GMP Training

(Insert manufacturer's name)

Objectives

- To review basic GMP requirements in the manufacture of products

Manufacture

- WHO Definition: All operations of purchase of materials and products, production, quality management, release, storage and distribution of products.

Design -Critical

- *Building*
- *Airconditioning*
- *Commissioning*

Air Classification System

Grade	*At rest*		*In operation*	
	maximum permitted number of particles/m^3			
	0.5 - 5.0 µm	> 5 µm	0.5 - 5.0 µm	> 5 µ
A	3 500	0	3 500	0
B	3 500	0	350 000	2 000
C	350 000	2 000	3 500 000	20 000
D	3 500 000	20 000	not defined	not defined

Air Conditioning

- Ventilation systems

  Appropriately designed ventilation system with air supply and extraction systems

  Supply or incoming air should be filtered

  Proper airflow patterns

Facility

To reach Grade B, C and D, the number of air changes should be appropriate to the size of the area, number of personnel, equipment present

- Minimum of 20 air changes per hour
- Good airflow pattern in the area
- HEPA filtered air
- Suitable methods to determine particulate matter and micro *e.g. ISO*

Facility

- Warning system to indicate failure in air supply
- BMS

Equipment

- Effective cleaning of equipment prior
- Maintenance and repairs from outside the clean area
- Planned maintenance, validation and monitoring

Facility Recertification

- Temperature, pressure and humidity
- Air changes CR – 20/hour,
- Airflow patterns
- Clean up time/recovery
- Filter integrity
- Airflow velocity

Clothing

Protection of operator and product

Personnel should not move between areas producing different products

Garments disposable

Cleaning

- *Cleaning programme, appropriate cleaning, records for internal and external*

- Effective cleaning and disinfection

  choice of materials and chemicals, validation

Cleaning

- Frequent, thorough cleaning of areas necessary
- Written programme
- Regular monitoring to detect resistant strains of microorganisms
- Chemical disinfection
- Monitoring of disinfectants and detergents

Cleaning

- Cleaning and cleaning validation
- Separate cleaning agents for each BSC
- Cleaning-*all cleaning and disinfecting solutions carefully prepared and expiry dated*
- SOP for cleaning and sub contract cleaning
- Environmental monitoring SOP

Production

- Careful attention to:
- Environment
- Personnel
- Transfer procedures

Production

- Work-flow- *designed to avoid potential contamination*
- *production areas restricted to authorized personnel- the more critical the area - fewer number of persons there*
- Production:

  Separation in time

  Followed by appropriate cleaning

  Validated cleaning procedure

Production

Line clearance

- Process of checking

  all materials and documentation from the previous product removed

  area and equipment thoroughly cleaned

  Complete sign in/sign out check

Production

- Entry

  personnel and/or equipment

  materials
- Separate areas for operations

GMP Requirements for Products

- Specific points relating to minimizing risks of contamination

  microbiological

  particulate matter

Environmental Monitoring

Microbiological

- Air samples
- Settle and Contact plates

EM

- Monitoring of clean areas
- Monitoring of personnel and surfaces after critical operations
- Frequent monitoring in areas where aseptic operations are carried out

EM

- Monitoring during operation
- Alert and action limits for particulate and micro
- Action taken when exceeded
- Area grades should be proven (e.g. validation runs,, environment, time limits - based on microbiological contamination/bioburden found)

Environmental Monitoring

- Limits of detection established
- Alert and action, and monitoring trends of air quality

Table 1. Limits for microbial contamination

Grade	Air sample (CFU/m3)	Settle plates (90mm diameter) (CFU/4hours)	Contact plates (55mm diameter) (CFU/plate)	Glove print (5 fingers) (CFU/glove)
A	< 3	< 3	< 3	< 3
B	10	5	5	5
C	100	50	25	-
D	200	100	50	-

Production

Airborne particulate classification

WHO GMP	US 209E	US Customary	ISO/TC (209)	EEC GMP
Grade A	M 3.5	Class 100	ISO 5	Grade A
Grade B	M 3.5	Class 100	ISO 5	Grade B
Grade C	M 5.5	Class 10 000	ISO 7	Grade C
Grade D	M 6.5	Class 100 000	ISO 8	Grade D

Staff Training

- Minimum number of staff in clean areas
- Training to include

  initial and regular

  Manufacturing and GMP
- Special cases

  supervision in case of outside staff

  decontamination procedures

Staff Training

High standards of hygiene and cleanliness

- No shedding of particles
- No introduction of microbiological hazards
- Changing and gowning procedure