

# Drug stability testing in Hong Kong – lessons to share



**Dr TSANG Kay Yan**

*MBChB (CUHK), MRCP(UK), PDipID(HKU)  
FHKCP, FHKAM(Medicine), FRCP(Gasg), FRCP(Edin)*

**Associate Consultant**

**Department of Medicine & Geriatrics  
Princess Margaret Hospital , HKSAR**

# Outline

- 1. Healthcare burden faced in Hong Kong**
- 2. Inception of OPAT service @ Princess Margaret Hospital, Hong Kong**
- 3. Introduction of elastomeric devices**
- 4. Setting up local drug stability database**
  - Why should we bother it? How to start off?**
  - What are the details of drug stability methodology and results ?**
  - What hurdles have we encountered ?**
  - How should we address and overcome such?**
- 5. Challenges and Opportunities**

# ***Healthcare burden in Hong Kong***

# Emergency attendance Bed Occupancy in Medicine

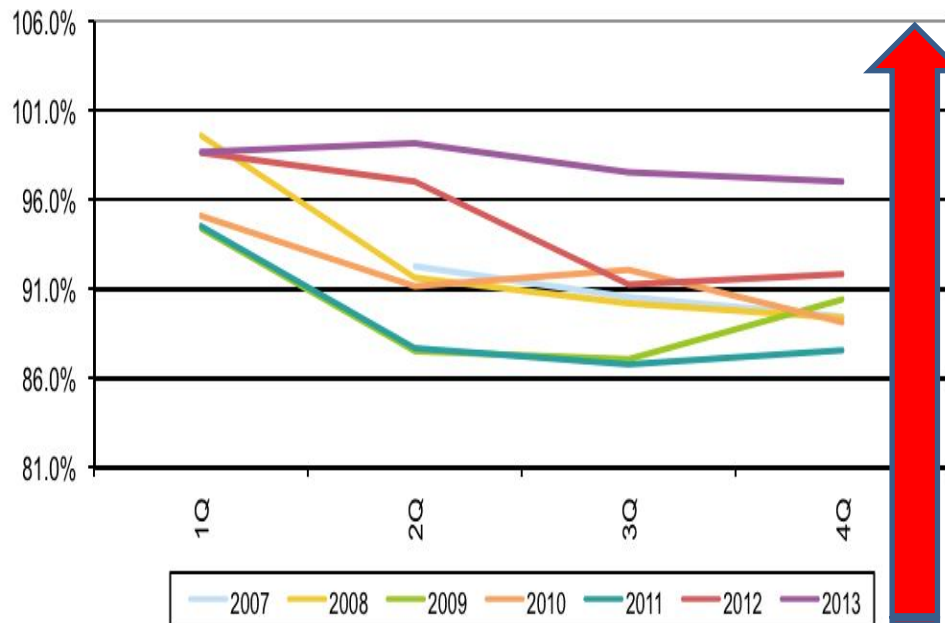
HA Overall - Average number of A&E first attendance per day  
in acute hospitals in 2013 (up to 14 Dec)

二零一三年 (截至十二月十四日)  
公立急症醫院急症室平均每天首次求診數字



A&E: Accident and Emergency Department  
Info source: Service Statistics & Review, HAHO; Hong Kong Observatory

Monthly Trend of Inpatient Bed Occupancy Rate  
[HA Overall, MED, Acute, Quarterly, 2007-2013]





# Bed occupancy in Medicine, PMH

## Department of M&G, PMH Daily Bed Situation after All Totally Discharged for the Month of January 2014

Date	Total no. of Patients (A)		Extra Patients		No. of Admissions		Discharges (Incl. Confirmed T/O other Dept/ Hosp and Death)						Occupancy Rate after all discharged		Other Information											
							Already Discharged		Pending Discharge (B)		Total Discharge				Outflow other Dept	LKB						OLMH				
							M		F		M		F			M		F		Called		Confirmed		Waiting		Confirmed
	M	F	M	F	C/C	E/C	M	F	M	F	M	F	M	F		M	F	M	F	M	F	M	F	M	F	
1	214	200	38	51	7	74	1	1	9	5	10	6	115%	128%	26	14	3	3	2	3	40	45	0	0	0	0
2am	236	209	59	57	2	61	6	1	20	25	26	26	122%	121%	25	20	3	2	2	1	39	43	0	0	0	1
2pm	223	204	46	52	2	61	24	25	26	19	50	44	111%	122%	23	20	3	3	3	2	41	44	0	0	1	3
3am	251	220	74	68	12	106	3	2	33	21	36	23	123%	131%	25	22	6	0	6	0	43	47	0	0	2	5
3pm	244	214	67	62	12	106	25	14	34	39	59	53	119%	115%	26	20	6	3	5	3	43	51	1	0	4	6
4	232	201	55	49	12	72	6	4	35	16	41	20	111%	122%	27	20	2	2	2	2	48	46	1	0	3	5
5	207	193	30	41	7	67	4	2	7	7	11	9	113%	122%	19	17	2	0	2	0	41	52	0	0	0	4
6am	242	198	65	46	1	52	3	1	21	26	24	27	125%	113%	25	23	2	3	2	3	37	46	0	1	0	2
6pm	225	192	48	40	1	52	23	22	28	30	51	52	111%	107%	22	24	5	5	5	5	39	49	0	2	0	0
7am	229	188	52	36	17	64	4	1	29	19	33	20	113%	111%	20	25	2	2	2	2	44	50	0	0	1	1
7pm	226	177	49	25	17	64	22	24	27	28	49	52	112%	98%	21	24	5	2	4	2	44	50	1	0	0	1
8	229	177	52	25	11	81	4	1	19	19	23	20	119%	104%	21	23	4	2	4	2	53	51	0	0	0	2
9am	243	180	66	28	10	83	6	1	30	29	36	30	120%	99%	22	17	4	3	3	3	46	48	0	1	2	3
9pm	226	163	49	11	10	83	29	26	20	18	49	44	116%	95%	19	15	5	4	4	4	49	44	0	1	2	2
10am	247	184	70	32	7	87	6	1	33	22	39	23	121%	107%	15	22	3	2	3	2	49	47	0	0	3	2
10pm	241	184	64	32	7	87	21	15	26	23	47	38	121%	106%	10	12	3	6	2	6	52	45	1	1	3	2
11	244	180	67	28	12	74	2	7	20	26	22	33	127%	101%	18	13	4	0	4	0	56	44	1	0	1	1
12	226	172	49	20	3	75	0	0	16	3	16	3	119%	111%	20	12	3	5	0	5	50	30	0	0	0	0
13am	240	194	63	42	1	73	1	0	25	15	26	15	121%	118%	20	17	3	0	3	0	56	39	0	0	0	1
13pm	228	185	51	33	1	73	31	17	19	20	50	37	118%	109%	17	17	3	1	2	1	51	47	0	0	0	3
14	238	192	61	40	7	68	4	2	24	18	28	20	121%	114%	10	17	6	4	6	4	54	45	0	0	2	3
15	228	191	51	39	16	73	2	0	28	19	30	19	113%	113%	12	17	7	2	5	2	40	47	1	0	1	1
16	215	187	38	35	11	53	7	3	28	17	35	20	106%	112%	11	14	6	3	6	3	49	47	1	0	2	1
17am	234	203	57	51	8	96	2	0	25	30	27	30	118%	114%	9	16	4	2	4	2	43	46	0	0	1	2
17pm	224	191	47	39	8	96	25	18	25	27	50	45	112%	108%	10	12	6	3	6	2	41	49	0	0	1	3
18	225	190	48	38	7	69	3	2	33	30	36	32	108%	105%	15	9	4	7	2	4	41	42	0	1	0	1
19	213	183	36	31	11	82	3	2	7	12	10	14	116%	113%	15	8	2	1	2	1	35	38	0	0	0	0
20am	229	197	52	45	6	64	3	0	20	18	23	18	118%	118%	19	14	2	1	2	0	40	44	0	0	0	2
20pm	225	188	48	36	6	65	18	17	21	14	39	31	115%	114%	19	19	3	3	1	3	47	44	1	1	0	2
21	223	186	46	34	10	49	4	1	30	30	34	31	109%	103%	20	26	3	3	3	4	44	47	0	1	1	2

one2free 3G 上午11:20 92%

訊息 +852 9665 7629 編輯

2012年7月31日下午12:16

<CaMS> G: M&G over 110% high bed occupancy call for male 113% & female 119%

2012年7月31日下午12:57


<CaMS> P: Dr Kwong 64610163

2012年7月31日下午4:22

<CaMS> P: 64610126 Dr. HO Wing Bing (M&G)

2012年7月31日下午4:32

<CaMS> G: M&G over 110% high bed occupancy call for male 110% & female 112%



Over 67% of our calendar days with either male or female wards > 100% bed occupancy  
Around 30% of our calendar days with both male and female wards > 100% bed occupancy

No single month can be exempted from observing  
either one of the above phenomenon, ie seasoning effect no longer exist



**Acute admission**



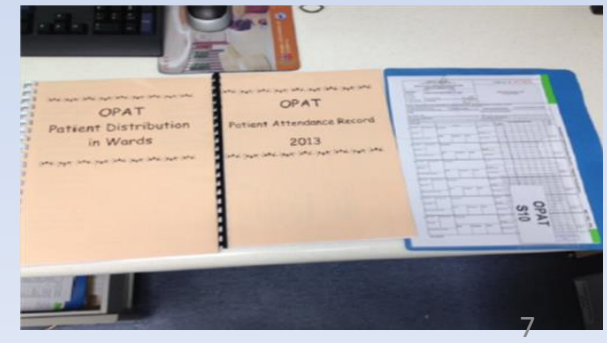
**Convalescent Hospitals**



**Opening up Canvas Beds**



# Inception of OPAT service @ PMH







**OPAT Service @PMH  
starting from Jan 2013**







OPAT Clinic @ PMH

# Antibiotic Infusion Device Options



**Elastomeric devices**



**Bags, flow restrictors/pumps**



## CADD-PLUS® AMBULATORY PUMP

The medication ordered by the Infectious Diseases physician (or Surgical/Medical team), will be delivered by an infusion device called CADD-PLUS® pump. This pump can be programmed to deliver the medication at a continuous rate or to deliver a specified amount of drug at a set programmed interval (both at up to 125mls per hour). The pump stores the programmed and historical information that the clinician required for the specific therapy.



Adaptation from CADD-Legacy™ PLUS  
Operation Manual - SMC EEL TEC  
Inc., supplied by Smith Medical  
Australia Pty Ltd

If the patient is receiving medication over a 24 hour period, then changing the device is a simple exercise. Stop the infusion and turn off the CADD-Plus® pump, disconnect from the patient and clean end of catheter. It will then be necessary to reconstitute the prescribed medication (as per guidelines), in an aseptic manner, and then inject into the intravenous fluid bag, and the CADD® Administration Set attached. Once this is done the CADD® Administration Set is connected to the CADD-Plus® pump it can be primed, and then the CADD® Administration Set is connected to the patient's CIVAD.

Note: Some education will be required on programming and setting up the CADD-Plus® pump prior to the clinician using it.



**24hr Syringe pumps**

## MINI-BAG Plus An integral part of the Baxter Integrated Closed System Reduces risk of BSLs



- Connected components reduce contamination risk.
- Helps protect patients against BSLs
  - Flexible, fully collapsible plastic bags reduce risk of medical errors
  - Ensures delivery of the entire medication volume
  - Reduces possibility of complications resulting from delivery of the wrong drug
- Connected components increase convenience.
- Saves time over manual screening
  - Fewer reconstitution steps
  - Ready-to-use delivery system eliminates possibility of needlestick injury

- Flexible, fully collapsible plastic bags
- Less drug waste, and cleanup
- Easier than glass to store and dispose of
- Val remains attached throughout infusion
- Spikes in plastic spikes
- System can be disposed of as a whole
- Non-vented container
- Reduced risk of accidental drug exposure to nurse
- Universal 20 mm neck vials
- 50 ml and 100 ml bags

## Ecoflac® Connect

The new standard in single-dose, closed system admixture



**Closed system admixture devices**

## "PEEL"

PEEL FOIL STRIP FROM DRUG CHAMBER



## "POP"

SQUEEZE BAG TO OPEN FIRST SEAL BETWEEN THE DILUENT AND DRUG POWDER



## "SHAKE"

SHAKE THOROUGHLY TO MIX



## "POP"

SQUEEZE BAG TO OPEN SECOND SEAL RELEASING SOLUTION TO SET PORT



## "GO"

REMOVE FOIL TAB FROM SET PORT AND SPIKE BAG



**Pre-compounded infusion bags**



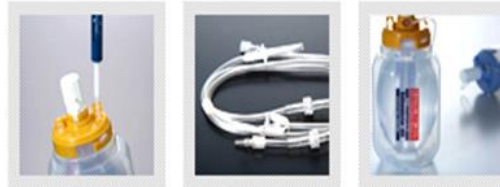
# Why using elastomeric infusion devices?

- **More “antimicrobial bullets” available for OPAT**
- **In alignment with antimicrobial stewardship agenda**
  - Use the narrower and more appropriate spectrum agent for specific organisms
  - Avoid overusing once daily dosing longer half life antimicrobials
    - Examples: Ceftriaxone, Daptomycin, Teicoplanin, Ertapenem
  - To optimize the antimicrobials pharmacokinetic properties
- **Less technical or electronic issues or manipulations imposed on patients**

# Elastomeric devices



**COOPDECH Balloonjector 200/300**  
(Portable Disposable Infuser)



**Accufuser®**



**Braun Easypump™**



**Kimberly-Clark**

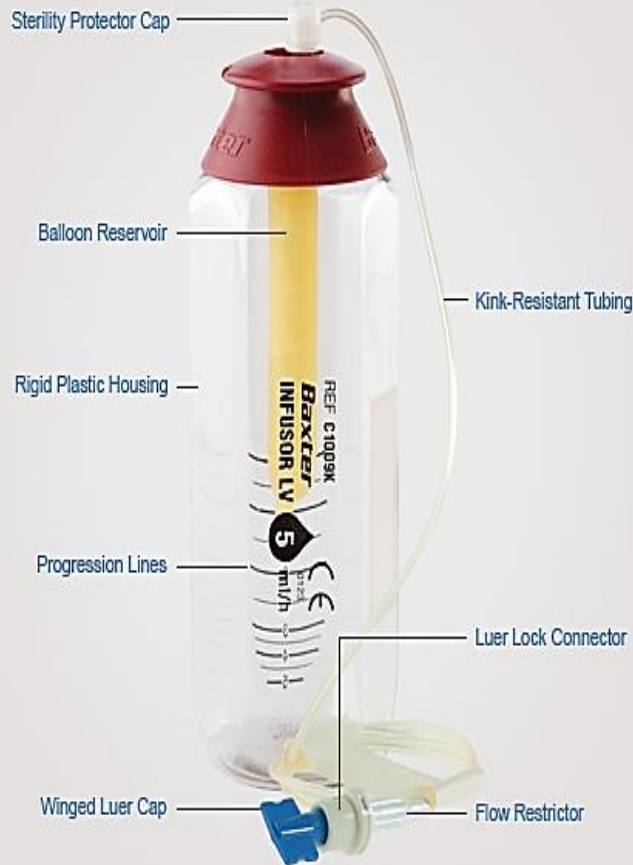


**Baxter LV infusers**



***Which one to choose ?***

# Baxter INFusor LV10 (240 ml)



The screenshot shows the Baxter Australia website. The header includes the Baxter logo, navigation links (Home, Healthcare Professionals, Patients & Caregivers, Suppliers, Careers, Investors, News & Sustainability, About Baxter), and a search bar. The main banner features a healthcare professional in a lab coat and mask, with the text: "Baxter is proud to be a member of The Australian Medicines Industry. As part of the Australian Medicines Industry we are delivering on our promise: to help all Australians live healthier, longer and more fulfilling lives." Below the banner are sections for "Latest News" (Baxter Australia News and Baxter Global News) and "Therapies & Services" (Healthcare Professionals, Patients & caregivers, Product Information). The right sidebar contains links to "Baxter Professional", "Scientific Excellence", "Customer Charter", and "Australia Product Catalogue".

**Baxter**

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**Baxter is proud to be a member of The Australian Medicines Industry**

As part of the Australian Medicines Industry we are delivering on our promise: to help all Australians live healthier, longer and more fulfilling lives.

**Latest News**

**BAXTER AUSTRALIA NEWS**

Jan 14, 2013  
» Baxter ANZ Continues to Drive Sustainability Initiatives

Dec 07, 2012  
» New Baxter Cartons

Nov 30, 2012  
» \$3.4m Pharmacy Compounding Facility re-opens in Coorparoo, QLD

**BAXTER GLOBAL NEWS**

Jun 25, 2014  
» Baxter's Fifteenth Sustainability Report Highlights Commitment to Innovative Programs and Sustainable Design

Apr 17, 2014  
» Baxter Reports Strong First Quarter Financial

Mar 27, 2014

**Therapies & Services**

Healthcare Professionals | Patients & caregivers

**Product Information**

Choose a product

» Doing business with us  
» Product Catalogue  
» Training and Education

**Baxter Professional**  
Our new website for Healthcare Professionals. Register today!  
» Read more

**Scientific Excellence**  
Discover what Baxter scientists focus on  
» Read More

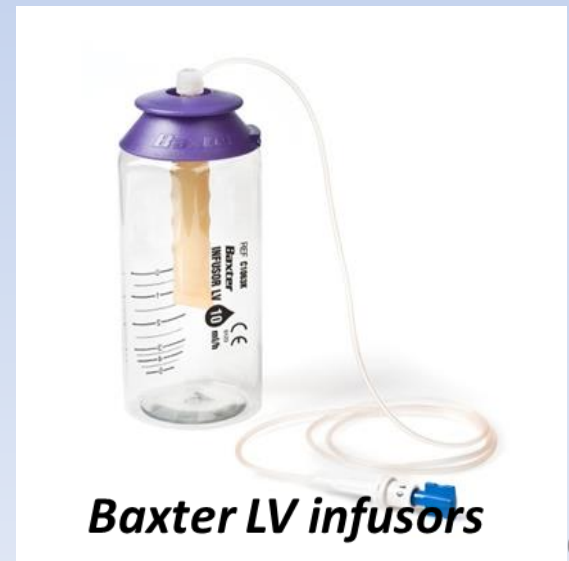
**Customer Charter**  
View Baxter Australia's customer charter.  
» Read more

**Australia Product Catalogue**  
Information for



***Why ?***

# Elastomeric devices





## B. Braun Access Port Systems

### EASYPUMP® ELASTOMERIC INFUSION PUMPS

#### DRUG STABILITY TABLE



**B. BRAUN**  
SHARING EXPERTISE

Medication	Concentration	Diluent	Stability			
			Room Temp.	Refrigerated	Frozen	Ref.
ACYCLOVIR Na	10 mg/mL	NS	10 days	30 days**	-	1
AMIKACIN SO <sub>4</sub>	10 mg/ mL	NS	24 hours	10 days	30 days	1
	10-20 mg/ mL	NS	24 hours	28 days	-	16
AMINOPHYLLINE	5-25 mg/ mL	NS	24 hours	28 days	-	16
New concentration !						
AMPHOTERICIN B**	0.2 mg/ mL	D5W	24 hours	10 days	-	1
AMPICILLIN Na	20 mg/ mL	NS	8 hours	3 days	-	1
AMPICILLIN Na - SULBACTAM Na	30-15 mg/ mL	NS	-	3 days	-	2
AZITHROMYCIN	1-2 mg/mL	NS/D5W	24 hours	7 days	-	8
AZLOCILLIN	50 mg/mL	NS	24 hours	7 days	-	2
AZTREONAM	13.3 - 26.7 mg/mL	NS	7 days	7 days	-	3
	20-30 mg/mL	NS	-	14 days	-	2
	5-20 mg/mL	NS	-	28 days	-	12
	60 mg/mL	NS	24 hours	28 days	-	12
	20 mg/mL	NS	-	30 days (4°C)	-	22
	40 mg/mL	NS	-	30 days (4°C)	-	22
	60 mg/mL	NS	-	30 days (4°C)	-	22
BLEOMYCIN SULFATE	1.07 IU/mL	NS	24 hours 5 days (37°C)	-	-	16 16
BUPIVACAINE HCl	0.25% 0.5%	-	7 days 7 days	-	-	10 10
CASPOFUNGIN Acetate	0.2, 0.28, 0.5 mg/mL	NS	60 hours	14 days	-	9
New !						
CEFAZOLIN Na	20 mg/mL	NS	24 hours	7 days	-	1
CEFEPIME	20 mg/mL	NS	24 hours	14 days	-	2
	40 mg/mL	Water for injection	-	15 days (8°C)	-	13
CEFOPERAZONE Na	2-50 mg/mL	NS/D5W	24 hours	5 days	3 weeks	10
CEFOTAXIME Na	18.66 mg/mL	NS	24 hours	-	-	1
CEFOTAXIME Na	10-20 mg/mL	NS/D5W	-	5 days	13 weeks	8
CEFOTETAN DISODIUM	10-40 mg/mL	NS/D5W	24 hours	4 days	1 week	8
	20 mg/mL	NS/D5W	-	-	60 days	8
New concentration !						
CEFOXITIN Na	10, 20 mg/mL	NS/D5W	24 hours	7 days	-	8
New concentration !						
CEFTAZIDIME	20 mg/mL	NS	18 hours	7 days	84 days	1
	5-30 mg/mL	NS	-	28 days	-	12
	5-40 mg/mL	NS	24 hours	14 days	-	2
	60 mg/mL	NS	-	14 days	14 days	15
	60 mg/mL	NS	-	14 days	-	12
CEFTIZOXIME Na	20, 40 mg/mL	NS/D5W	48 hours	7 days	-	8
CEFTRIAXONE Na	20 mg/mL	NS	72 hours	-	-	1
CEFTRIAXONE Na	10, 20, 40 mg/mL	NS/D5W	72 hours	10 days	-	8
	10-40 mg/mL	NS/D5W	-	-	26 weeks	8
New concentration !						
CEFUROXIME Na	1-30 mg/mL	NS/D5W	24 hours	7 days	6 months	8,9
CIPROFLOXACIN	2 mg/mL	None	24 hours	28 days	-	16
CISPLATIN**	0.5 mg/mL	NS	28 days	-	-	8
New concentration !						
CLINDAMYCIN PO <sub>4</sub>	10 mg/mL	NS	24 hours	10 days	-	1
CLINDAMYCIN PO <sub>4</sub>	6, 9, 12 mg/mL	NS/D5W	16 days	32 days	8 weeks	8
CYCLOPHOSPHAMIDE	4.5 mg/mL	NS	7 days	7 days	-	3
DAPTOMYCIN	20 mg/mL	NS	-	10 days	-	17
New !						
DEFEROXAMINE MESYLATE	5 mg/mL	NS	12 days	-	-	2
	5-160 mg/mL	NS	-	28 days	-	12
	73 mg/mL	NS	7 days	28 days	-	16
DOXORUBICIN HCl	2 mg/mL	NS	-	48 hours	-	1
DOXYCYCLINE	0.1 mg/mL-1 mg/mL	NS/D5W	48 hours	3 days	-	8
	1 mg/mL	D5W	-	-	8 weeks	8

# List of Drug Stability from Baxter

Benzylpenicillin										
Salt	Source	Form	Container	Diluent(*)	Concentration	Unit	-20°C	2-8°C	25°C	33°C
K	Pfizer	Powder	Infusor	D5W	20K - 60K	U/ml		7 d	+ 24 h	

Ceftriaxone										
Salt	Source	Form	Container	Diluent(*)	Concentration	Unit	-20°C	2-8°C	25°C	33°C
Na2 7/2H2O	Roche	Powder	Intermediate	WFI	30 mg/ml	30 d		10 d		
Na2 7/2H2O	Roche	Powder	Intermediate	NS	40 mg/ml	30 d				
Na2 7/2H2O	Roche	Powder	Intermediate	D5W	5 mg/ml			28 d	+ 24 h	
Na2 7/2H2O	Roche	Powder	Intermediate	D5W	5 mg/ml	30 d				
Na2 7/2H2O	Roche	Powder	Intermediate	NS	5 mg/ml			28 d	+ 48 h	
Na2 7/2H2O	Roche	Powder	Intermediate	D5W, NS	5 - 40 mg/ml			21 d	+ 24 h	
Na2 7/2H2O	Roche	Powder	Intermediate	D5W, NS	5 - 40 mg/ml	30 d				

Cefazolin										
Salt	Source	Form	Container	Diluent(*)	Concentration	Unit	20°C	2-8°C	25°C	33°C
Na	Smith Kline & French	Powder	Infusor	D5W	10 - 40	mg/ml		17 d	+ 4 d	

Piperacillin (I)+ tazobactam (II)										
Salt	Source	Form	Container	Diluent(*)	Concentration	Unit	-20°C	2-8°C	25°C	
(I)Na (II)Na	(I)Lederle (II)Lederle	(I)Powder (II)Powder	Intermediate	D5W	(I)1.25 - 10 (II)0 - 80	(I)mg/ml (II)mg/ml	35 d	+		24 h
(I)Na (II)Na	(I)Lederle (II)Lederle	(I)Powder (II)Powder	Intermediate	DEW	(I)1.25 - 10 (II)0 - 80	(I)mg/ml (II)mg/ml		7 d	or	24 h
(I)Na (II)Na	(I)Lederle (II)Lederle	(I)Powder (II)Powder	Intermediate	NS	(I)1.25 - 10 (II)0 - 80	(I)mg/ml (II)mg/ml	35 d	+		24 h
(I)Na (II)Na	(I)Lederle (II)Lederle	(I)Powder (II)Powder	Intermediate	NS	(I)1.25 - 10 (II)0 - 80	(I)mg/ml (II)mg/ml		7 d	or	24 h

Vancomycin									
Salt	Source	Form	Container	Diluent(*)	Concentration	Unit	-20°C	2-8°C	25°C
HCl	Actavis	Powder	Intermediate	NS	5-10	mg/ml		48 h	24 h
HCl	Hospira	Powder	Intermediate	NS	5	mg/ml		4 d	24 h
HCl	Lilly	Powder	Intermediate	D5W, NS	10 - 20	mg/ml	30 d	+	24 h
HCl	Lilly	Powder	Intermediate	D5W, NS	10 - 20	mg/ml		10 d	or 24 h
HCl	Lilly	Powder	Intermediate	D5W	10 - 20	mg/ml	31 d	+	10 d or 24 h
HCl	Lilly	Powder	Intermediate	D5W	10 - 20	mg/ml			10 d
HCl	Lilly	Powder	Intermediate	WFI	15	(mg/ml)			10 d


Cefepime										
Salt	Source	Form	Container	Diluent	Concentration	Unit	-20°C	2-8°C	25°C	33°C
2HCl H2O	Bristol - Myers Squibb	Powder	Intermediate	D5W, NS	1	mg/ml		14 d		+ 48 h
2HCl H2O	Bristol - Myers Squibb	Powder	Intermediate	D5W, NS	1	mg/ml	63 d	+ 7 d		+ 48 h
2HCl H2O	Bristol - Myers Squibb	Powder	Intermediate	D5W, NS	1	mg/ml	63 d			+ 3 d
2HCl H2O	Bristol - Myers Squibb	Powder	Intermediate	NS	1	mg/ml				4 d
2HCl H2O	Bristol - Myers Squibb	Powder	Intermediate	D5W	1 - 5	mg/ml				48 h
2HCl H2O	Bristol - Myers Squibb	Powder	Intermediate	NS	1 - 5	mg/ml				3 d
2HCl H2O	Bristol - Myers Squibb	Powder	Intermediate	D5W, NS	1 - 60	mg/ml	63 d			+ 24 h
2HCl H2O	Bristol - Myers Squibb	Powder	Intermediate	D5W, NS	5 - 60	mg/ml		Precipitation		

Flucloxacillin										
Salt	Source	Form	Container	Diluent	Concentration	Unit	-20°C	2-8°C	25°C	33°C
Na H <sub>2</sub> O	Wockhardt	Powder	Intermediate	NS, WFI	10 - 20	mg/ml	10 d			
Na H <sub>2</sub> O	Wockhardt	Powder	Intermediate	NS, WFI	10 - 20	mg/ml	10 d		+ 24 h (1)	+ 6 h

(1) Related compounds not taken into account for shelf life calculation

> ANTIBIOTIC > CEFOPERAZONE						Issue Date : 19/Jul/2001					X
Salt	Source	Form	Container	Diluent	Concentration	Unit	-20°C	2-8°C	25°C	33°C	
Na	Roerig	Powder	Intermediate	D5W	2 - 50	mg/ml	30 d	+		24 h	
Na	Roerig	Powder	Intermediate	D5W	2 - 50	mg/ml		10 d	or	24 h	
Na	Roerig	Powder	Intermediate	NS	2 - 50	mg/ml		10 d	or	24 h	
Na	Roerig	Powder	Intermediate	WFI	25	mg/ml		10 d			

<b>Limits :</b> BP: no monograph for injection USP 90.0 - 120.0 %	<b>Comments :</b> a - Shelf Life limited by study design b - Shelf Life limited by intrinsic stability of the drug
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> ANTIBIOTIC > CEFTRIAZONE					Issue Date : 07/Mar/2003					
Salt	Source	Form	Container	Diluent	Concentration	Unit	-20°C	2-8°C	25°C	33°C
Na	Roche	Powder	Glass or Intermediate or Minibag	D5W or NS	5	mg/ml		28 d	+ 24 h	
Na	Roche	Powder	Glass or Intermediate or Minibag	D5W or NS	5 - 40	mg/ml		21 d	+ 24 h	1
Na	Roche	Powder	Intermediate	D5W or NS	5 - 40	mg/ml	30 d	+	+ 24 h	
Na	Roche	Powder	Intermediate	WFI	30	mg/ml		10 d		
Na	Roche	Powder	Vial	D5W or NS	2.5	mg/ml		7 d		a 2
Na	Roche	Powder	Vial	D5W or NS	2.5	mg/ml			24 h	b 2

<b>Comments :</b> 0 - Shelf Life allocated against BP limits. 1 - 40 mg/ml solutions may precipitate if stored longer than 21 days at 2-8°C. 2 - Calculated against BP limits. a - Shelf Life limited by study design b - Shelf Life limited by intrinsic stability of the drug
--

ANTIBIOTIC > CEFTAZIDIME					Issue Date : 16/Sep/2003					✖
Salt	Source	Form	Container	Diluent	Concentration	Unit	-20°C	2-8°C	25°C	33°C
Na	?	?	Glass	D5W	200	mg/ml	30 d			
Na	?	?	Glass	D5W	200	mg/ml	24 d			
Na	?	?	Intermediate	D5W or NS	200	mg/ml	21 d			
Na	Glasco/Wellcome	Powder	Vial	D5W or NS	0.1	mg/ml		7 d		
Na	Glasco/Wellcome	Powder	Vial	D5W or NS	0.1	mg/ml				
Na	Glass	Powder	600	NS	5	mg/ml	14 d		24 h	8
Na	Bi Lilly, Glaxo	Powder	Glass or Minibag	D5W	5	mg/ml	5 d		24 h	
Na	Bi Lilly, Glaxo	Powder	Glass or Minibag	D5W	5	mg/ml	7 d		8 h	
Na	Bi Lilly, Glaxo	Powder	Glass or Minibag	D5W	5	mg/ml	7 d		24 h	1
Na	Bi Lilly, Glaxo	Powder	Glass or Minibag	D5W or NS	5 - 80	mg/ml	3 d		8 h	
Na	Bi Lilly, Glaxo	Powder	Glass or Minibag	NS	5	mg/ml	7 d		24 h	
Na	Bi Lilly, Glaxo	Powder	Glass or Minibag	NS	5	mg/ml	7 d		48 h	
Na	Bi Lilly, Glaxo	Powder	Infusor	D5W	10 - 40	mg/ml	24 d		14 h	
Na	Bi Lilly, Glaxo	Powder	Intermediate	D5W	5 - 40	mg/ml	30 d		24 h	
Na	Bi Lilly, Glaxo	Powder	Intermediate	D5W	5 - 40	mg/ml	30 d		24 h	
Na	Bi Lilly, Glaxo	Powder	Intermediate	NS	5 - 40	mg/ml	20 d		24 h	
Na	Bi Lilly, Glaxo	Powder	Intermediate	NS	5 - 80	mg/ml	24 d		7 d	
Na	Bi Lilly, Glaxo	Powder	Intermediate	WFI	20	mg/ml	10 d			
Na	Bi Lilly, Glaxo	Powder	Minibag	NS	40	mg/ml	50 d		12 h	
Na	Bi Lilly, Glaxo	Powder	Minibag	NS	5 - 40	mg/ml			14 d	
Na	Bi Lilly, Glaxo	Powder	Minibag	NS	40	mg/ml	80 d		7 d	
Na	Bi Lilly, Glaxo	Powder	Minibag	NS	10 - 20	mg/ml			14 d	
Na	Bi Lilly, Glaxo	Powder	Minibag	NS	10 - 25	mg/ml	150 d		24 h	
Na	Bi Lilly, Glaxo	Powder	Minibag	NS	10 - 25	mg/ml	150 d			

<b>Limits :</b> BP: no monograph for injection Cefazidime / USP: 90.0 - 105.0% of initial	<b>Comments :</b> 1 - Short term stability study: 7 days at 2-8°C or 48 hours at R.T. a - Shelf Life limited by study design b - Shelf Life limited by intrinsic stability of the drug
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> ANTIBIOTIC > CLOXACILLIN						Issue Date : 18/Dec/2002					<input type="button" value="X"/>
Salt	Source	Form	Container	Diluent	Concentration	Unit	-20°C	2-8°C	25°C	33°C	
Na	Beecham	Powder	Glass	D5W	2	mg/ml			< 8 h		3
Na	Beecham	Powder	Vial	D5W	2	mg/ml			24 h		1
Na	Beecham	Powder	Vial	D5W	2	mg/ml			8 h		

<b>Limits :</b> BP: 90.0 - 105.0 % of initial USP: 90.0 - 120.0 %	<b>Comments :</b> 1 - Data within USP limits but out of BP limits / 48 h compatibility study at 23°C / iodometry 2 - Data within BP and USP limits. 3 - Data within BP and USP limits / 48 h compatibility study at 23°C / iodometry a - Shelf Life limited by study design b - Shelf Life limited by intrinsic stability of the drug
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> ANTIBIOTIC > GENTAMICIN					Issue Date : 06/Mar/2003					✖	
Salt	Source	Form	Container	Diluent	Concentration	Unit	-20°C	2-8°C	25°C	33°C	
S04	Schering -Plough	Liquid	Glass	D5W	0.32 - 1	mg/ml				4	
S04	SoloPack	Bulk Powder	Infusor	NS	0.8 - 2.4	mg/ml		17 d	+ 17 d	2	
S04	Elkins-Sinn, Roussel	Liquid	Intermediate	D5W	0.5 - 5.0	mg/ml		10 d		1	
S04	Elkins-Sinn, Roussel	Liquid	Intermediate	D5W	0.5 - 5.0	mg/ml		30 d	+	24 h	2
S04	Elkins-Sinn, Roussel	Liquid	Intermediate	NS	5	mg/ml			24 h	1	
S04	Elkins-Sinn, Roussel	Liquid	Intermediate	NS	0.5 - 5.0	mg/ml		10 d		1	
S04	Elkins-Sinn, Roussel	Liquid	Intermediate	NS	0.5	mg/ml		10 d		2	
S04	Elkins-Sinn, Roussel	Liquid	Intermediate	NS	0.5 - 5.0	mg/ml		30 d	+	24 h	2
S04	Elkins-Sinn, Roussel	Liquid	Intermediate	WFI	2.5	mg/ml		10 d		2	
S04	?	N/A	Minibag	D5W	0.8	mg/ml		120 d	+	24 h	3
S04	Schering -Plough	Liquid	Vial	D5W	0.32 - 1	mg/ml			2 d	4	
S04	Schering -Plough	Liquid	Vial	D5W or NS	0.5	mg/ml		7 d	or 48 h	a	

<b>Limits :</b> BP: 92.4 - 115.8 % (97.0/1.05 - 110.0/0.95) / Fiducial limits NLT 95% and NMT 105% of estimated potency / Upper fiducial limit of error NLT 97.0% and lower fiducial limit of error NMT 110.0% of stated amount USP: 90.0 - 125.0 % of initial	<b>Comments :</b> 1 - Data within USP limits but out of BP limits. 2 - Data within BP and USP limits 3 - Frozen study performed at -10°C 4 - Data within BP and USP limits / 48 h compatibility study at 23°C / Microbiological assay 5 - Calculated against BP limits a - Shelf Life limited by study design b - Shelf Life limited by intrinsic stability of the drug
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> ANTIBIOTIC > IMPENEM (I) + CILASTATIN (II)						Issue Date : 06/Mar/2003				
Salt	Source	Form	Container	Diluent	Concentration	Unit	-20°C	2-8°C	25°C	33°C
(I) Na	MSD	Powder	Glass	D5W	5.0 (I) + 5.0 (II)	mg/ml			8 h	
(I) Na	MSD	Powder	Glass	D5W	2.5 (I) + 2.5 (II)	mg/ml		24 h		
(I) Na	MSD	Powder	Glass	D5W	2.5 (I) + 2.5 (II)	mg/ml			16 h	
(I) Na	MSD	Powder	Glass	NS	5.0 (I) + 5.0 (II)	mg/ml			11 h	
(I) Na	MSD	Powder	Glass	NS	2.5 (I) + 2.5 (II)	mg/ml			16 h	
(I) Na	MSD	Powder	Glass	NS	2.5 (I) + 2.5 (II)	mg/ml		24 h	+ 9 h	
(I) Na	MSD	Powder	Intermediate	D5W	2.5 (I) + 2.5 (II)	mg/ml		24 h	+ 9 h	
(I) Na	MSD	Powder	Intermediate	D5W	5.0 (I) + 5.0 (II)	mg/ml			8 h	
(I) Na	MSD	Powder	Intermediate	D5W	2.5 (I) + 2.5 (II)	mg/ml			16 h	
(I) Na	MSD	Powder	Intermediate	NS	5.0 (I) + 5.0 (II)	mg/ml		24 h	+ 9 h	
(I) Na	MSD	Powder	Intermediate	NS	5.0 (I) + 5.0 (II)	mg/ml			13 h	
(I) Na	MSD	Powder	Intermediate	NS	2.5 (I) + 2.5 (II)	mg/ml			18 h	
(I) Na	MSD	Powder	Intermediate	NS	2.5 (I) + 2.5 (II)	mg/ml		48 h	+ 16 h	
(I) Na	MSD	Powder	Intermediate	NS	2.5 (I) + 2.5 (II)	mg/ml			24 h	+ 9 h
(I) Na	Merck Sharp Dohme	Powder	Vial	D5W or NS	0.5 (I) + 0.5 (II)	mg/ml		72 h		

<b>Limits :</b> Impenem (I) + Cilastatin (II) / BP: no monograph Impenem (I) + Cilastatin (II) / USP: 90.0 - 115.0 % (I and II) from initial	<b>Comments :</b> a - Shelf Life limited by study design b - Shelf Life limited by intrinsic stability of the drug
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> ANTIBIOTIC > MEROPENEM					Issue Date : 19/Dec/2002					✖
Salt	Source	Form	Container	Diluent	Concentration	Unit	-20°C	2-8°C	25°C	33°C
N/A	Zeneca	Powder	9060 or Intermediate or Minibag	NS	5	mg/ml		3 d	+ 6 h	
N/A	Zeneca	Powder	Intermediate	IS	5 - 40	mg/ml		18 h	+ 6 h	
✖ Limits :					✖ Comments :					
Applied limits: 90.0 - 110.0 % of initial					a - Shelf Life limited by study design					
B.P. no monograph					b - Shelf Life limited by intrinsic stability of the drug					
I.S.D. no monograph										

[Home](#) > [Products](#) > [Infusion Therapy](#) > [Elastomeric Pumps](#) > [Easypump®](#)

## Products

### Infusion Therapy

Infusion- and Injection  
Solutions

Drug Admixture

Administration Sets

Infusion & Transfusion  
Accessories

Automated Infusion  
Systems

Venipuncture and  
Injection

### Elastomeric Pumps

► [Product-QuickFinder](#)

# Easypump®

## Disposable Infusion Pumps

### Description

Easypump® is a disposable elastomeric pump for the infusion of cytotoxic drugs, antibiotics and pain relief. This device allows patients to be mobile while receiving their treatment, and offers a safe, simple alternative to electronic devices. Easypump® can be used either in the hospital or in the home setting.

### Advantages

- Wide range of flow rates and fill volumes to aid adaptation to different treatment regimes
- Easy to use as there is no need to vary flow rates
- Comfortable and discreet for the patient
- Air and particle venting filters for security
- Colour coded for easy identification of volumes and flow rates
- Facilitates home treatment, especially when combined with Celsite® access ports and Surecan® with Wings needles

### Indication

Long, short or medium duration infusions for a wide range of medications, including cytotoxic drugs, antibiotics and pain relieving drugs.

### Note

Easypump® is available in a range of flow rates from 0.5-250 ml/hour and a choice of fill volumes from 50-500 ml.



### More Info

#### Pictures (1)

Easypump®

JPEG [21 KB]

Not all products are registered and approved for sale in all countries or regions. Indications of use may also vary by country and region. Please contact your country representative for product availability and information. Product images are for reference only.

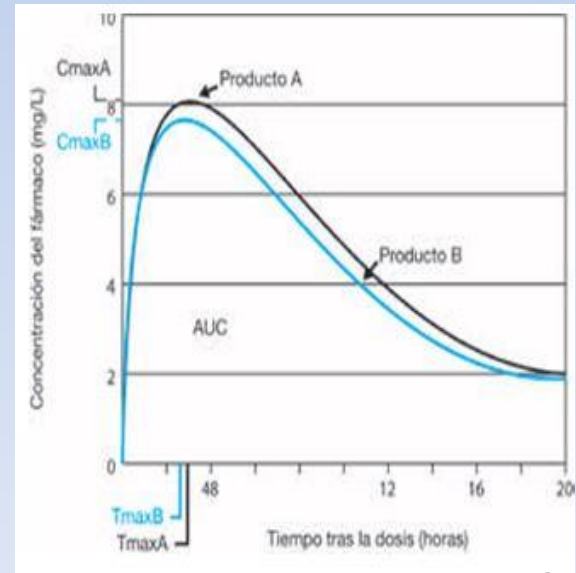


***Why should we bother  
drug stability results ?***

**A generic medicine** is defined as a product having the same qualitative and quantitative composition in active ingredients, as well as the same pharmaceutical form, as the reference medicine and whose bioequivalence has been shown by adequate bioavailability studies.

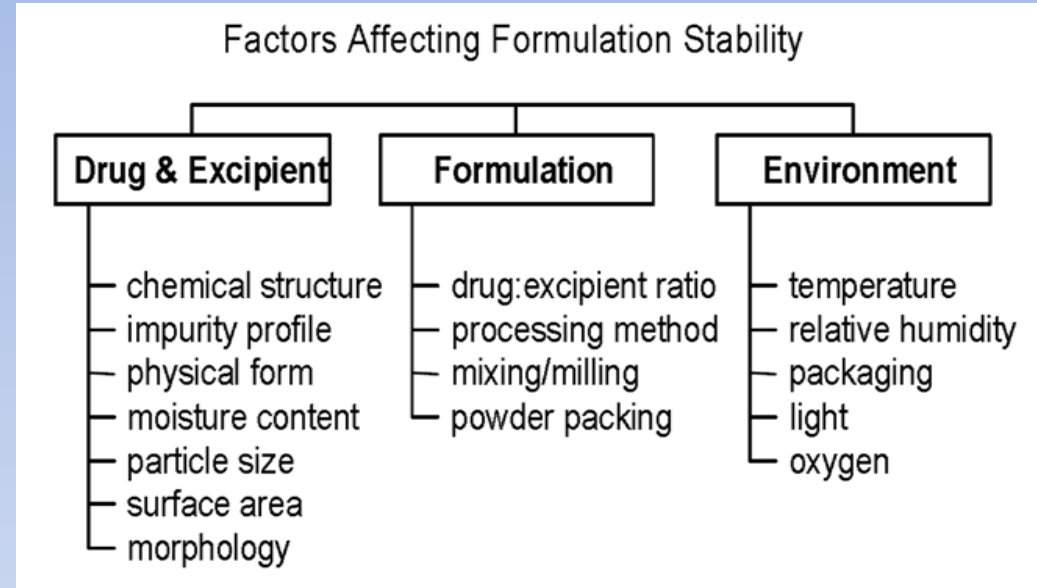
**Bioavailability** is defined as the amount and speed at which the active ingredient is absorbed from a pharmaceutical form and reaches the site of action. Bearing in mind that **an active ingredient is in balance between systemic circulation and the site of action**, it is assumed that **drug values** in blood represent drug bioavailability. Bioavailability is assessed using pharmacokinetic parameters, including: **AUC, Cmax and Tmax**.

**Bioequivalence** is the comparison between the bioavailability of a medicine under study and the bioavailability of a reference drug. It is accepted that a study product is bioequivalent to the reference product when its values (especially the **AUC**) are **within the 90% confidence interval (80–125%)**.

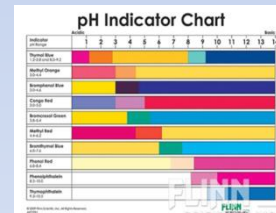


# Importance of drug stability

- Extensive chemical degradation => a substantial loss of potency
- Degradation products may result in adverse events or be unsafe
- Instability may cause
  - Undesired change in performance, i.e. dissolution/bioavailability
  - Substantial changes in physical appearance of the dosage form causing product failures
- Requirement for approval by regulatory agencies



Minor differences in excipient composition, preservatives, pH, tonicity of solutions or other inactive components do exist between the generic and the reference medicine because of avoidance of violating patents





# Importance of drug stability

## Kinetics of reactions

- Complex reactions

## Factors affecting reaction rate

- Temperature

- Arrhenius equation:  $k = Ae^{-E_a/RT}$
- The Arrhenius plot

## Factors affecting reaction rate

- Solvent

- pH of aqueous solvents
  - Acid, base, and water catalyzed reactions, mostly hydrolysis
  - Leading to various kinetic profiles: L, V, U
  - More complex shapes of kinetic profiles if the compound has (multiple)ionizable functionality
- Composition: medium effect on chemical reactions

## Factors affecting reaction rate

- Light
- Oxygen
- Co-solutes
  - Buffer salts: catalysis
  - Surfactants: different environment in the micelles
  - Complexation agents: different environment, e.g. cyclodextrin
  - Antioxidants and/or chelating agents

## Common degradation routes

- Solvolysis/hydrolysis
  - Most frequently encountered hydrolysis – ester
  - Typically pseudofirst order
  - Intramolecular catalysis and steric factors
- Photolysis/oxidation
- Racemization
  - May cause substantial decrease in biological activities: e.g. Pilocarpine, tetracycline
- Others
  - e.g. decarboxylation

Drug compatibility and stability in a fluid reservoir and administration set of a disposable pump are also important when selecting a disposable infusion device. Some disposable pumps are made from materials not typically used for fluid containers and administration lines. Therefore, users must not assume that drug stability and compatibility data for commonly used medical materials, such as PVC and polypropylene, will be applicable to disposable pumps.

Separate data on drug stability and compatibility with the fluid container and fluid-contacting parts of the disposable pump are therefore necessary. Restrictions on storage time

Am J Health-Syst Pharm—Vol 63 Jul 1, 2006

? PVC (non-polyvinyl chloride)  
? DEHP [di(2-ethylhexyl)phthalate]

The membranes of elastomeric pumps are made of various elastomers, both natural and synthetic (e.g., isoprene rubber, latex, and silicon), and can be made of a single or multiple layers. The type of elastomer and the geometry of the elastomeric balloon determine the pressure generated on the fluid when the balloon is stretched.<sup>2</sup> Multiple-layer elastomeric membranes can generate higher pressures than the single-layer



# Setting up local drug stability database for elastomeric device

- **Lacking sufficient stability data on existing local generic antibiotics which have no significant differences in terms of bioavailability and bioequivalence studies**
  - Tender bid exercise once every 2-3 years for each antibiotic
  - Mostly from mainland China, India, Philippines
- **Differences between textbook, commercial database, journal articles in terms describing ....**
  - Brand name of antibiotic /elastomeric device; Diluents used
  - Temperature range; Dosage range
  - Testing methodologies.



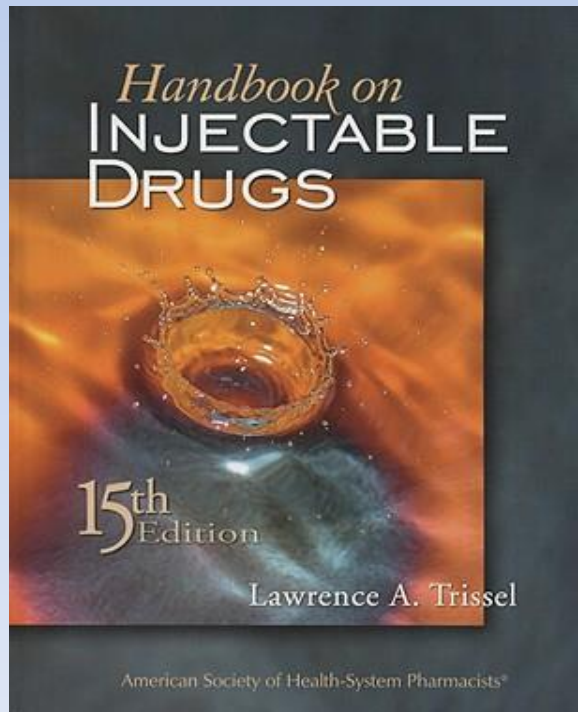
# Example 1.

Desirable therapeutic dosage range and diluent not met

**Baxter**

Benzylpenicillin										
Salt	Source	Form	Container	Diluent(*)	Concentration	Unit	-20°C	2-8°C	25°C	33°C
K	Pfizer	Powder	Infusor	D5W	20K - 60K	U/ml		7 d	+ 24 h	

Textbook Reference



## PENICILLIN G POTASSIUM (BENZYL PENICILLIN POTASSIUM) AHFS 8:12.16.04

**Products** — Penicillin G potassium is available in vial sizes of 5 million and 20 million units. (1-1/06) The commercial products contain sodium citrate and citric acid as buffers. Depending on the route of

Pump Reservoir(s)	Conc.	Frozen	REF	RT
Home pump; Home-pump Eclipse	10,000 units/mL <sup>a</sup> 20,000 units/mL <sup>b</sup>	30 days	24 hr 4 days	24 hr 24 hr
Intermate	100,000 units/mL <sup>a,b</sup>	30 days	10 days	24 hr
Intermate HPC	20,000 to 60,000 units/mL		7 days	24 hr
ReadyMed	50,000 units/mL <sup>b</sup>	4 weeks	14 days	48 hr

<sup>a</sup>In dextrose 5%.

<sup>b</sup>In sodium chloride 0.9%.

Only 1 drug concentration

# Example 2.

**Baxter**

## Ceftriaxone

Salt	Source	Form	Container	Diluent(*)	Concentration	Unit	-20°C	2-8°C	25°C	33°C
Na2 7/2H2O	Roche	Powder	Intermediate	WFI	30 mg/ml			10 d		
Na2 7/2H2O	Roche	Powder	Intermediate	NS	40 mg/ml	30 d				
Na2 7/2H2O	Roche	Powder	Intermediate	D5W	5 mg/ml			28 d	+ 24 h	
Na2 7/2H2O	Roche	Powder	Intermediate	D5W	5 mg/ml	30 d				
Na2 7/2H2O	Roche	Powder	Intermediate	NS	5 mg/ml			28 d	+ 48 h	
Na2 7/2H2O	Roche	Powder	Intermediate	D5W, NS	5 - 40 mg/ml			21 d	+ 24 h	
Na2 7/2H2O	Roche	Powder	Intermediate	D5W, NS	5 - 40 mg/ml	30 d				



**The Chinese University of Hong Kong**  
**School of Pharmacy**  
 Bioanalytical Unit

Rm 823, 8th Floor, Lo Kwee-Seong Integrated Biomedical Sciences Building,  
 Area 39, Shatin, N.T., Hong Kong

Drug	Concentration	Time (h) at 30°C After refrigeration (2-8°C) for	
		4 days	9 days
Ceftriaxone (Generic)	5 mg/mL	+36 h	+24 h
	40 mg/mL	+28 h	+16 h



# Setting up local drug stability database for elastomeric device

- Quality control and Medication safety issues
- Take reference to the standard practice of PIVAS (Pharmacy Intravenous Admixture Service) in Hospital Authority i.e., Brand-specific stability of antibiotic requirement
- To ensure the concentration of targeted antimicrobial within the elastomeric device is well above the 90-95% potency line.



# What variables to consider?

- **Clinical factor**

- Spectrum of common pathogens
- Selection of preferred antimicrobial agents from each class
- Prioritization the testing of antimicrobials

- **Patient factor**

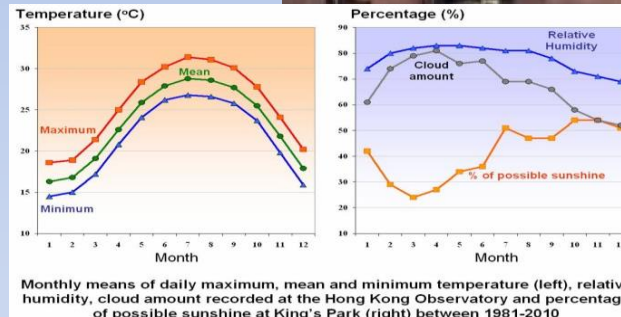
- Convenience (daily vs weekly FU)

- **Operational factor**

- Local temperature variation
- Clinic based or home based
- Delivery of elastomeric device

- **Practical**

- availability of compounding sessions /week
- manpower issue
- how to address long holidays
- supply chain of specific brand antibiotics
- determine the brand of elastomeric device
- budget calculation for antimicrobials' testing based on the dosage range( including renal dosing), sampling time points and preferred temperature setting



pH and temperature effects on the hydrolysis of three  $\beta$ -lactam antibiotics: Ampicillin, cefalotin and cefoxitin

Shannon M. Mitchell<sup>a</sup>, Jeffrey L. Ullman<sup>b,\*</sup>, Amy L. Teel<sup>a</sup>, Richard J. Watts<sup>a</sup>

<sup>a</sup> Department of Civil and Environmental Engineering, Washington State University, 405 Spokane Street, Pullman, WA 99164, USA

<sup>b</sup> Department of Agricultural and Biological Engineering, University of Florida, PO Box 110570, 1741 Museum Road, Gainesville, FL 32611, USA

## Compounding Infusors

PMH Aseptic Clean Room

Antibiotics are reconstituted and compounded in laminar flow hood



***How should we address or overcome these issues?***

**Table 3.** National comparisons from the International OPAT Outcomes Registry<sup>a</sup>

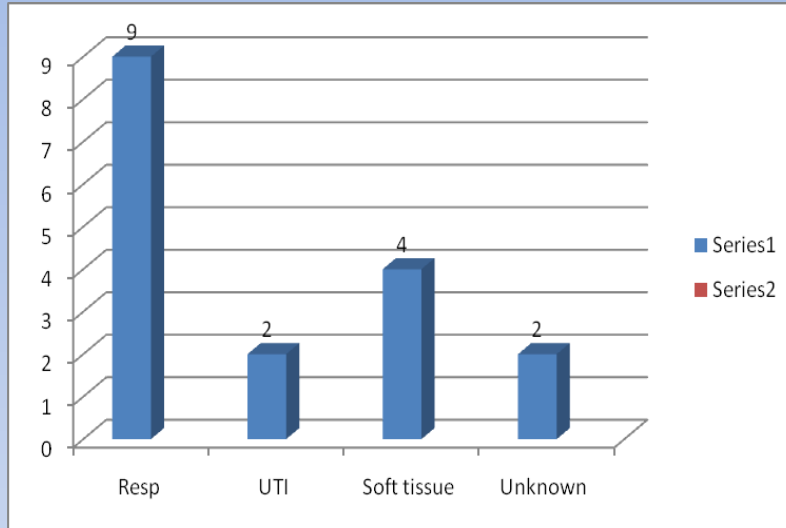
	UK	Italy	Canada	USA
Top diagnoses				
cellulitis	44.8	9.9	22.7	19.3
osteomyelitis	19.1	18.6	15.7	13.1
prosthetic joint infection	7.2	0.5	4	2.2
post-operative wound infection	4.9	1.4	1.6	11.1
septic arthritis	3	5.7	7.9	3.3
bronchitis	0.2	14	20	0.9
pneumonia	0.7	15	0.8	3.1
bacteraemia	1.2	0	0.3	4.9
wound infection—other	3	0	0.9	3.7
Top antibiotics				
ceftriaxone	49.6	36.8	6.6	32.8
teicoplanin	31	18.3	0	0
gentamicin	7.9	0.7	4.4	2.3
meropenem	3.7	0.2	2	0.4
vancomycin	2.5	0.7	7.7	18.8
cefazolin	0.3	0	23.3	5.5
ceftazidime	0	5.7	12.8	3.3
tobramycin	0	0.2	11.9	2.2
amikacin	0	8.7	0.2	0.2
levofloxacin	0	3.2	0.4	1.3
clindamycin	0	0.5	15	3.3
oxacillin	0	0	0	3.3
Antibiotic route				
iv	100	71	100	99.7
im	0	29	0	0.3
Site of care				
infusion centre—hospital	52.6	50.2	9.2	0
home—visiting nurse/doctor	24.2	19	15	7.2
administered by self/family member	19.9	29.5	45.7	60.6
nursing home	2.5	0	0.4	1
infusion centre—clinic	0.5	0.7	0	29.5

<sup>a</sup>All values are percentages.**Table 1.** Infections treated with outpatient parenteral antimicrobial therapy (OPAT) and the antibiotics used in 4 studies or sites.

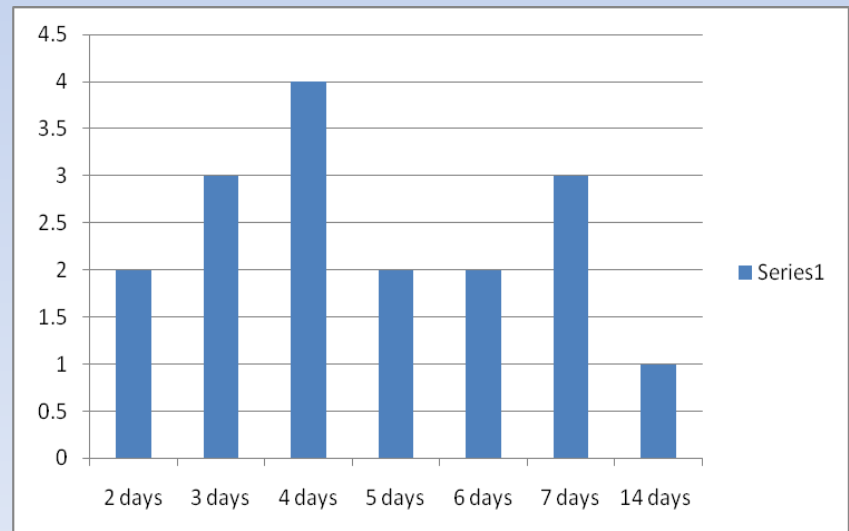
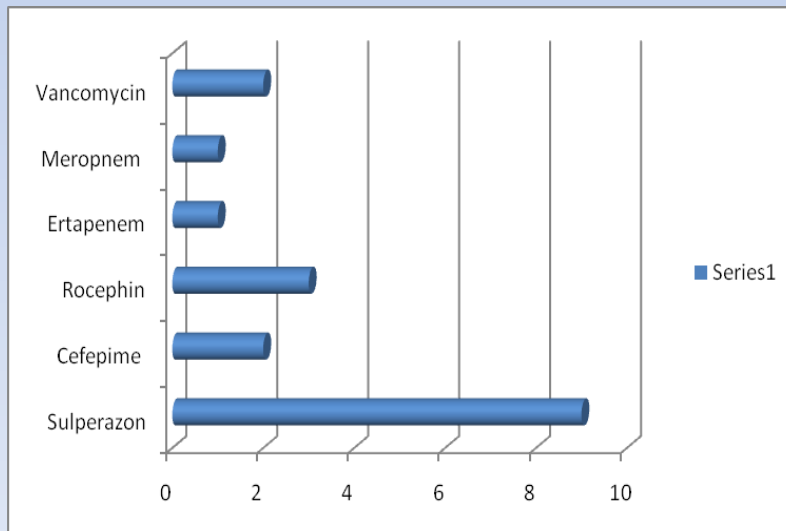
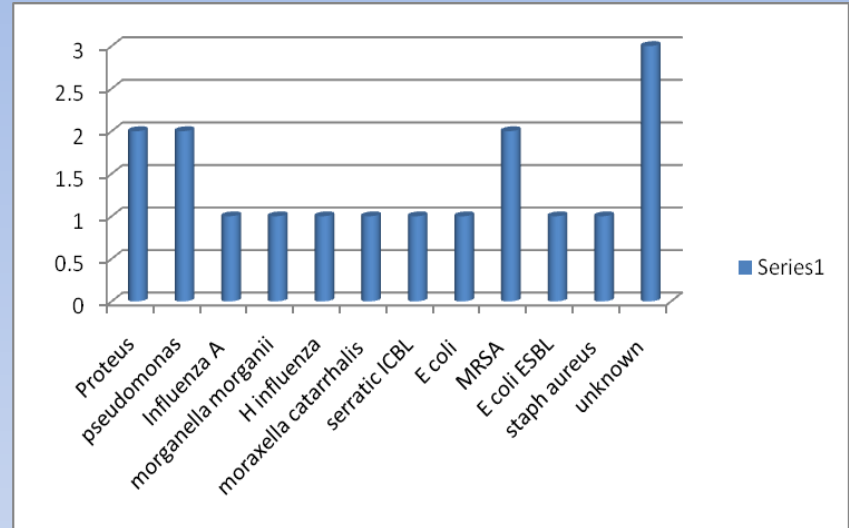
OPAT Network (1996–2002) <sup>a</sup>	Cleveland Clinic (1986–2000) <sup>b</sup>	Minneapolis area (1978–1990) <sup>c</sup>	Children's Hospital San Diego (2000) <sup>d</sup>
Type of infection, ranked by frequency (% of OPAT courses)			
Skin and soft tissue (23)	Musculoskeletal	Cellulitis (15)	Bacteremia (16)
Osteomyelitis (15)	Infected devices	Osteomyelitis (13)	Pyelonephritis (13)
Septic arthritis/bursitis (5)	Bacteremia	Late-stage Lyme disease (10)	Meningitis (13)
Bacteremia (5)	Intra-abdominal	Pyelonephritis and UTI (9)	Intra-abdominal (8)
Wound (4)	Skin and soft tissue	Septic arthritis (7)	Cellulitis (7)
Pneumonia (4)	...	Other (46)	Osteomyelitis (7)
Pyelonephritis (3)	...	...	Wound (7)
Antimicrobial, ranked by frequency of use (% of OPAT courses)			
Ceftriaxone (33)	Vancomycin (31)	...	Ceftriaxone (42)
Vancomycin (20)	Penicillins (20)	...	Meropenem (11)
Cefazolin (6)	Antivirals (12)	...	Cefazolin (11)
Oxacillin/nafticillin (5)	Cephalosporins (9)	...	Cefepime (6)
Aminoglycosides (5)	Aminoglycosides (5)	...	Ceftazidime (6)
Clindamycin (3)	Other $\beta$ -lactams (4)	...	Vancomycin (6)
Ceftazidime (3)	...	...	...

# PMH pilot trial in 2009

Site of Infection



Causative organisms



Antimicrobial agents used

Duration of treatment courses



# NOT ALL antibiotics suitable for elastomeric infusion pump

**Table 5. Properties of commonly prescribed antimicrobials at various temperatures.**

CID 2004;38:1651

Drug	Half-life in h	Phlebitis risk rating <sup>b</sup>	Optimal dilution, mg/mL <sup>c</sup>	Duration of stability, by storage temperature <sup>a</sup>		
				-20°C	5°C	25°C
Acyclovir <sup>d</sup>	2–3.5	1	5	ND	37 d	>37 d
Amphotericin B	24–360	3	0.1	ND	35 d	5 d
Liposomal amphotericin B	24–360	2	4	ND	24 h	5 d
Amphotericin B lipid complex	24–360	2	1	ND	48 h	6 h
Ampicillin	1	2	30	ND	48 h	8 h
Ampicillin-sulbactam	1	2	20	ND	48 h	8 h
Caspofungin	>48	1	0.2–0.3	ND	24 h	1 d
Cefazolin	1–2	1	10–20	30 d	10 d	1 d
Cefoperazone	1.5–25	1	40	96 d	80 d	80 d
Ceftazidime	1.4–2	1	1–40	90 d	21 d	2 d
Ceftriaxone	5.4–10.9	1	10–40	180 d	10 d	3 d
Cefuroxime	1–2	1	5–10	30 d	180 d	1 d
Chloramphenicol	1.5–4	1	10–20	180 d	30 d	30 d
Clindamycin	2–3	1	6–12	56 d	32 d	16 d
Doxycycline <sup>e</sup>	22–24	2	0.1–1	56 d	48 h	3 d
Erythromycin lactobionate	1.5–2	3	0.1–0.2	30 d	14 d	1 d
Ertapenem	4	2	20	ND	24 h	6 h
Ganciclovir	2.5–3.6	1	5	364 d	35 d	5 d
Gentamicin	2–3	1	0.6–1	30 d	30 d	30 d
Imipenem-cilastatin	0.8–1.3	2	2.5–5	ND	2 d	10 h
Linezolid	4.5	1	2	ND	ND	ND
Meropenem	1.5	1	5–20	ND	24 h	4 h
Nafcillin	0.5–1.5	3	2–40	90 d	3 d	1 d
Oxacillin	0.3–0.8	2	10–100	30 d	7 d	1 d
Penicillin G <sup>f</sup>	0.4–0.9	2	0.2	84 d	14 d	2 d
Vancomycin	4–6	2	5	63 d	63 d	7 d

**TABLE 6. STABILITY OF SELECTED ANTIMICROBIAL DRUGS  
FOR OUTPATIENT PARENTERAL THERAPY.\***

DRUG	RECOMMENDED DILUENT	CONCENTRATION (mg/ml)†
<b>Adequate stability‡</b>		
Nafcillin	Water or normal saline	80
Oxacillin	Water	50 or 100
Ticarcillin–clavulanate	Water or normal saline	10–100
Cefazolin	Water	73.2
Cefuroxime	Water	≤30
Cefoxitin	Water	40
Ceftriaxone	Normal saline	40
Ceftazidime	Water	30 or 60
Vancomycin	Water or normal saline	10
Amikacin	5% dextrose in water	20
Gentamicin	5% dextrose in water	5.45
Tobramycin	5% dextrose in water	3.2
Pentamidine	Normal saline or 5% dextrose in water	3
Ganciclovir	Normal saline or 5% dextrose in water	5
Amphotericin B§	5% dextrose in water	0.1
<b>Intermediate stability¶</b>		
Acyclovir	Normal saline or 5% dextrose in water	5
Erythromycin	Water or normal saline	20
Penicillin G sodium	Water	180,000 U/ml
<b>Poor stability**</b>		
Ampicillin	Water or normal saline	60
Imipenem–cilastatin	Normal saline	5
Doxycycline	Normal saline	2
Trimethoprim– sulfamethoxazole	5% dextrose in water	0.8–4

# Stability of doripenem in polyvinyl chloride bags and elastomeric pumps

JARED L. CRANDON, CHRISTINA SUTHERLAND, AND DAVID P. NICOLAU

Given the substantial costs associated with inpatient hospital visits, much focus has been placed on minimizing the length of hospital stay. One population that

## Continuous Infusions of Meropenem in Ambulatory Care: Clinical Efficacy, Safety and Stability

Laurens Manning<sup>1,2\*</sup>, Cameron Wright<sup>3</sup>, Paul R. Ingram<sup>4,5</sup>, Timothy J. Whitmore<sup>4</sup>, Christopher H. Heath<sup>4,6</sup>, Ingrid Manson<sup>3</sup>, Madhu Page-Sharp<sup>7</sup>, Sam Salman<sup>1</sup>, John Dyer<sup>2</sup>, Timothy M. E. Davis<sup>1</sup>

<sup>1</sup> School of Medicine and Pharmacology, University of Western Australia, Fremantle Hospital, Fremantle, Western Australia, Australia, <sup>2</sup> Department of Infectious Diseases, Fremantle Hospital and Health Service, Fremantle, Western Australia, Australia, <sup>3</sup> Pharmacy Department, Fremantle Hospital and Health Service, Fremantle, Western Australia, Australia, <sup>4</sup> Department of Microbiology and Infectious Diseases, Royal Perth Hospital, Perth, Western Australia, Australia, <sup>5</sup> School of Pathology and Laboratory Medicine, University of Western Australia, Perth, Western Australia, Australia, <sup>6</sup> School of Medicine and Pharmacology, University of Western Australia, Royal Perth Hospital, Perth, Western Australia, Australia, <sup>7</sup> School of Pharmacy, Curtin University, Bentley, Western Australia, Australia

has drawn is patients receiving antibiotics.<sup>1</sup> patients are the hospital der of their strategy has treatment-as loss in posit The introdu tomeric infu feasibility of devices adn sion without an electrical pump.<sup>3</sup>

Regarding: administrati cally prepare macy and d home for ad care professi

**Purpose.** The stability of doripenem 500 and 1000 mg in polyvinyl chloride (PVC) bags and elastomeric pumps at various storage temperatures was evaluated.

injection and 7 days in 9% dextrose injection. A white precipitate, which returned to solution by shaking, was noted after thawing the frozen containers. Whether thawed

### Abstract

**Objectives:** Concerns regarding the clinical impact of meropenem instability in continuous infusion (CI) devices may contribute to inconsistent uptake of this method of administration across outpatient parenteral antimicrobial therapy (OPAT) services.

**Methods:** We retrospectively reviewed the clinical efficacy and safety of CIs of meropenem in two Australian tertiary hospitals and assessed its stability under simulated OPAT conditions including in elastomeric infusion devices containing 1% (2.4 g) or 2% (4.8 g) concentrations at either 'room temperature' or 'cooled' conditions. Infusate aliquots were assayed at different time-points over 24 hours.

**Results:** Forty-one (82%) of 50 patients had clinical improvement or were cured. Adverse patient outcomes including hemato-, hepato- and nephrotoxicity were infrequent. Cooled infusers with 1% meropenem had a mean 24-hour recovery of 90.3%. Recoveries of 1% and 2% meropenem at room temperature and 2% under cooled conditions were 88%, 83% and 87%, respectively. Patients receiving 1% meropenem are likely to receive >95% of the maximum deliverable dose (MDD) over a 24-hour period whilst patients receiving 2% meropenem should receive 93% and 87% of the MDD under cooled and room temperature conditions, respectively.

**Conclusions:** Meropenem infusers are likely to deliver ~95% MDD and maintain effective plasma concentrations throughout the dosing period. These data reflect our local favourable clinical experience with meropenem CIs.

**Citation:** Manning L, Wright C, Ingram PR, Whitmore TJ, Heath CH, et al. (2014) Continuous Infusions of Meropenem in Ambulatory Care: Clinical Efficacy, Safety and Stability. PLoS ONE 9(7): e102023. doi:10.1371/journal.pone.0102023

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**Funding:** The elastomeric infusion devices, temperature monitoring strips, meropenem for infusion, ertapenem internal standard and ice bricks were provided free of charge by Baxter Healthcare, Timstrip UK Ltd, Ranbaxy Australia Pty Ltd, Merck & Co., Inc. and Interaction Branding Pty Ltd, respectively. TD was supported by a National Health and Medical Research Council of Australia Practitioner Fellowship. Internal funding for this work was provided by the School of Medicine and Pharmacology, University of Western Australia and the Department of Infectious Diseases, Fremantle Hospital and Health Service. Additional funding for the development of the meropenem assays was provided through a National Health and Medical Research Council of Australia project grants 634343 and 101212. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

**Competing Interests:** The elastomeric infusion devices, temperature monitoring strips, meropenem for infusion, ertapenem internal standard and ice bricks were provided free of charge by Baxter Healthcare, Timstrip UK Ltd, Ranbaxy Australia Pty Ltd, Merck & Co., Inc. and Interaction Branding Pty Ltd, respectively. This does not alter the authors' adherence to PLOS ONE policies on sharing data and materials.

\* Email: laurens.manning@uwa.edu.au

## Stability of doripenem, imipenem and meropenem at elevated room temperatures

Sir,

Room temperature stability of a pharmaceutical preparation is generally assessed at 25 °C; however, actual room temperatures may be substantially higher in many settings. These temperatures may lead to reduced stability, yielding lower than expected in vivo concentrations. At worst, a decrease in antimicrobial exposure may result in clinical failure or development of resistance. Additionally, prolonged infusions are frequently used to help optimise the pharmacodynamics of  $\beta$ -lactams, which further amplifies stability concerns since the antibiotic must remain stable throughout the 2–4-h infusion. Here we determined the stability of doripenem, imipenem and meropenem at three temperatures exceeding 25 °C.

Commercially available 500 mg vials of doripenem (Doribax®; Ortho-McNeil-Janssen), imipenem/cilastatin (Primaxin®; Merck) and meropenem (Merrem®; AstraZeneca) were reconstituted with 10 mL of normal saline and were then diluted in 90 mL of normal saline to produce 5 mg/mL solutions. Six bags were made for each antibiotic at each storage temperature and the stability of all three antibiotics was determined in unison at 30 °C, 35 °C and 40 °C. Duplicate 1 mL samples were taken from each bag immediately after preparation (0 h) and at 1, 2, 3, 4, 5, 6, 8, 10, 12, 16 and 24 h and then frozen at –80 °C until assayed. Visual assessment of colour and clarity was made and the pH was determined using an Orion PerpHecT® 320 pH meter (Thermo Fisher Scientific) at each time point. Samples were independently analysed using validated, stability-indicating high-performance liquid chromatography assays and the average concentration at each time point was utilised. Forced degradation of each antibiotic was performed and no interfering peaks were noted. Drug potency was determined as percentage of the initial (0 h) concentration remaining. Solutions maintaining  $\geq 90\%$  of the initial concentrations were considered stable. The interday coefficient of variations (CV) for each antibiotic was  $\leq 5.1\%$  and the intraday CV was  $\leq 6.6\%$ .

A summary of doripenem, imipenem and meropenem stability at each temperature is shown in Table 1. At 30 °C, imipenem, meropenem and doripenem were stable for 6, 12 and 16 h, respectively. The respective stability was reduced to 4, 8 and 12 h when stored at 35 °C and to 3, 6 and 8 h at 40 °C. Doripenem and meropenem solutions ranged from colourless to slightly yellow, whilst imipenem ranged from colourless to brown. No precipitate was identified in any solution. The pH ranged from 4.26–5.28, 4.63–7.44 and 7.33–7.74 for doripenem, imipenem and meropenem, respectively.

**Table 1**  
Summary of doripenem, imipenem and meropenem stability (time to reach <90% initial concentration) at 30 °C, 35 °C and 40 °C.

Drug	Temperature		
	30 °C	35 °C	40 °C
Doripenem	16 h	12 h	8 h
Imipenem	6 h	4 h	3 h
Meropenem	12 h	8 h	6 h

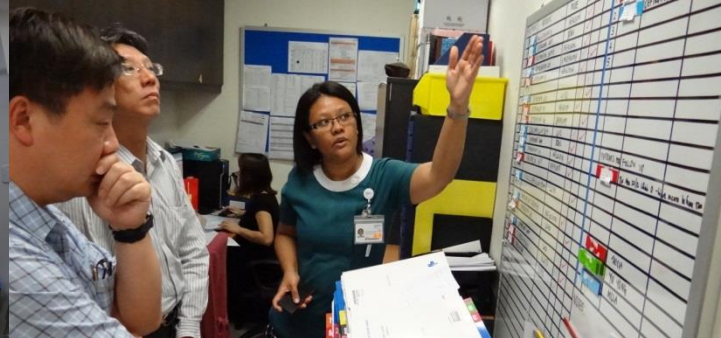


# OPAT : Setting the Scene

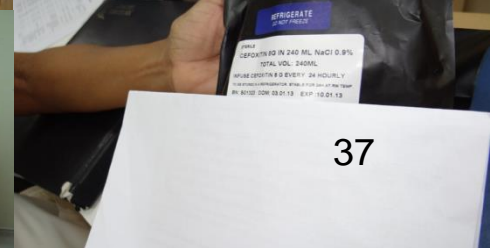
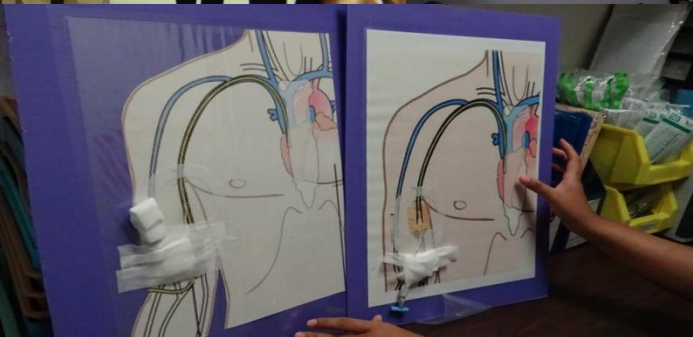
Dilip Nathwani  
Birmingham, October 2009

Ninewells Hospital & Medical School  
Dundee DD1 9SY





National  
University  
Hospital









# Antibiotics in Elastomers (Eg, Infusors) - Stability Data

DRUGS	CONCENTRATION/UNIT	AMOUNT OF DRUGS	LV10 (1DAY)	RECONSTITUTION	DILUENT	2-8 DEG C	25 DEG C
Amikacin SO <sub>4</sub>	0.25-20 mg/ml	60-4800mg	YES	NA	DSW or NS	28 days	+48hrs
Amphotericin B	0.2-0.5mg/ml	48-120 mg	YES	WFI	DSW	9days	+24hrs
	0.5-5mg/ml	120-1200 mg			DSW	9days	+24hrs
Aztreonam	5-60mg/ml	1200-14400 mg	YES	WFI	DSW or NS	28days	+24hrs
	1-5 mg/ml	240-1200 mg			DSW or NS	7days	+48hrs
Cefepime	1-5 mg/ml	240-1200 mg	YES	WFI	DSW or NS	14days	+24hrs
	5-60 mg/ml	1200-14400 mg			DSW or NS	-	24hrs
Cefoxitin	5-60 mg/ml	1200-14400 mg	YES	WFI	DSW / NS / WFI	10days	-
	60 mg/ml	1400 mg			NS	10days	-
	5 mg/ml	1200 mg			NS	-	24hrs
	30 mg/ml	7200 mg			WFI	10days	-
Ceftazidime	5-40 mg/ml	1200-9600 mg	YES	WFI	NS	10days	24hrs
	5-40 mg/ml	1200-9600 mg			DSW	5days	24hrs
Ceftioxone	5-40 mg/ml	1200-9600 mg	YES	WFI	DSW or NS	21days	+24hrs
Cephazolin	5-40 mg/ml	1200-9600 mg	YES	WFI	WFI	10days	24hrs
	10-40 mg/ml	2400-9600 mg			WFI	17days	+4days
Clindamycin	2-12 mg/ml	480-2880 mg	YES	NA	DSW or NS	10days	24hrs
Erythromycin	2.5-10 mg/ml	600-2400 mg	YES	WFI	DSW	10days	-
	2.5-10 mg/ml	600-2400 mg			NS	10days	24hrs
Flucloxacillin	5-60 mg/ml	1200-14400 mg	YES	WFI	NS or WFI	10days	+48hrs
Gentamicin	0.5-5 mg/ml	120-1200 mg	YES	NA	DSW or NS	10days	24hrs
	0.8-2.4 mg/ml	192-576 mg			NS	17days	+17days
Piperacillin	10-80 mg/ml	2400-19200 mg	YES	NS	DSW	14days	+24hrs
	10-80 mg/ml	2400-19200 mg			NS	14days	24hrs
Benzylpenicillin	25-100KU/ml	6-24MU	YES	CCCITBUF	NS	19days	+2hrs at 30°C
	0.5-4.8 mg/ml	120-1152 mg			DSW or NS	10days	24hrs
Tobramycin	0.5-5 mg/ml	120-1200 mg	YES	NA	DSW	7days	+24hrs
	0.5-5 mg/ml	120-1200 mg			NS	7days	+48hrs
Tazocin	11.25-90 mg/ml	2700-21600 mg	YES	WFI	DSW or NS	7days	24hrs
	5-20 mg/ml	1200-4800 mg			DSW or NS	11days	+3days
Vancomycin	10-20 mg/ml	2400-4800 mg	YES	WFI	DSW or NS	10days	24hrs
	10-20 mg/ml	2400-4800 mg			DSW	17days	+3days

## LIST OF ANTIBIOTICS SUITABLE FOR OPAT

Abx	Diluent	Dose per day	Conc	Fill Volume (ml)	Pump #	Duration
Aztreonam	N/S	3000mg	20mg/ml	150	270-54	24hr
		*1200 - 14400mg	5 - 60mg/ml	240	LV10	24hr
Amphotericin	D5	48 - 1200mg	0.2 - 5mg/ml	240	LV10	24hr
Cefazolin	N/S	3000mg	20mg/ml	150	270-54	24hr
		*1200 - 9600mg	5 - 40mg/ml	240	LV10	24hr
Cefepime	N/S	2000mg	13.3mg/ml	150	270-54	24hr
		2000mg	20mg/ml	150	270-54	24hr
		6000mg	40mg/ml	150	270-54	24hr
		*240 - 1200mg	1 - 5mg/ml	240	LV10	24hr
Cefoxitin	N/S	3000mg	20mg/ml	150	270-54	24hr
		*1200 - 14400mg	5 - 60mg/ml	240	LV10	24hr
Ceftazidime	N/S	3000mg	20mg/ml	150	270-54	24hr
		2000mg	8mg/ml	250	270-24	24hr
		6000mg	40mg/ml	150	270-54	24hr
		*1200 - 9600mg	5 - 40mg/ml	240	LV10	24hr
Ceftriaxone	N/S	1000mg	20mg/ml	100	100-48	48hr
		2000mg	40mg/ml	100	100-48	48hr
~5-40mg/ml (B.Braun)		4000mg	31.3mg/ml	255	270-54	48hr
		3000mg	23.5mg/ml	255	270-54	48hr
Flucloxacillin	N/S	*1200 - 14400mg	5 - 60mg/ml	240	LV10	24hr
Pip/Tazo	N/S	4.5g TDS (13.5g)	80mg/ml (pip)	150	270-54	24hr
		*2400 - 19200mg	10-80mg/ml (pip)	240	LV10	24hr
Vancomycin	D5	500mg	10mg/ml	100	100-48	48hr
		750mg	15mg/ml	100	100-48	48hr
~up to 50mg/ml (B.Braun)		1000mg	20mg/ml	100	100-48	48hr
		1250mg	25mg/ml	100	100-48	48hr
		1500mg	30mg/ml	100	100-48	48hr
		2000mg	40mg/ml	100	100-48	48hr
		2250mg	45mg/ml	100	100-48	48hr
		2500mg	50mg/ml	100	100-48	48hr
		3000mg	23.5mg/ml	255	270-54	48hr
		4000mg	31.4mg/ml	255	270-54	48hr
Doripenem	N/S	750mg	5mg/ml	150	270-54	24hr
		1500mg	10mg/ml	150	270-54	24hr
Penicillin	N/S	6-24MU	25-100kU/ml	240	LV10	24h

\* To be used ONLY if Easypump is NOT suitable.

Possible if hep-lock is done after infusion is completed

Abx	Diluent	Dose per day	Conc	Volume	Pump #	Duration
Cefepime	N/S	4000mg	20mg/ml	200	270-24	18h

### Not suitable

Meropenam	N/S	1g TDS (3g)
		2g TDS (6g)

### Flow Rates

LT100-48  
LT270-54  
LT270-24

2ml/hr  
5ml/hr  
10ml/hr

Baxter LV10 10ml/hr

07052012

### SGH PHARMACY SCHEDULE FORM

Abx Regimen: Vancomycin 500mg OM Administration rate: 2ml/hr Pump: 100-48  
Stability: 7 Days @ 2-8°C Duration: 6 weeks from 3/12/13  
48H @ 24HRT

Month	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
Inf time	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A
# Pump																															
# Vials																															

COSTING # Bags = 12

# Vials = 12 x 3 = 36

Abx Vancomycin 500mg 34.10 x 36 = \$1247.60  
Disposal pump @ \$30.90 x 12 = \$478.80  
Drug prep fee - complex @ \$16.70 x 12 = \$224.40

Prepared by: Hazirah Checked by: Wing Yee

Outpatient Antibiotic Therapy  
Telephone: 63266727 Fax: 63241837

Pharmacy  
Telephone: 63214398 Fax: 63265554





1<sup>st</sup> Working Group Meeting for OPAT in Nov 2013

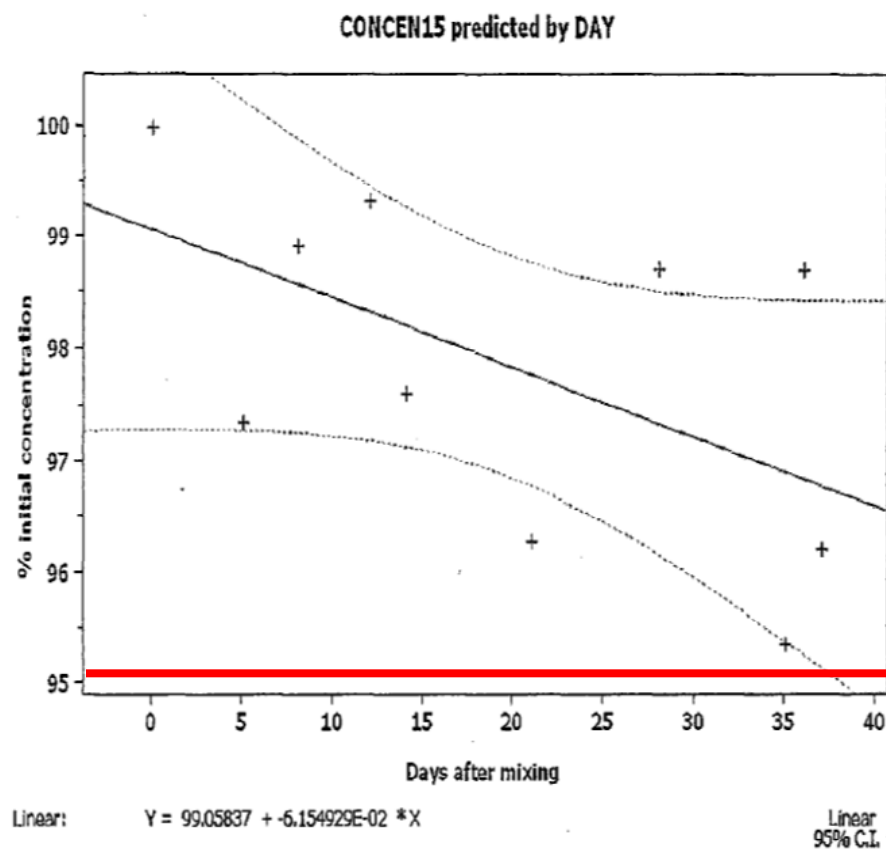


***What are the details of  
antibiotic stability testing?***

Test	Methodology	Criteria
Chemical stability	-HPLC assay according to the BP/USP/manufacture's method of assay at day 0 and at each sampling point. -Linear regression analysis	-Initial concentration (Day 0)=100% -Use pharmacopoeial limits (e.g. 95 to 105% of labeled potency), if not available, use limits set out by the manufacturer as acceptable limits -95% confidence limits to be calculated -The shelf life is the duration after fresh preparation that the lower fiducial curve meets the lower pharmacopoeial /manufacturer limit
PH	BP/EP/USP method	-Product expiry is indicated by two successive excursions +/- 1 PH unit compared with the freshly prepared solution
Color	Visual inspection	-Color of the test sample shall not differ significantly from that of the freshly prepared solution
Particles	Visual inspection	-No particle shall be detected upon visual inspection
Degradation	-A freshly prepared solution stored at 40-50 °C/ 75% RH ±5%RH exposed to light for 7-10 days to develop degradation products, detectable by HPLC trace	The trace is compared with that of the freshly prepared sample (at time 0) to identify peaks not present in the freshly prepared sample. At each time point throughout the study comparison with the "fresh" and degraded traces will assist in identifying emergence degradants.
	The solution is to be chromatographed according to the assay method as a reference to analyze the degradation products. No need to identify degradants	

# Linear Regression Concept for stability determination

An example: Flucloxacillin Sodium 15mg/mL in sodium chloride 0.9% stored in the dark at 2-8°C



Drug	Concentration	Assay Specification	Acceptance limit
Buffered Benzylpenicillin	50ku/ml	USP	90% -110%
	100ku/ml		
Flucloxacillin	8.33mg/mL	BP	95-105%
	50mg/ml		
Cefoxitin	12.5mg/ml	CP (中國藥典)	90% -110%
	50mg/ml		
Cefoperazone- Sulbactam	5mg/ml	Manufacturer	90-110%
	20mg/ml		
Ceftriaxone	5mg/mL	USP	90-110%
	40mg/mL		
Cefepime	4mg/mL	USP	90%-110%
	30mg/mL		
Ceftaroline	2.5mg/ml	Manufacturer	95%-105%
	7.5mg /ml		
Doripenem	5mg/mL	Manufacturer	95%-105%
	10mg/mL		
Piperacillin/Tazobactam	11.25mg/mL	Manufacturer	90%-110%
	90mg/mL		

# Ultra High Performance Liquid Chromatographic (UPLC) system



- a thermostat column oven (ACQUITY UPLC CH-A 186015042, from WATERS)
- a delivery pump (ACQUITY UPLC I-CLASS BSM 186015000, from WATERS)
- an autosampler (ACQUITY UPLC I-CLASS Sample Manager-FTN 186015046, from WATERS)
- a variable –wavelength absorbance detector (ACQUITY UPLC I-CLASS e<sup>2</sup> PDA Detector 176015091, from WATERS)
- chromatography data system (WATERS EMPOWER).
- Measurements of pH were determined with a precision pH meter (FiveEasy, METTLER-TOLEDO)



# Drug Stability testing Protocol : 2013 version

Test	Day 0 (upon receiving)	Day 1 (24h)	Day 4 (96h)	Day 9 (216h)	Day 11 (264h)	Day 14 (336h)
pH						
Colour Change						
Particle precipitation						
Degradation (Part 1)	Sample Pre-stressed					
Degradation (Part 2)						
Storage at 2-8°C	Series 1 (Infusor 1,2,3) Series 2 (Infusor 4,5,6) Series 3 (Infusor 7,8,9)	Series 1 (Infusor1-3)	Series 1 (Infusor 1-3) Series 2 (Infusor 4-6)	Series 1 (Infusor 1-3)  Series 3 (Infusor 7-9)	Series 1 (Infusor 1-3)	Series 1 (Infusor 1-3)
Storage at controlled room temp 30°C ±2°C / 65±5%RH after 2-8 °C			Series 2 (Infusor 4-6)	+24h	Series 3 (Infusor 7-9)	+24h
			Series 2 (Infusor 4-6)	+48h	Series 3 (Infusor 7-9)	+48h
			Series 2 (Infusor4-6)	+72h	Series 3 (Infusor 7-9)	+72h
			Series 2 (Infusor 4-6)	+96h	Series 3 (Infusor 7-9)	+96h
Stability indicated by HPLC Assay	initial conc.	% initial conc.	% initial conc.	% initial conc.	% initial conc	% initial conc.

# Summary of Drug Stability Testing: 2013 initial protocol

Drug	Concentration	Time (h) at 30°C After refrigeration (2-8°C) for	
		4 days	9 days
Ceftriaxone (Livon, China)	5 mg/ml	+36h	+24h
	40 mg/ml	+28h	+16h
Cefepime (Bristol-Myers Squibb , Italy)	4 mg /ml	Regression analysis of day 4-8 or day 9-13 drug conc. remaining vs time data both yielded a statistically significant negative correlation coefficient value. Concentration in almost all samples are above 90% potency line which lies above the 95% lower confidence bound of the regression line of the day 4-8 and of the day 9-13 data respectively. No expiration date can be assigned	
	30 mg /ml	Regression analysis of day 4-8 or day 9-13 drug conc. Remaining vs time data both yielded a statistically significant negative correlation coefficient value. Concentration in almost all samples are below the 90% potency line which lies above the 95% lower confidence bound of the regression line. No expiration date can be assigned	
Piperacillin / Tazobactam (GlaxoSmithKline, India)	11.25 mg/ml	+48h	+72h
	90 mg/ml	+24h	+24h

# Cefepime 4 mg/ml

Figure 4.4.1

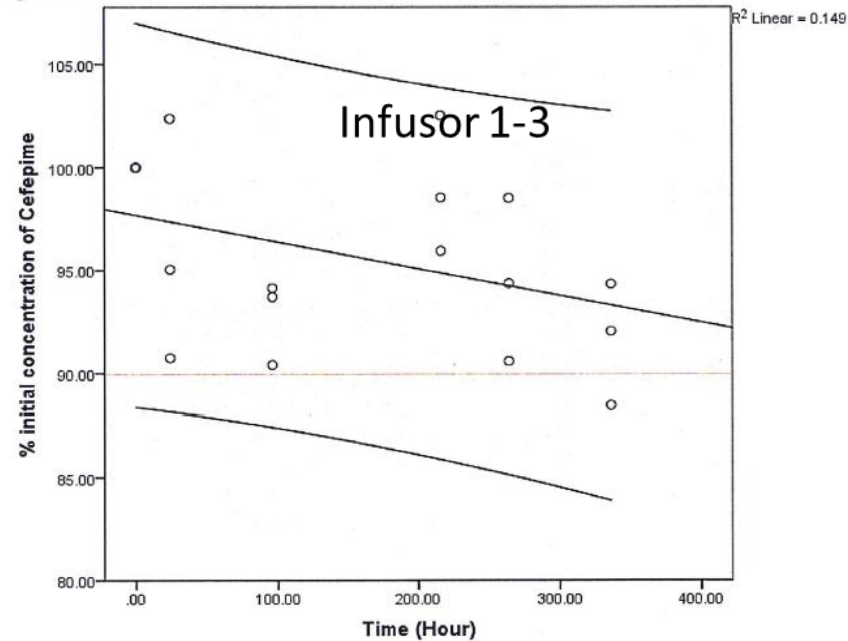
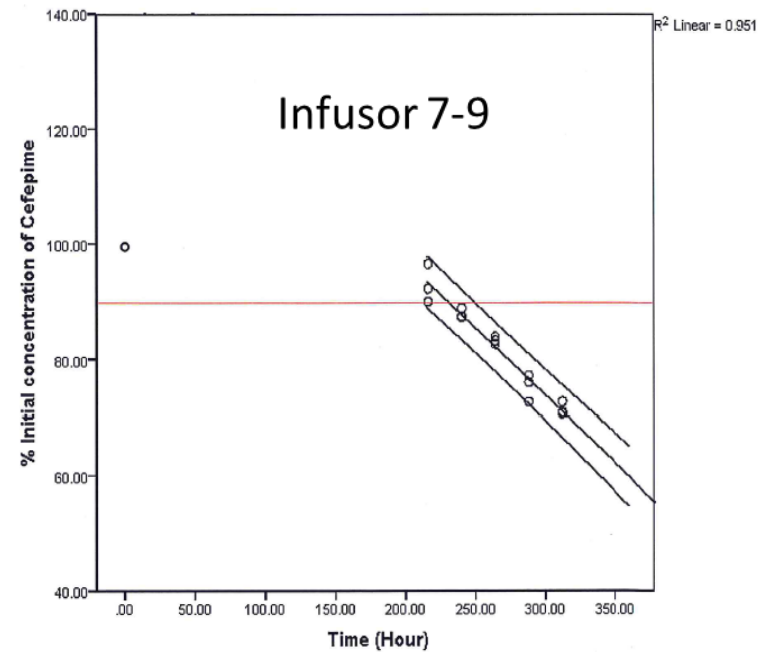
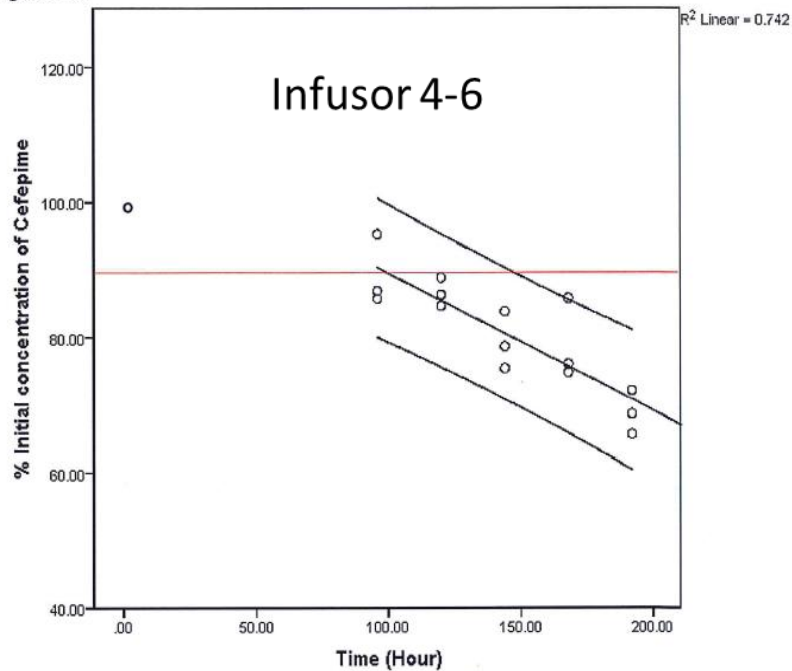
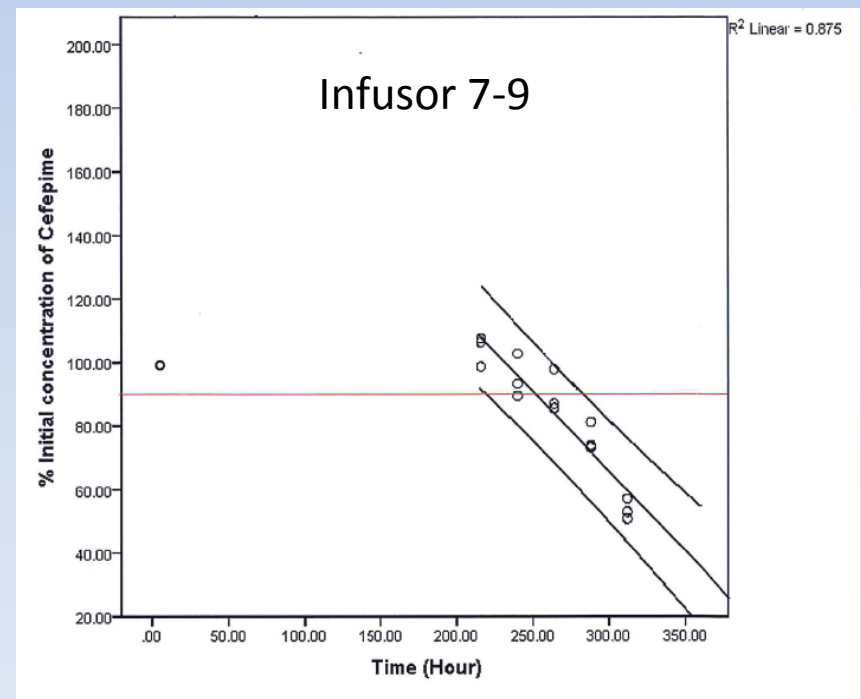
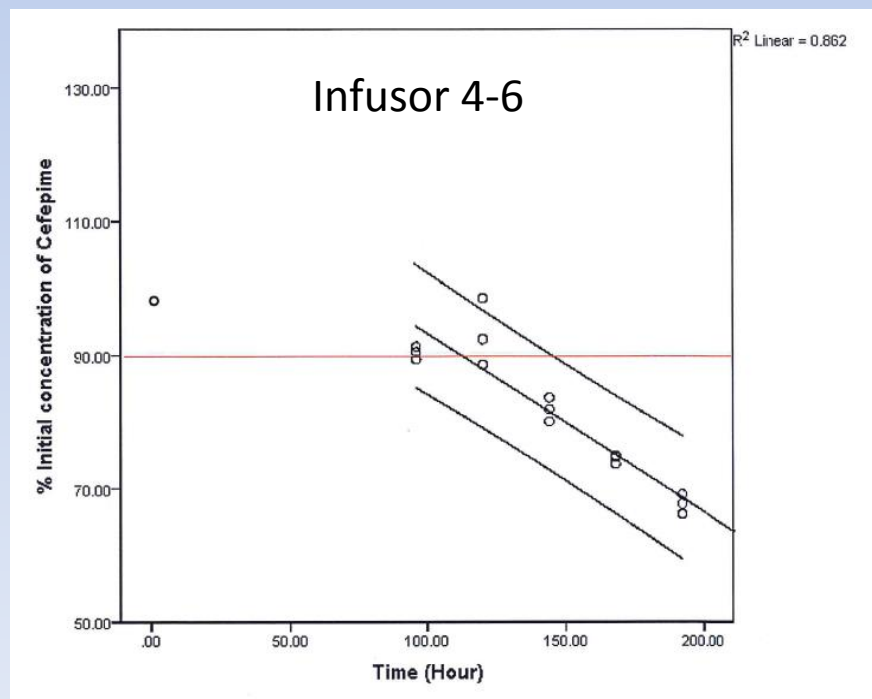
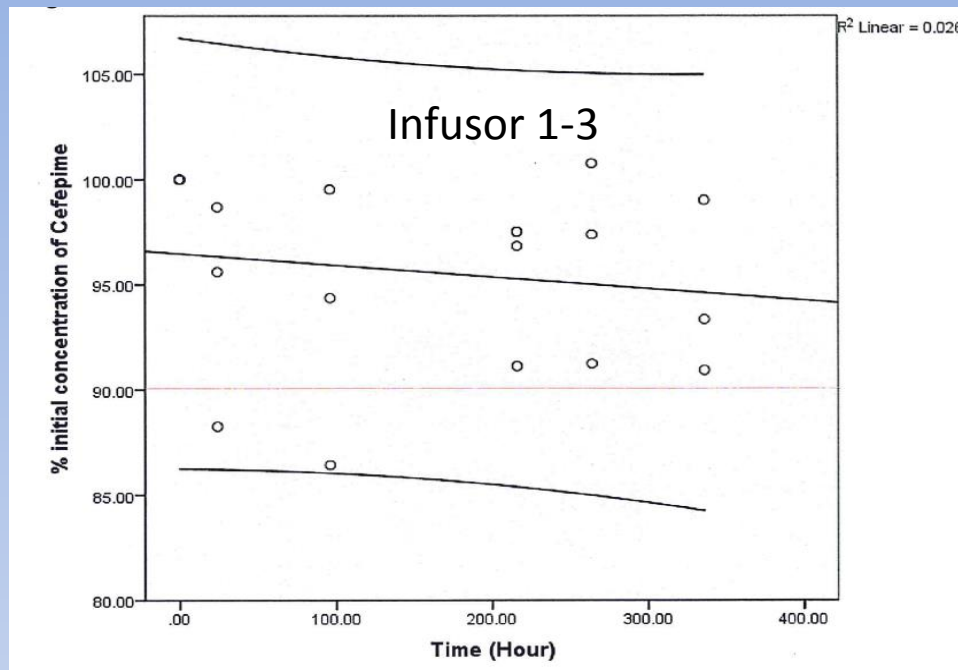


Figure 5.4.1



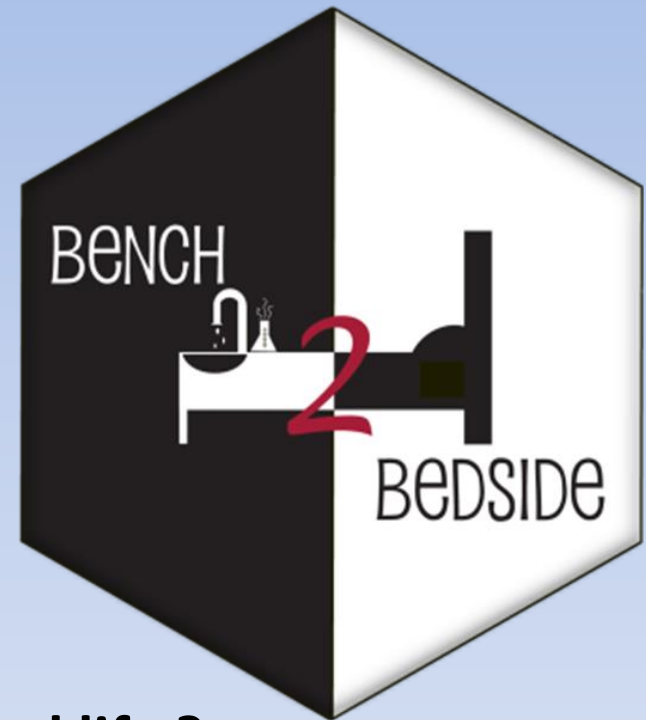
# Cefepime 30 mg /ml





# Interim review

- Anything wrong with our protocol?
- Can we revise and improve it?
- What are the adjustable variables ?
  - Sampling time points
  - Temperature condition
- How to revise and apply practically in real life ?



# Drug Stability testing Protocol : 2014 revised version

Test	Day 0 (upon receiving)	Day 1 (24h)	Day 7 (168h)	Day 9 (216h)	Day 11 (264h)	Day 14 (336h)
pH						
Colour Change						
Particle precipitation						
Degradation (Part 1)	Sample Pre-stressed					
Degradation (Part 2)						
Storage at 2-8°C	Series 1 (Infusor 1,2,3) Series 2 (Infusor 4,5,6) Series 3 (Infusor 7,8,9)	Series 1 (Infusor1-3)	Series 1 (Infusor 1-3) Series 2 (Infusor 4-6)	Series1 (Infusor 1-3)  Series 3 (Infusor 7-9)	Series1 (Infusor 1-3)	Series1 (Infusor 1-3)
Storage at controlled room temp 25 °C ±2°C / 65±5%RH after 2-8 °C			Series 2 (Infusor 4-6)	+6h	Series 3 (Infusor 7-9)	+6h
			Series 2 (Infusor 4-6)	+24h	Series 3 (Infusor 7-9)	+24h
			Series 2 (Infusor4-6)	+30h	Series 3 (Infusor 7-9)	+30h
			Series 2 (Infusor 4-6)	+48h	Series 3 (Infusor 7-9)	+48h
Stability indicated by HPLC Assay	Initial conc.	% initial conc.	% initial conc.	% initial conc.	% initial conc	% initial conc.

# Summary of Drug Stability Testing: 2014 revised protocol

Drug	Concentration	Time (h) at 25°CAfter refrigeration (2-8°C) for	
		7 days	9 days
Buffered Benzylpenicillin (Pfizer, Italy)	50 ku/ml	+48h	+48h
	100 ku/ml	+48h	+48h
Cefoxitin (Shenzhen Zhijun Pharmaceutical, China)	12.5 mg/ml	+29h	+21h
	50 mg/ml	+31h	+20h
Cefoperazone / Sulbactam (ShenZhen Lijian Pharmaceutical, China)	5 mg/ml	+27h	+16h
	20 mg/ml	+48h	+34h
Ceftaroline (Astrazeneca, Italy)	2.5 mg/ml	+6h	+3h
	7.5 mg/ml	+8h	+2h
Doripenem (Janssen-Cilag, Japan)	2 mg /ml	Regression analysis of day 7-11 or day 9-13 drug conc. remaining vs time data both yielded a statistically significant negative correlation coefficient value. The 95% potency line lies much above the 95% lower confidence bound of the regression line of the day 7-11 and of the day 9-13 respectively	
	10 mg/ml	Regression analysis of day 7-11 or day 9-13 drug conc. remaining vs time data both yielded a statistically significant negative correlation coefficient value. The 95% potency line lies much above the 95% lower confidence bound of the regression line of the day 7-11 and of the day 9-13 respectively	
Drug	Concentration	Time (h) at 20°CAfter refrigeration (2-8°C) for	
Flucloxacillin (Wockhardt, UK)	50mg/ml	+18h	+4h

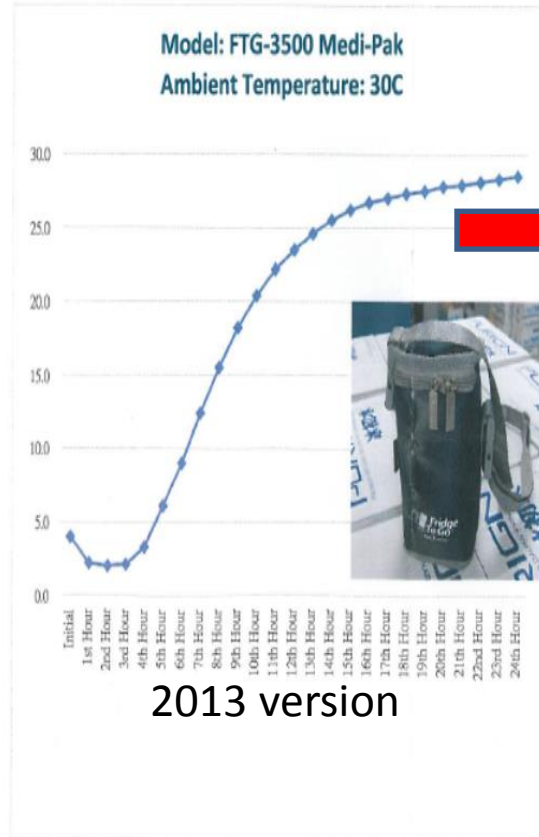
# Simulated ambient temperature testings in a tailored made cooler bag

- To ensure the elastomeric device under desirable temperature condition within carrying bag

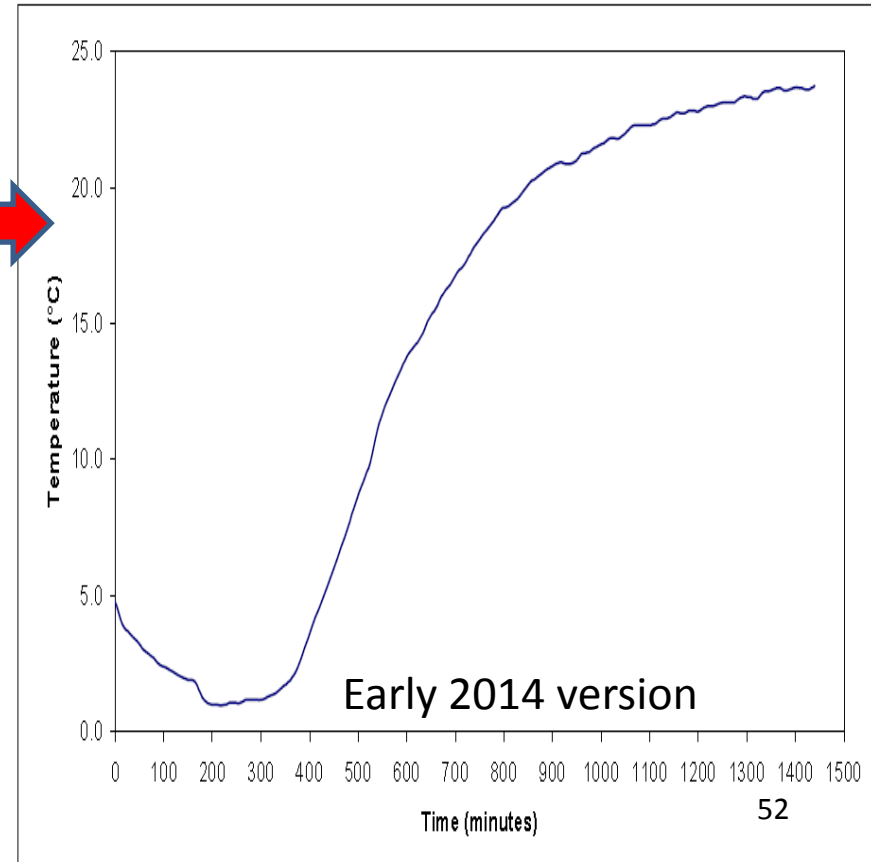


Cooling Performance TEST of Fridge-to-go® portable Fridge Bag for Medicine of D5 provided by Princess Margaret Hospital

TEST A	
Medicine of D5	
taken right from Fridge	
DURATION	TEMPERATURE °C
Initial	4.0
1st Hour	2.2
2nd Hour	2.0
3rd Hour	2.1
4th Hour	3.3
5th Hour	6.1
6th Hour	9.0
7th Hour	12.4
8th Hour	15.5
9th Hour	18.2
10th Hour	20.4
11th Hour	22.2
12th Hour	23.5
13th Hour	24.6
14th Hour	25.5
15th Hour	26.2
16th Hour	26.7
17th Hour	27.0
18th Hour	27.3
19th Hour	27.5
20th Hour	27.8
21th Hour	27.9
22nd Hour	28.1
23rd Hour	28.3
24th Hour	28.5



Appendix





# Elastomeric Related Antibiotic Stability Database

[illegible]

# Challenges & Opportunities

- **NO ideal testing protocol at this moment ....**
  - Manpower constraints
  - Drug budget and Laboratory Testing budget constraints
  - Limited Compounding sessions and such service not available in every hospital
- **Looking for collaborations.....**
  - Standardizing the testing protocol
  - Strengthening our antimicrobials' stability database through overseas collaboration
  - Minimize the wastage of resources and time in testing on some brand specific antibiotics
  - Publications

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**Thank You**





# Outpatient Parenteral Antimicrobial Therapy (OPAT) Workshop 2014, Hong Kong

## OPAT GLOBAL OVERVIEWS, STANDARDS AND OUTCOMES



**Dr Sanjay Patel**  
Consultant  
Southampton Children's Hospital  
The United Kingdom



**Prof Dale Fisher**  
Senior Consultant & Head  
National University Hospital  
Singapore



**Dr David Lye**  
Senior Consultant  
Tan Tock Seng Hospital  
Singapore



**Dr Ryota Hase**  
Senior Consultant  
Kameda Medical Center  
Japan



**Mr Mark Gilchrist**  
Consultant Pharmacist  
Imperial College Healthcare  
NHS Trust, the United Kingdom



**Ms Zuraidah Sulaiman**  
Advanced Practice Nurse  
National University Hospital  
Singapore



**Ms Zhong Lihua**  
Senior Staff Nurse  
Tan Tock Seng Hospital  
Singapore



**Dr TSANG Kay-yan**  
Associate Consultant  
Princess Margaret Hospital  
Hong Kong



**CO-ORGANIZERS:**



**DATE**  
4<sup>TH</sup> - 5<sup>TH</sup>  
DECEMBER 2014

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LECTURE THEATRE, 7/F, BLOCK H,  
PRINCESS MARGARET HOSPITAL

**TIME**  
8:30A.M. - 5:00P.M.