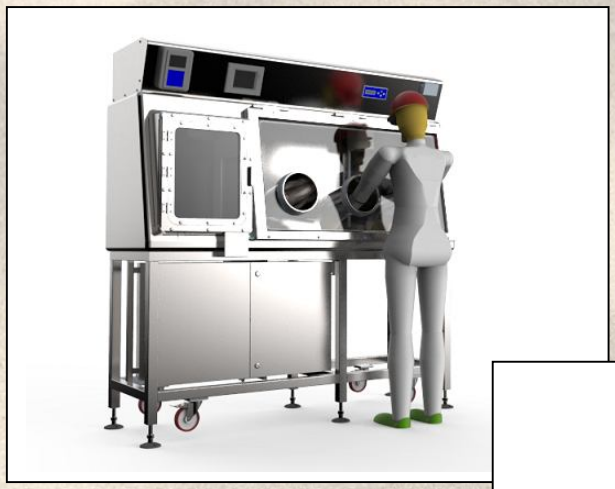
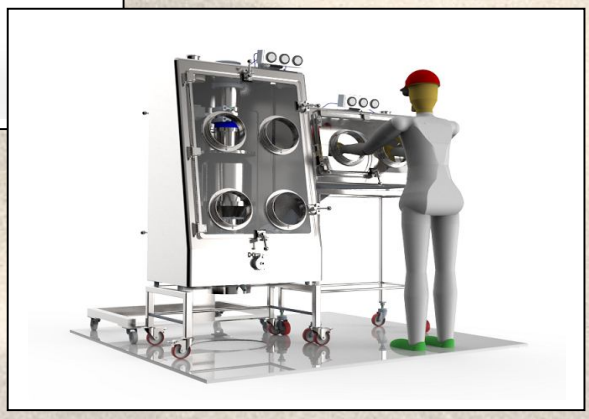
nuova guseo

Reliability - Experience - Advanced Technology

ISOLATION TECHNOLOGY





NUOVA GUSEO s.r.l. – COSTRUZIONI MECCANICHE

ISOLATION TECHNOLOGY

In the past years there has been an ever increasing attention given to containment aspects by the pharmaceutical & chemical industries.

In particular due to the increase of the toxicity of treated products This trend has brought to the fore the technologies related to a specific method of production: **isolation technology**

In case of manipulation of active ingredients (API or HAPI), it is necessary to proceed to a classification of these substances by OEL index (Operator Exposure Limit) or OEB (Operator Exposure Band) in order to identify the management system more suitable

The index OEL defines the average concentration (g/m^3) of a substance measured for 8 hours in the air breathed by an operator in the work environment. Therefore the term "containment" refers to the process of input of a biological agent (active medicinal products, pathogens) or of another substance within a local defined

.

EVALUATION OF THE OCCUPATIONAL EXPOSURE LEVEL OF SOME PHARMACEUTICAL COMPOUNDS

INTRODUCTION

For the OEL's evaluation has been utilised the following Formula:

$$OEL = \frac{NOEL\ (mg/Kg/day) * BW\ (Kg)}{V\ (m^3/day) * S(days) * SF * \alpha *} = [mg/m^3]$$

- NOEL=No Observable Effect Level = LD_{50} * 0.00005 [mg/Kg/day]
- BW = Body weight [Kg]
- V = volume of air breathed in an 8 hour work day [m^3] = (10 m^3)
- S = time in days to achieve a plasma steady state = we will set 1
- SF = safety factor:
  - 10 x = using subchronic in lieu of chronic tox studies
  - 10 x =using animal data in lieu of human data
  - 10 x = intraspecies variation
  - 10 x = using estimation of the NOEL
  - 10 x = if the substance is carcinogen and or teratogenic or sensitising
- α = percent of compound absorbed from inhalation = 100

THE OEB INDEX

The index OEB (1, 2, 3, 4, 5) is assigned on the basis of the toxicity of a given substance in a pure state in order to a classification of the plants, thanks to which it is possible to select devices and manufacturing processes more suitable for a given product.

OEB	Range of OEL (µg/m^3)	Toxicological / Pharmacological proprieties
OEB 1	**> 1.000**	**Harmful, and/or low pharmacological activity**
OEB 2	**100 – 1.000**	**Harmful, and/or moderate pharmacological activity**
OEB 3	**10 - 100**	**Moderate toxic and/or high pharmacological activity**
OEB 4	**1 - 10**	**Toxic and/or very high pharmacological activity**
OEB 5	**< 1**	**Extremely toxic and/or extremely high pharmacological activity**

INDIVIDUATING THE CONTAINMENT STRATEGY

1) *MATERIAL FORM (DUST POTENTIAL)*

HIGH – Fine light powders with dust cloud potential.

MEDIUM – Granular or crystalline, visible dust, settles quickly.

LOW – Pellets or non-friable solids

2) *DURATION OF TASK*

SHORT TERM – A task duration of <30mins is considered short.

LONG TERM – 30mins or longer

3) *SCALE OF OPERATION*

SMALL SCALE – Lab Scale/Pilot Plant –gr to kg

MEDIUM SCALE – 10 –100kg

LARGE SCALE – over 100kg

EXPOSURE POTENTIAL MATRIX

INFORMATION COLLATED CAN BE INPUT INTO A MATRIX TO DETERMINE THE EXPOSURE POTENTIAL OF THE COMPOUND

SCALE OF OPERATION	MATERIAL FORM (DUST POTENTIAL)			DURATION OF TASK
	LOW	MEDIUM	HIGH	
SMALL (gm to kg)	EP 1	EP 1	EP 2	SHORT
	EP 1	EP 2	EP 3	LONG
MEDIUM (10 -100kg)	EP 1	EP 2	EP 3	SHORT
	EP 2	EP 3	EP 3-4	LONG
HIGH (+100kg)	EP 2	EP 3	EP 3	SHORT
	EP 3	EP 4	EP 4	LONG

EQUIPMENT SELECTION MATRIX*

CONTAINMENT STRATEGY SELECTION BASED ON EXPOSURE LEVELS AND EXPOSURE POTENTIAL

	Exposure Potential 1	Exposure Potential 2	Exposure Potential 3	Exposure Potential 4
OEB1	Level 1	Level 1	Level 1	Level 2
OEB2	Level 1	Level 2	Level 2	Level 3
OEB3	Level 2	Level 3	Level 3	Level 4
OEB4	Level 3	Level 3	Level 4	Level 4
OEB5	Level 4	Level 4	Level 4	Level 4
Below than 10 ng/m^3	Level 5	Level 5	Level 5	Level 5

*Institution of Chemical Engineers (IChemE)

LEVEL 1 - Controlled General Ventilation
LEVEL 2 - Local Exhaust Ventilation
LEVEL 3 - Barrier Isolation Systems
LEVEL 4 - Closed Handling within Isolator
LEVEL 5 - Robotic handling, total containment

BARRIER ISOLATORS

A barrier isolator is an enclosure designed to prevent the leakage of the products contained in the environment concerned into the external environment or the penetration of substances of the external environment into the internal environment, or both at the same time.

The main applications of a glove box is the segregation of a series of operations by granting, at the same time, a triple protection level:

- protection of the operator;
- protection of the processed product;
- protection of the environment.

The **protection of the operator** from dangerous product contamination is granted by the physical barrier represented by the isolator, by the negative air pressure regime to the external environment and by the manipulation and transfer devices suitable in order to avoid any direct contact with the product during the different phases of the process.

The **protection of the product** from external polluting substances is granted by an absolute filtration system (Hepa type, usually H13 efficiency level) installed on the air inlet.

The protection of the environment is granted by proper filtration system (Hepa type, H13 or H14 efficiency level) installed on the air outlet. This device allows the expulsion of the inner air only after treatment in order to protect both, environment and operator.

In case of multi-chamber isolator it each chamber hat to be equipped with a proper filtration system.

According to the ISO 14644-7, further characteristics of a state of the art isolator are represented by:

a high finishing degree in order to avoid the heap of treated substances while the control of the air flows minimise the contact of product with the internal surface of the glove boxes; all this in order to facilitate the cleaning operations at product change

an internal washing system with the relevant a draining bottom where the contaminated liquid is conveyed

an ergonomic design for easy access to all internal surfaces and work: areas, and with respect to the process undertaken.

a minimum size and number of access devices consistent with operation, cleaning and maintenance.

built-in test facilities and **appropriate alarms**

appropriate to process and routine operation transfer device(s)

glove ports and glove cuff rings devices designed for ease of change,

testing and security of operation.

INTERNATIONAL REFERENCE STANDARDS

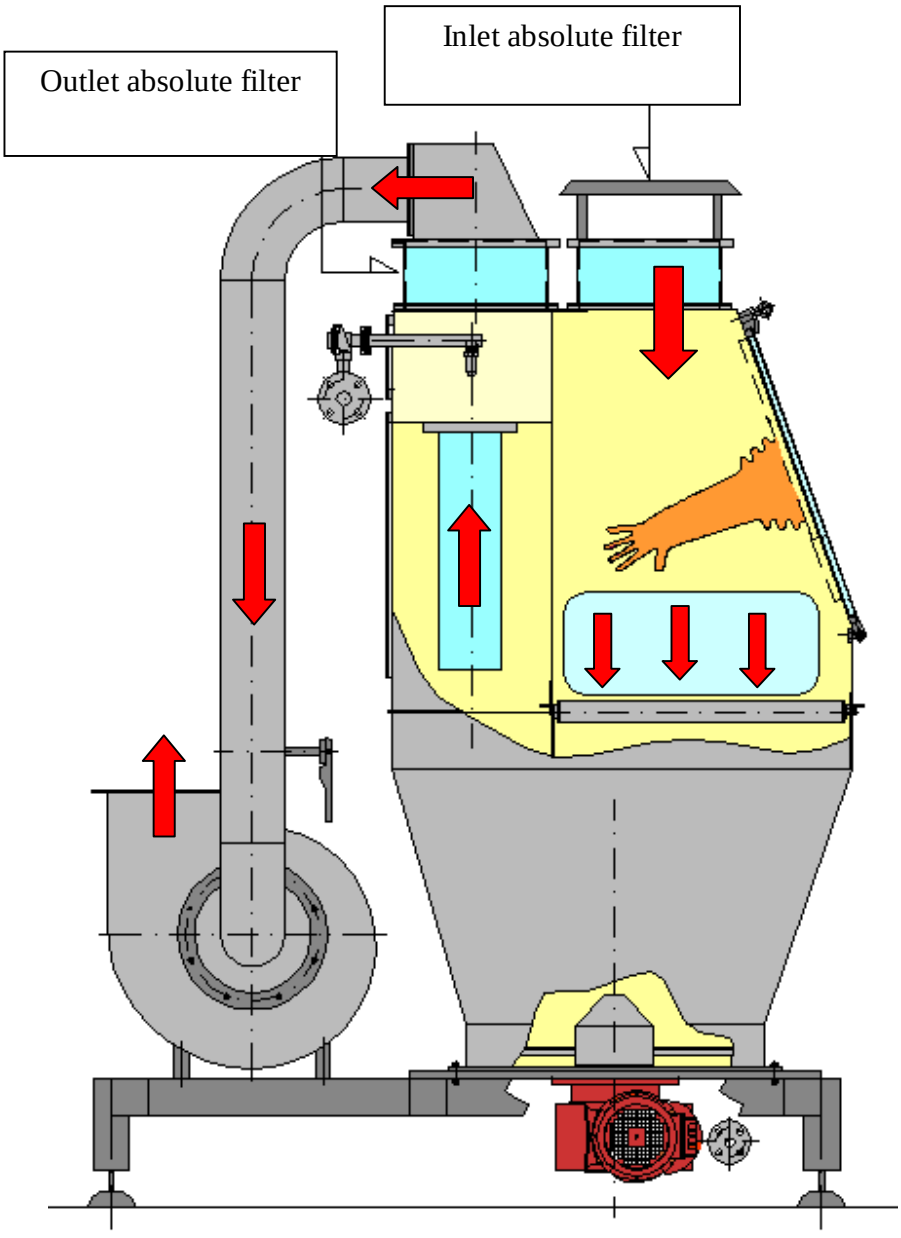
ISO 14644-7 Separative devices (clean air hoods, glove boxes, isolators, and mini-environments

ISO 10648-1 Containment enclosure – Part 1 Design principles

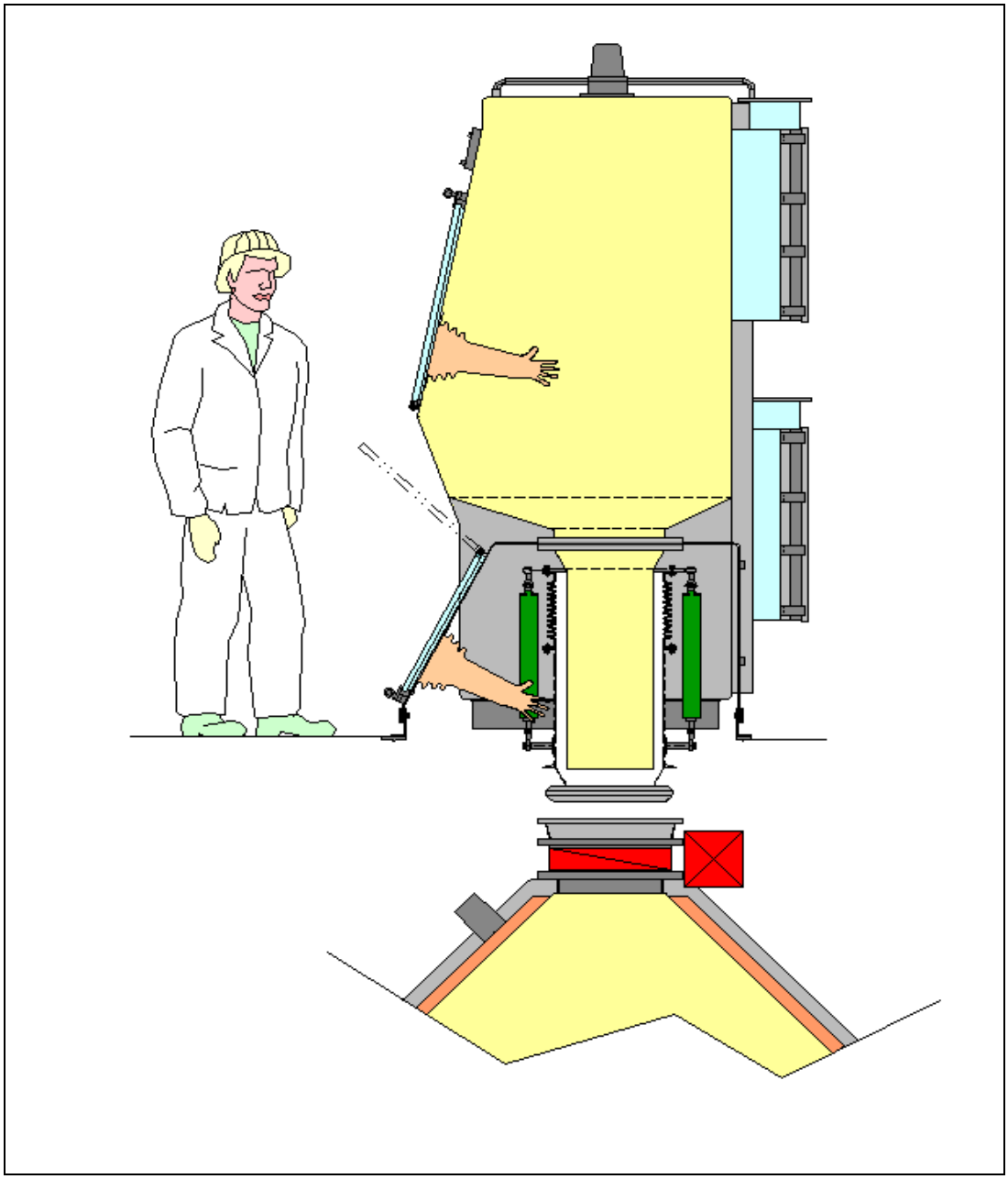
ISO 10648-2 Containment enclosure – Part 2 Classification according to leak tightness and associated checking method

AGS-G001-2007 (American Glovebox Society)

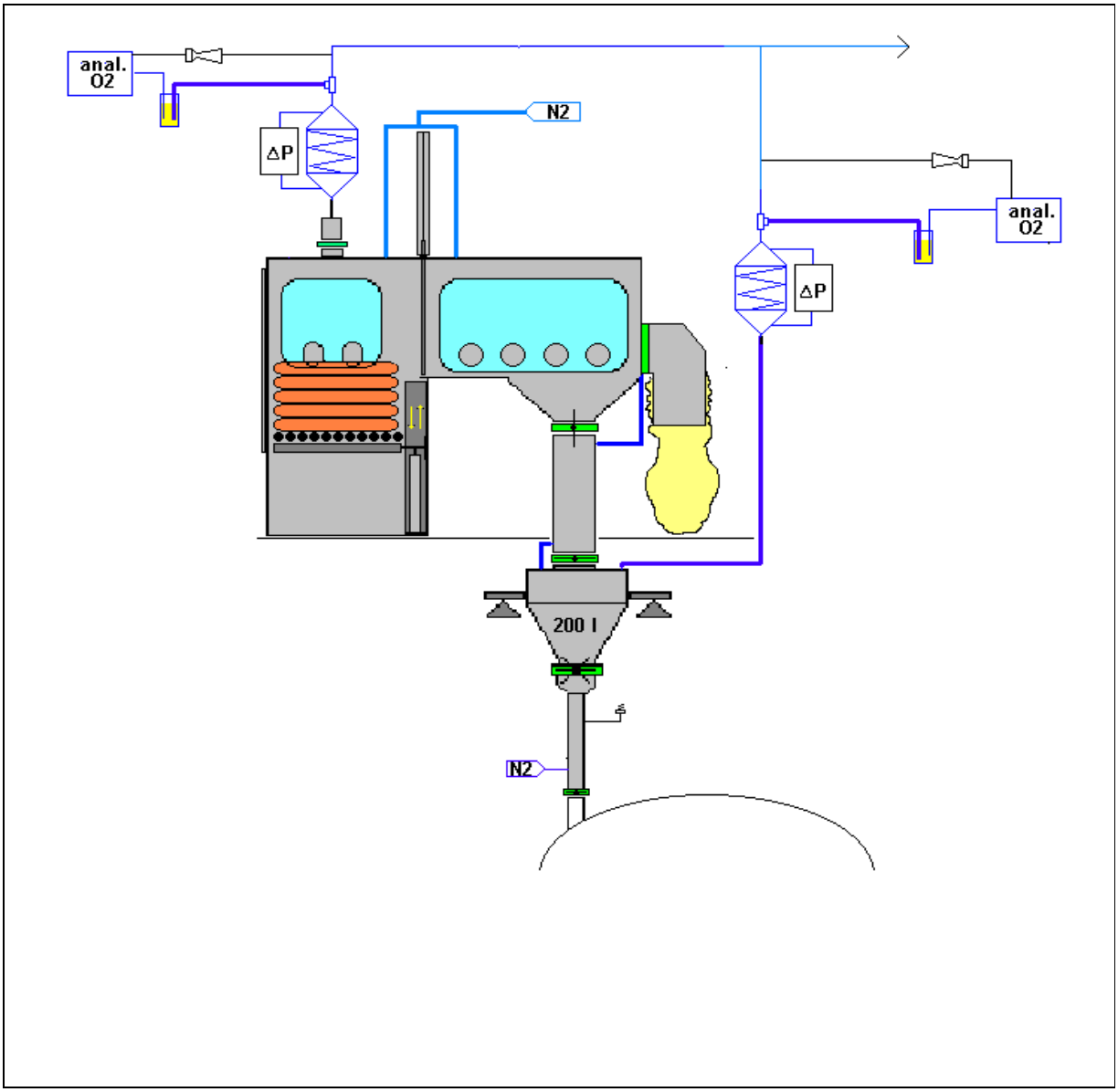
EXAMPLES OF APPLICATIONS



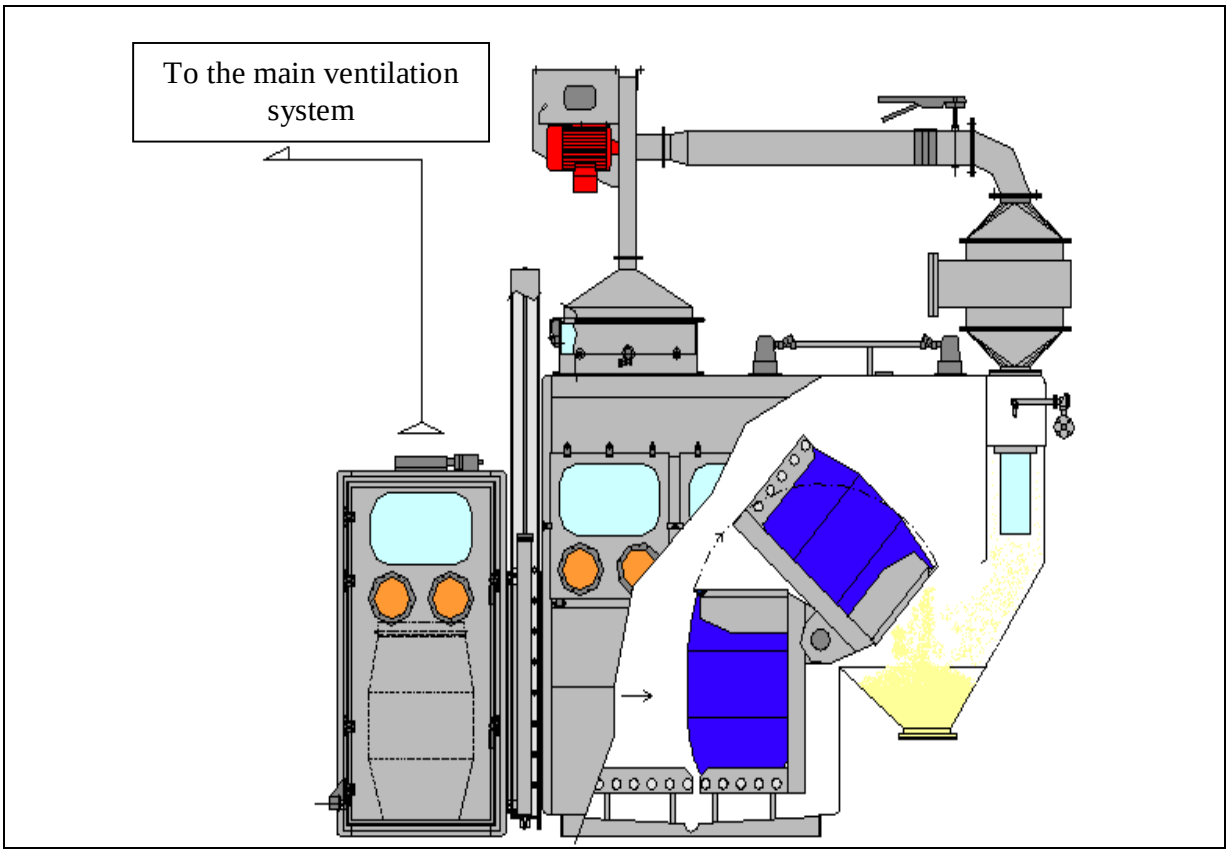
BAGS OPENING AND DISCHARGING GLOVE BOX FOR TOXIC PRODUCTS



CHARGING GLOVE BOX FOR BICONICAL DRYER



REACTOR LOADING AND DOSING STATION FOR HIGHLY ACTIVE PRODUCTS



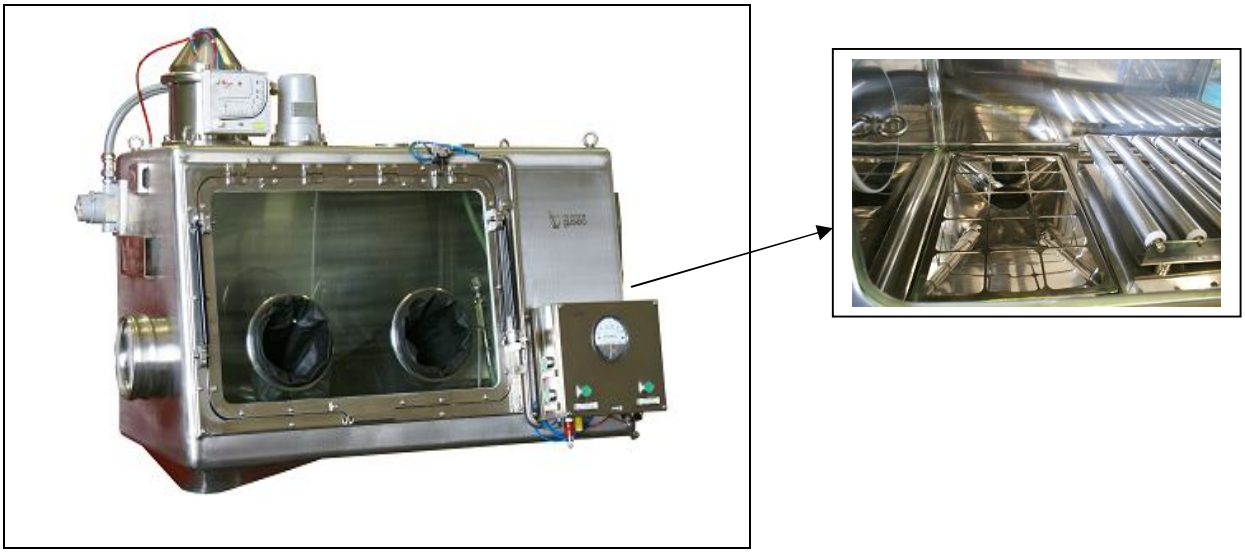
DRUM OVERTURNING GLOVE BOX WITH PRE-CHAMBER

FILTER DRYER STATIC DISCHARGE ISOLATOR

PADDLE DRYER STATIC DISCHARGE ISOLATOR FOR SAMPLING

ISOLATOR FOR PILOT SCALE MICRONIZATION UNIT M100

LABORATORY ISOLATOR WITH INTEGRATED WEIGHING UNIT



DOUBLE CHAMBER REACTOR CHARGING ISOLATOR WITH INTERNAL DETAIL

LAB-SCALE WEIGHING AND SAMPLIG ISOLATOR OPERATING IN INERTED ATMOSPHERE

DRUM DISCHARGING ISOLATOR

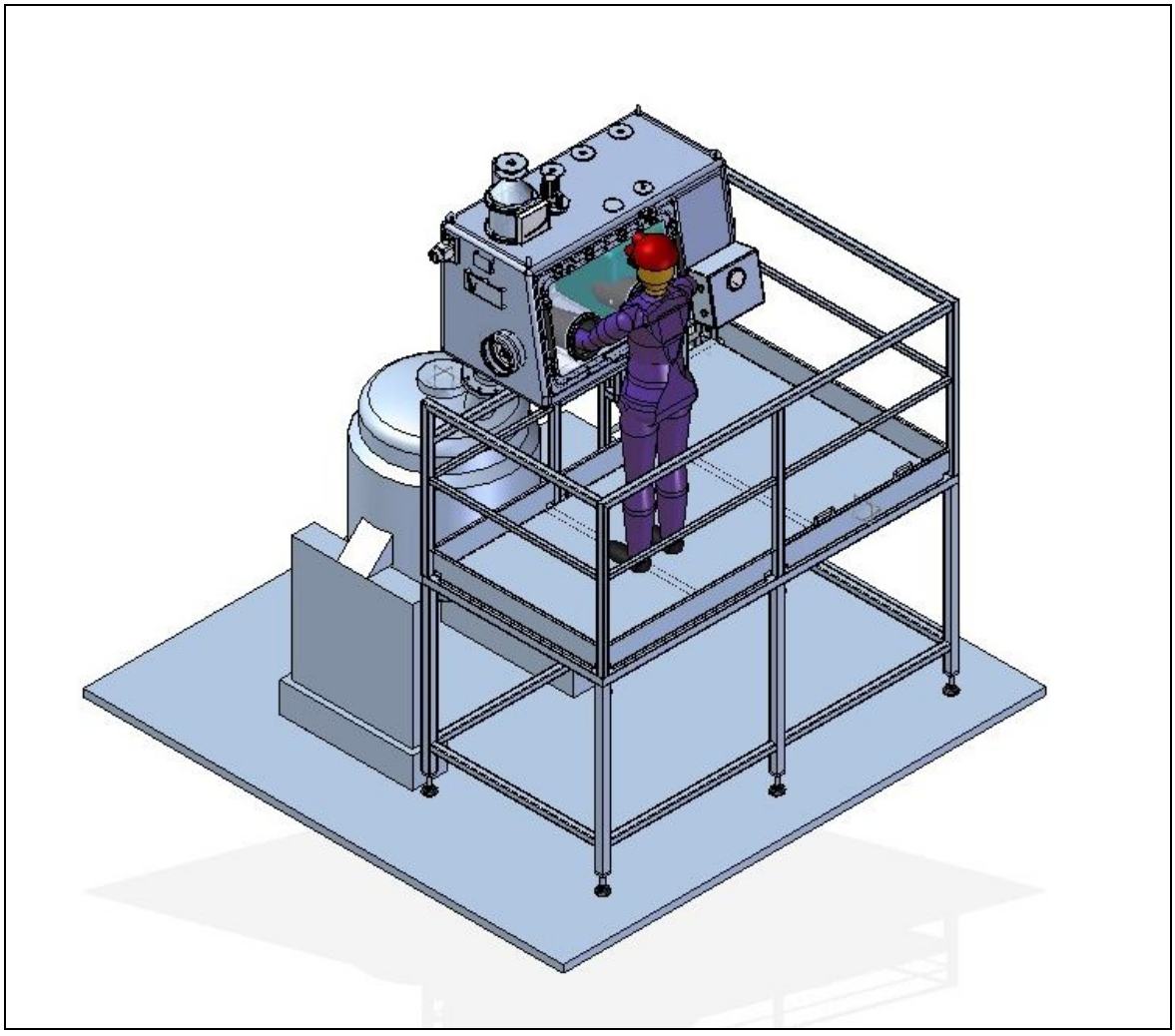
EXAMPLES OF INSTALLED UNITS

MULTI-CHAMBER ISOLATOR FOR CHEMICAL SYNTESIS ACTIVITIES

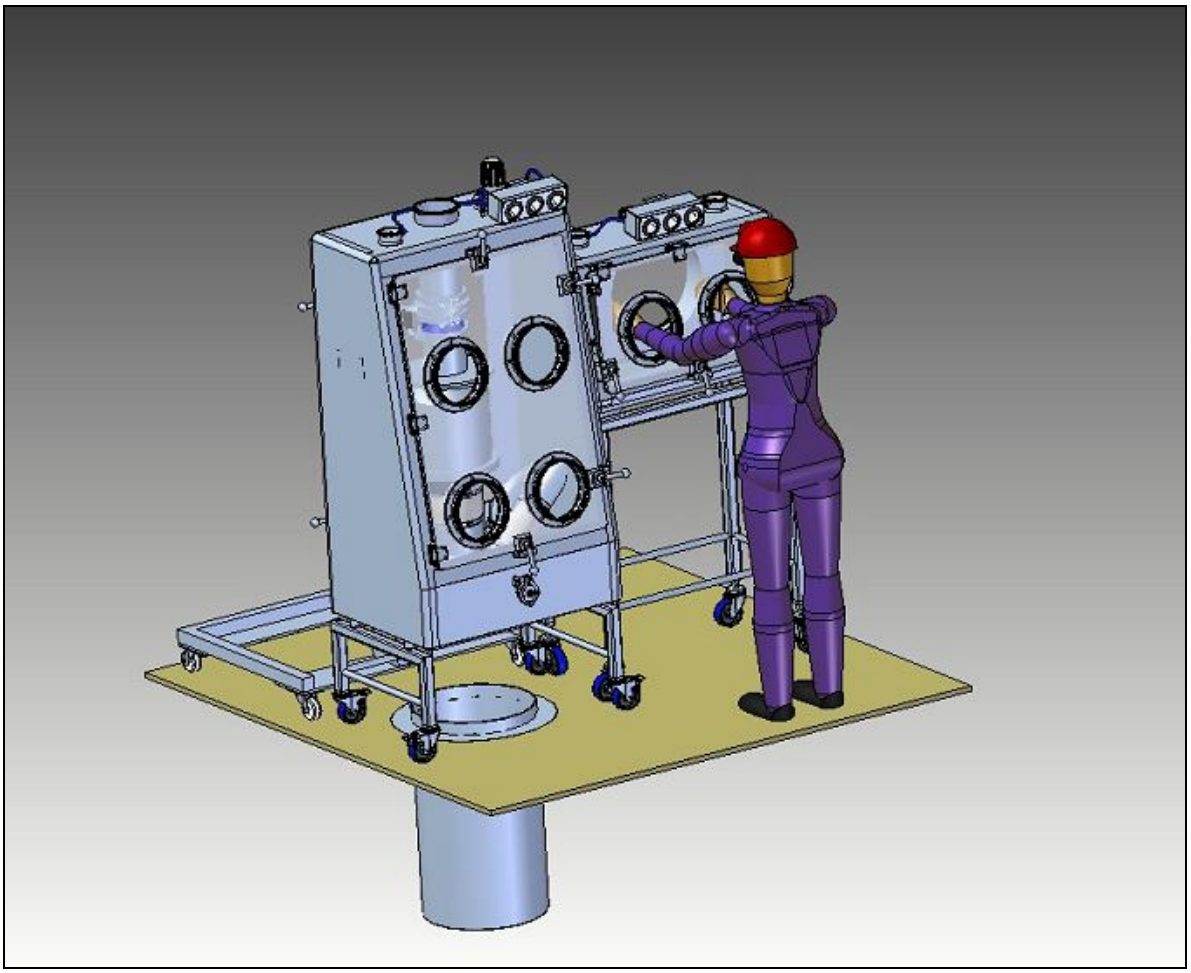
DOUBLE CHAMBER WEIGHING AND DISPENSING ISOLATOR

DOUBLE CHAMBER ISOLATOR FOR PRODUCTION SCALE CONE MILL

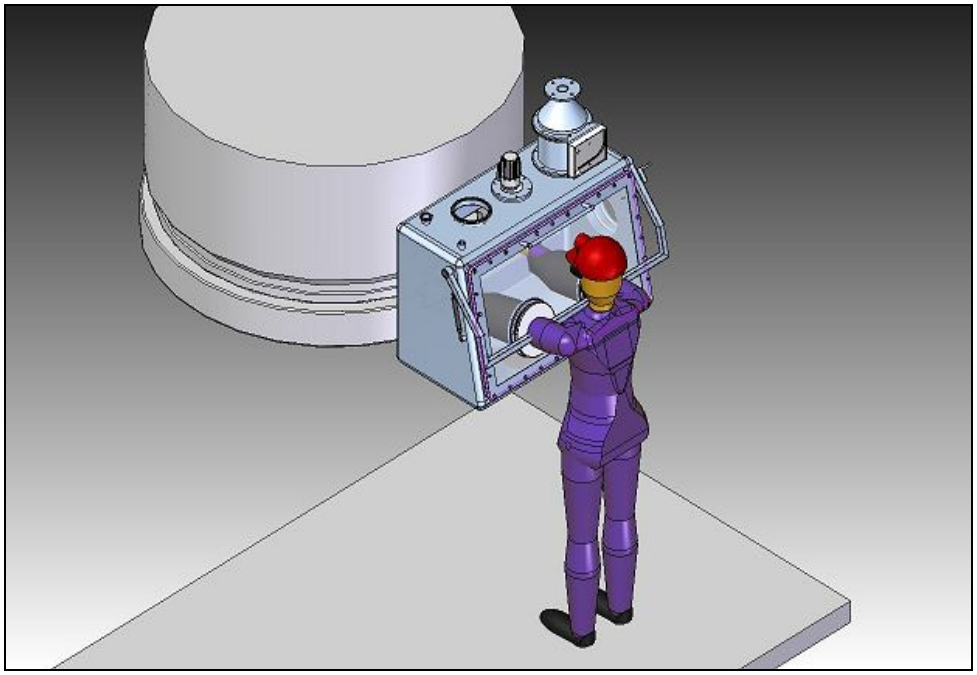
3D VIEWS

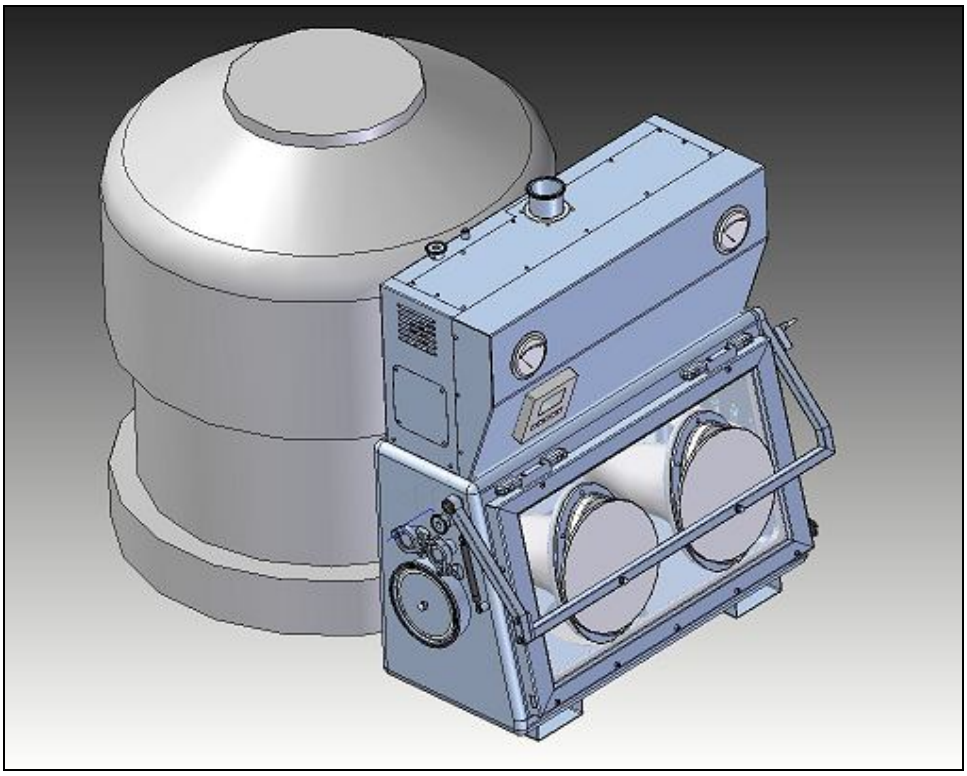


REACTOR CHARGING ISTALLATION

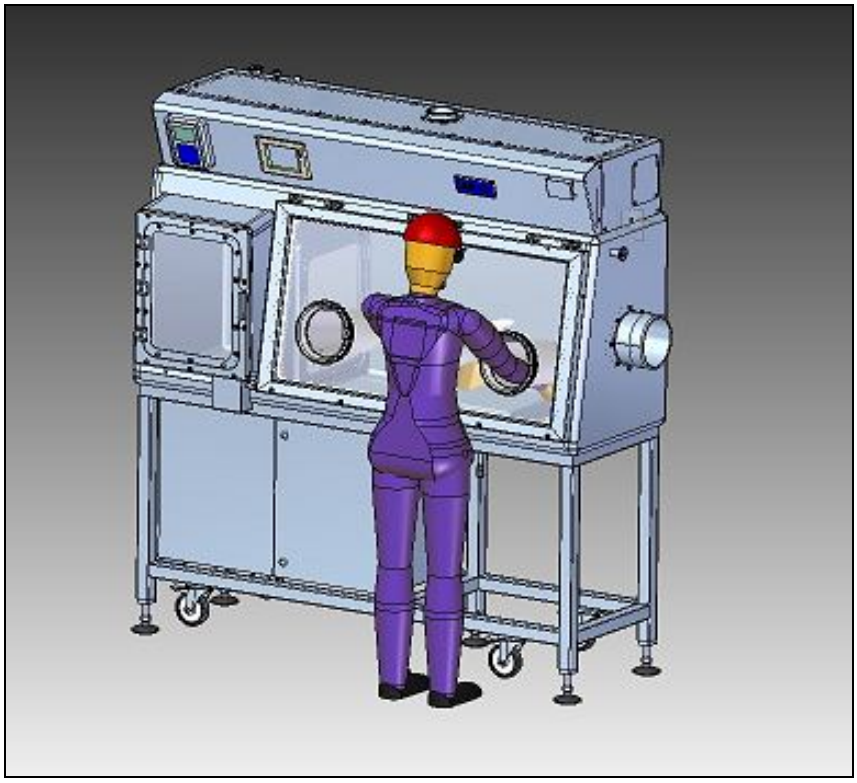


DOUBLE CHAMBER ISOLATOR FOR SIEVING STATION





FILTER DRYER DISCHARGING STATIC AND ACTIVE ISOLATORS



LABORATORY WEIGHING AND DISPENSING ISOLATOR

For further request for information do not hesitate to contact us!

NUOVA GUSEO s.r.l. – COSTRUZIONI MECCANICHE
Sede e Stabilimento: Via Dante 8
29010 Villanova sull'Arda (Pc) Italy
Registro Imprese PC, Codice Fiscale e Partita IVA:
IT 00310330337
N. R.E.A.: 97797 Capitale Sociale EURO: 10.400,00 i.v.

Tel.: +39 (0)523 837149 – 837187
Fax: +39 (0)523 837498
E-mail: nguseo.commerciale@tin.it
Website: www.nuovaguseo.eu