

# CGMP Vaccine Facility Design in compliance with Biosafety Regulations

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**A .Basic Information Needed**

# 1. Type of Vaccines

ex) virus, bacteria, rickettia....

# 2. Biohazard class of vaccine agents

- a. Class 1: Bacillus subtilis
- b. Class 2: Hepatitis B
- c. Class 3: Japanese encephalitis B
- d. Class 4: Ebola

### 3. Biohazard classification of infectious agents

BSL-1: Unlikely to cause human disease

BSL-2: To cause human disease with moderate risk

- Percutaneous injury, ingestion, mucous membrane exposure

BSL-3: To cause human disease with high risk

- Potential for aerosol transmission
- Not ordinarily transmitted from one individual to another

BSL-4: To cause human disease with life-threatening risk

- Aerosol transmitted lab. Infection or unknown risk of transmission
- Readily transmitted from one individual to another

## 4. Safety equipment (ex. BSC) requirement

BSL-1: Not required

BSL-2: Class II BSCs for manipulations causing splashes or aerosols of infectious materials

BSL-3: Class II or III BSCs for all open manipulations of agents

BSL-4: a. Cabinet Lab : Class III BSCs

b. Suit Lab. : Class I or II BSCs with full-body, air-supplied positive pressure personnel suit

## 5. Assignment of bio-safety level (Facilities)

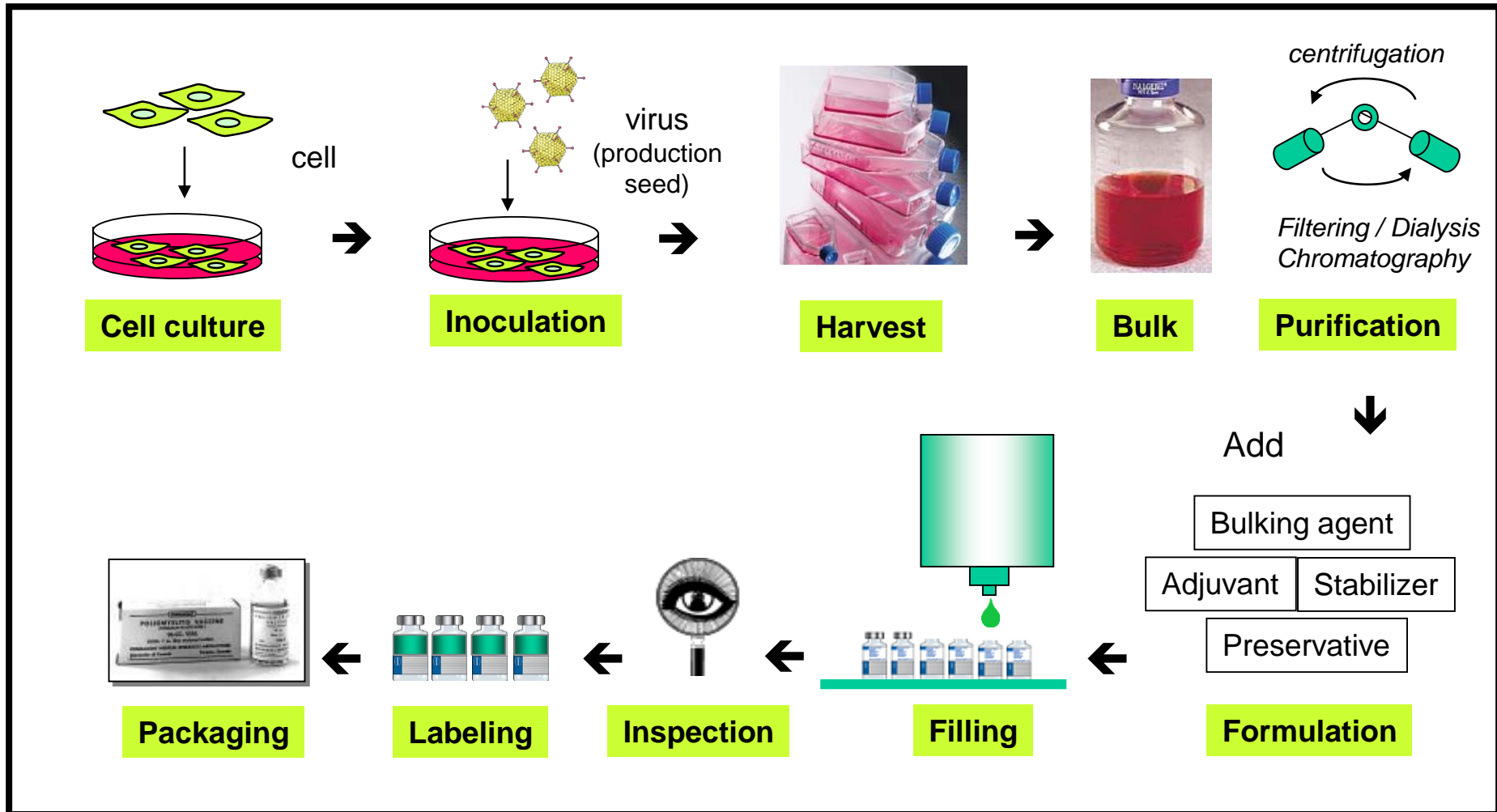
- a. Principle No.1: The same BSL as assigned to the agent itself  
ex) tetanus, diphtheria, vaccinia etc. →BSL-2
- b. Principle No.2: Upgraded BSL assigned to the agent  
ex) pertussis, BCG etc. in large scale production →BSL-3
- c. Principle No.3: Downgraded BSL assigned to the vaccine strains  
ex) Junin candid #1, Yellow fever 17-D etc. →BSL-2

6. Total number of vaccine doses to be produced :  
ex)  $20 \times 10^6$  doses per year
7. Single-dose vials or multi-dose vials
8. Size of vials
9. Freeze-dried vaccines or liquid vaccines
10. Yearly working months  
ex) 10 months per year

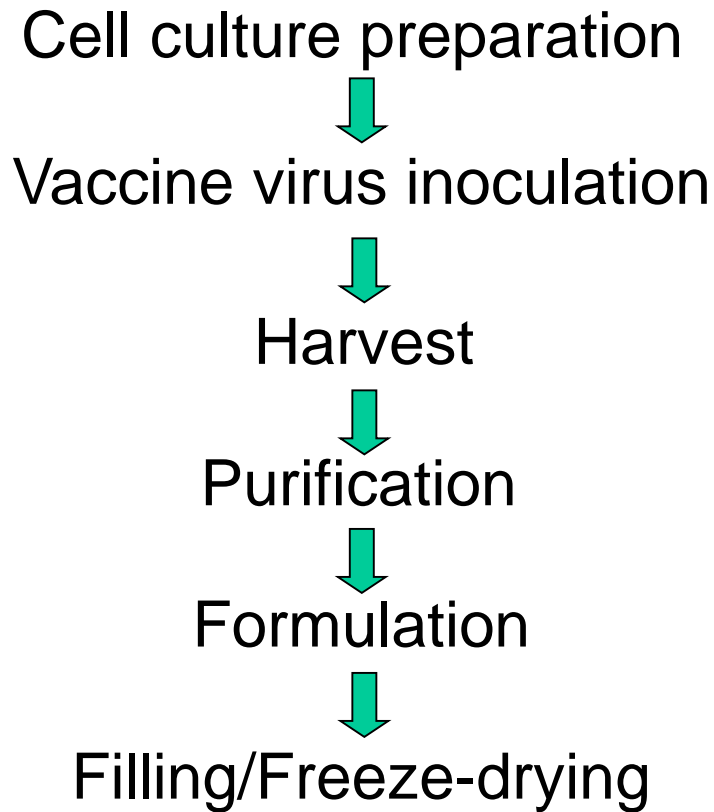
# B. Overall Manufacturing Process



# Virus Vaccine Production



## ex) virus vaccine production



**C. Determine the Size & Number  
of Rooms & Equipment/Systems**

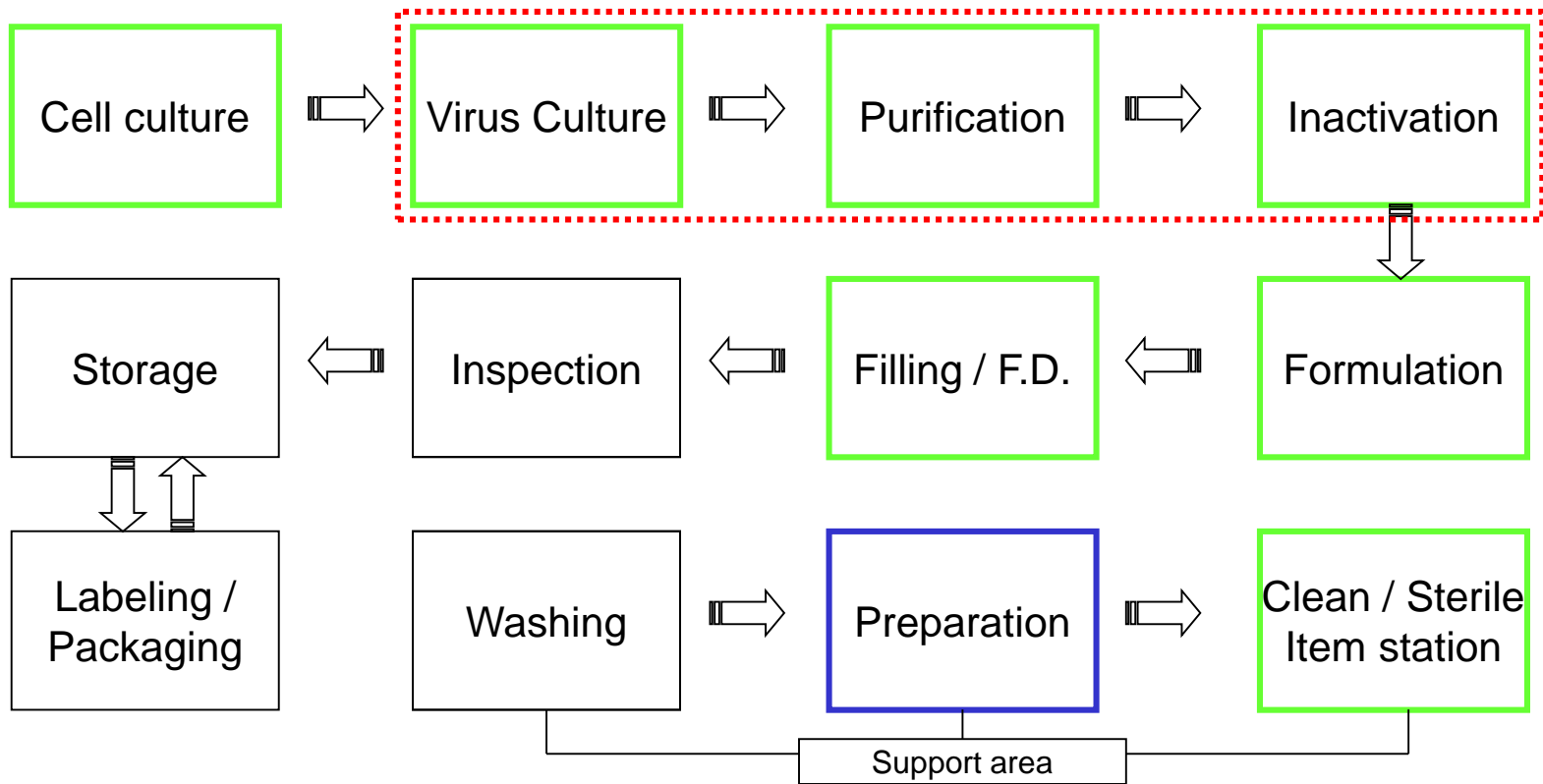
1. Adequate space for operation, cleaning & maintenance
2. Equipment:  
ex) Freeze-dryer, Filling apparatus....
3. Systems:  
ex) HVAC, WFI, Clean Steam....

## D. Conceptual Layout

# Schedule of minimum air requirements for various manufacturing spaces

Typical rooms	Particle count ( $\geq 0.5\mu\text{m}$ )	Filter required	Pressure (inches of water)	Air changes per hour
Warehouse or equivalent	Not defined	Disposable	Not defined	1
Packaging Cafeteria Offices Lounge	Not defined	Disposable	Not defined	15-20
Laboratory or equivalent	$\leq 100,000$	30-65% NIST	0.05	20
Manufacturing nonsterile products	10,000 -100,000	95% NIST	0.05	20-30
Manufacturing sterile products Wash area equipment product container/closures	$\leq 10,000$	HEPA	0.05	30-60
Fill-seal room	$\leq 10,000$	HEPA	0.05	30-60
Over work surface	$\leq 100$	HEPA	0.05	Laminar 300-600

# 1. Process Block Flow Diagram with Air Cleanliness and Infectious Area shown



Air Cleanliness(Dynamic) : — non-controlled, — class 100,000  
— class 10,000  
Infectious area : . . . . .

## 2. Draw the layout in accordance with the following concepts.

### a. Clean vs. Dirty Area concept

- 1) Flow of material
- 2) Flow of product
- 3) Flow of personnel
- 4) Flow of waste
- 5) Flow of air

### b. Infectious vs. Non-infectious Area concept

- 1) Determine the biohazard class
- 2) Follow the Biosafety Requirements



# 3. Biosafety Requirements on Facilities

\* Note: O = required, P = preferred/recommended, - = not required or not applicable

	Items	BSL-1	BSL-2	BSL-3	BSL-4	
					Cabinet	Suit
1	Clothing change room	-	-	O	O	O
2	Double door entry with interlock	-	-	O	O	O
3	Lockable doors	-	O	O	O	O
4	Self-closing doors	-	O	O	O	O
5	Sink for hand washing(manual or automatic)	O	O	-	-	-
	Sink for hand washing(automatic)	-	-	O	O	O
6	Windows with fly screens	O	O	-	-	-
	Windows sealed	-	P	O	O	O
7	Bench tops impervious to water and resistant to chemicals	O	O	O	O	O
8	Sturdy lab. furniture	O	O	O	O	O
9	Furniture & equipment spaced for cleaning	O	O	O	O	O
10	Lab. (furniture) for easy decontamination	-	O	O	O	O
11	Decontaminating device in facilities	-	O	O	O	O
	Double door autoclave	-	-	P	O	O

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	Items	BSL-1	BSL-2	BSL-3	BSL-4	
					Cabinet	Suit
12	Eye wash station	-	O	O	O	O
13	Water shower in change room	-	-	P	O	O
	Chemical shower in change room	-	-	-	-	O
14	Mechanical ventilation system (directional flow)	-	P	O	O	O
15	Exhaust air not recirculated	-	P	O	O	O
16	Exhaust air HEPA-filtered	-	-	O	-	-
	Exhaust air via 2 HEPA-filters in series	-	-	-	O	O
17	Negative air pressure	-	P	O	O	O
18	Pressure-monitoring device	-	P	O	O	O
19	Walls, floors & ceilings for easy cleaning	O	O	O	O	O
	Walls, floors & ceilings for easy decontamination	-	O	O	O	O
20	Coved floor coverings	-	-	P	O	O
21	Penetrations in surfaces sealed	-	-	O	O	O

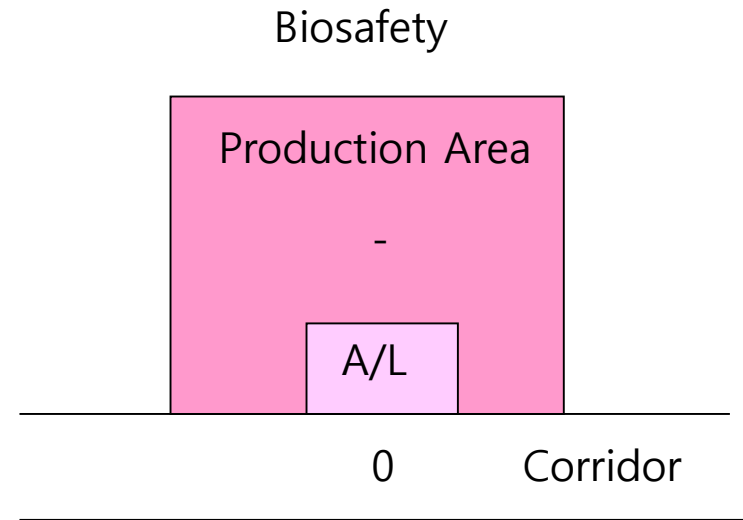
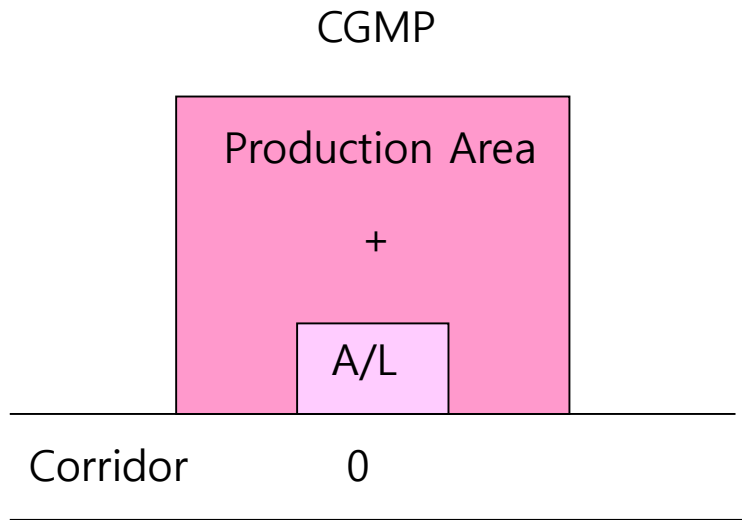
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	Items	BSL-1	BSL-2	BSL-3	BSL-4	
					Cabinet	Suit
22	Openings sealable for decontamination	-	-	O	O	O
23	Vacuum lines protected with HEPA filter	-	O	O	-	-
	Vacuum lines protected with 2 HEPA filters in series	-	-	-	O	O
24	Biological safety cabinet	-	O	O	O	O
25	Decontamination of liquid effluents from inner change room, cabinet room sink and floor drains	-	-	-	O	O
26	Prevention of reversed air flow	-	-	O	O	O
27	Annual re-verification of facilities	-	-	O	O	O
28	Appropriate communication system	-	-	P	O	O
29	Emergency power source	-	-	P	O	O
30	Sewer vents with 2 in-line HEPA filters	-	-	-	O	O

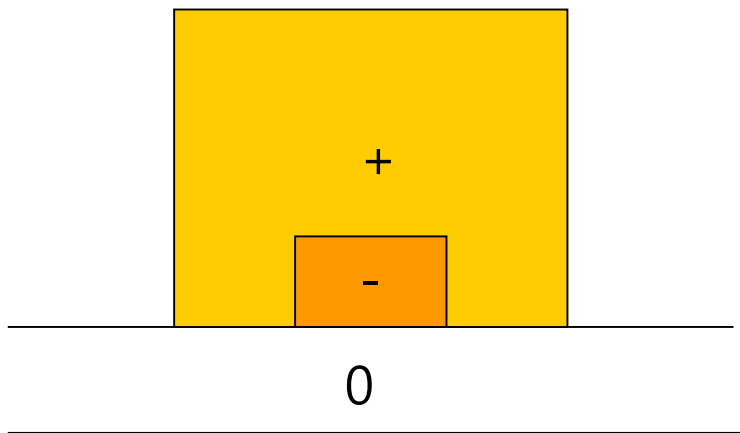
# 4. Harmonization of CGMP & Biosafety

## a. Typical Layout required by CGMP & Biosafety

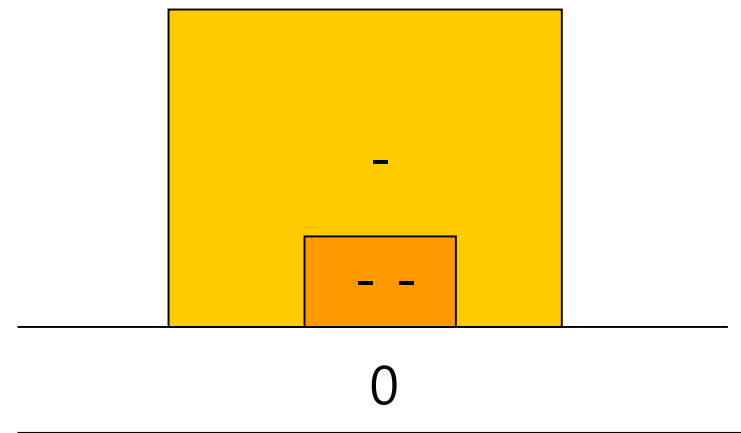


# 4. Harmonization of CGMP & Biosafety

b. Using sink type air-lock

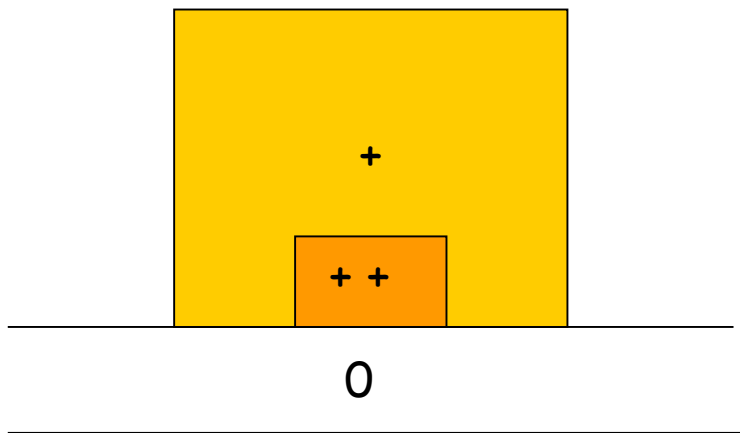


or

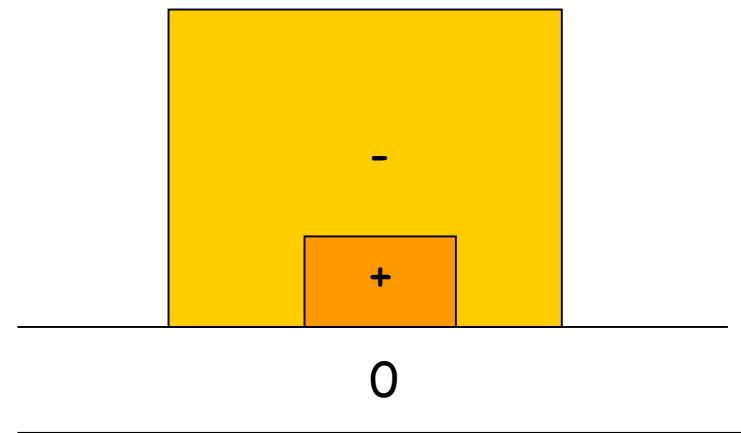


# 4. Harmonization of CGMP & Biosafety

c. Using bubble type air-lock



or



# E. Incorporate Support Areas

1. Equipment Area
2. Penthouse
3. Interstitial Space
4. Sewage Treatment Facilities
5. Storage Area



# F. Evaluation & Construction

# 1. Conceptual Layout

- a. Internal Review: User/Consultant
- b. External Review: Regulatory Agency

# 2. Basic Design

- a. Generated by Architectural/Engineering Co.
- b. Reviewed by Internal & External Experts.

### 3. Detailed Design

- a. Generated by Architectural/Engineering Co.
- b. Reviewed by Internal & External Experts.

### 4. Construction under User's/ Expert's Supervision

# G. Typical layout for GMP production facilities

# Viral Vaccine Manufacturing facilities

