



# INTRAVENOUS ADMIXTURE SYSTEM

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# Intravenous Admixture System

- Hospital pharmacist have been involved with the preparation of parenteral dosage forms for several decades
- Was only compounding sterile intravenous, intrathecal, ophthalmic, and irrigating solutions that were not available commercially





# Intravenous Admixture System

- The first needle was made from a quill attached to an animal bladder
  - Lack of aseptic techniques and sterile, pure drugs caused failure in parenteral therapy until 19<sup>th</sup> century
- 



# Intravenous Admixture System

- Through effort of Pasteur and others (Lister, Koch, Jenner, Hunter and Seibert) aseptic technique, bacteriologic filtration methods, and pyrogen free diluents were developed
  - Gained recognition by the national formulary and U.S. pharmacopeia (USP)
- 

# Intravenous Admixture System

- 40% of hospital inpatients receive IV preparations (and it is continue raising!)
- replacing fluids and electrolytes, provide nutrition and administer medication



# Intravenous Admixture System

- Parenteral comes from a Greek words “para” and “enteron” =outside the intestine
- Injection medication into veins and through subcutaneous tissue





# Basic Intravenous Therapy

- Intravenous (IV) route of administrations is the most common route that parenteral dose are administered today.
  - Other parenteral dosage forms are:
    1. intramuscular (IM)
    2. subcutaneous (SubQ)
    3. intradermal (ID)
    4. epidural
  - IV fluid is in a large-volume parenteral (LVP), usually more than 100 mL
- 



## Risks of Intravenous Therapy

- Infection – results if a product contaminated with bacteria is infused into a patient.
- Air embolus – incidence is low, because many solutions are administered using infusion pumps equipped with an alarm that sound when air is in the IV line. These are called **air-in-line alarms**.
  - in adults it takes 150 or 200 mL of air (much less in infants or pediatric patient) given quickly to result in harm.



## Risks continued...

- Allergic reaction – when a patient has an allergic reaction to a substance given parenterally the reaction is usually more severe than if the same substance was given by another route (e.g. mouth, topically, or rectally)
    - one reason for this is that substances given parenterally cannot be retrieved like substances given by other routes.
  - Incompatibilities – if an incompatibility exists, the drug might precipitate, be inactivated, or adhere to the container. Incompatible solutions should not be administered to patients.
- 



# Risks continued..

- **Extravasation** – occurs when the catheter punctures and exits the vein under the skin, causing drugs to infuse or infiltrate into the tissue.
  - Particulate matter – refers to particles present in parenteral products. When injected into the bloodstream can cause adverse effects to the patient. Examples:
    - microscopic glass fragments
    - hair
    - lint or cotton fibers
    - undissolved drug particles
    - fragments of rubber stoppers
- 



# Risks continued..

- Pyrogens – the by-products or remnants of bacteria, can cause reactions (e.g. fever and chills) if injected in large enough amounts.
- Phlebitis – Irritation of the vein. Caused by:
  - the drug being administered (due to its chemical properties or its concentration)
  - the location of the IV site
  - a fast rate of administration
  - the presence of particulate matter
  - the patient usually feels pain or discomfort along the path of the vein (often severe) and red streaking may also occur



# Intravenous Admixture System

- In 2012 WHO published: nosocomial infection rate of **15 %** for developing countries (based on rates in South Africa) e' a **5 %** mortality rate.
  - Ineffective IC & inappropriate use of antimicrobial agents in health care facilities has resulted in the emergence of **MDR bacteria**.
- 



# Intravenous Admixture System

**Root causes of nosocomial infections and MDR problems in hospitals include the following—**

- Lack of an IC infrastructure and poor IC practices & basic training (procedures)
  - Inadequate facilities and techniques for hand hygiene
  - Lack of isolation precautions and procedures. Large medical and surgical wards
  - Use of advanced, complex treatments without adequate supporting training and infrastructure,
  - Inadequate sterilization, disinfection, and hospital cleaning procedures
- 



# Intravenous Admixture System

- *One of the most important recommendations of WHO IC guidelines:*

## Careful Use of Intravascular Catheters, Intravenous Fluids, and Medications:

- Medication admixtures to IV solutions should be prepared centrally by **qualified pharmacy personnel**. If this is not possible,
- specific policies and procedures should be prepared for nurses who should be certified competent before they are allowed to prepare admixtures.
- **Use all lipid and parenteral nutrition solutions promptly.**



# Intravenous Admixture System

- Admixture system” refers to sterile IV solutions that are prepared by using one or more medications or electrolytes and will be administered via the parenteral route
  - Admixture also could be irrigation, ophthalmic, and intrathecal solutions
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# Intravenous Admixture System





# Intravenous Admixture System

the responsibility of the pharmacy are:

## Contamination

- The pharmacy must maintain a clean area out of the direct flow of traffic with a vertical or horizontal laminar air flow hood to prepare IV admixtures
- 



# Intravenous Admixture System

the responsibility of the pharmacy are:

## Compatibility

- A pharmacist education should prepare him/her to deal with problems of physical, chemical, and therapeutic incompatibilities and to design suitable alternatives when these problem arise
- 



# Intravenous Admixture System

the responsibility of the pharmacy are:

## Stability

- Drug stability information must be readily accessible to the pharmacist in order to determine optimum conditions for drug storage prior and after preparation
  - The stability of a drug at ideal storage conditions will help to establish a reasonable expiration date for the product
  - Product sterility, overall integrity also inspected
- 



# Intravenous Admixture System

the responsibility of the pharmacy are:

## Cost

- Preparation in the pharmacy is more economically than individual nurses on a patient unit
  - The overall cost of drug, diluents procurement, storage, preparation time, and waste is less in pharmacy based admixture program
  - Nurse based program needs coordination of efforts to obtain drugs from the pharmacy as well as diluents solutions from central supply
- 



# Intravenous Admixture System

the responsibility of the pharmacy are:

## Cost (cont')

- In pharmacy frequently administered medications can be obtained in bulk containers which decreases drug procurement cost, and can be prepared in batches, which decreases both labor and waste
  - Nursing time associated with administration to patients is minimized
  - The amount of unused and wasted parenteral is likely to decrease when a pharmacy IV admixture program is used
- 



# Intravenous Admixture System

the responsibility of the pharmacy are:

## Errors

- Reduced in a pharmacy based admixture program
  - It has been less likely for the pharmacist than the other health professionals to make errors in pharmaceutical calculation
  - Standardized dosing charts, showing pre-calculated drug doses and dilutions, contained in admixture area can also reduced the potential of error
- 



# Intravenous Admixture System

the responsibility of the pharmacy are:

## Process

- First pharmacist will determine dosage, diluents, volume of diluent, and rate of administration are correct
  - Next the label will be checked against the original order
  - The final solution with additives will then be checked against the label to ensure that the proper dose has been prepared
    - ***“Read the label three times”***
- 





# Intravenous Admixture System

## Components of an IV program

- Preparation area
  - Policies and procedures
  - Personnel
  - Storage space
  - Admixture systems
- 

# Intravenous Admixture System

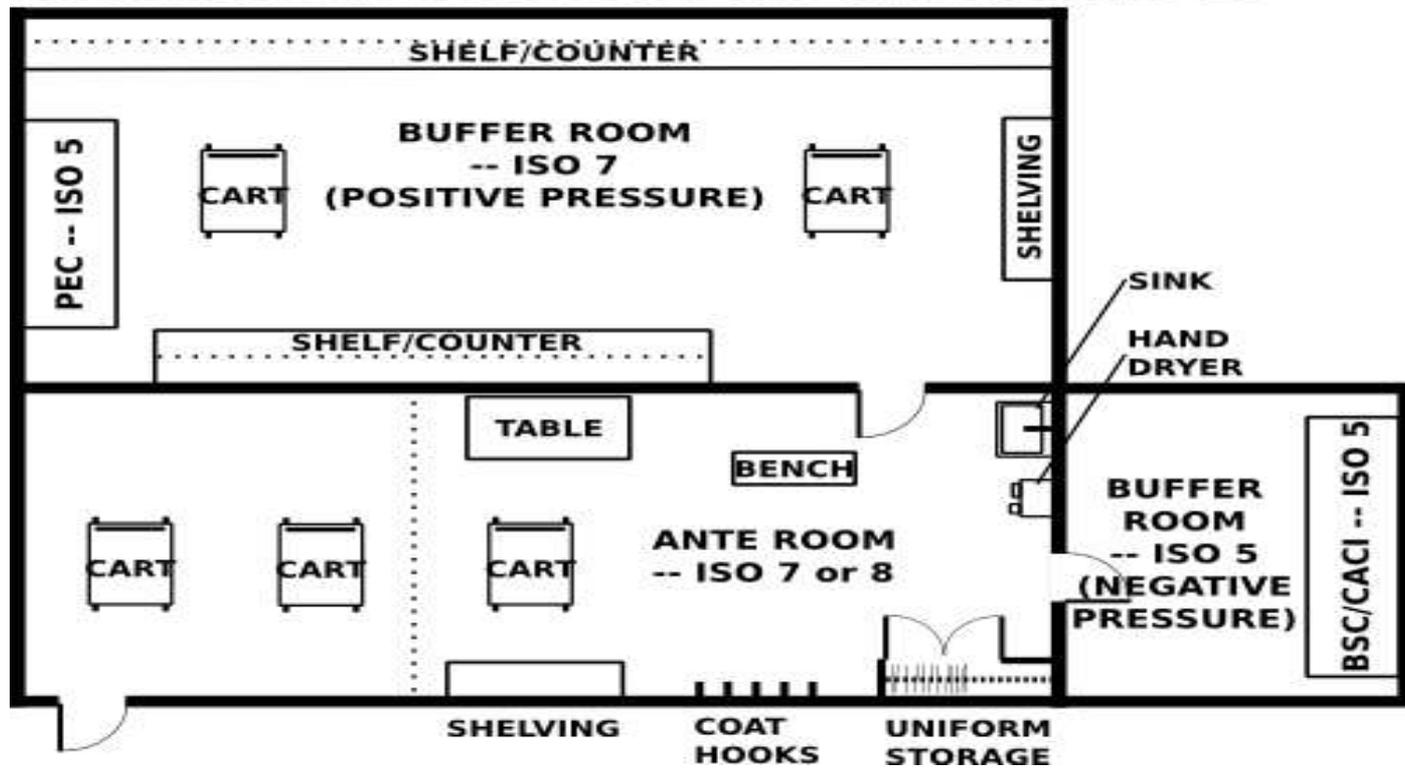
## Components of an IV program

### Preparation area

- Ideally in separate room in the pharmacy  
“clean room”
- Size vary



## EXAMPLE OF CLEAN ROOM FLOOR PLAN SUITABLE FOR HIGH-RISK LEVEL CSPs AND HAZARDOUS DRUGS



# Intravenous Admixture System

**Table 19-1. Preparation area\***

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- Tiled, washable floor covered with a coat of vinyl or epoxy sealant to provide a continuous surface
  - Hand-washing facilities
  - Laminar air-flow hoods: horizontal and/or vertical air-flow
  - Refrigerator
  - Preparation equipment: needles, syringes, alcohol prep pads, gloves, masks, gowns, receptacles for disposables, small-volume parenterals, diluents, and solutions
  - Good lighting
  - Adequate counter space
  - Restricted area or minimized traffic flow
  - Prohibition of smoking, beverages, food, and unauthorized personnel
- 

\*Some references recommend that only sterile equipment be kept in the preparation area.



USP 800 for clean room area



# Intravenous Admixture System

## Components of an IV program

### Policies and procedures

- Guidelines for preparing parenteral products should be outlines in the pharmacy's policy and procedure manual
  - Detailed information regarding preparation, labeling, storage and expiration dating of parenteral products should be readily available in the pharmacy
  - These policy help to provide quality control for the parenteral products
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# Intravenous Admixture System

Components of an IV program

Polices and procedures

- *Stability*

Rigorous stability testing by the

- pharmaceutical manufacturer
- Independent investigators
- Put in your mind that stability is affected by place, environmental condition, diluent used to administer the product, other drugs that may be mixed with
- **Stability and sterility! Gives the expiration date**





# Intravenous Admixture System

Components of an IV program

Policies and procedures

- *incompatibility*

Physical: visible change e.g. precipitation

Chemical: may or not visible change, deterioration or inactivation of an active ingredient

Therapeutic: drug-drug or drug-disease interaction that lead to potentiating of drug effect, drug toxicity, deterioration



# Intravenous Admixture System

Components of an IV program

Polices and procedures

- ***Aseptic Technique***

Method of handling sterile products, a sterile parenteral dosage form is free from living microorganisms, particulate matter, and pyrogens

It refers to the ability of personnel who prepare these IV solutions to handle these products in the clean environment of a laminar or vertical air flow hood without introducing viable microorganisms into the product



# Intravenous Admixture System

## Components of an IV program

### Sterile compounding area

- Sterile parenteral solutions must be free of living microorganisms and relatively free of particles and pyrogens.
- A sterile compounding area should be cleaned daily and segregated from normal pharmacy operations, patient specimens, nonessential equipment, and other materials that produce particles. Examples:
  - traffic flow should be minimized.
  - floors should be disinfected periodically.
  - trash should be removed frequently and regularly.



# Intravenous Admixture System

Components of an IV program

Polices and procedures

- *Labeling and check systems*

Reviewed against the patient's current medication profile



# Intravenous Admixture System

## Labeling & checking system

Properly label the IV with the following information:

- Patient name, ID number and room number (if inpatient)
  - Bottle or bag sequence number, when appropriate
  - Name and amount of drug(s) added
  - Name and volume of admixture solution- Auxiliary labeling
  - Approximate final total volume of the admixture.
  - Prescribed flow rate (in mLs per hour)
  - Date and time of scheduled administration
  - Date and time of preparation
  - Expiration date
  - Initials of person who prepared and person who checked the IV admixture
  - Auxiliary labeling – supplemental instructions and precautions
- 



# Intravenous Admixture System

Components of an IV program

Policies and procedures

- *Quality assurance and control*

A system of checks and balances, aseptic environments, and the pharmacist's access to both the patient's medication profile and the final product provide more stringent quality control over parenteral therapy

Routine inspection of all laminar air flow hoods must be performed, routine hood maintenance



# Intravenous Admixture System

## Components of an IV program

### Polices and procedures

- *Quality assurance and control (cont')*

A typical IV order for a patient would entail the following activities

1. A pharmacy copy of the physician's original order is prepared, containing the patient's name, room number, IV fluids, additive(s), and flow rate.
2. The Rx order is entered into the patient's profile by a pharmacist who checks for drug interactions, proper dose, compatibilities, duplication of medication, allergies, length of therapy and other patient therapies
3. A label is prepared and checked against the original order
4. The parenteral product is prepared by the pharmacist or by an experienced technician



# Intravenous Admixture System

## Components of an IV program

### Polices and procedures

- *Quality assurance and control (cont')*

A typical IV order for a patient would entail the following activities

5. The prepared product is then checked against the label and original order by a pharmacist. Dosage, ingredients, auxiliary labels, compatibility, route, rate, absence of particulate mater, discoloration, and container integrity are verified.
  6. Upon delivery of the IV product to the patient unit, the solution is once again checked by the person who will be administering the drug
  7. Whenever possible, IV admixture should be refrigerated until shortly prior use
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# Intravenous Admixture System

Components of an IV program

Polices and procedures

- *Auxiliary label*

There need arise after a potential medication error occurs on the patient-care



# Intravenous Admixture System

**Table 19-4. Auxiliary labels\***

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<b>Note dosage strength</b> —	to be placed on concentrated solutions which are double or triple the strengths that are normally used (these types of solutions may be used on patients who are fluid restricted)
<b>Must activate before use</b> —	to be placed on unactivated ADD-Vantage <sup>®</sup> solutions

**Protect from light**

**Do not refrigerate — Do not allow to freeze**

**Caution: Chemotherapeutic agent — Dispose of properly**

**Caution: Vesicant/Tissue irritant**

**For epidural use only**

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\*Some of the labels listed above must be specially ordered.



# Intravenous Admixture System

Components of an IV program

equipments

- *Laminar air flow hoods*
  - *Refrigerator*
  - *references*
- 

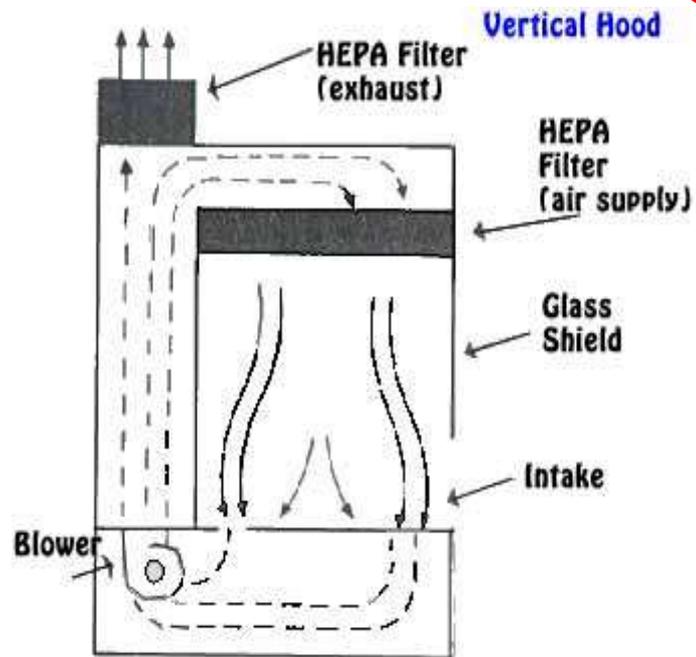
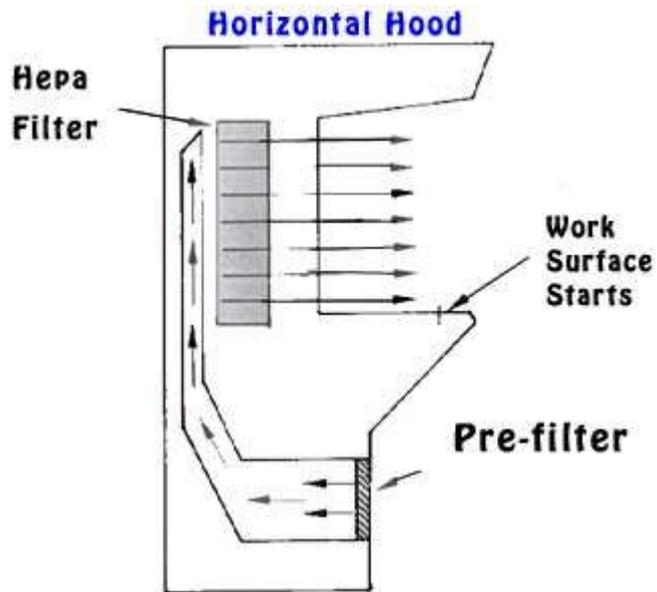
# Intravenous Admixture System

## Components of an IV program equipments

- *Laminar air flow hoods*
  - **False sense of security**
  - It uses high efficiency particulate air (HEPA) filtration could be horizontal or vertical
  - Hoods do not sterilize an environment but maintain it clean
  - Should be inspected every 6 months



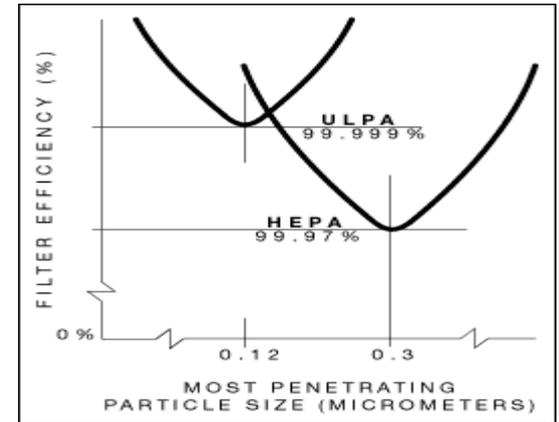
BSC



# HEPA vs ULPA

**HEPA:** High Efficiency Particulate Air , it's efficacy ➤  
is 99.99% at 0.3microns

**ULPA:** Ultra Low Penetration Air, it's efficacy is ➤  
99.999% at between 0.1 to 0.2microns.



# Types of BSC:

Class	Min Inflow Velocity (fpm)	Recirc. Air	Exhaust Air	Exhaust Alternatives	Biosafety Level
I	75	0%	100%	Inside room / Hard Duct	1,2,3
II A1	75	70%	30%	Inside room / Thimble Duct	1,2,3
II A2	100	70%	30%	Inside room / Thimble Duct	1,2,3
II B1	100	30%	70%	Hard duct only	1,2,3
II B2	100	0%	100%	Hard duct only	1,2,3
III	Closed P>0.5"WG	0%	100%	Inside room / Hard Duct	1,2,3,4



# *Bio Safety Level (BSL)*

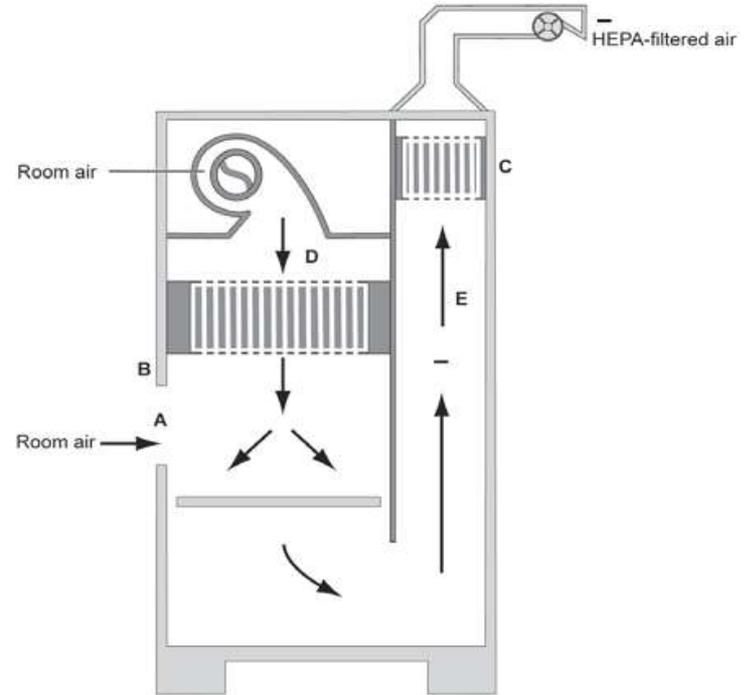
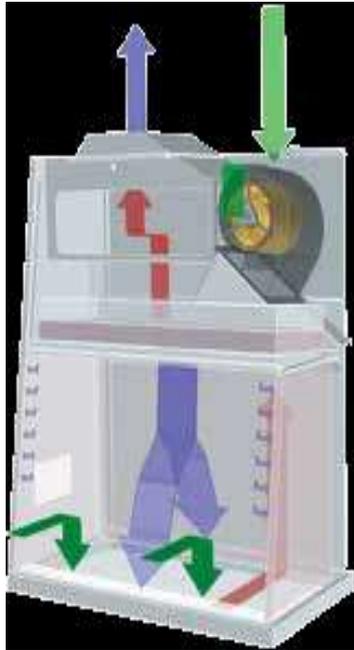
Level	Lethality	Cure	Example
1	Safe	Yes	B.Subtilis
2	Some	Some	HIV
3	Serious	Some	M. Tuberculosis
4	Extreme	Non	Numerous virus that cause hemorrhagic Disease e.g.Ebola



# Biological Safety Cabinet Selection:

Type of protection	BSC Selection
Personnel Protection, microorganisms in Risk Groups 1-3	Class I, Class II, Class III
Personnel Protection, microorganisms in Risk Groups 4, glove box laboratory	Class III
Personnel Protection, microorganisms in Risk Groups 4, suit laboratory	Class I, Class II
Product Protection	Class II, Class III
Volatile radionuclide / chemical protection, re-circulated back to work zone	Class II Type B1, Class II Type A2 vented to outside
Volatile radionuclide / chemical protection, no re-circulation back to work zone	Class I, Class II Type B2, Class III vented to outside

# Class II B2 BSC Airflow



# Clean room classification:

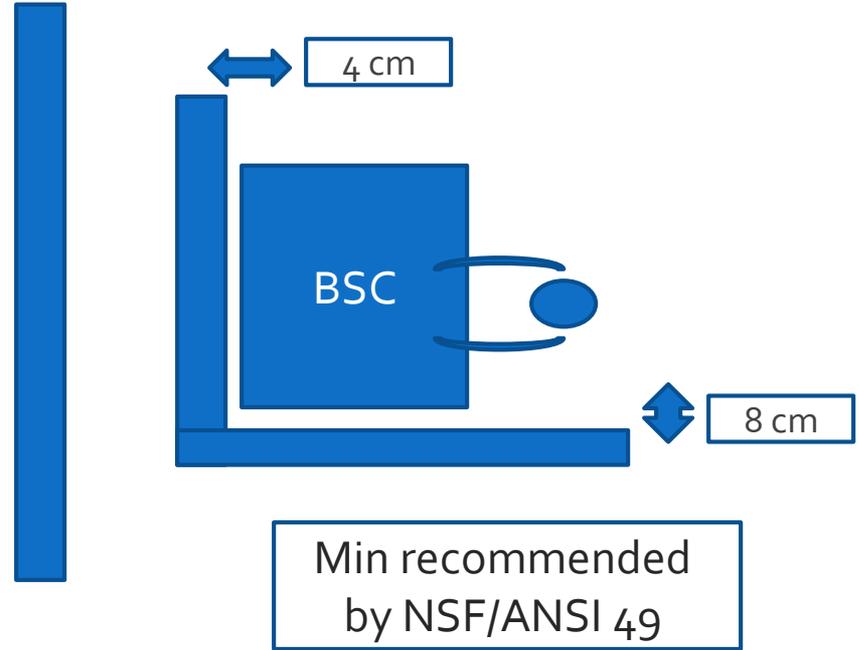
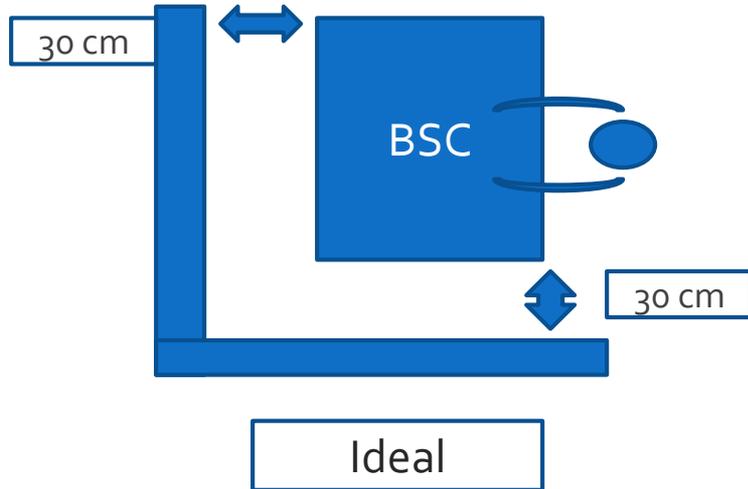
- Cleanrooms are classified according to the number and size of particles permitted per volume of air.
- **ISO 14644-1 cleanroom standards**

ISO classification number (N)	Maximum concentration limits (particles/m <sup>3</sup> of air) for particles equal to and larger than the considered sizes shown below (concentration limits are calculated in accordance with equation (1) in 3.2)					
	0,1 µm	0,2 µm	0,3 µm	0,5 µm	1 µm	5 µm
ISO Class 1	10	2				
ISO Class 2	100	24	10	4		
ISO Class 3	1 000	237	102	35	8	
ISO Class 4	10 000	2 370	1 020	352	83	
ISO Class 5	100 000	23 700	10 200	3 520	832	29
ISO Class 6	1 000 000	237 000	102 000	35 200	8 320	293
ISO Class 7				352 000	83 200	2 930
ISO Class 8				3 520 000	832 000	29 300
ISO Class 9				35 200 000	8 320 000	293 000

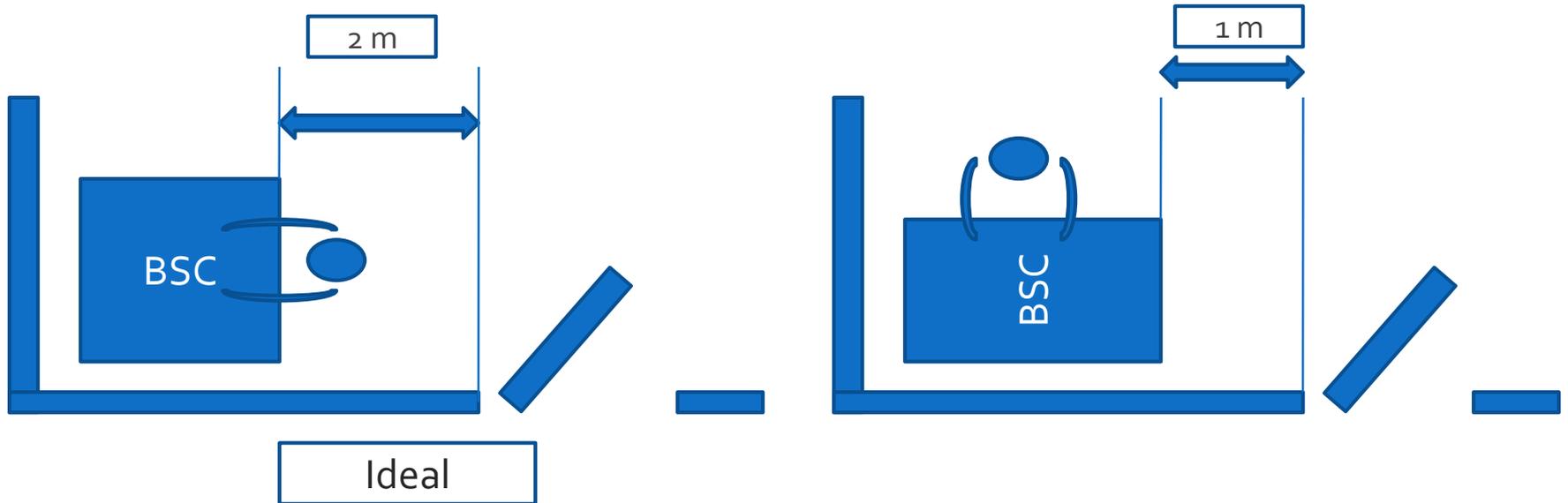
NOTE Uncertainties related to the measurement process require that concentration data with no more than three significant figures be used in determining the classification level

# Cabinet installation

## Distance to Wall

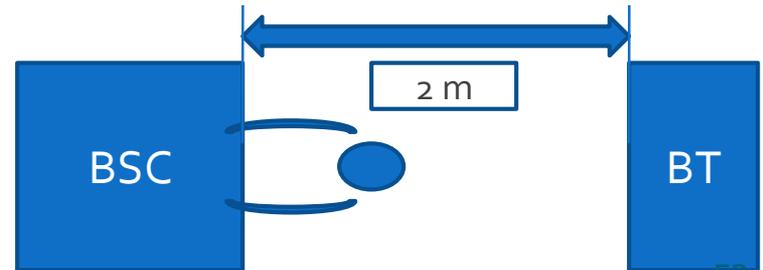
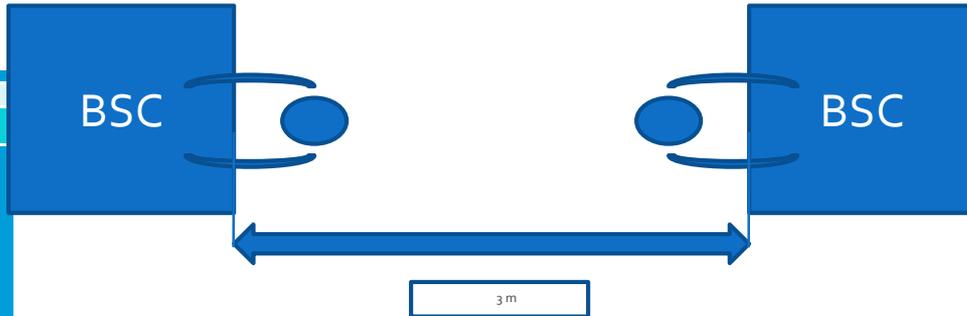
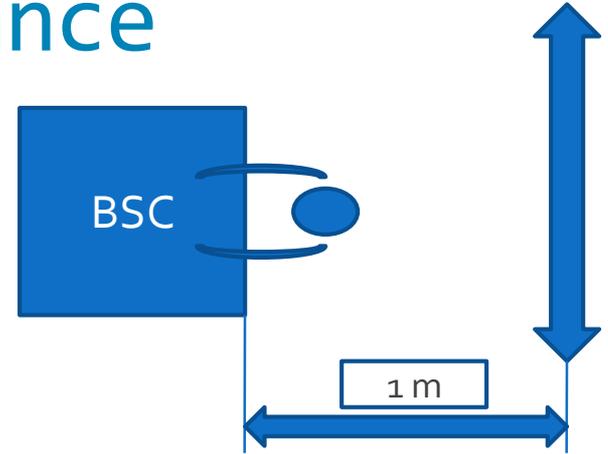
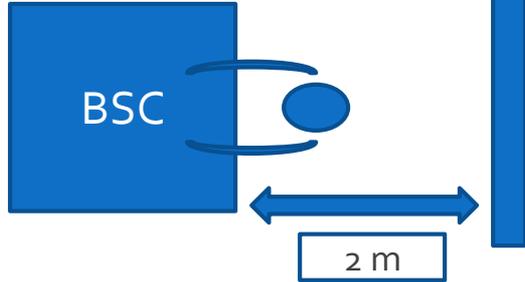


# Distance to Door





# Front clearance





# Intravenous Admixture System

Components of an IV program

equipments



- *refrigeration*
  - The introduction of a needle into a sterile product is associated with risk of contamination
  - Microbial growth is retarded under refrigeration

# Intravenous Admixture System

Components of an IV program  
equipments



- *References*

- Handbook of injectable drug from ASHP
- We referenced compatibility and stability charts are also necessary in an IV preparation area (manufacturer)
- Standardized compounding charts



# Intravenous Admixture System

**Table 19-5.** Examples of charts for admixture preparation

<i>Drug</i>	<i>Size</i>	<i>Diluent</i>	<i>Amount to add</i>	<i>Approximate final diluted concentration</i>	<i>Expiration date (days)</i>
Cefazolin	250 mg	Bacterio- static water	2 mL	125 mg/mL	10*r
	500 mg		2 mL	250 mg/mL	10 r
	1 g		2.5 mL	400 mg/mL	10 r
	10 g		45 mL	1,000 mg/mL	10 r
Nafcillin	500 mg	Bacterio- static water	1.7 mL	500 mg/2 mL	7 r
	1 g		3.4 mL	1,000 mg/4 mL	7 r
	2 g		6.8 mL	1,000 mg/4 mL	7 r
	10 g		43.0 mL	1,000 mg/5 mL	7 r

Methylprednisolone concentrations for syringes:

40 mg/mL:	30 mg=0.75 mL	20 mg=0.5 mL	10 mg=0.25 mL	48 hr r
125 mg/mL:	100 mg=1.6 mL	80 mg=1.3 mL	60 mg=0.96 mL	48 hr r

Gentamicin concentrations for syringes or minibags:

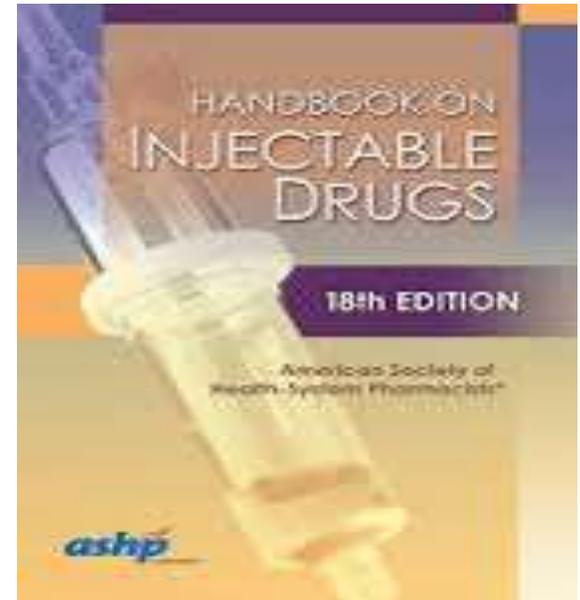
40 mg/mL vial:	10 mg=0.25 mL	50 mg=1.25 mL	90 mg=2.25 mL
	15 mg=0.375 mL	55 mg=1.375 mL	95 mg=2.375 mL
	20 mg=0.5 mL	60 mg=1.5 mL	100 mg=2.5 mL
	25 mg=0.625 mL	65 mg=1.625 mL	105 mg=2.625 mL
	30 mg=0.75 mL	70 mg=1.75 mL	110 mg=2.75 mL
	35 mg=0.875 mL	75 mg=1.875 mL	115 mg=2.875 mL
	40 mg=1.0 mL	80 mg=2.0 mL	120 mg=3.0 mL
	45 mg=1.125 mL	85 mg=2.125 mL	125 mg=3.125 mL

\*r = refrigerated.

# Intravenous Admixture System

Components of an IV program  
equipments

- *References*
- [www.globalrph.com](http://www.globalrph.com)
- [www.medscape.com](http://www.medscape.com)
- [www.lexicomponline.com](http://www.lexicomponline.com)
- [www.uptodate.com](http://www.uptodate.com)
- [www.micromedex.com](http://www.micromedex.com)





# Intravenous Admixture System

Components of an IV program

## Personnel

Carefully trained

Who will prepare? Pharmacist or technician

Proper training in aseptic technique and sterile product information is necessary (training courses, self study programs)



# Intravenous Admixture System

**Table 19-7. Steps involved in starting or expanding an IV admixture program**

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1. Review State and hospital governing regulations.
  2. Review current recommendations from agencies or organizations that have standards of practice.
  3. Prepare and gain support for rationale in starting or expanding a program.
  4. Obtain approval from hospital administration.
  5. Evaluate space and equipment requirements for different types of systems. Rely on help from manufacturers of different systems in coordinating data. Visit other hospital pharmacies to view actual systems in use.
  6. Assess personnel requirements. The financial impact and availability of additional personnel may necessitate compromise in choosing one type of system over another.
  7. Experiment with different types of systems. Manufacturers will readily help with trial evaluations.
  8. Maintain communication between pharmacy and nursing when evaluating systems. Different systems may be more suitable for particular nursing units. The final program may contain several types of admixture systems.
  9. Prepare or update a thorough policy and procedure manual for the type of system(s) that will be used.
-

# ASHP Guidelines on Handling Hazardous Drugs





# Routes of Exposure.

- Numerous studies showed the presence of hazardous drugs in the urine of health care workers.
- **Hazardous drugs enter the body through :-**
  1. Inhalation.
  2. Accidental injection
  3. Ingestion of contaminated foodstuffs or mouth contact with contaminated hands.
  4. Dermal absorption.
    - While inhalation might be suspected as the primary route of exposure, air sampling studies of pharmacy and clinic environments have often demonstrated low levels of or no airborne contaminants



# Recommendations

1-Environment.

2-Ventilation Controls.

3-Personal Protective Equipment.



# 1. Environment

- Hazardous drugs should be stored in an area with sufficient general exhaust ventilation to dilute and remove any air born contaminants.
  - Due to the hazardous nature of these preparations, a contained environment where air pressure is **negative** to the surrounding areas or that is protected by an airlock or **anteroom** is preferred.
- 



## 2. Ventilation Controls

- Ventilation or engineering controls are devices designed to eliminate or reduce worker exposure to chemical, biological, radiological, ergonomic, and physical hazards.
  - Ventilated cabinets are a type of ventilation or engineering control designed for the purpose of worker protection.
  - These devices minimize worker exposure by controlling the emission of airborne
- 



## 3. Personal protective equipment

- Gloves
  - Gowns
  - Face mask
  - Eye goggle
- 

# 3. Personal protective equipment

## Gloves:

- Powder-free latex gloves are preferred because powder particulates can contaminate the sterile processing area and absorb hazardous drug contaminants, which may increase the potential for dermal contact.



# 3. Personal protective equipment

## Gowns and over head

- compounding in the laminar flow hood, administration, spill control, and waste management to protect the worker from contamination by fugitive drug generated during the handling process.



# 3. Personal protective equipment

## Face mask and Eye goggle

- Also these kits used as protective tools from spilling and prevent inhalation of cytotoxic drugs



# Intravenous Admixture System

Small volume IV infusion

Manufacture's drug packaging

- Glass ampoules
- Single dose vials

Drug in solution, lyophilized or powdered drugs

- Multiple dose containers

Drug in solution, lyophilized or powdered drugs

- Prefilled syringes





# Intravenous Admixture System

Specialized admixtures

- Nutritional
- chemotherapy



Oscar Pistorius