Cleanroom Basics

Controlling the environment

What is a cleanroom?

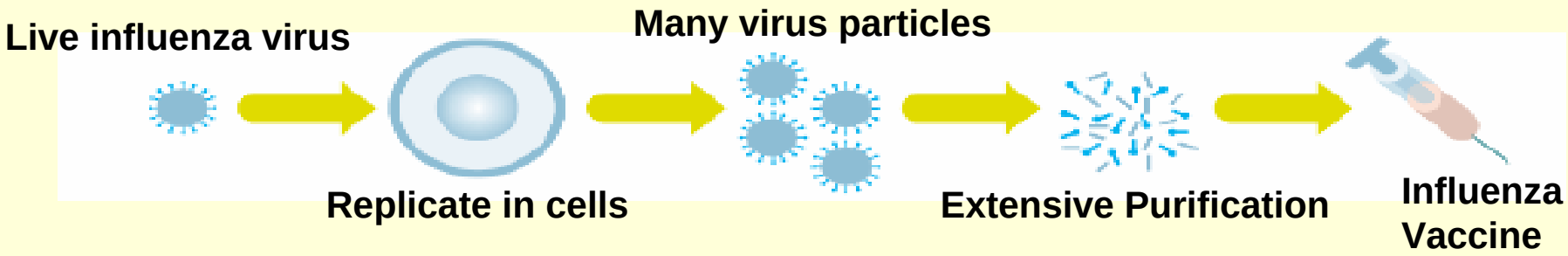
ISO 14644-1:

- *'A room in which the concentration of airborne particles is **controlled**, and which is constructed and used in a manner to minimise the **introduction**, **generation**, and **retention** of particles & microbes inside the room and in which other relevant **parameters**, e.g. temperature, humidity, and pressure, are controlled as necessary.'*

Who's being protected from *What?*

Protecting the Product

- The quality of biopharmaceuticals depends on the absence of contamination from beginning to end of the production process.



Contamination Control

- Environmental Control
  - Atmospheric
  - Materials and supplies
  - Entrance and exit
  - Cleaning and maintenance
- Personnel Control
  - Activity
  - Personal Hygiene
  - Gowning

How Clean?

- Cleanrooms are classified according to the degree of cleanliness required of the manufacturing step.
- Upon receiving a classification, the room must be maintained to meet the specifications for:
  - Cleanliness
  - Temperature
  - Humidity
  - Pressure
  - Number of air changes/hr.
  - Flow rate (CFM)

Classification of Cleanrooms

ISO 16644-1 Air Cleanliness Classes for Cleanrooms and Clean Zones		
ISO Classification #	SI	English (Former FED-STD-209E)
ISO Class 3	M 1,5	1
ISO Class 4	M 2,5	10
ISO Class 5	M 3,5	100
ISO Class 6	M 4,5	1,000
ISO Class 7	M 5,5	10,000
ISO Class 8	M 6,5	100,000

*The required standard of cleanliness of a room is dependent on the task performed in it; the more susceptible the product is to contamination the better the standard.

Sources of Contamination

- **Facilities:**
  - walls, floors, ceilings, paint, coatings, construction material (sheet rock, saw dust etc.), air conditioning debris
- **Equipment/Supplies:**
  - Particles from friction and wear, lubricants & emissions, vibrations, brooms, mops, items brought into cleanroom, cleanroom debris
- **People:**
  - Skin flakes and oil, hair, spittle, cosmetics & perfume, clothing debris (lint, fibers, etc.)

Potential Contaminates

- Microorganisms
  - Viruses, bacteria, fungus
- Particles
  - Clothing fibers, equipment, paint

Controlling Contamination:

Air Quality

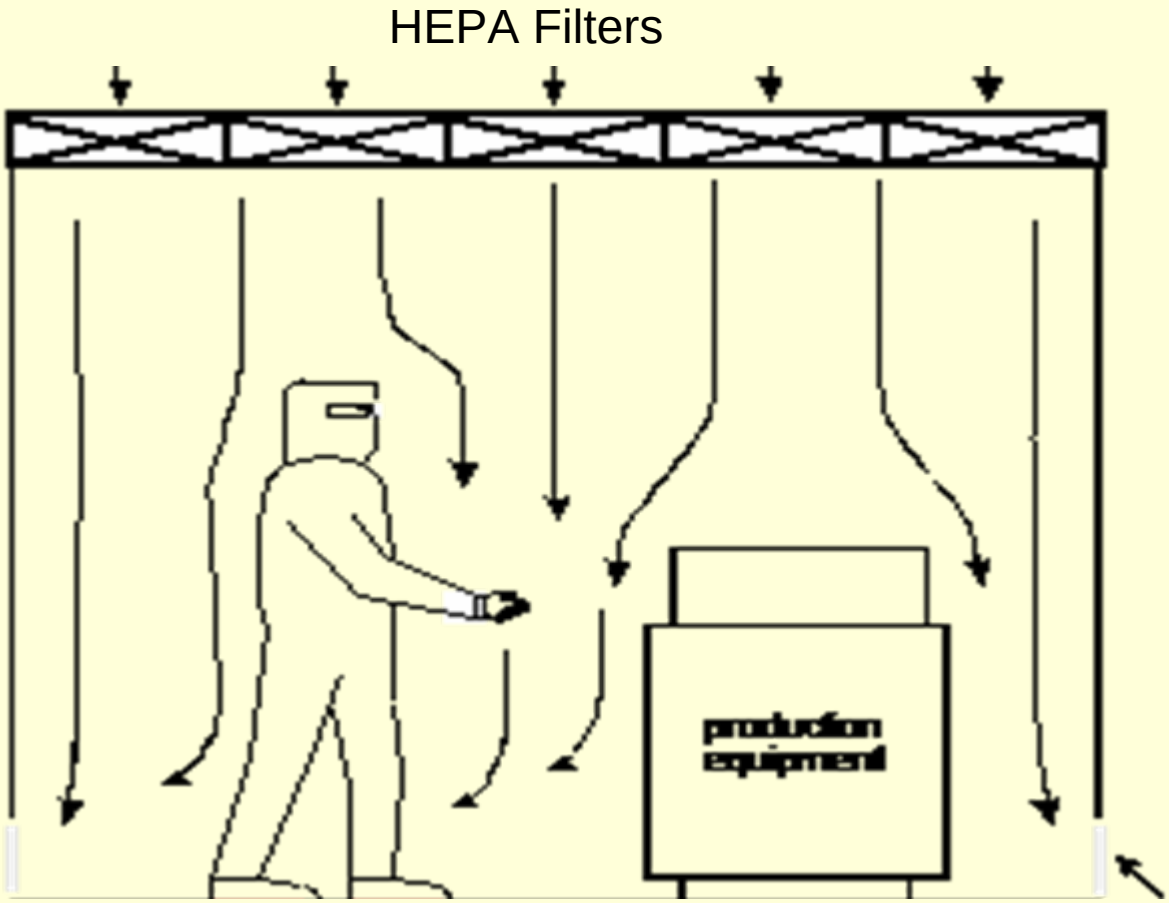
- Filtration
  - Pre-filtered in air handling units
  - HEPA (High Efficiency Particulate Air) filtered prior to entering cleanroom. Removes 99.99% of particles (typically 0.3um).
  - Air is not recycled
- Temperature
  - Maintained to reduce microbial growth (viruses, spores, fungi, bacteria)
- Humidity
  - Effects static, and growth of microbes

Employee Comfort

Class 10,000 Specifications: Temperature 72 +/- 2.5^{o}F, Humidy 45+/- 5%

Laminar Flow

Air flows with uniform velocity in parallel layers, with no disruption between the layers.



http://www.s2c2.co.uk/docs/Cleanroom_Design_Intro.html

Air extracted through vents low on walls.

Why Laminar Flow?

- Non-turbulent air flow, reduces the possibility of contamination caused by the movement of particles
- “Scrubs” the room with air flowing from ceiling to floor

Air Change
"*The solution is dilution*"

- Air Change
  - A volume of air equivalent to the room volume that enters and exits a room.

  For example: 60 air changes an hour means that a volume of air equivalent to the room passes through the room each minute.

  *FDA guidelines only specify a minimum of 20 air changes per hour. The number of air changes required to meet specification is determined for each individual cleanroom.

Cleanroom Architecture

- Elimination of spaces and crevasses that trap particles:
  - Recessed lighting and vents
  - “Coved” floor
  - Covered light switches
  - Specialized furniture (wheels, low particle emitting, stainless steel)
  - Epoxy paint on walls and floors

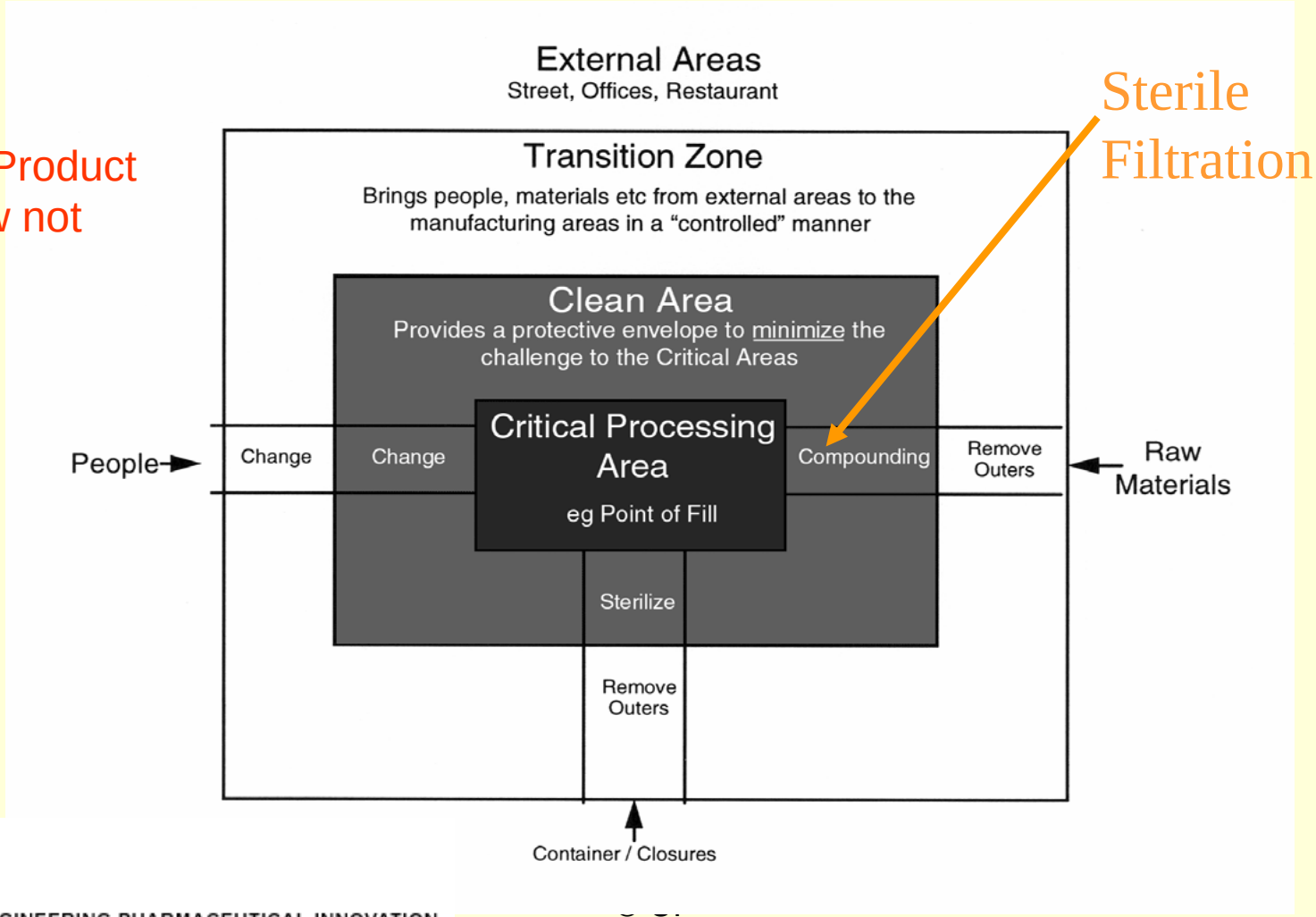
CLEANROOM ARCHITECTURE

- Maintained at a positive air pressure
  - Indicated by pressure gauge or indicator

  - Forces air to travel only OUT of the cleanroom, preventing dirty outside air from coming in.

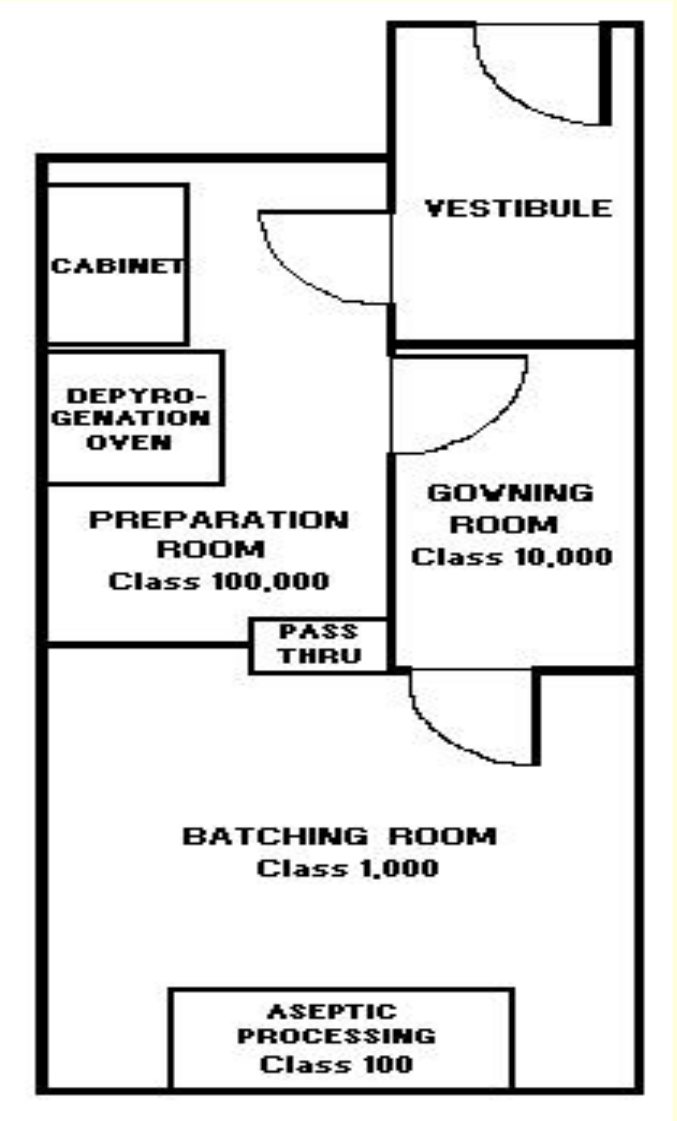
Nested Zones

Note: Product outflow not shown



CLEANROOM ARCHITECTURE

- Interlocking door system
  - Door to “dirtier” area must be closed before door to “clean” area can be opened.
  - Personnel must come in and out of the cleanroom through the gowning room. buffer zone.
  - An open, non-air locked door can add billions of particles per cubic ft



HUMANS IN CLEANROOMS

(The biggest source of contamination)

PEOPLE ACTIVITY	PARTICLES/MINUTE (0.3 microns and larger)
Motionless (Standing or Seated)	100,000
Walking about 2 mph	5,000,000
Walking about 3.5 mph	7,000,000
Walking about 5 mph	10,000,000
Horseplay	100,000,000

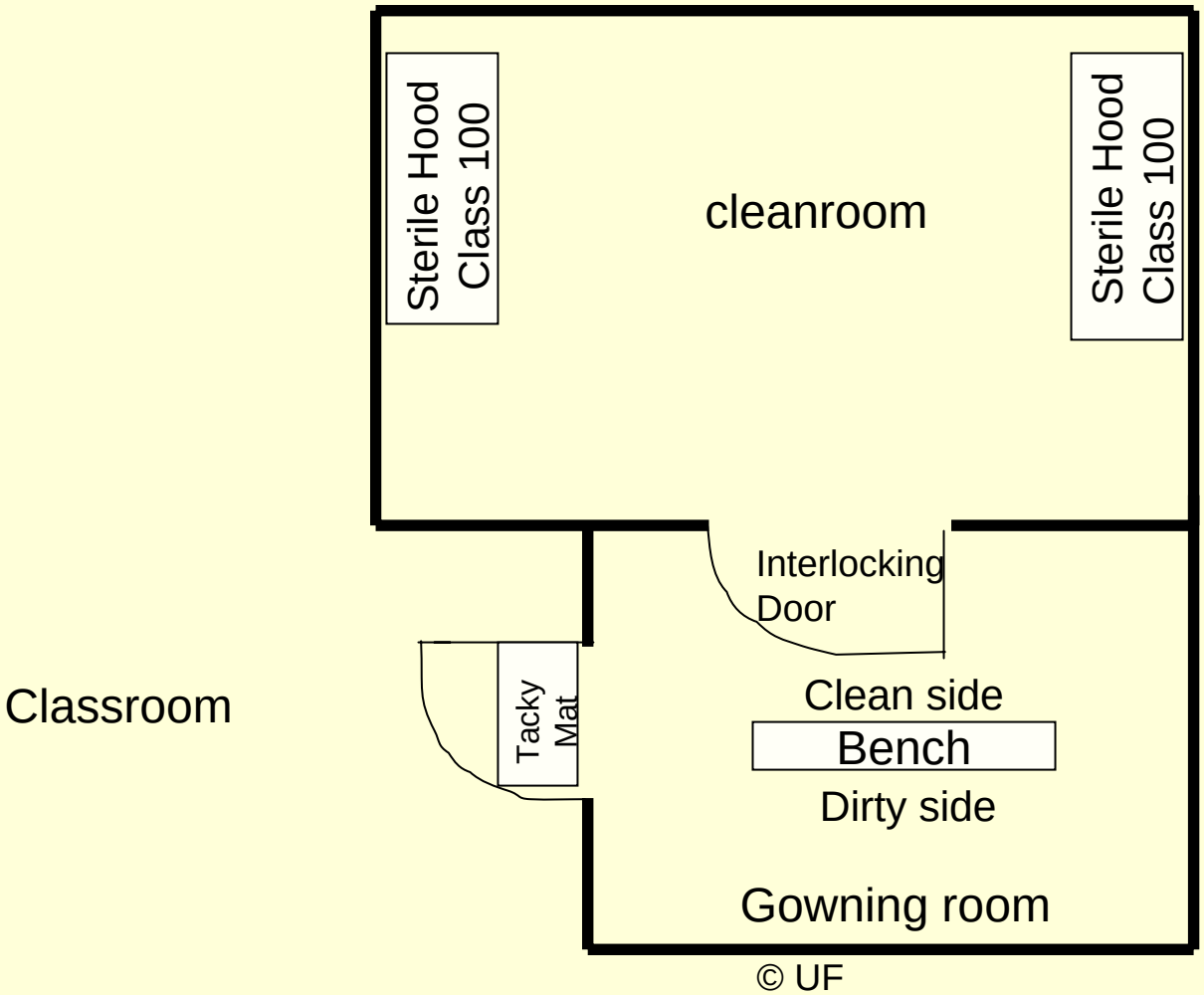
http://www.coastwidelabs.com/Technical%20Articles/Cleaning%20the%20Cleanroom.htm

Must “Gown-In” prior to entering cleanroom

Minimum Gowning Requirements

	ISO Class 8	ISO Class 7	ISO Class 6	ISO Class 5	ISO Class 4
Hair Cover	x	x	x	x	x
Hood				x	x
Beard Cover	x	x	x	x	x
Face Mask		x	x	x	x
Frock	x	x			
Coverall			x	x	x
Shoe Covers	x	x	x	x	x
Boots				x	x

Entering the Cleanroom



General Cleanroom Regulations

- No personal items such as jewelry, keys, watches, matches, lighters and cigarettes
- No eating, smoking or gum chewing
- No cosmetics such as lipstick, eye shadow, eyebrow pencil, mascara, eye liner, false eye lashes, fingernail polish, hair spray, mousse, or the heavy use of aerosols, after shaves and perfumes.
- Approved skin lotions are sometimes allowed to reduce skin flaking.

Actions Prohibited in Cleanrooms

- Fast motions such as running, walking fast or horseplay.
- Sitting or leaning on equipment or work surfaces.
- Writing on equipment or garments.
- Removal of items from beneath the cleanroom garments.
- Wearing torn or soiled garments.
- Allowing hands to touch anything other than product-related work

Minimizing particles

- Only approved cleanroom paper.
- Only approved ball point pens for writing
- Use of paper or fabric towels are prohibited

-Two surfaces rubbing generates billions of particles per cubic ft.

-Equipment should be specialized for cleanroom use (brushless centrifuges)

Cleaning the Cleanroom

- Cleaning is the essential element of contamination control.
  - Disinfectants filtered
  - Mops/Buckets autoclaved
  - Disinfectants rotated every two weeks
  - Only cleanroom approved wipers allowed
  - Clean top to bottom, cleanest area to dirtiest

Clean?

- When can the cleanroom be cleaned?
  - Need to work around production schedule
- How frequently does it need to be cleaned?
  - Depends on use
- What is clean and how is it measured?

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