

# LA PREVENTION EN PRATIQUE

COLLECTIVE AND PERSONAL PROTECTIVE EQUIPMENT USED  
WHEN HANDLING CYTOSTATIC / CYTOTOXIC PRODUCTS

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# CENEXI-LABORATOIRES THISSEN S.A.

# Creating Innovative Partnerships

Cenexi is a global provider of contract development and manufacturing services.

We offer pharmaceutical and biotechnology customers a comprehensive portfolio of drug product outsourcing services.



# Creating Innovative Partnerships

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We are a leader in sterile product manufacturing, with specialization **in sterile products including potent drugs**, but also broad capabilities across solid dosage forms, including tablets and capsules.

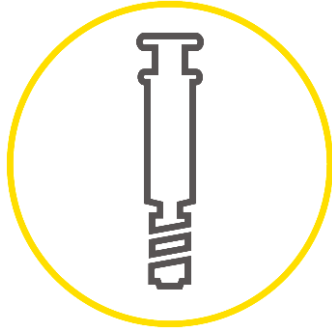


# Company Timeline

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- 2020 ● Projection for annual revenue to almost double from 2015 – 2020.
  - 2015 ● Change in shareholders to Cathay Capital, Management.
  - 2012 ● Acquisition of a production site in Thissen, Belgium.
  - 2011 ● Acquisition of production site in Osny, France.  
Creation of Cenexi Services.
  - 2008 ● Change in shareholders to Chequers Capital and Indigo Capital.  
Cenexi becomes a completely independent company.
  - 2004 ● Creation of Cenexi in Fontenay-sous-Bois, France.  
Key shareholder: Roche.

# Braine-l'Alleud Facility



**ONCOLOGY –  
PREFILLED SYRINGES**



**ONCOLOGY –  
STERILE AND  
LYOPHILIZED VIALS**

**THISSEN, BELGIUM**

8,000 Sq m



## Dosage forms

- Sterile & Lyophilized Vials (Oncology)
- Prefilled Syringes (Oncology)
- Syrups



**SYRUPS**

# Sterile Product Development Center

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From formulation development to pre-clinical, clinical batches and exhibition batches, the SPDC is able to handle any sterile products :

- Vial (cyto and non cyto)
- Freeze dry (cyto and non cyto)
- Pre filled syringe (cyto and non cyto)

Once developed and registered the products are transferred to all plants of the group.

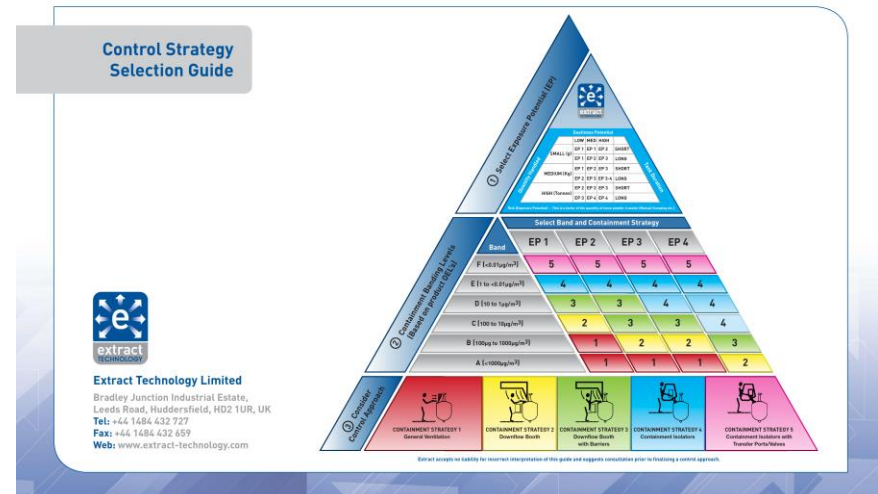
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# PRODUCT CLASSIFICATION

# Product Classification

## Data used to classify the products

- EP: Exposure Potential
- OEL: Occupational Exposure Limit
- SDS: Safety Data Sheet
- Pharmacological and Toxicological information
- Control Strategy Selection Guide



# Product Classification

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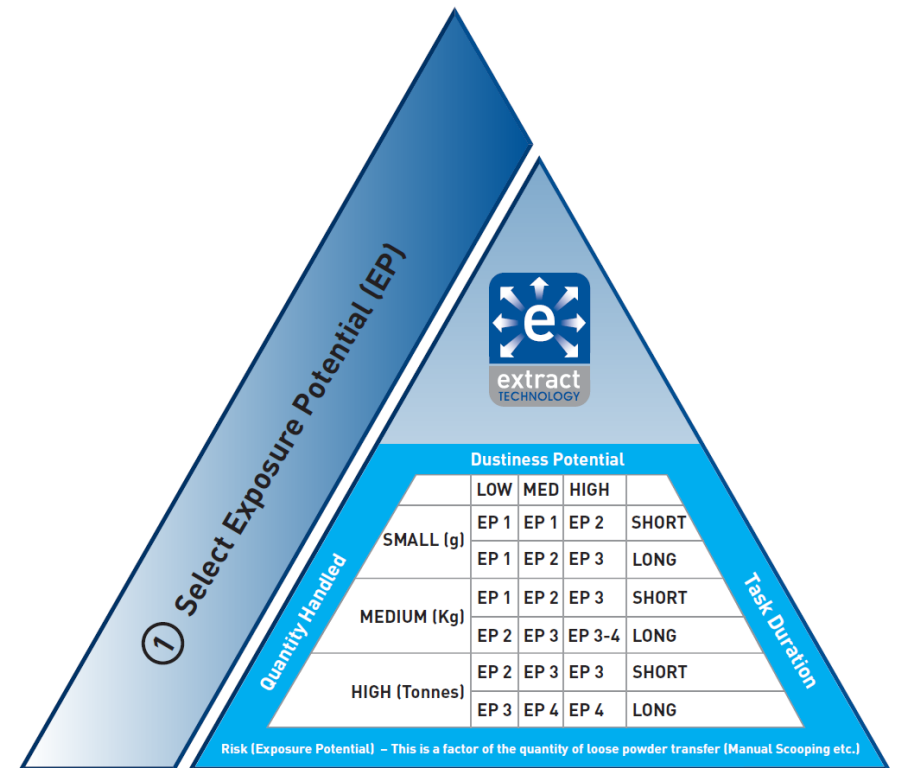
## Selection of the product

- Pure API (powder)
- Lyophilized Finished Product
- Liquid Finished Product

# Product Classification

## Process

- Selection of the Exposure Potential (from EP 1 to EP 4) based on:
  - Dustiness Potential
  - Quantity Handled
  - Task Duration



# Product Classification

## Process

- Containment Banding Levels (from 1 to 5) based on:
  - Product OEL's (\*)
  - Exposure Potential (see previous slide)

		Select Band and Containment Strategy			
		EP 1	EP 2	EP 3	EP 4
② Containment Banding Levels (Based on product OEL's)	Band				
	F (<0.01µg/m <sup>3</sup> )	5	5	5	5
	E (1 to <0.01µg/m <sup>3</sup> )	4	4	4	4
	D (10 to 1µg/m <sup>3</sup> )	3	3	4	4
	C (100 to 10µg/m <sup>3</sup> )	2	3	3	4
	B (100µg to 1000µg/m <sup>3</sup> )	1	2	2	3
A (<1000µg/m <sup>3</sup> )	1	1	1	2	

# Product Classification

## Process

(\* ) other parameters in addition or when OEL's values are not available

OEB	OEL vapor (ppm)	Therapeutic dose	H statements	Oral LD50 (mg/kg)	Inhalation LD50 (mg/l/4 h)	Percutaneous LD50 (mg/kg)	Irritating	Sensitizing	Genotoxicity Carcinogenicity	Reprotoxicity
1	> 1000	$100 \leq x$	Not classified	> 2000	> 5	> 2000	No or low irritating	Negative	Negative	No evidence
2	100 – 1000	$10 \leq x \leq 100$	H302, H304, H312, H315, H319, H332, H336	200 à 200	1 à 5	400 à 2000	Eye and/or skin irritating	Skin low sensitizing	Negative	Some evidence on animals
3	10 – 100	$1 \leq x \leq 10$	H301, H311, H317, H318, H331, H335, H361f, H361d	25 à 200	0,25 à 1	50 à 400	Eye and/or skin high irritating Respiratory irritating	High skin sensitizing Low respiratory sensitizing	Positive genotoxicity in vitro, not confirmed in vivo Carcinogenicity C3	Low effect on animals Classified R3
4	1 – 10	$0,1 \leq x \leq 1$	H300, H310, H314, H330, H334, H340, H341, H350, H350i, H351, H360D, H360F, H370, H371, H372, H373	0,5 à 25	0,005 à 0,25	1 à 50	Corrosive: skin burns	High respiratory sensitizing	Positive genotoxicity in vitro and in vivo Carcinogenicity C1 / C2	High effect on animals and/or suspected on humans Classified R1 / R2
5	< 1	$0,01 \leq x \leq 0,1$		< 0,5	< 0,005	< 1			High genotoxicity or carcinogenicity potential	

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# COLLECTIVE AND PERSONAL PROTECTIVE EQUIPMENT

# Collective and Personal Protective Equipment

## Process of selection

### ○ Control approach:

- General ventilation
- Downflow booth
- Downflow booth with barriers
- Containment isolators
- Containment isolators with transfer ports / valves



# Collective and Personal Protective Equipment

## In practice



- Control approach vs area of handling / collective protective equipment available

Equipments:	HVAC	Laminar flow	Biological enclosure	cRABS	Isolator
Production	Decontamination	Freeze-dryer (un)loading	Capping + PPE's (*)	Filling (***)	Formulation (****)
Pilot	/	/	/	Vial filling / Freeze-dryer (un)loading / Capping / Decontamination	Formulation / Syringe filling
Quality Control	/	/	Biological enclosure + PPE's (*)	Biological enclosure + PPE's (**)	/
Development	/	Laminar flow	/	RABS (***)	/

# Collective and Personal Protective Equipment

## Personal Protective Equipment

- Additional PPE's (needed to complete the CPE's in order to assure personal safety):

(\*) Gloves / Chirurgical mask / Tyvek

(\*\*) Gloves / P3 mask / Tyvek

- PPE's vs CPE's (needed when the CPE's can no be used):

(\*\*\*) Gloves / Powered Air Purifying Respirator / Tyvek

(\*\*\*\*) Gloves / Supplied Air Respirator / Tyvek



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# CLEANING / EMERGENCY

# Cleaning / Emergency

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## Cleaning

- 3 steps :
  - Pre-rinsing agent to solubilize the cytostatic / cytotoxic product:
    - Product dependent
    - Mandatory before handling cytostatic / cytotoxic product
  - Cleaning agent
  - Disinfection agent (µbiological effect)

# Cleaning / Emergency

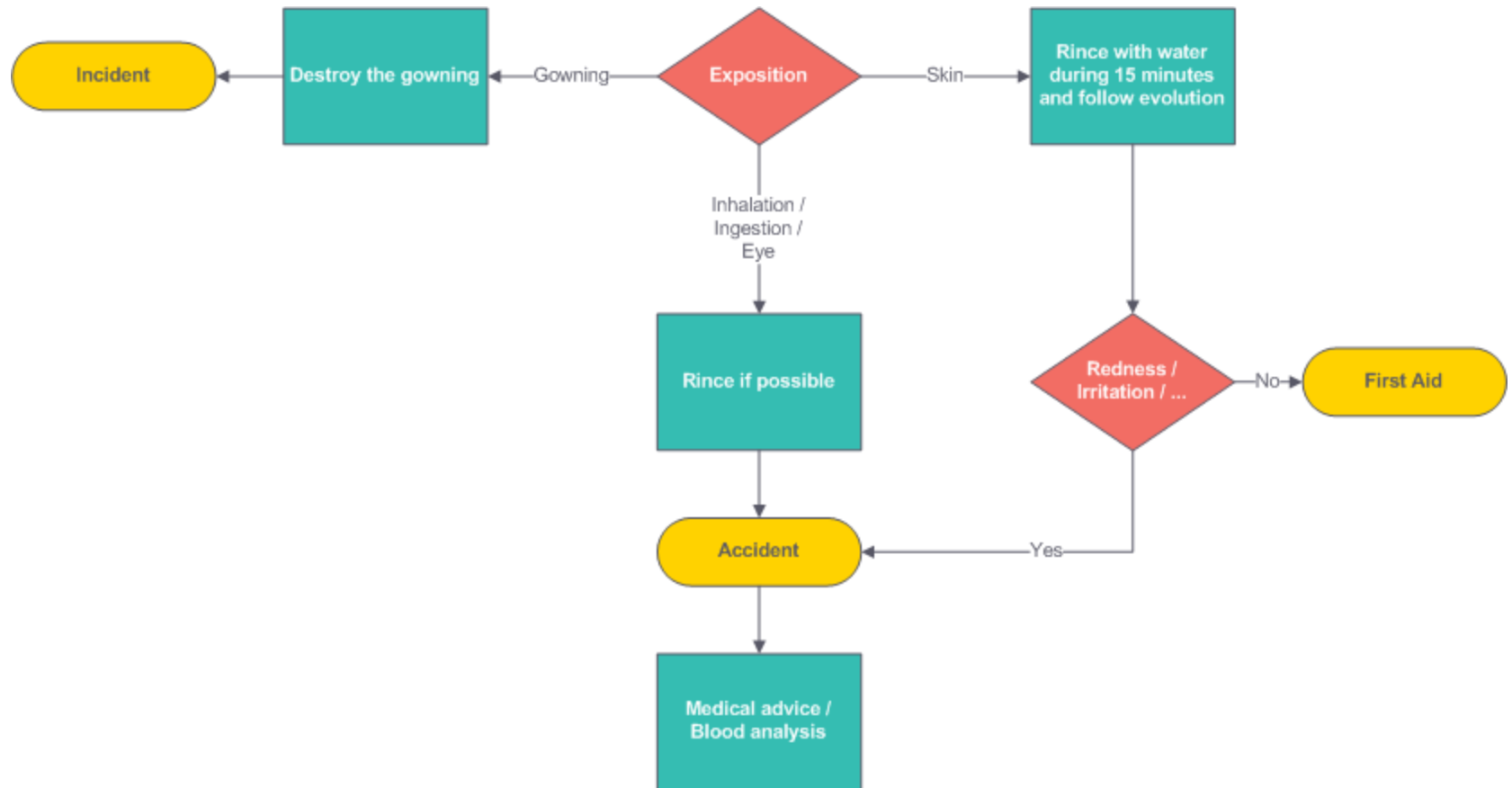
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## Accidental contamination

- Alert people present in the area
- Leave the area
- Return to the area with the safety gowning
- Absorb the product
- Start the cleaning (see previous slide)

# Cleaning / Emergency

## People exposition



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# QUESTIONS & ANSWERS

**cenexi**

creating innovative partnerships

# THANK YOU FOR YOUR ATTENTION

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