



## **La strategia del contenimento nella manipolazione di HAPI**

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# Premessa: Legge 81

## Art. 222. :Definizioni

- g) pericolo: la proprieta' intrinseca di un agente chimico di poter produrre effetti nocivi;
- h) rischio: la probabilita' che si raggiunga il potenziale nocivo nelle condizioni di utilizzazione o esposizione.

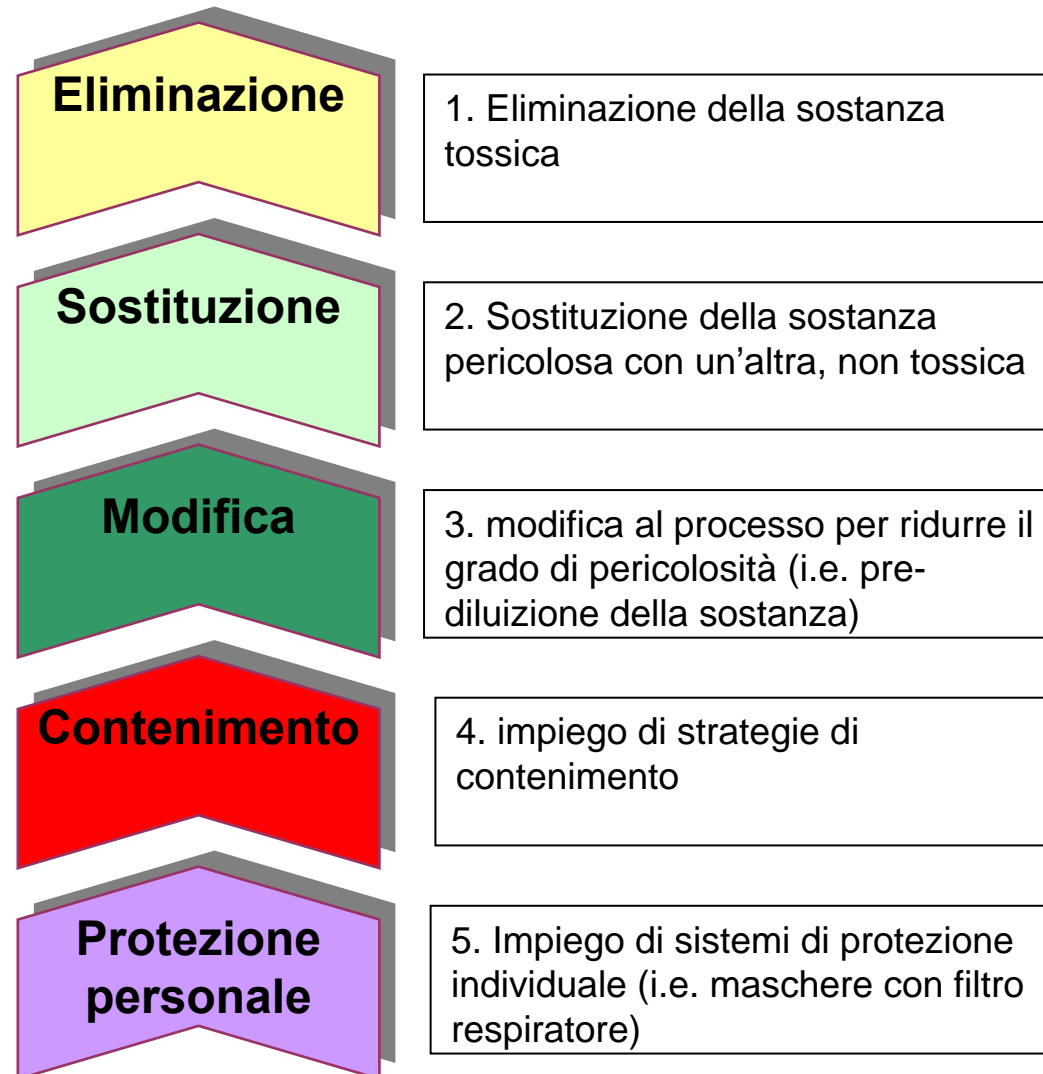
## Art. 223. Valutazione dei rischi

1. Nella valutazione di cui all'articolo 28, il datore di lavoro determina, preliminarmente l'eventuale presenza di agenti chimici pericolosi sul luogo di lavoro e valuta anche i rischi per la sicurezza e la salute dei lavoratori derivanti dalla presenza di tali agenti, prendendo in considerazione in particolare:
  - c) **il livello, il tipo e la durata dell'esposizione;**
  - d) le circostanze in cui viene svolto il lavoro in presenza di tali agenti, compresa la **quantita'** degli stessi;
  - e) **i valori limite di esposizione** professionale o i valori limite biologici; di cui un primo elenco e' riportato negli allegati XXXVIII e XXXIX;
  - f) gli effetti delle misure preventive e protettive adottate o da adottare;
2. ... Nella valutazione medesima devono essere incluse le attivita', **ivi compresa la manutenzione e la pulizia**, per le quali e' prevedibile la possibilita' di notevole esposizione o che, per altri motivi, possono provocare effetti nocivi per la salute e la sicurezza, anche dopo l'adozione di tutte le misure tecniche.

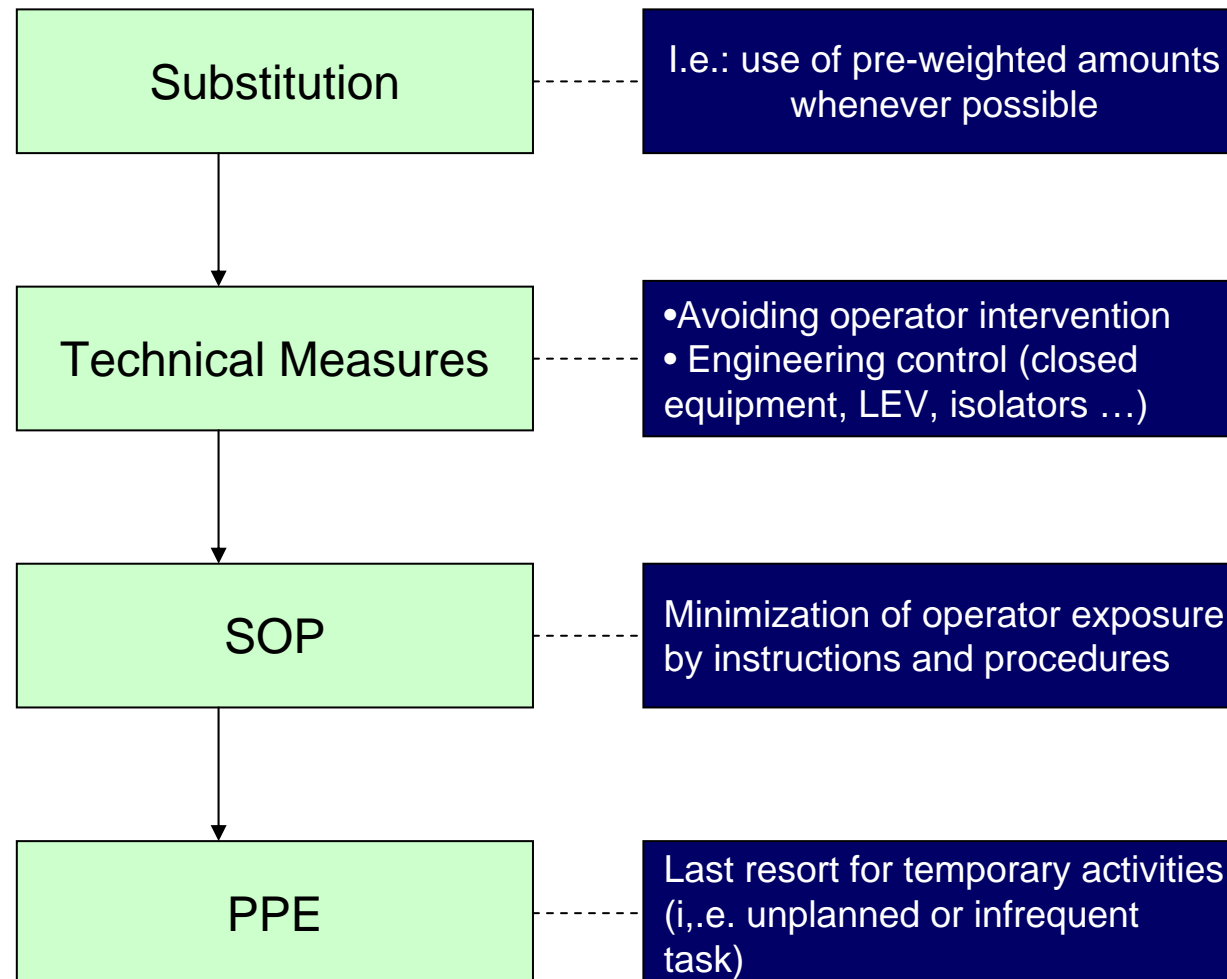
# Agenda

- Premessa: gerarchia degli interventi
- Contenimento primario e secondario
- Approccio al contenimento
- Le strategie per il contenimento
- Conclusione

# Scala degli interventi

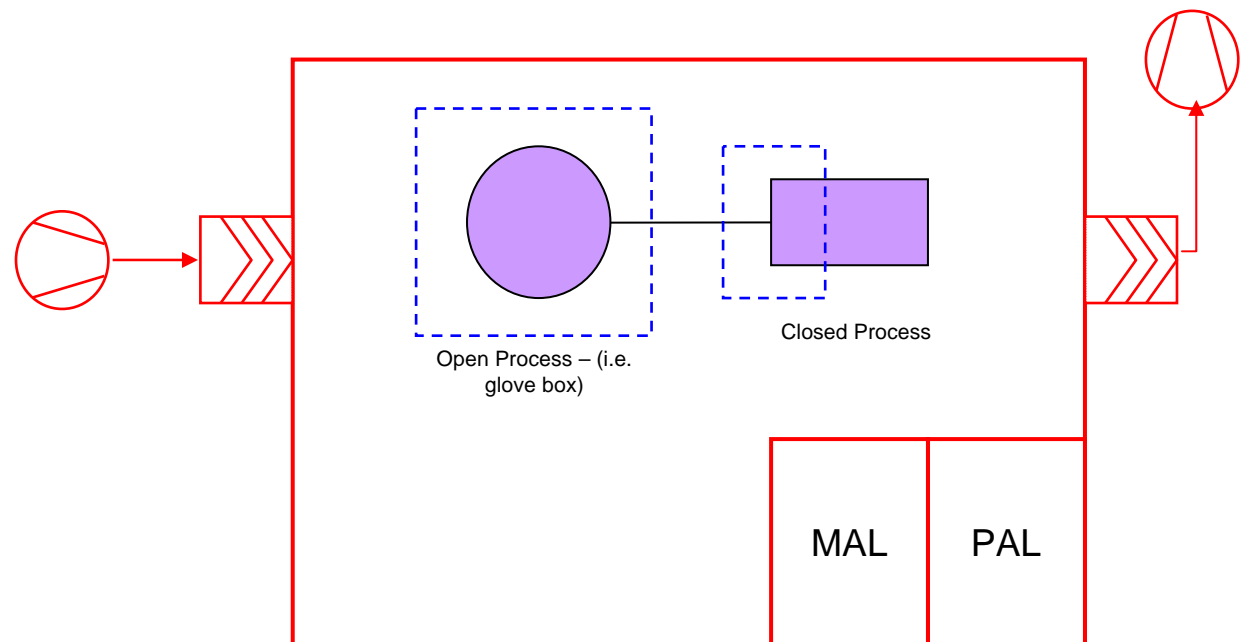


# Gerarchia delle misure di controllo

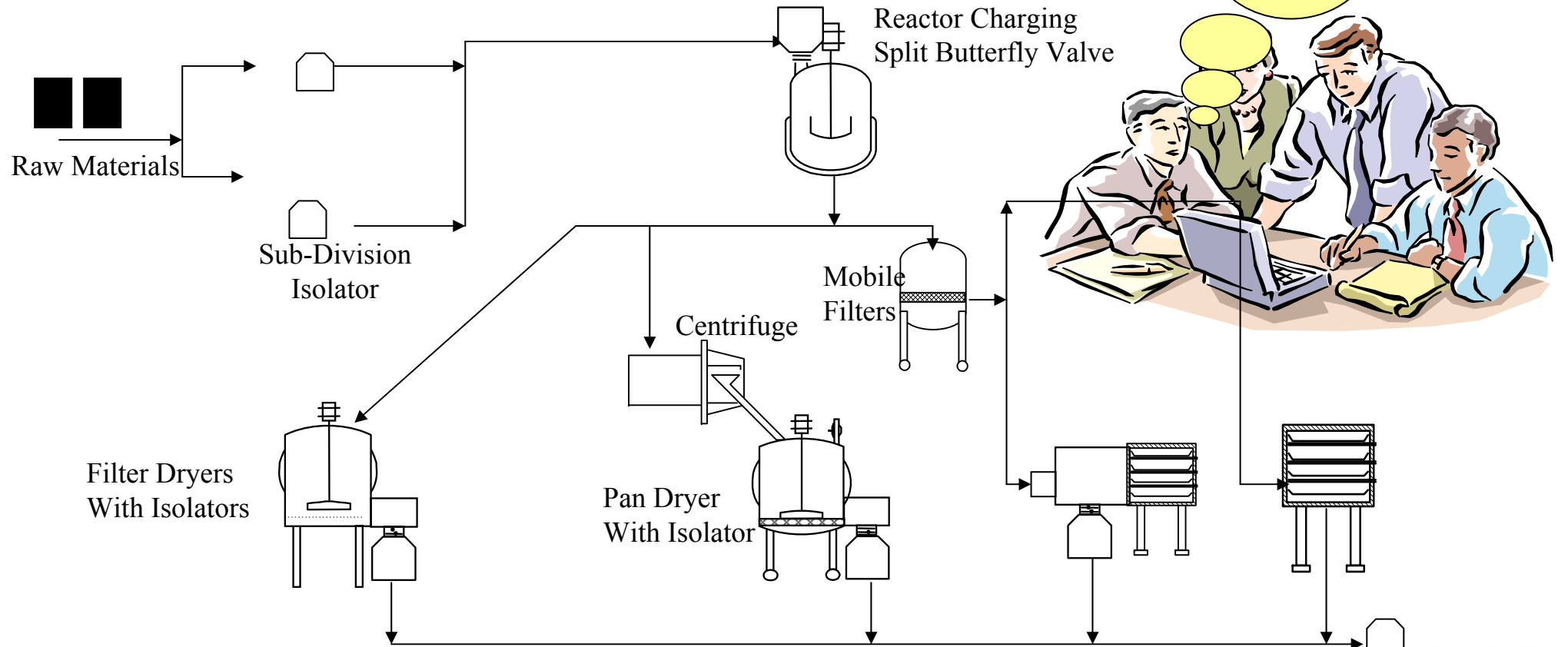
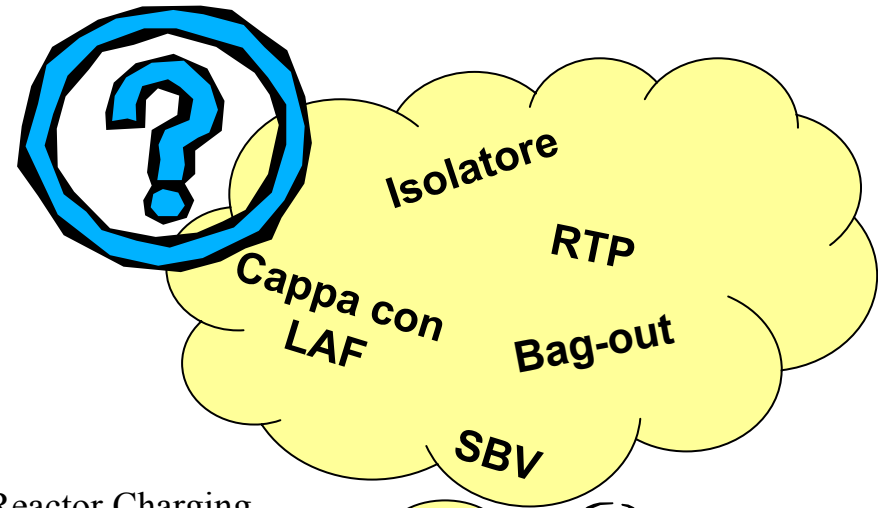


# Contenimento primario e secondario

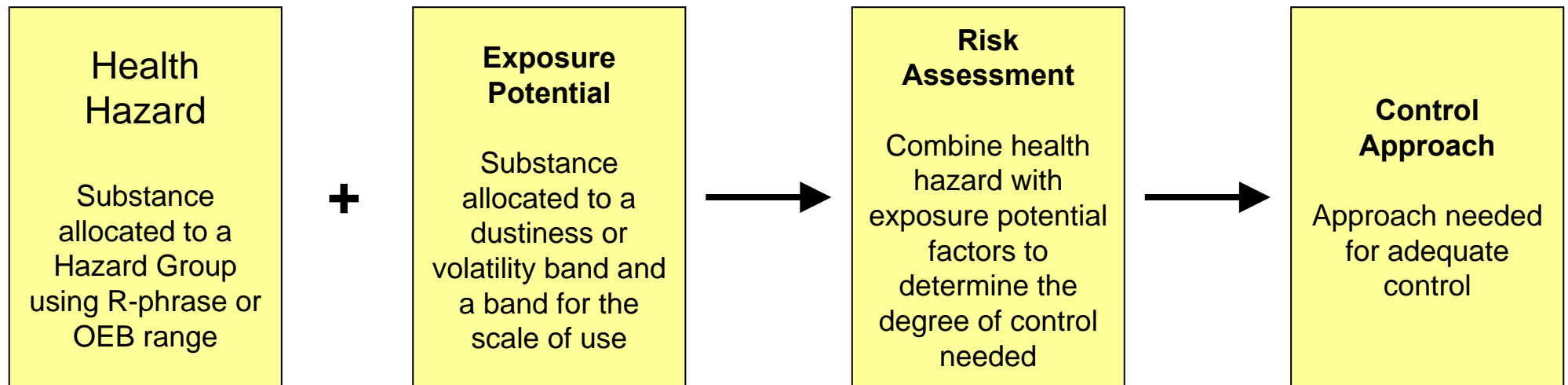
- Il contenimento primario (in blu) si basa su apparecchiature di processo chiuse e su barriere attorno alle parti critiche della apparecchiatura stessa
- Il contenimento secondario si basa su come è realizzato il locale di processo, gli accessi e l'impianto HVAC



# Contenimento: come fare?

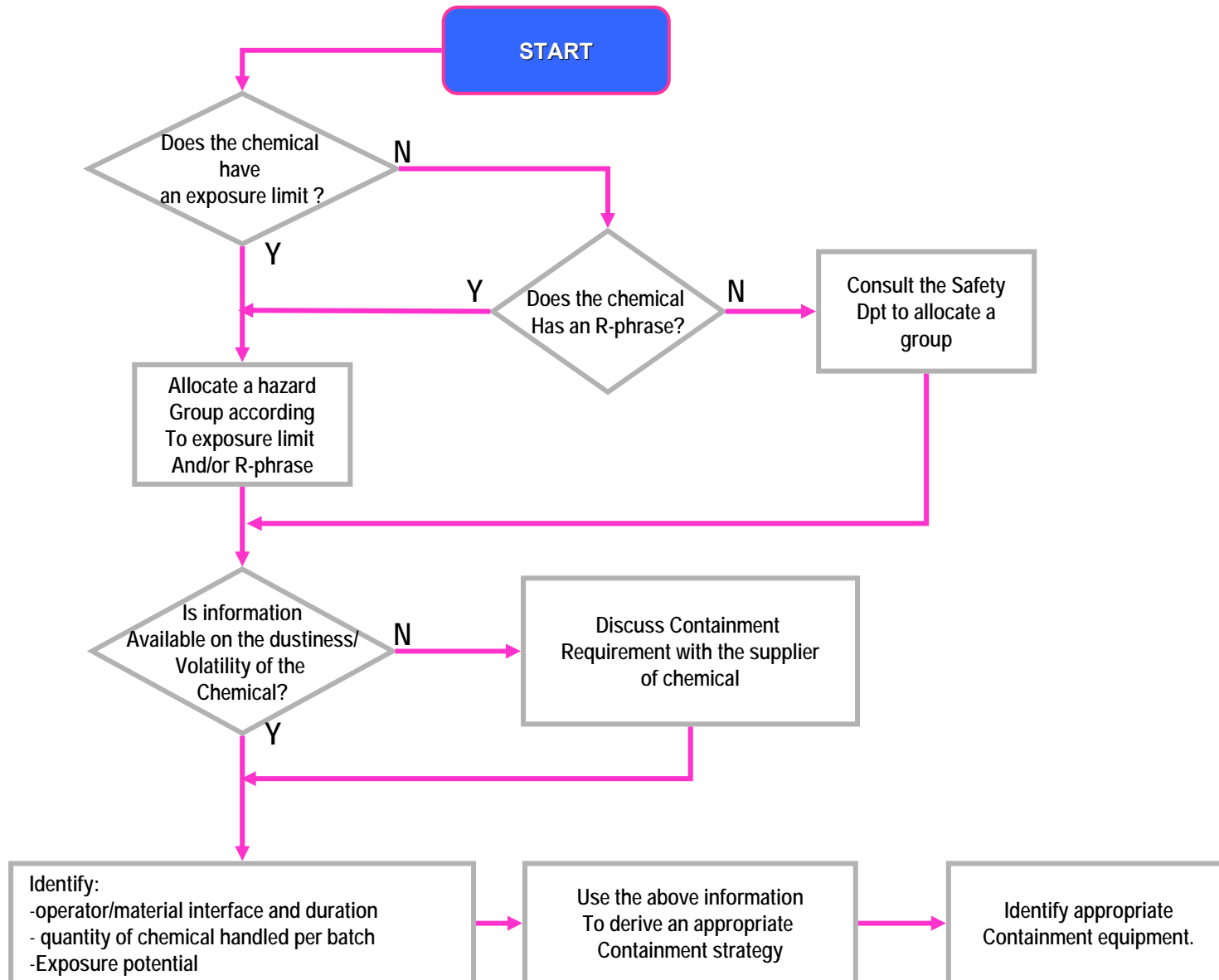


# Assignment of Containment strategy

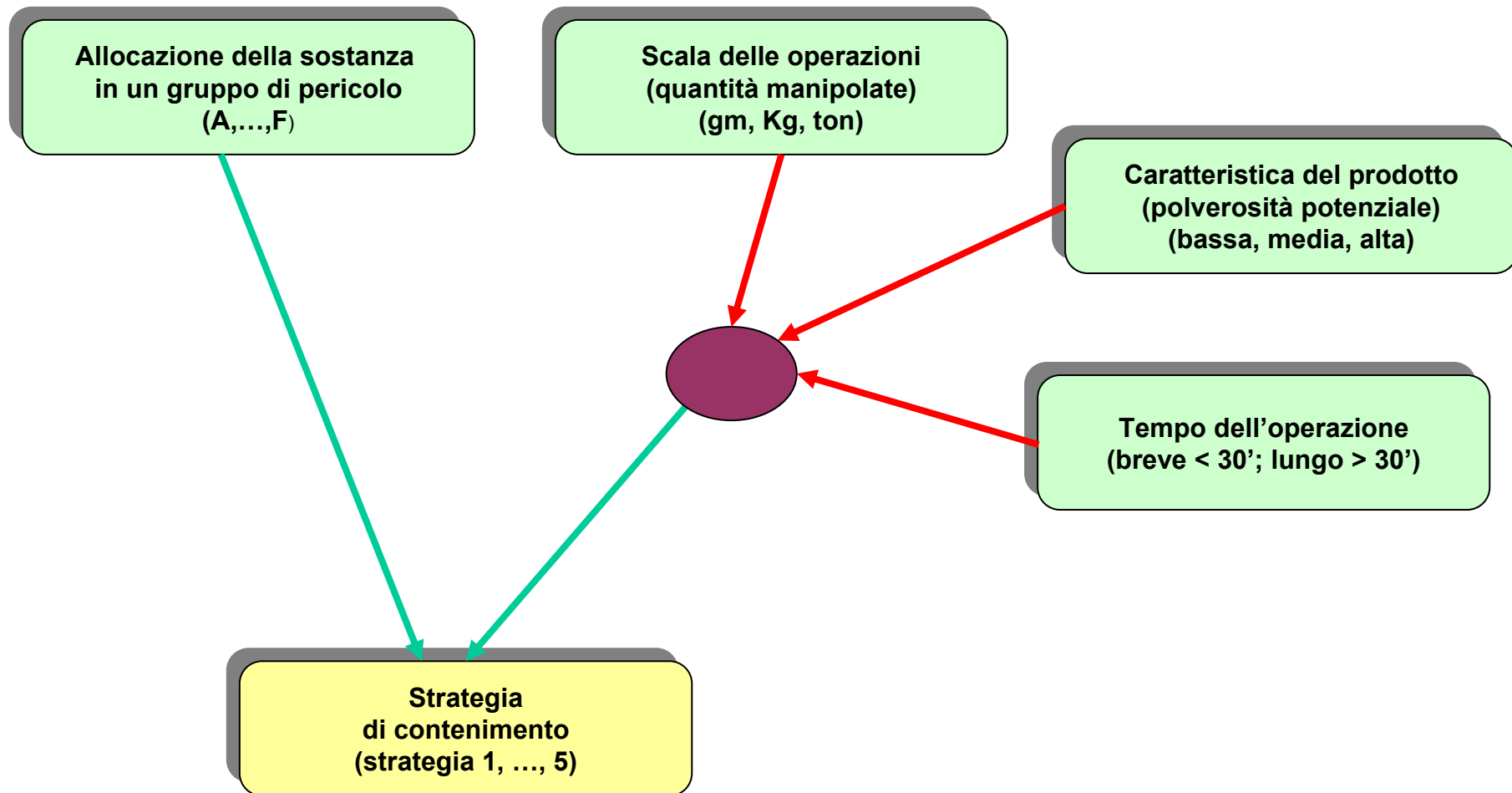




# La Strategia di contenimento: Flow chart



# Identificazione della strategia di controllo



# Esempio schemi di selezione

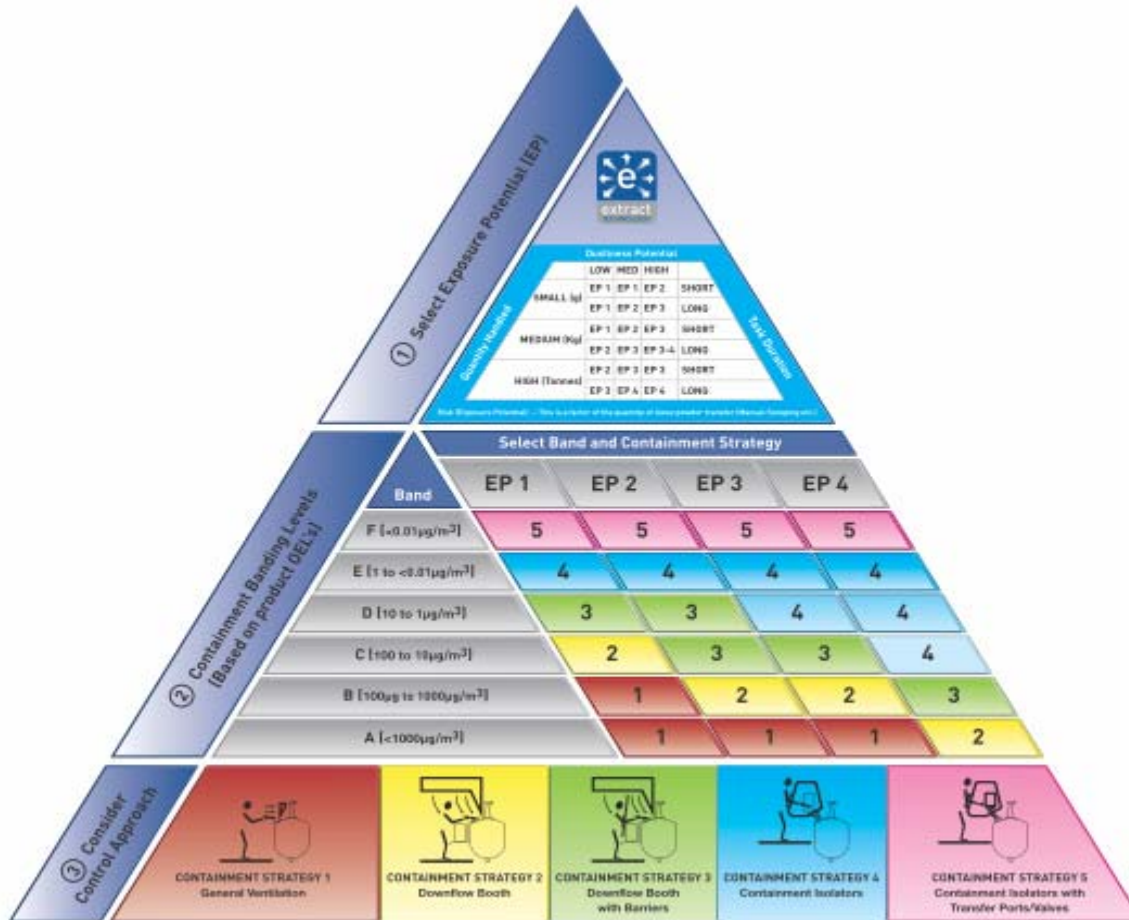
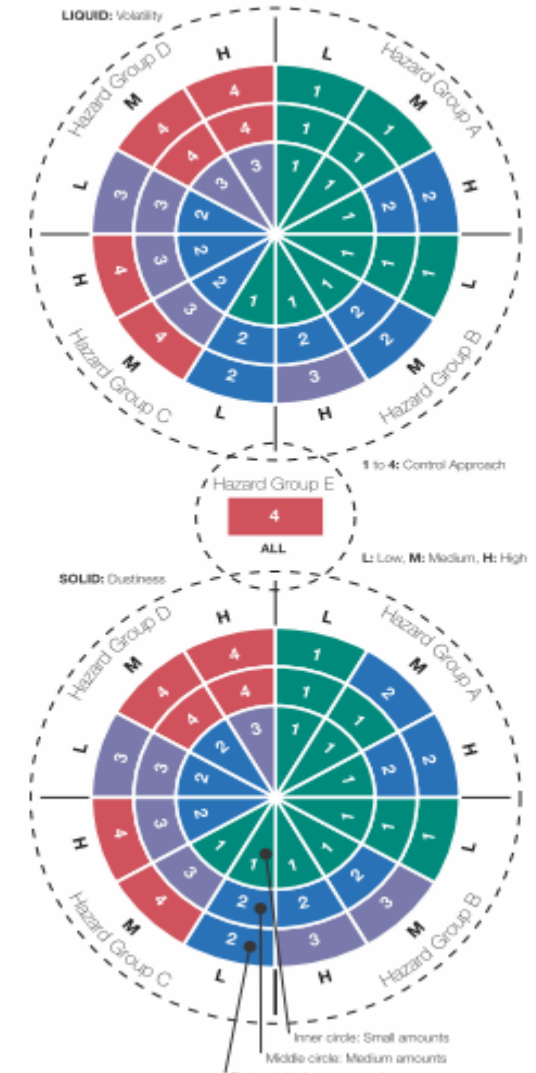
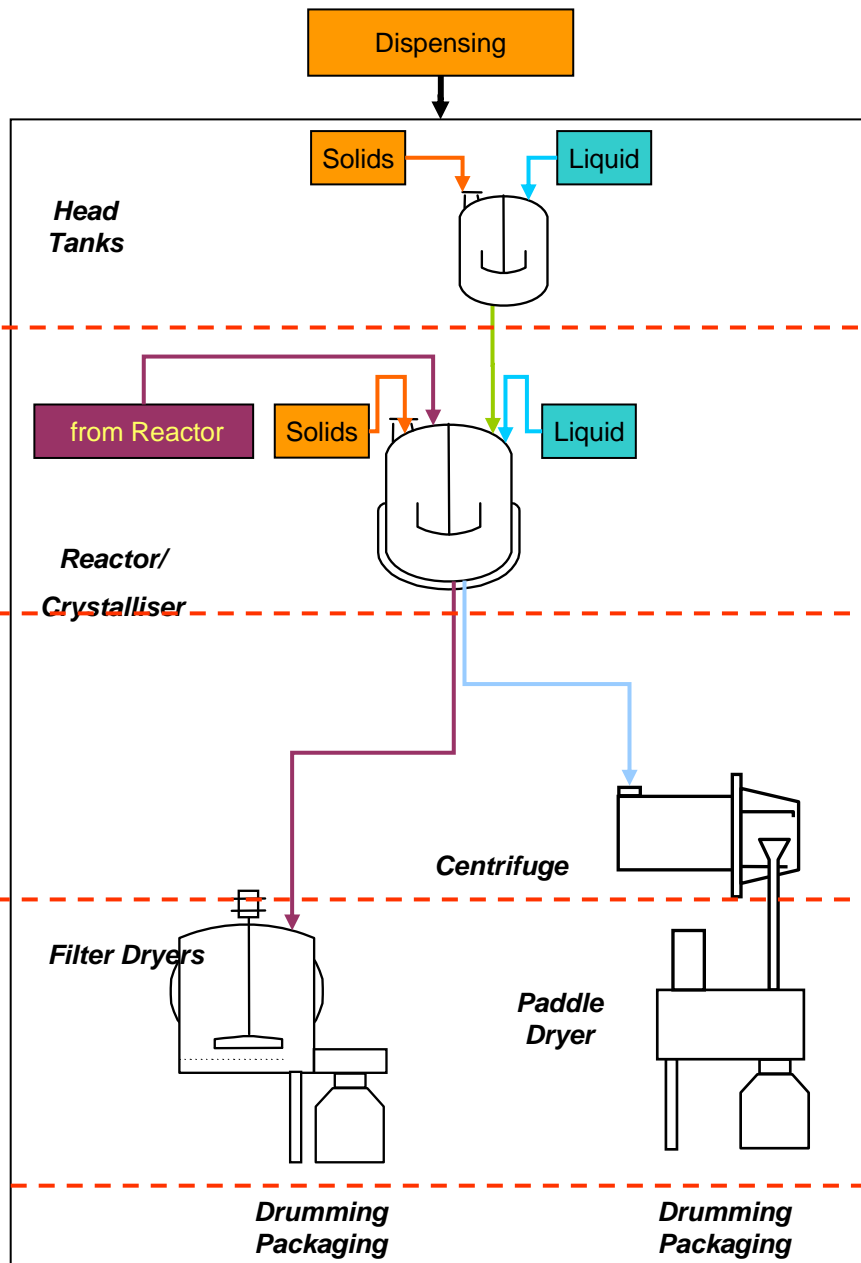


Figure 2



# Il processo produttivo



| Task       | Subs. | Phys.  | Quantity | OEB -µg/m3 (ppm) | Durat. |
|------------|-------|--------|----------|------------------|--------|
| Dispensing | solid | medium | Medium   |                  | < 60'  |

|                 |        |          |        |  |       |
|-----------------|--------|----------|--------|--|-------|
| Solid Charg.    | solid  | medium   | Medium |  | < 60' |
| Liquid charging | liquid | medium v | Medium |  | < 60' |

|                 |        |          |        |  |       |
|-----------------|--------|----------|--------|--|-------|
| Solid Charg.    | solid  | medium   | Medium |  | < 60' |
| Liquid charging | liquid | medium v | Medium |  | < 60' |
| Piping connec.  | liquid | medium   | medium |  | < 60' |
| Cleaning        |        |          |        |  |       |

|                 |        |          |        |  |       |
|-----------------|--------|----------|--------|--|-------|
| Centrif. Disch. | slurry | Medium   | Medium |  | < 60' |
| Clening         | Slurry | medium v | Medium |  | < 60' |

|           |       |        |        |  |       |
|-----------|-------|--------|--------|--|-------|
| Discharge | solid | Medium | Medium |  | < 60' |
| Cleaning  | solid | Medium | Medium |  | < 60' |
| Packaging | solid | Medium | Medium |  | < 60' |

# Analisi delle singole fasi produttive e definizione della categoria di controllo

|   | OEL<br>mcg/m <sup>3</sup> /R-<br>phase | Hazard<br>Allocation | m [kg] | Quantity | volatility | Duration of<br>operation | Exposure<br>Potential<br>(EP) | Control<br>Strategy |
|---|--|----------------------|--------|----------|------------|--------------------------|-------------------------------|---------------------|
| <b>Liquid</b>                             |  |                      |        |          |            |                          |                               |                     |
| Liquid A                                  | R 22                                   | OEB B                | 570    | Large    | Low        | long                     | EP3                           | CS2                 |
| Liquid B                                  | 1000 ppm                               | OEB A                | 2160   | Large    | High       | long                     | EP4                           | CS2                 |
| DMSO (Filter rinsing)                     | 250 ppm                                | OEB A                | 178    | Large    | Low        | long                     | EP3                           | CS1                 |
| <b>Solid</b>                              |  |                      |        |          |            |                          |                               |                     |
| Wet cake (OEL 0.5 mcg/m <sup>3</sup> )    | 0,5 mcg/m <sup>3</sup>                 | OEB E                | 130    | Medium   | Medium     | long                     | EP3                           | CS4                 |
| Dry Product (OEL 0.5 mcg/m <sup>3</sup> ) | 0,5 mcg/m <sup>3</sup>                 | OEB E                | 110    | Medium   | Medium     | long                     | EP3                           | CS4                 |
| Solid A                                   | 0,5 mcg/m <sup>3</sup>                 | OEB E                | 380    | Large    | Low        | long                     | EP3                           | CS4                 |

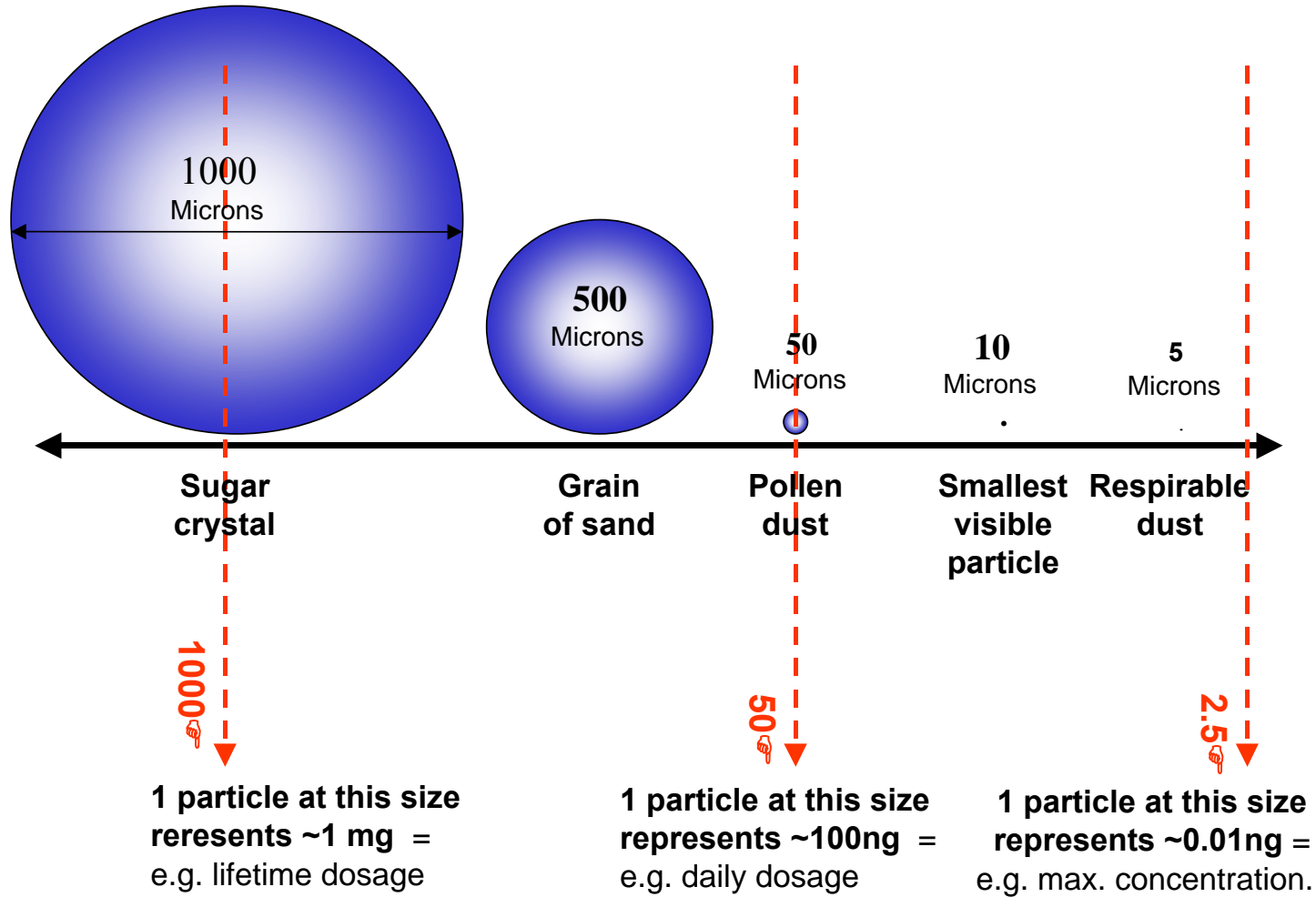
# Strategia di contenimento primario CS4

| Process Operation   | CS4  |
|---|--|
| Dispensing of dry solids  | Use of already dispensed material strongly recommended. Otherwise isolator technology required, to be places within a secondary containment.   |
| Charging of dry solids  | <ul style="list-style-type: none"> <li>• More than one chamber charging isolator (risk analysis if a nitrogen neutralization is required): isolator to be placed within a secondary containment.</li> <li>• PTS / DCS to be placed within a secondary containment</li> </ul> |
| Charging of wet cake into the dryer                                     | Use filter dryer or centrifuge directly coupled to dryer.  |
| Material / powder Transfer (e.g. charging and discharging of equipment) | Use gravity transfer wherever possible : direct connection between processing units or Isolator  |
| Sampling of dry solids from filter drier                                | Discharging isolator fitted with RTP or bag in / bag out system and discharging door fitted with sampling orifice.   |
| Discharging of paddle driers, filter driers                             | Into drums using an offloading booth fitted with continuous liner (if sufficient height available). The whole discharging station to be placed within a secondary containment.   |

# Contenimento secondario: check list

|                           |   |
|---------------------------|---|
| Description               | OEL= xxx mcg/m3 – OEB Y   |
| General concept           | Open or closed handling? Workstation with LEV   |
| Process Room              | Process rooms with all plants installed or process room segregated from the technical are?  |
| Access                    | Restricted access to work area required to authorized, properly trained personnel.<br>Airlock with special features? (i.e. showers, pressure control ..). MAL and PAL?  |
| Materials of Construction | Highly cleanable, moisture/chemical resistant, non-porous materials...  |
| Floors and wall surface   | Characteristics of floors (i.e. seamless, chemical resistant, drainable ...)<br>Characteristics of wall (i.e. non-porous, chemical resistant, easily cleanable ...)   |
| HVAC                      | Recirculation or once-through?<br>GEV or LEV? Air changes<br>HEPA Filtration?<br>Pressure cascade<br>Safety replace system –Redundancy - Maintainability  |
| Cleaning procedure        | Compressed air is permitted? Water mist?  |
| PPE                       | Type of PPE during normal operation<br>Type of PPE during open handling steps, maintenance, cleaning, emergency ...)  |
| Procedure                 | Normal operation<br>decontamination of equipment and surfaces<br>cleaning of process equipment and rooms (especially in case of CIP or WIP)<br>waste disposal<br>Detection and measures in case of a loss of containment or HVAC failure<br>Emergency procedures<br>Maintenance |

# What is Nanogm/m<sup>3</sup> Containment?

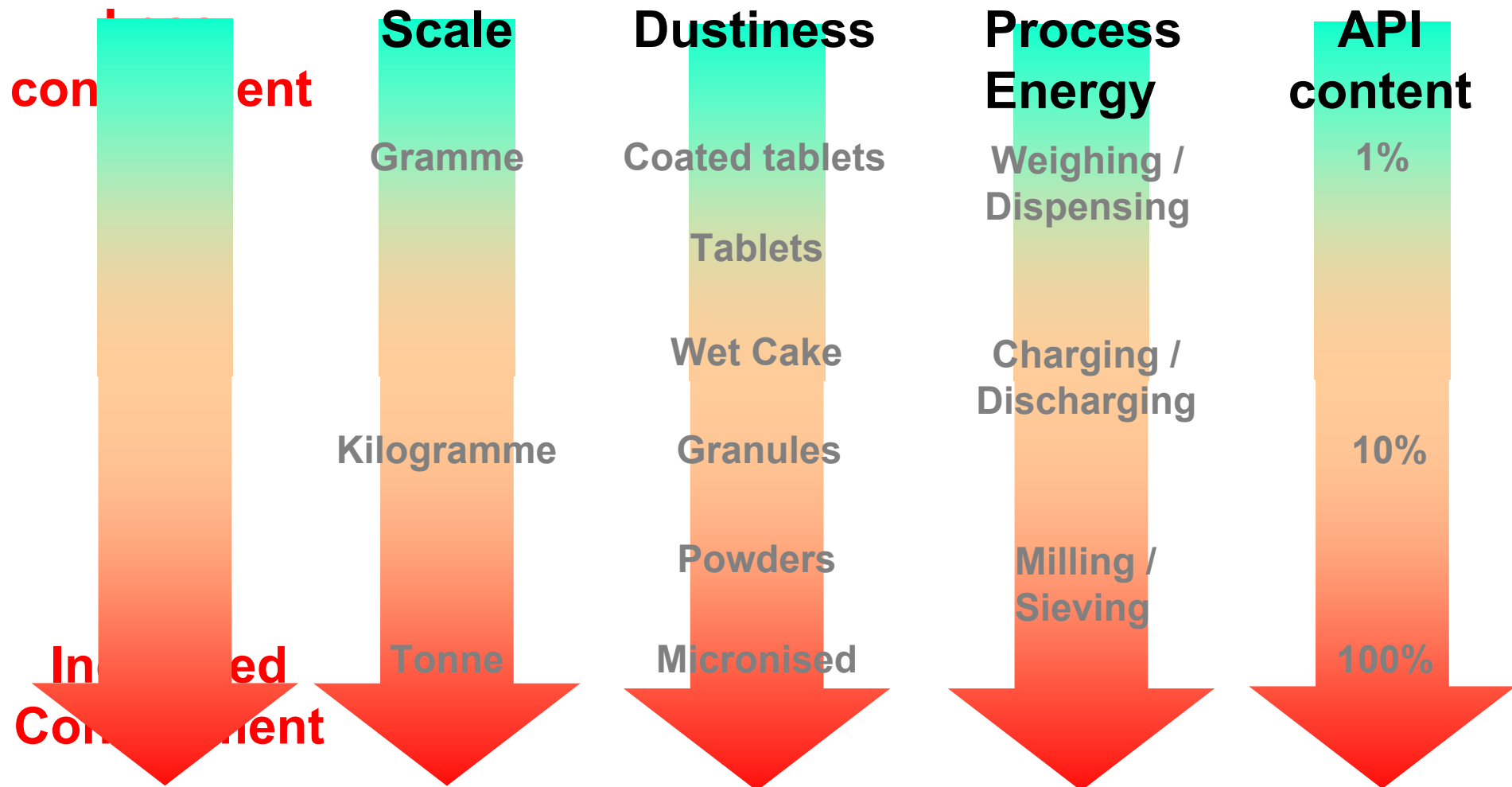




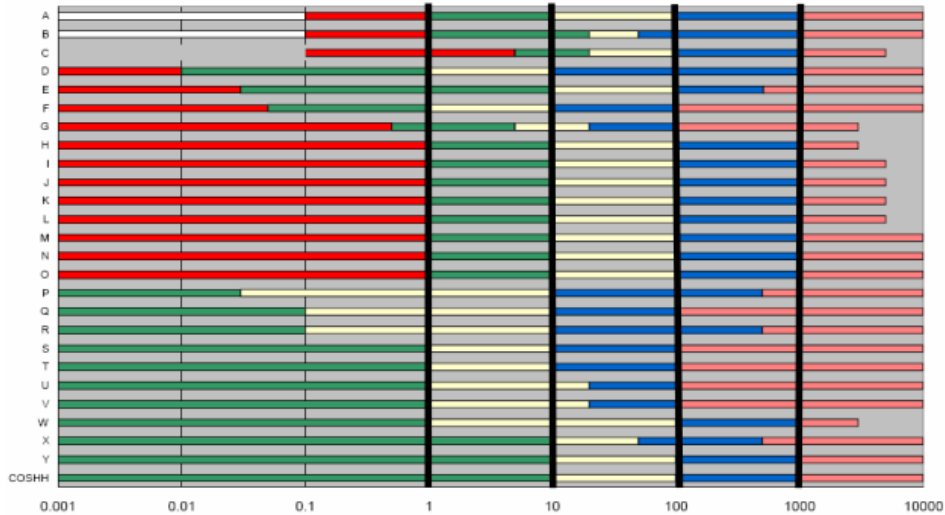
# Contenimento: OEB - #/ft3 – CR standard

| Potency Bands                     | Potency Bands: International Program on Chemical Safety   | PARTICLE DIAMETER, (micrometers)                  |   |  | ALLOWABLE DUST PARTICLES TO BE ≤ OEL       |                               |                               | COMPARE TO CLEAN ROOM STANDARDS<br>See Note below. |                     |
|-----------------------------------|---|---|---|--|--|-------------------------------|-------------------------------|--|---------------------|
|                                   |   | Occupational Exposure Limits Expressed in:        |   |  | # particles / ft <sup>3</sup>              | # particles / ft <sup>3</sup> | # particles / ft <sup>3</sup> | Federal Standard 209E                              | ISO 146441          |
|                                   |   | 10 <sup>-3</sup> g/m <sup>3</sup><br>(milligrams) | 10 <sup>-6</sup> g/m <sup>3</sup><br>(micrograms) | 10 <sup>-9</sup> g/m <sup>3</sup><br>(nanograms) |  |                               |                               |  |                     |
| Band 1<br>(Low Toxicity)          | Band A<br>(Not harmful, not irritating, low pharmaceutical activity)  | 10  | 10,000  | 10,000,000                                       | 283  | 283,000                       | 2,270,000,000                 |  |                     |
|                                   |   | 1   | 1,000   | 1,000,000  | 28.3                                       | 28,300                        | 227,000,000                   |  |                     |
| Band 2<br>(Intermediate Toxicity) | Band B<br>(Harmful, may be irritant and/or moderate pharmacological effect)   | 0.1   | 100   | 100,000  | 2.83                                       | 2,830                         | 22,700,000                    |  |                     |
|                                   |   | 0.01  | 10  | 10,000   | 2.83 per 10 ft <sup>3</sup>                | 283                           | 2,270,000                     |  | Class 9:<br>997,000 |
| Band 3<br>(Potent)                | Band C<br>(Moderate toxic and/or high pharmacological activity)   | 0.001   | 1   | 1,000  | 2.83 per 100 ft <sup>3</sup>               | 28.3                          | 227,000                       | Class 100,000                                      | Class 8:<br>99,700  |
|                                   |   | 0.0001  | 0.1   | 100  | 2.83 per 1,000 ft <sup>3</sup>             | 2.83                          | 22,700                        | Class 10,000                                       | Class 7:<br>9,970   |
| Band 4<br>(Highly Potent)         | Band E<br>(Extremely toxic, may be corrosive, sensitizing or genotoxic and/or extremely high pharmaceutical activity. Often referred to as potent.) | 0.00001   | 0.01  | 10   | 2.83 per 1,000,000 ft <sup>3</sup>         | 0.283                         | 2,270                         | Class 1,000  | Class 6:<br>997     |
|                                   |   | 0.000001  | 0.001   | 1  | 2.83 per 1,000,000,000 ft <sup>3</sup>     | 0.0283                        | 227                           | Class 100  | Class 5:<br>99.7    |
|                                   |   | 0.0000001   | 0.0001  | 0.1  | 2.83 per 1,000,000,000,000 ft <sup>3</sup> | 0.00283                       | 22.7                          | Class 10   | Class 4:<br>9.97    |
|                                   |   |   |   |  |  |                               |                               |  |                     |

# Approccio al contenimento: fattori di rischio (stessa OEB)



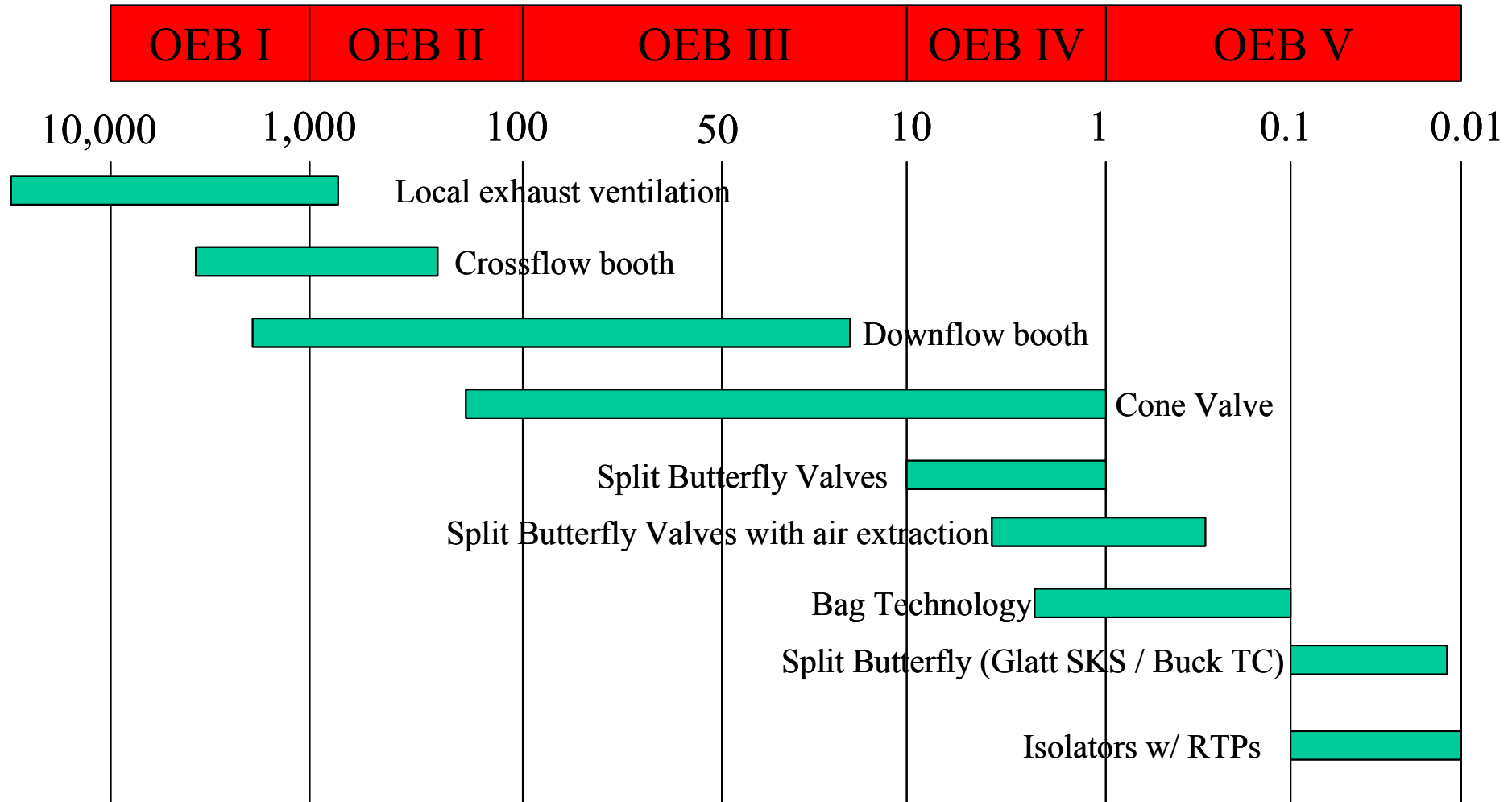
# Esempi categorie OEB



| Category/<br>Criteria | 1                             | 2                               | 3a                            | 3b                              | 4                              |
|-----------------------|-------------------------------|---------------------------------|-------------------------------|---------------------------------|--------------------------------|
| Potency               | >100 mg/day                   | 100-10 mg/day                   | 10-0.01 mg/day                |                                 | <0.01 mg/day                   |
| OEL range             | >100 $\mu\text{g}/\text{m}^3$ | 20-100 $\mu\text{g}/\text{m}^3$ | 5-20 $\mu\text{g}/\text{m}^3$ | 0.01-5 $\mu\text{g}/\text{m}^3$ | <0.01 $\mu\text{g}/\text{m}^3$ |
| Acute Toxicity        | none – slight                 | slight; reversible              | moderate – severe             |                                 | extreme - lethal               |

# Categorie API e contenimento primario

OEL ( $\mu\text{g}/\text{m}^3$ )



# Contenimento con controllo dei flussi d'aria

- LEV and Capture hoods
- Charge cutes with extract
- Shaped hoods and extracted booths
- Down-flow unidirectional airflow booths
- DFB with barriers and work station

OEB1

OEB1/2

OEB2/3

OEB3

OEB 4



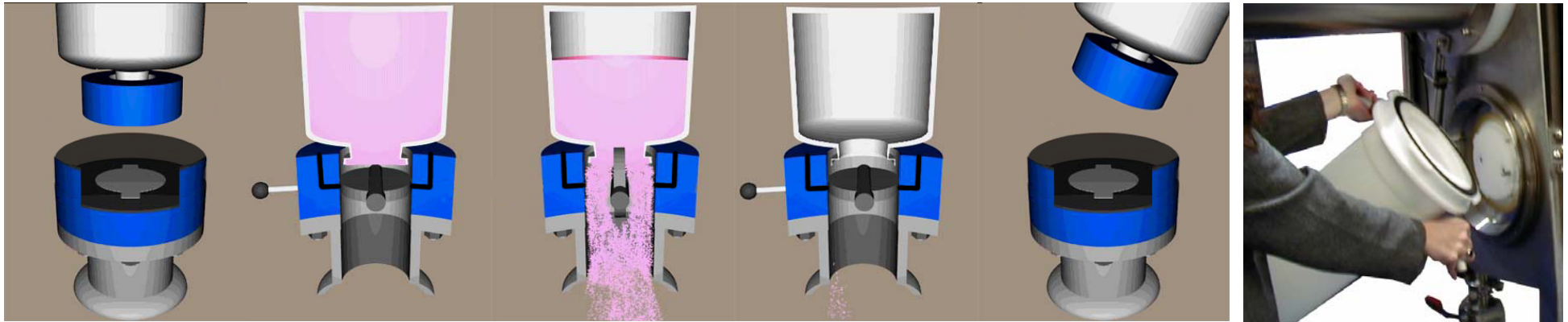
# Sistemi di connessione

- Split Butterfly Valves
- High Containment SBV extract
- RTP

OEB 3

OEB 4/5

OEB 4/5



# Connessioni flessibili

- Continuous liner OEB 3
- FIBC + extracted box OEB 3
- FIBC + isolators OEB 4/5
- Flexible room PPE
- Flexible enclosure and bags OEB 3
- Flexible Isolator OEB 3



**JACOBS**



# Sistemi chiusi

- Fume Hoods
- Biosafety Cabinet
- Rigid Isolator
  - Single chamber/multiple
  - Active pressure management
- Rigid Isolator
  - Closed operation within isolator
  - RTP transfer system

OEB 3

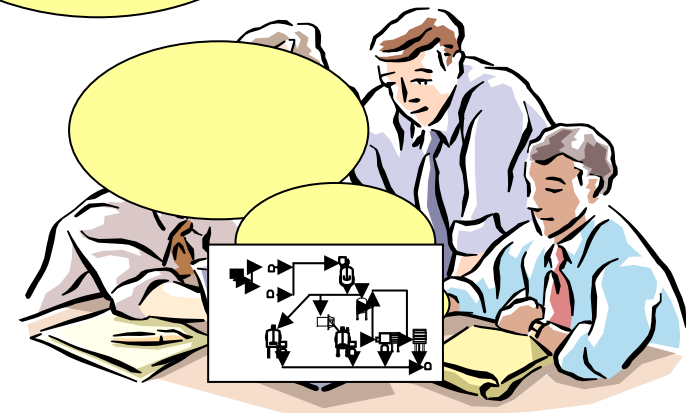
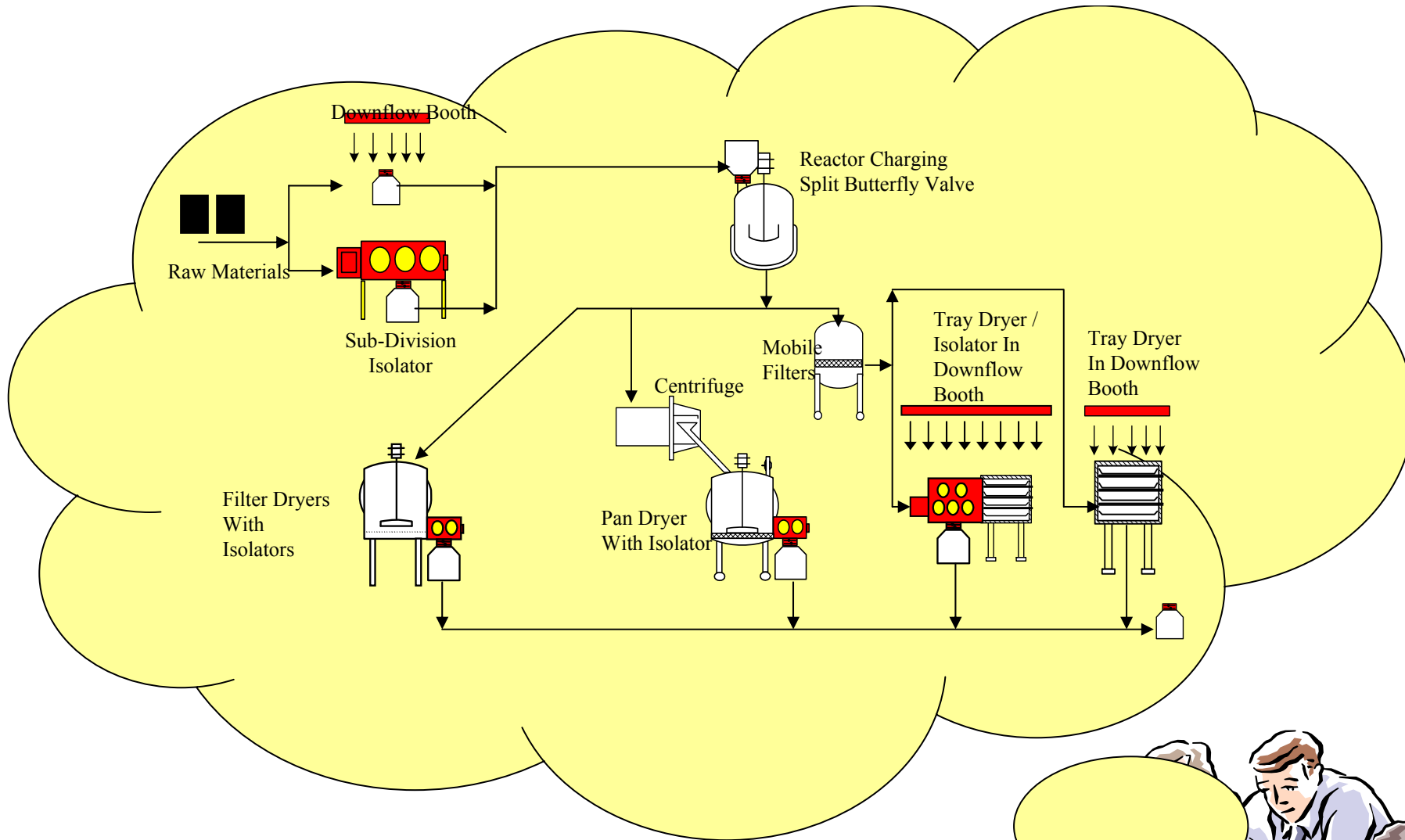
OEB 3/4

OEB 4

OEB 5







**Conclusione: conoscere per agire**