Supplementary Training Modules on GMP

Air Handling Systems

Heating
Ventilation and
Air Conditioning (HVAC)

Part I: Introduction and overview

Air Handling Systems

Objectives

To understand:

1. The need and reason for pharmaceutical air handling systems
1. The technical requirements for air handling systems
2. Different types of air handling systems
3. Qualification and monitoring requirements

Air Handling Systems

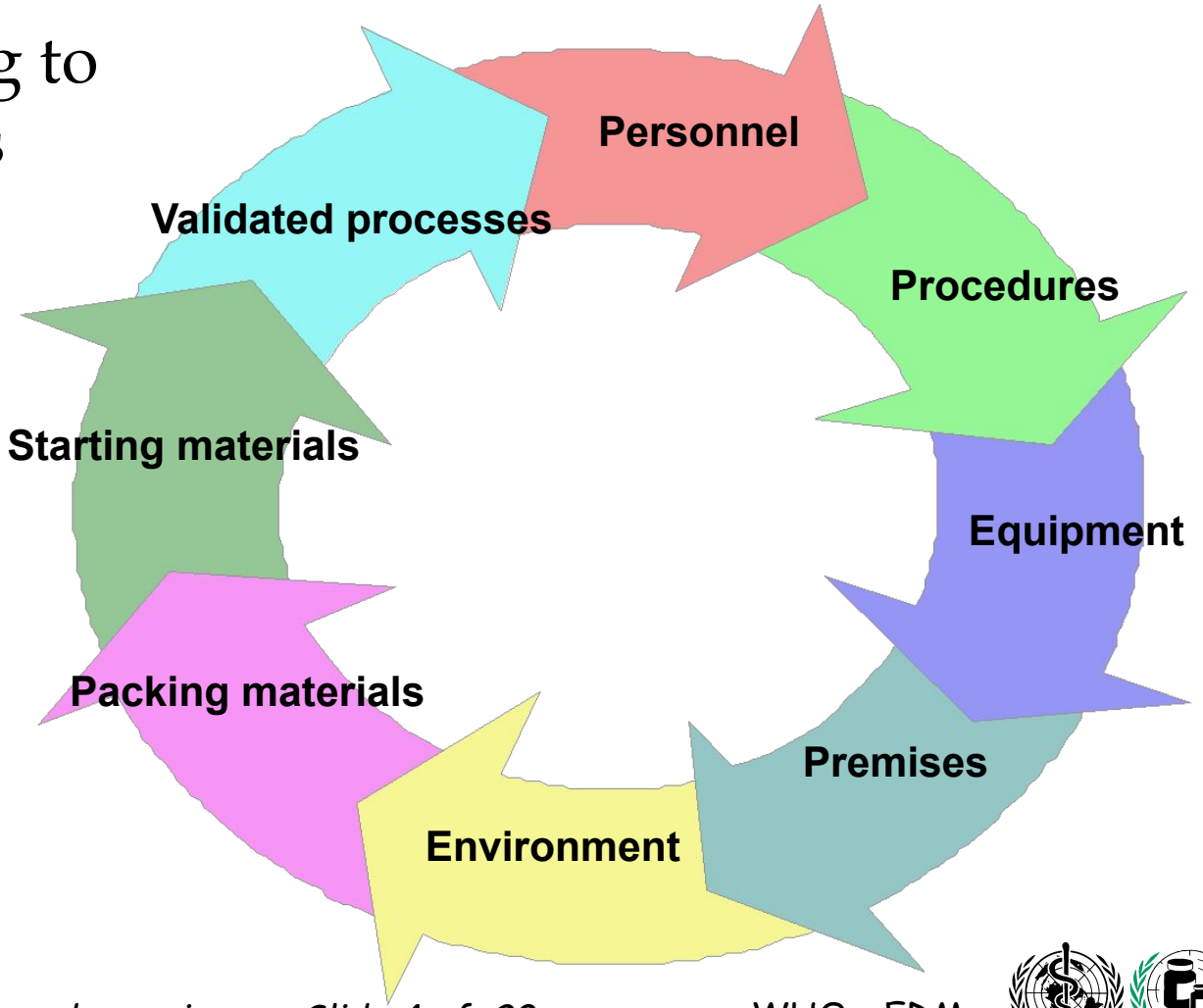
Factors that contribute to quality products:

1. Starting materials and packaging materials
2. Validated processes
3. Personnel
4. Procedures
5. Equipment
6. Design and quality of premises
7. Manufacturing environment

Inadequacies in the above factors will lead to sub-standard products.

Air Handling Systems

Factors contributing to quality products



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The manufacturing environment is critical for product quality

1. Light
2. Temperature
3. Humidity
4. Air movement
5. Microbial contamination
6. Particulate contamination
7. Uncontrolled environment can lead to product degradation
   - *product contamination*
   - *loss of product and profit*

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What are contaminants ?

Contaminants are

1. Products or substances other than product manufactured
2. Foreign products
3. Particulate matter
4. Micro-organisms
5. Endotoxins (degraded micro-organisms)

Cross-contamination is a particular case of contamination

Cross-Contamination (1)

What is Cross-Contamination ?

Definition of Cross-Contamination:

Contamination of a starting material, intermediate product, or finished product with another starting material or product during production. **(WHO)**

Annex 1, Glossary

Air Handling Systems

Cross-Contamination (2)

From where does Cross-Contamination originate?

1. Poorly designed air handling systems and dust extraction systems
2. Poorly operated and maintained air handling systems and dust extraction systems
3. Inadequate procedures for personnel and equipment
4. Insufficiently cleaned equipment

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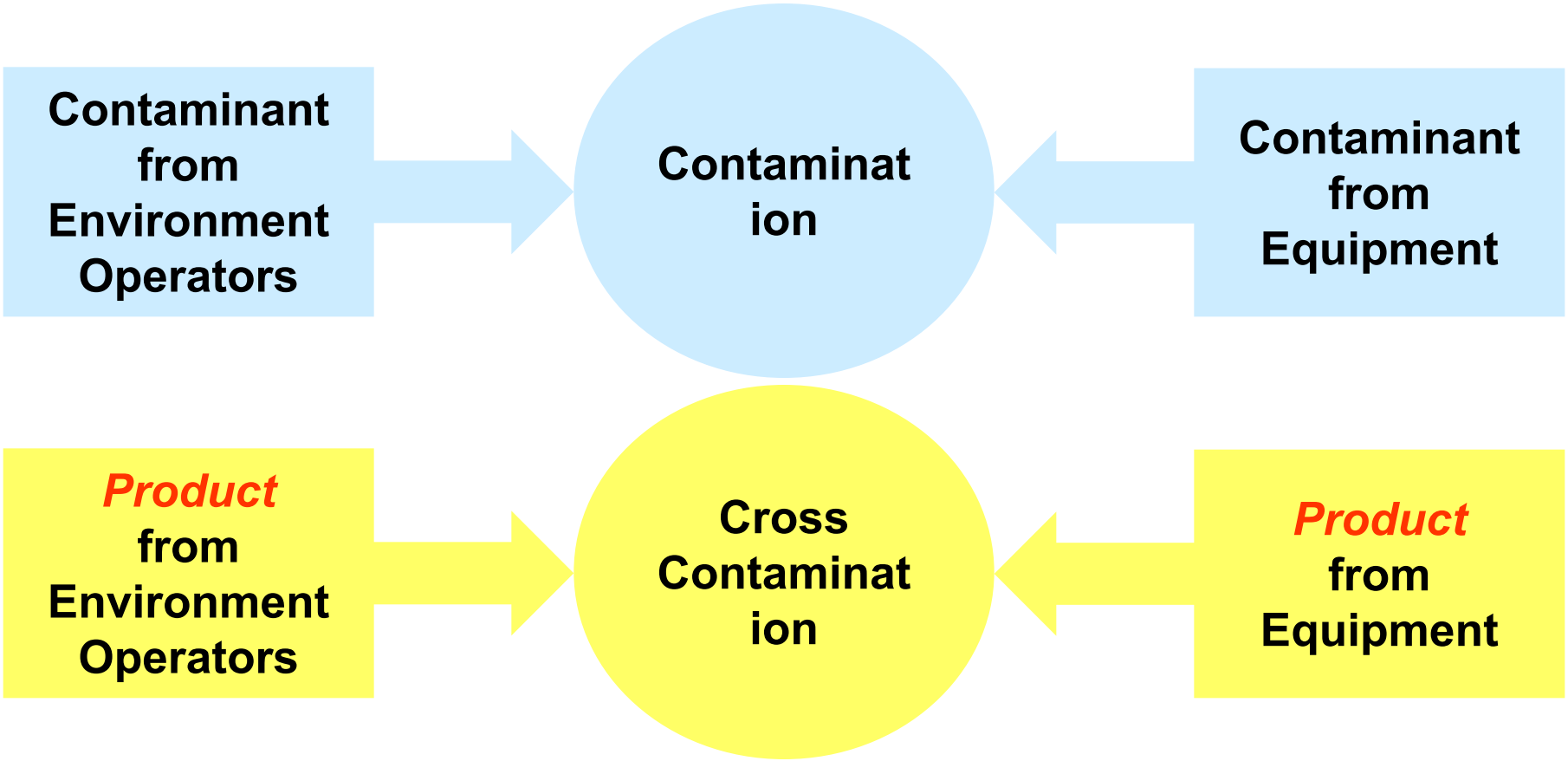
Cross-Contamination (3)



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Cross-Contamination (4)

Cross-contamination can be minimized by:

1. Personnel procedures
2. Adequate premises
3. Use of closed production systems
4. Adequate, validated cleaning procedures
5. Appropriate levels of protection of product
6. Correct air pressure cascade

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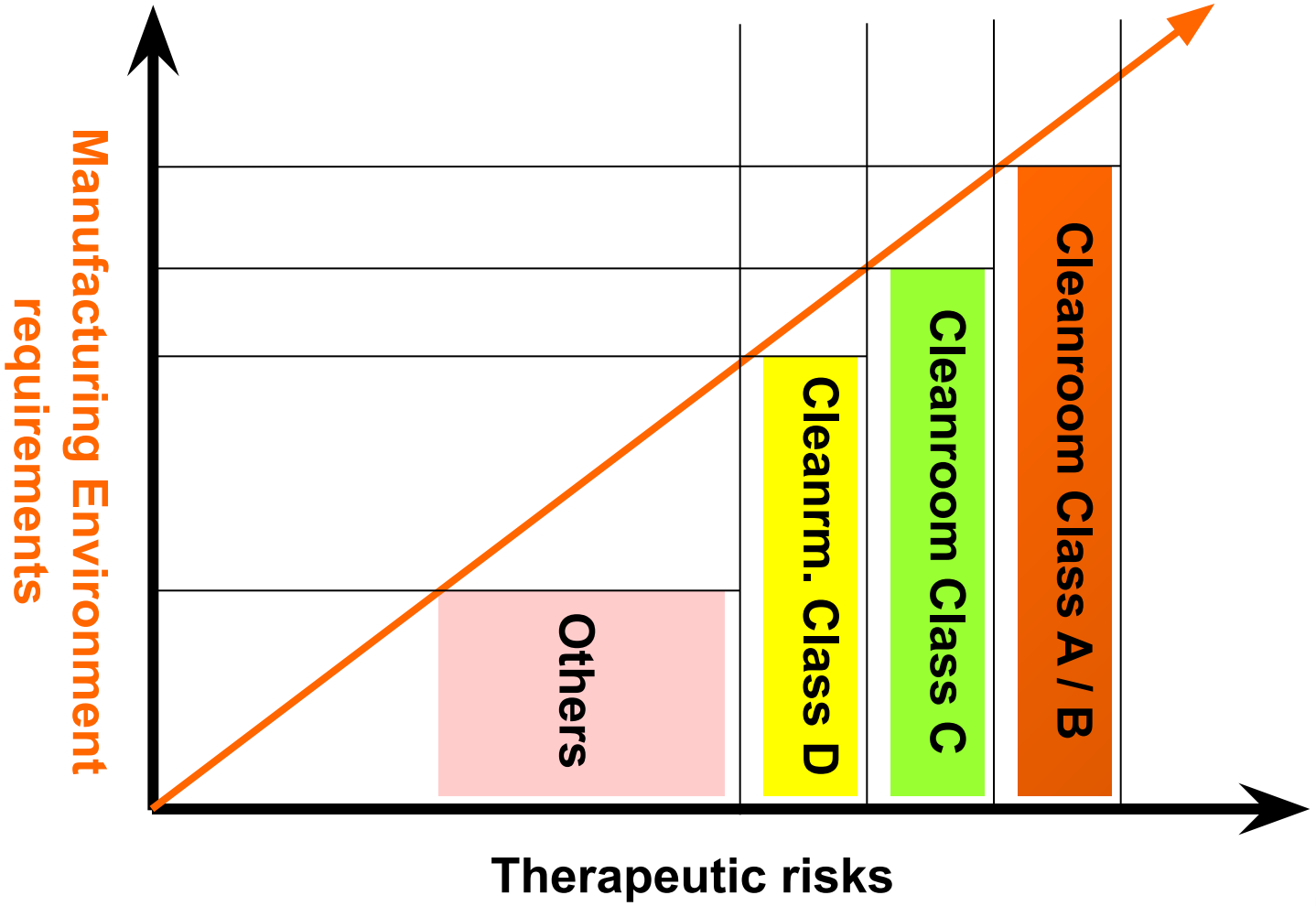
Level of Protection Concept

1. Defines environmental requirements
2. Helps prevent contamination and cross-contamination
3. Allows production under optimal hygiene conditions
4. Takes into account
    - *product sensitivity to contamination*
    - *therapeutic risk*

Air Handling Systems



Air Handling Systems

Levels of Protection

Parameters to be defined:

1. Air cleanliness requirements (filters type and position, air changes, air flow patterns, pressure differentials, contamination levels by particulate matter and micro-organisms)
2. Personnel and material transfer methods
3. Permitted operations
4. Building design and finishes

Annex 1, 17.3, 17.4

Air Handling Systems

Levels of Protection

Types of Cleanroom Classes

- International
  - ***WHO*** *A, B, C, D*
- National
  - *EC, PIC/S, TGA, etc. : A, B, C, D*
  - *US FDA : critical and controlled*
  - *ISPE: level 1, 2 or 3 or cleanroom class*
  - *Companies : various others*

Annex 1, 17.3, 17.4

Air Handling Systems

Levels of Protection

All operations within a pharmaceutical facilility must be correlated to well-defined cleanroom classes, and can be included in a hygiene concept.

Example:

Cleanroom Class	A	B	C	D
Washing of containers				X
Preparation of solution for terminal sterilisation			X	
Preparation of solutions for aseptic filling	X	X	X	
Depyrogenisation of containers	X			
Filling for terminal sterilisation			X	
Filling for aseptic process	X			
etc.				

Annex 1, 17.3, 17.4, 17.5

Air Handling Systems

Levels of Protection

Based on the cleanroom class requirements, various Levels of Protection have to be created, including:

- Correlation between process operations and cleanroom classes
- Type of operation permitted in each Level of Protection
- Definition of cleanroom class (parameters, building materials, room requirements, HVAC systems)
- Requirements for personnel and material in the different classes (clothing, training, type of materials, etc.)
- Requirements on entry conditions for personnel and material (change procedures)

Parameters influencing Levels of Protection (1)

Annex 1, 17.4

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Parameters influencing Levels of Protection (2)

1. Number of particles in the air
2. Number of micro-organisms in the air or on surfaces
3. Number of air changes for each room
4. Air velocity
5. Air flow pattern
6. Filters (type, position)
7. Air pressure differentials between rooms
8. Temperature, humidity

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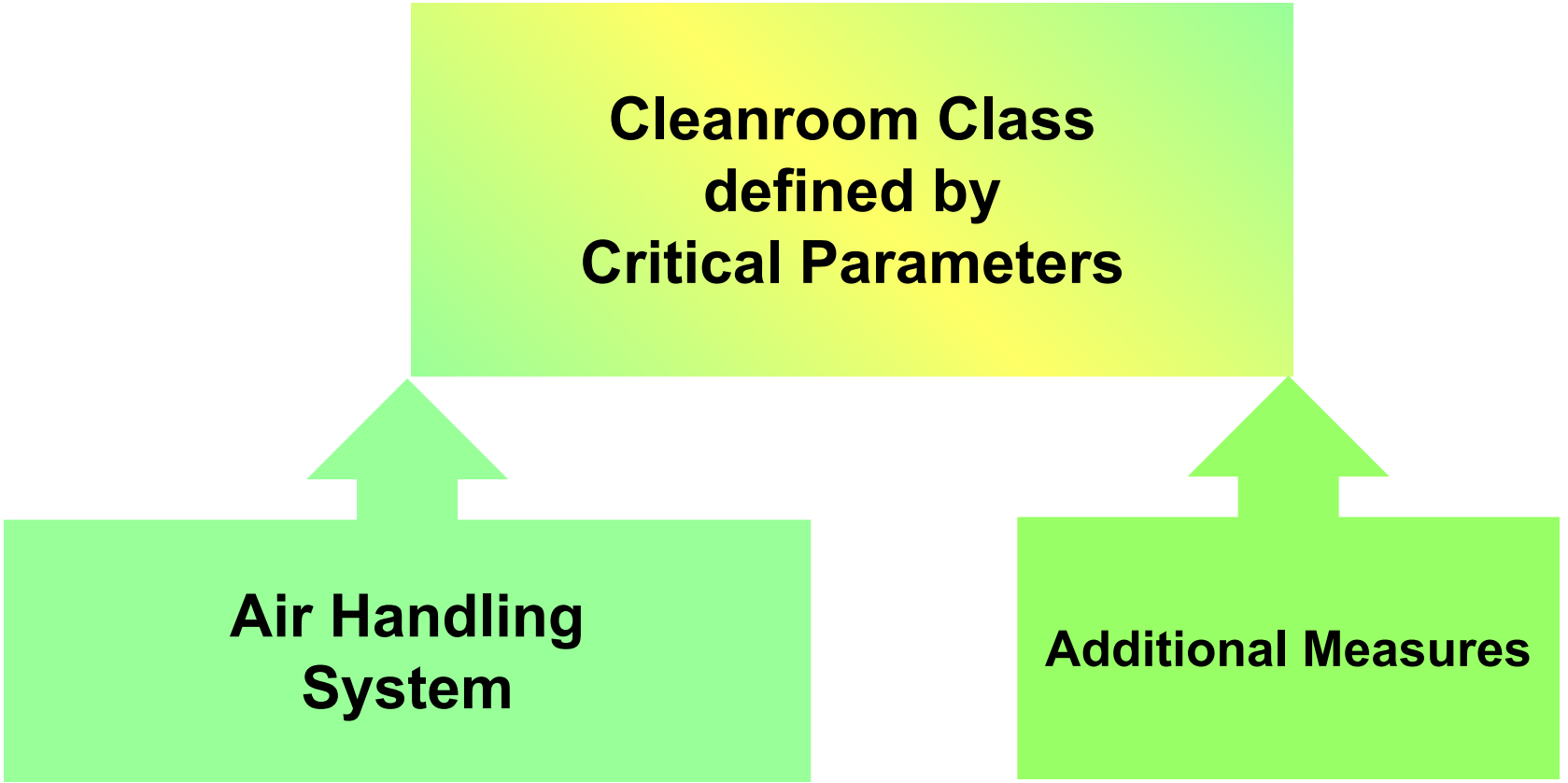
Parameters influencing Levels of Protection (3)



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Parameters influencing Levels of Protection (4)

Air handling systems:

- Are the main tool for reaching required parameters
- But are not sufficient as such
- Need for additional measures such as
  - *appropriate gowning (type of clothing, proper changing rooms)*
  - *validated sanitation*
  - *adequate transfer procedures for materials and personnel*

Annex 1, 17.10 to 17.16