Setting-up: Focus on Quality Assurance & Audit

Ng Hui Cheng
National Cancer Centre

Quality Assurance (QA)

- Refers to a program for the systematic monitoring and evaluation of the various aspects of a service or facility to ensure that standards of quality are being met
- Gives CONFIDENCE in a product

Quality Assurance (QA)

2 Key Principles

"Fit for Purpose"

- The product should be suitable for the intended purpose

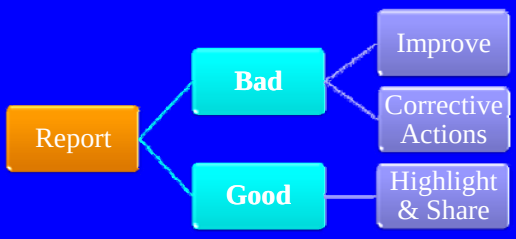
"Right First Time"

- Error-free

Audit

- Verify the effectiveness of a quality management system
- Hands-on management tool for achieving continual improvement

Audit



Why Do We Need QA?

Patients' Perspective

- Incorrectly prepared or contaminated pharmacy-prepared products can lead to patient morbidity and mortality
- Increased risk of infection in cancer patients who are immunocompromised and receiving chemotherapy
- Cytotoxic drugs have narrow therapeutic index – error in preparation may lead to overdosing

Why Do We Need QA?

Healthcare Personnel's Perspective

- Occupational exposure
  - Dermal contamination
  - Airborne contamination
  - Oral contamination
- Signs and symptoms
  - Skin rashes
  - Infertility, miscarriage, birth defects
  - Leukemia, other cancers

Standards & Guidelines

Standards	Guidelines
USP <797> United States Pharmacopoeia	ASHP American Society of Health-System Pharmacists
OSHA Occupational Safety and Health Administration	HOPA Haematology/Oncology Pharmacy Association
JCAHO Joint Commission on Accreditation of Healthcare Organizations	ISOPP International Society of Oncology Pharmacy Practitioners
	NIOSH National Institute for Occupational Safety and Health

What Can Affect Quality?

DRUG

Drug

- Packaging
  - Primary containers
  - Labeling
- Material Safety Data Sheet (MSDS)
- Storage
- Transportation
  - Warehouse to Pharmacy

PERSONNEL

Personnel

- **Education and training**
- Health considerations
- Hygiene
- Staffing levels

Education & Training (1)

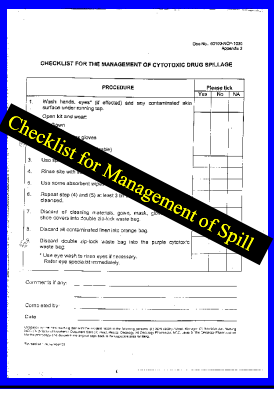
- Recognized qualification / certified training program in accordance with local regulations
- Personal Portfolio
- Structured learning program
- Aseptic technique validation test

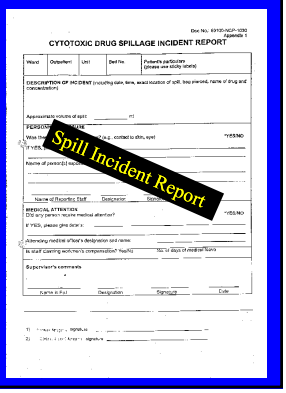
Education & Training (2)

1. **Cleaning** of biohazard safety cabinet / isolator
2. **Safe handling** of cytotoxic drugs
   - Storage & transportation
   - Spill management
   - Needle stick injury
   - Cytotoxic waste management

Spill Management

- Spill kit must be
  - available in the work zone and within reach
  - checked regularly





Needle Stick Injury

Prevention

- Practice good aseptic technique
  - Do not re-cap needles manually
  - Do not over-fill sharps containers
  - Never use waste plastic bags to contain the needles/sharps
- Do not rush during preparation

Treatment

Cytotoxic Waste Management

- Designated cytotoxic waste bags
- Cytotoxic waste sharps containers

Education & Training (3)

4. **Drug knowledge**
- Continual education sessions
- Regular updates
- Regular assessment & evaluation of practice to verify compliance with procedures

5. **Personal Protective Equipment (PPE)**

PPE

- Appropriate selection and proper use of PPE
- To ensure sterility of the end product
- To protect the operator from hazardous drugs
- Type of PPE depends on the grade of room

PPE

Protective goggles
- Risk of projection
- Should be worn when cleaning a spill

Gown/ Coverall
- Disposable
- Non-linting
- Non-absorbent PE-coated polypropylene material

Boots/ Overshoes

Head covering

Mask
- Fluidshield N95
- Surgical mask do not offer protection against aerosols

Gloves
- Nitrile/ Neoprene/ Latex
- Permeability
- Non-powdered
- Double gloving
- Change every 30min or when damaged or contaminated

Personnel

- Education and training
- **Health considerations**
- Hygiene
- Staffing levels

Health Considerations

- Informed about the risks of occupational exposure to hazardous drugs
- No direct measurements to indicate total exposure to cytotoxic drugs
- Institutions should have a written policy for baseline and regular monitoring of staff involved in cytotoxic drug preparation

Medical Examinations

- Non-specific measurements

1. Full blood examination
2. Biochemistry evaluations
   - Liver function tests
   - Urea, creatinine, electrolytes
   - Urine dipstick / microscopic examination of urine for blood

Exclusions From Cytotoxic Preparation Work

- Illness
  - Upper respiratory infections
  - Cutaneous infections
  - On immunosuppressive therapy

Exclusions From Cytotoxic Preparation Work

- Family planning
  - Pregnant
  - Breastfeeding

- *Alternative work section if requested*
- *Institutions should develop a written policy on how to deal with this issue*

Exclusions From Cytotoxic Preparation Work

- Abnormal pathology results
  - They should not prepare cytotoxic drugs until the abnormality has been investigated
- Physical well-being
  - Back pain
  - Wrist sprain
  - Hand strain

Personnel

- Education and training
- Health considerations
- **Hygiene**
- Staffing levels

Hygiene

- Strict hygiene procedures should be developed and followed
  - ✕ Eating
  - ✕ Drinking
  - ✕ Chewing gum
  - ✕ Application of cosmetics
  - ✕ Rings, bracelets, other jewellery

Personnel

- Education and training
- Health considerations
- Hygiene
- **Staffing levels**

Staffing Levels

- Number of staff members available to cater to
  - Expected workload
  - Busiest period of the day
  - Complexity of products manufactured
- Staff roster
- Workload statistics

Staff Levels

- Work breaks
  - Staff allocation must be sufficient to allow for adequate breaks for those working in the cytotoxic cleanroom
  - No more than 2 hours be spent working at the cabinet or isolator without a break
  - Sufficient breaks must be provided to maintain concentration

FACILITIES & EQUIPMENT

Facilities & Equipment

- Controlled area – limited access
- Cleanliness
  - Limited personnel movement in and out
  - Full PPE
  - Limited storage of items within cleanroom
  - Low-particulate
  - Controlled temperature, humidity and pressure
  - Regular cleaning and maintenance
  - Check for surface contamination using wipe test

Protect product & operator

Facility - Cleanroom

- ISO 14644-1 international standard[1]
  - Classification of cleanroom air cleanliness
  - Replaces the Federal standard 209E
- Pharmaceutical Inspection Co-Operation Scheme (PIC/S) Guidelines[2]
  - Implementation and maintenance of harmonized GMP standards

[1]ISO (International Organization for Standardization) 14644-1: cleanrooms and associated controlled environments – Part 1: classification of air cleanliness. 1999.
[2]PIC/S Guide to Good Practices for Preparation of Medicinal Products in Pharmacies. http://www.picscheme.org/index.php.

ISO 14644-1

Classification is based on maximum level of particulate contamination

ISO 14644-1	Federal Std 209E		No. of particles/m³ of 0.5µm size
ISO Class	Gr[illegible]	[illegible]	
ISO 5	A	100	3,520
ISO 6	[illegible]	[illegible]	35,200
ISO 7	[illegible]	[illegible]	352,000
ISO 8	D	100,000	3,520,000

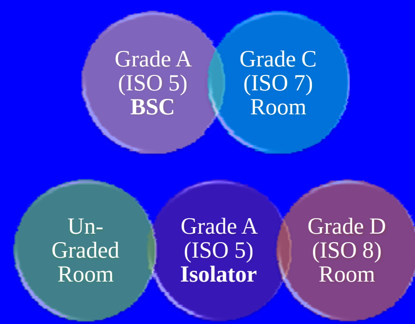
BSC / Isolator environment

Cleanroom Environment for BSC

Cleanroom environment for isolator

1. EudraLex http://legislafarma.iespana.es/procedimientos/laboratorios/000_EUDRALEX.pdf
2. PIC/S http://www.picscheme.org/index.php

Recommended Combinations



Cleanroom Settings

- Pressure differentials
  - Negative pressure room
  - Protect operator and environment from cytotoxic contamination
  - Prevent dissemination of contamination in the event of breakage
- Air changes
  - Minimum air change of 20 room volumes per hour
  - Air from the room should be exhausted out to prevent exposure of personnel
  - HEPA exhaust filter

Cleanroom Settings

- Temperature
  - 18 - 22°C
  - Prevent microbiological contamination
  - Ensure comfort of personnel
- Humidity
  - 30 – 70% relative humidity
  - Prevent corrosion and condensation on work surfaces
  - Ensure comfort of personnel

Facilities - Monitoring

•Establish an ongoing monitoring program

Microbiological contamination *To be performed on a regular basis.*	**Air velocity** *To be assessed on a regular basis, annually.*
Particulate contamination *To be assessed annually.*	**Pressure differentials** *To be checked before entry into cleanroom, daily.*
HEPA filtration *To be assessed annually.*	**Visual inspection of surfaces and joints**

** Specifications to be maintained depend on the grade of the room.*

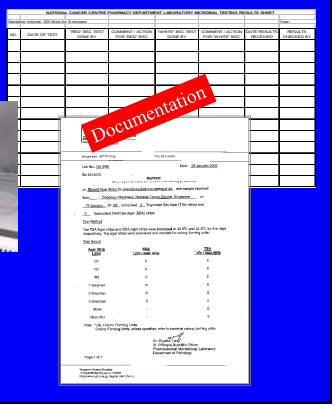
Facilities & Equipment – Certification

① Design
② Installation
③ Operation
④ Performance

Microbiological Testing

Passive air sampling

Active air sampling



Documentation

PROCEDURES / WORK PROCESSES

Procedures / Work Processes

- Standard operating procedures (SOP)
- Proper documentation
- Validation of final product

Validation - *Product*

- Validation of product *(Simulation)*
  - Microbiological quality
  - Concentration
  - Chemical stability
  - No cross contamination

Validation – *Work Processes*

- Validation of work processes
  - Reproducible
  - Checking mechanism
  - Ensure safety

Validation – *Computer Program*

- To confirm that the computer hardware and software systems perform to the required standards
- Accurate output
- Error-free

Audit

- By Internal staff
- By External personnel
- Regular and ongoing
- Scheduled *(informed)*
- Adhoc *(surprise)*

"If it is not written, it did not happen"

"If there is no certification, it is not validated"

SurfaceSafe

Uses
To clean and inactivate most anticancer drugs on chemotherapy work surfaces.

Description and Purpose
Surface Safe is made up of two packets and is packaged in boxes containing 15 double packets (15 pairs/box). Each pair of packets provides enough solution to treat about a 2-square-foot area.

Packet 1

- Contains a 5.5 x 10 in. towelette in a 2% (w/w) sodium hypochlorite $Na(OCl_2)$ soap solution
- Has a high level of oxidizing activity which inactivates potent anticancer agents

Packet 2

- Contains a 5.5 x 10 in. towelette in 1% (w/w) sodium thiosulfate with 0.9% (w/w) benzyl alcohol
- Rapidly inactivates the hypochlorite in the first packet to reduce toxic potential and long-term damage to insert surfaces [Note: This reaction is slightly exothermic (produces heat)]

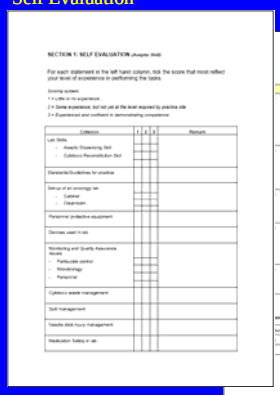
Operational Certifications

HEPA filter integrity test	Functional check of pressure regulation and alarms	Air change rate per hours
Particle count	Pressure differential	Noise level
	Light level	

A Typical Spill Kit

- Appropriate PPE
- Absorbent mats with plastic backing
- Disposable paper towels
- Cytotoxic waste bags
- Detergent
- Normal saline eyewash

Self Evaluation



Training Time-Table

Self-Appraisal

Program Evaluation

Education & Training (2)