotics (IV and PO)	Approx. Cost/day	Antibiotics (IV and PO)	Approx. Cost/day
Aminoglycosides		Macrolides	
Gentamicin	\$2.84	Erythromycin (V)	\$1.86
Tobramycin	\$12.00	Erythromycin (po)	\$0.40
Amikacin	\$8.50	Azithromycin (V)	\$18.15
Cephalosporins		Azithromycin (po)	\$5.14
Cefazolin	\$1.50	Clarithromycin	\$5.42
Cefepime	\$22.00	Other Antibiotics	
Cephalexin (po)	\$0.55	Clindamycin (IV)	\$16.00
Cefuroxime (po)	\$10.12	Clindamycin (po)	\$11.70
Cefuroxime (V)	\$17.10	Doxycycline (IV)	\$11.20
Ceftriaxone	\$21.10	Doxycycline (po)	\$0.16
Cefotaxime	\$20.00	Linezolid (IV)*	\$112.82
Ceftazidime	\$20.80	Linezolid (po)*	\$68.40
Miscellaneous B-lactam		Metronidazole (V)	\$2.00
Imipenem	\$52.24	Metronidazole (po)	\$0.16
Aztreonam	\$50.80	Netilmicin	\$1.88
Meropenem*	\$59.32	Synsard*	\$334.00
Penicillin		SKINIP (IV)	\$2.48
Penicillin G (IV)	\$30.00	SKINIP (po)	\$0.20
Pen VK (po)	\$0.21	Vancocin (IV)	\$13.20
Amoxicillin (po)	\$0.33	Vancocin (po)	\$17.00
Augmentin (po)	\$7.00	Antifungals	
Ampicillin (po)	\$0.30	Amphotericin B	\$7.32
Ampicillin (IV)	\$2.00	Ampho. B Lipid*	\$274.00
Clacilin	\$8.40	Caspofungin	\$250.00
Dicloxacillin (po)	\$0.22	Fluconazole (IV)	\$67.00
Empenoc*	\$44.25	Fluconazole (po)	\$9.30
Meropenem	\$35.68	Isavuconazole	\$37.00
Quinolones		Itraconazole	\$11.12
Ciprofloxacin (V)	\$25.00	Ketoconazole	\$2.61
Ciprofloxacin (po)	\$6.64	Voriconazole	\$125.00
Gatifloxacin (V)	\$15.00	Antivirals	
Gatifloxacin (po)	\$6.72	Acyclovir (IV)	\$11.40
*Dosing based on 70kg patient		Acyclovir (po)	\$1.50
*ID consult required		Ganciclovir (IV)	\$48.70
		Ganciclovir (po)	\$38.24
		Neovir	\$1,079.00

* ID consult required

Compounded Sterile Products

- Four specific categories
 - ◆ Low, Medium, High-risk level and Immediate Use
- Categories assigned based on potential for microbial contamination
- ISO = International Organization of Standardization

Table 1. ISO Classification of Particulate Matter in Room Air (limits are in particles of 0.5 μm and larger per cubic meter [current ISO] and cubic feet [former Federal Standard No. 209E, FS 209E])^{*}

Class Name		Particle Count	
ISO Class	U.S. FS 209E	ISO, m^3	FS 209E, ft^3
3	Class 1	35.2	1
4	Class 10	352	10
5	Class 100	3,520	100
6	Class 1,000	35,200	1,000
7	Class 10,000	352,000	10,000
8	Class 100,000	3,520,000	100,000

^{*} Adapted from former Federal Standard No. 209E, General Services Administration, Washington, DC, 20407 (September 11, 1992) and ISO 14644-1:1999, Cleanrooms and associated controlled environments—Part 1: Classification of air cleanliness. For example, 3,520 particles of 0.5 μm per m^3 or larger (ISO Class 5) is equivalent to 100 particles per ft^3 (Class 100) ($1 \text{ m}^3 = 35.2 \text{ ft}^3$).

Compounded Sterile Products

- Immediate use category
 - ◆ Intended only for emergency or immediate patient administration; not intended for storage (eg. batch)
- Low risk
 - ◆ Compounding entirely within ISO5 or better quality air using sterile ingredients; ISO class 5 device within ISO class 7 environment
 - ◆ CAI (ISO class 5 device) with proper documentation
- Low risk with 12 hour or less BUD
 - ◆ Designed to accommodate satellite pharmacies with LAFH or CAI (without proper documentation) that cannot be located within an ISO class 7 buffer area
 - ◆ All cleansing and garbing requirements apply
 - ◆ The segregated compounding area shall not be in a location that has unsealed windows or doors that connect to the outdoors or high traffic flow, or that is adjacent to construction sites, warehouses, or food preparation







Compounding
Aseptic
Isolators (CAI)



Compounded Sterile Products

- Immediate use category
 - ◆ Intended only for emergency or immediate patient administration; not intended for storage (e.g. batch)
- Low risk
 - ◆ Compounding entirely within ISO5 or better quality air using sterile ingredients; ISO class 5 device within ISO class 7 environment
 - ◆ CAI (ISO class 5 device) with proper documentation
- Low risk with 12 hour or less BUD
 - ◆ Designed to accommodate satellite pharmacies with LAFH or CAI (without proper documentation) that cannot be located within an ISO class 7 buffer area
 - ◆ All cleansing and garbing requirements apply
 - ◆ The segregated compounding area shall not be in a location that has unsealed windows or doors that connect to the outdoors or high traffic flow, or that is adjacent to construction sites, warehouses, or food preparation

Compounded Sterile Products

- Medium risk

- ◆ Compounding similar to low risk but requires more package manipulations or sterile products are combined for administration to multiple patients (e.g. batch)

- High risk

- ◆ Compounding sterile products from non-sterile ingredients

Compounded Sterile Products

- Expiration dating (manufacturers expiration date)
- Beyond-use-dates (BUD compounded preparations) – based on microbiologic limits determined by risk category

Compounded Sterile Products

■ Beyond-use-dates

- ◆ Low risk
 - ◆ Room temp = 48 hours; Refrigerated = 14 days
- ◆ Low risk with 12 hour or less BUD
 - ◆ Room temp = 12 hours; Refrigerated = 12 hours
- ◆ Medium risk
 - ◆ Room temp = 30 hours; Refrigerated = 9 days
- ◆ High risk
 - ◆ Room temp = 24 hours; Refrigerated = 3 days
- ◆ Immediate use category
 - ◆ Administration begins not later than one hour from completion of compounding





**AUTOMATIC
CAUTION
DOOR**









U.S. PHARMACOPEIA

USP General Chapter <797> Frequently Asked Questions

Revised January 12, 2010

Responses have been provided for informational purposes only, and should not be construed as an official interpretation of USP text or relied on to demonstrate compliance with USP standards or requirements.

- ▶ [General](#)
- ▶ [Microbial Contamination Risk Level Categories](#)
- ▶ [Beyond-Use Date \(BUD\)](#)
- ▶ [Cleaning and Disinfecting the Compounding Area](#)
- ▶ [Personnel Cleansing and Garbing](#)
- ▶ [Hazardous Drugs as CSPs](#)
- ▶ [Radiopharmaceuticals as CSPs](#)
- ▶ [Environmental Quality and Control](#)
- ▶ [Education and Training](#)

CSP FAQ

- **Q: Does the spiking of an IV bag, such as Normal Saline, constitute sterile compounding?**
- **A: Spiked IV bags containing no added drugs, one added drug, or two added drugs would be either Immediate-Use, Low-Risk Level with 12-Hour Beyond-Use Date, or Low-Risk Level CSPs, depending on the environmental quality and personnel cleansing and garbing.**

CSP FAQ

- **Q: What types of sterile compounds can nurses prepare on the floor? Can they draw up IV push medications?**
- **A: Only Immediate-Use CSPs (Compounded Sterile Preparations) may be prepared in worse (dirtier) than ISO Class 5 environments, such as in clinical patient care areas. Refer to the Immediate Use CSPs section for the six specific criteria.**

CSP FAQ

- **Q: Can nurses draw up IVP medications on the nursing unit? Can they keep the left over drug in a syringe in the patient's medication drawer for future dosing?**
- **A: Intravenous medications prepared in worse (dirtier) than ISO Class 5 environments are subject to the standards for Immediate-Use CSPs. Immediate-Use CSPs cannot be stored.**

CSP FAQ

- **Q: Is there a limit of how many times a vial can be entered by a nurse using a single dose vial on a nursing unit within 24 hours?**
- **A: This practice qualifies as an Immediate-Use CSP. A maximum of two stopper entries is permitted within one hour from when the preparation began for administration to the same patient.**

CSP FAQ

- **Q: Immediate use CSPs must be administered within one hour following preparation. Must administration be completed within that same hour? With low-risk level CSPs with 12 hour BUD, must administration be completed within those 12 hours?**
- **A: Administration of Immediate-Use CSPs must begin within 1 hour from the start of their preparation; there is no requirement for the duration of administration. For Low-Risk Level CSPs with 12-Hour or Less BUD, there administration must begin within 12 hours from the start of compounding, but there is no administration duration requirement.**

CSP FAQ

- **Q: Does the 28 day expiration on multi-dose vials apply to their use in additional compounding, or does it apply to only administration of that preparation?**
- **A: 28 days is the USP chapter <51> testing requirement for Multiple-Dose Containers to be used under any conditions. The BUD on some products may be labeled more or less than 28 days, at the discretion of the manufacturer.**

CSP FAQ

- **Q: Nursing is known to mix IVPB way ahead of time for administration. What is the BUD?**
- **A: The BUD for intravenous piggyback (IVPB) infusions depends on the conditions under which they were prepared. For example, when prepared under conditions of Immediate-Use CSPs, infusion must start within 1 hour of starting to prepare the CSP with no time limit to finish the infusion; when prepared under conditions of Low-Risk Level CSPs with 12-Hour or Less BUD, infusion must start within 12 hours of preparing the CSP with no time limit to finish the infusion; when prepared under conditions of Low-Risk Level CSPs, BUD is 48 hours at controlled room temperature (see USP General Notices and Requirements), 14 days at cold temperature (see USP General Notices and Requirements), and 45 days in solid frozen state between -25° and -10° , in the absence of direct sterility testing evidence that supports longer BUDs.**

CSP FAQ

- **Q: If a commercially available IV fluid (i.e., Lactated Ringers or Normal Saline) is spiked in anticipation of emergent administration, for example in an ambulance, trauma emergency bay or a trauma OR room, does the 1 hour expiration time apply to this situation?**
- **A: Yes. Since the spiking of an IV bag is considered sterile compounding, administration within the one hour time limit would be applicable. The individual performing this task should use appropriate aseptic technique and should perform (if possible) a thorough hand sanitization.**

CSP FAQ

- **Q: Do healthcare practitioners preparing immediate use parenteral products need to gown up, including gloves and mask?**
- **A: No. Immediate use compounding is exempt from all requirements of the Chapter. That does not preclude the process of performing scrupulous hand hygiene and adhering to appropriate proper aseptic compounding technique.**