

# WORKSHOP: TOXICOLOGY and SAFETY

- ➔ **Toxicology: examples related to As, Al, Be, Ga, In compounds.**  
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- 2- Toxicology and Speciation
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## Semiconductor (GaAlAs, GaInAsP....) chemical vapor deposition

### MOCVD

#### Gaseous sources

AsH<sub>3</sub> arsine

PH<sub>3</sub> phosphine

Metalorganics: In, Ga, Al...

#### Dopants

MOCVD: Metal Organic  
Chemical Vapor Deposition

### MBE

#### Solid sources

As, Ga, Al, P

Dopants: Be

MBE: Molecular Beam  
Epitaxy

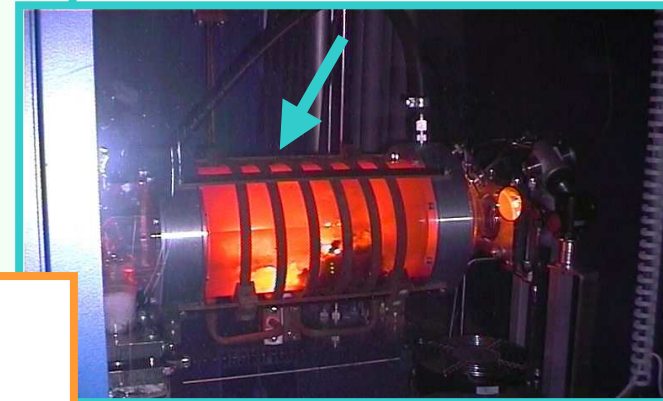


## Chemical vapor deposition

**MOCVD sources :  $\text{PH}_3$   $\text{AsH}_3$  and metalorganics based on Ga, In, Al...**



**Reaction chamber**

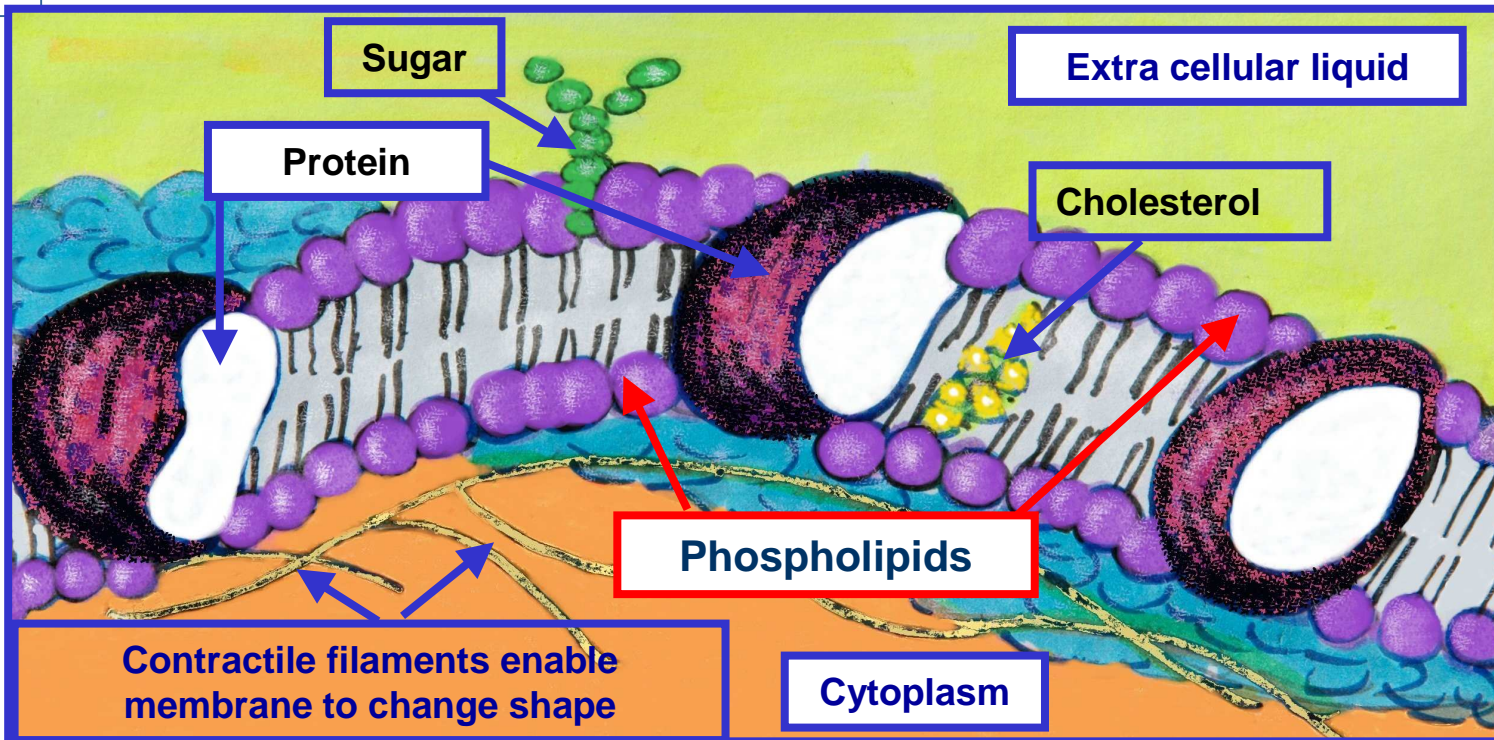


**MAINTENANCE HAZARDS : sources, by products : gases and particles (dust)**

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# Cell membrane arrangement and structure



Cell membrane  
(semipermeable)

## Toxicant interaction:

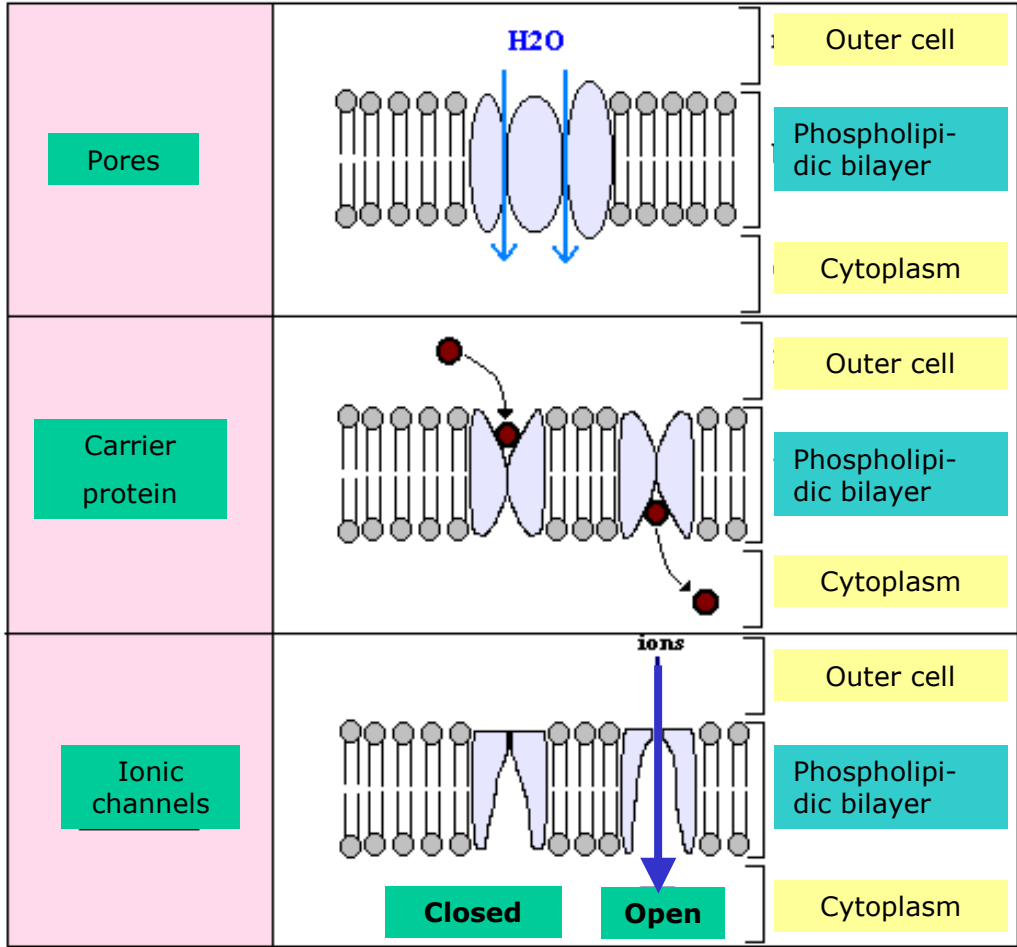
- on the surface of the cell - within the cell- in the extracellular (interstitial) space

## Toxicant transport:

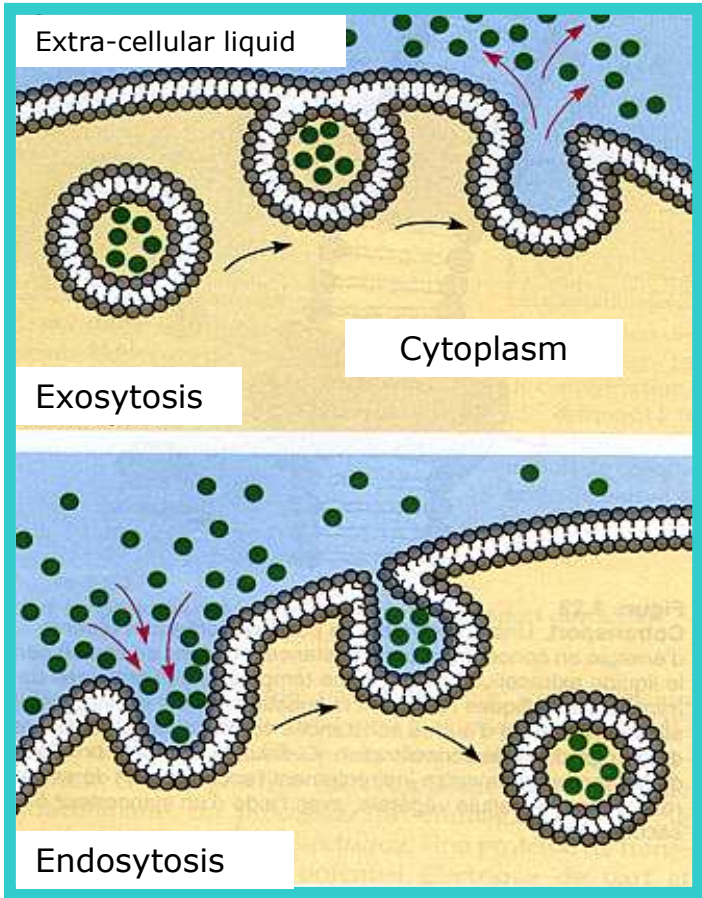
1- **Passive or spontaneous** : without energy, based on simple diffusion

2- **Facilitated diffusion** : assistance of specific carrier proteins

3- **Active transport with energy**, based on the consumption of ATP



**Facilitated transport**

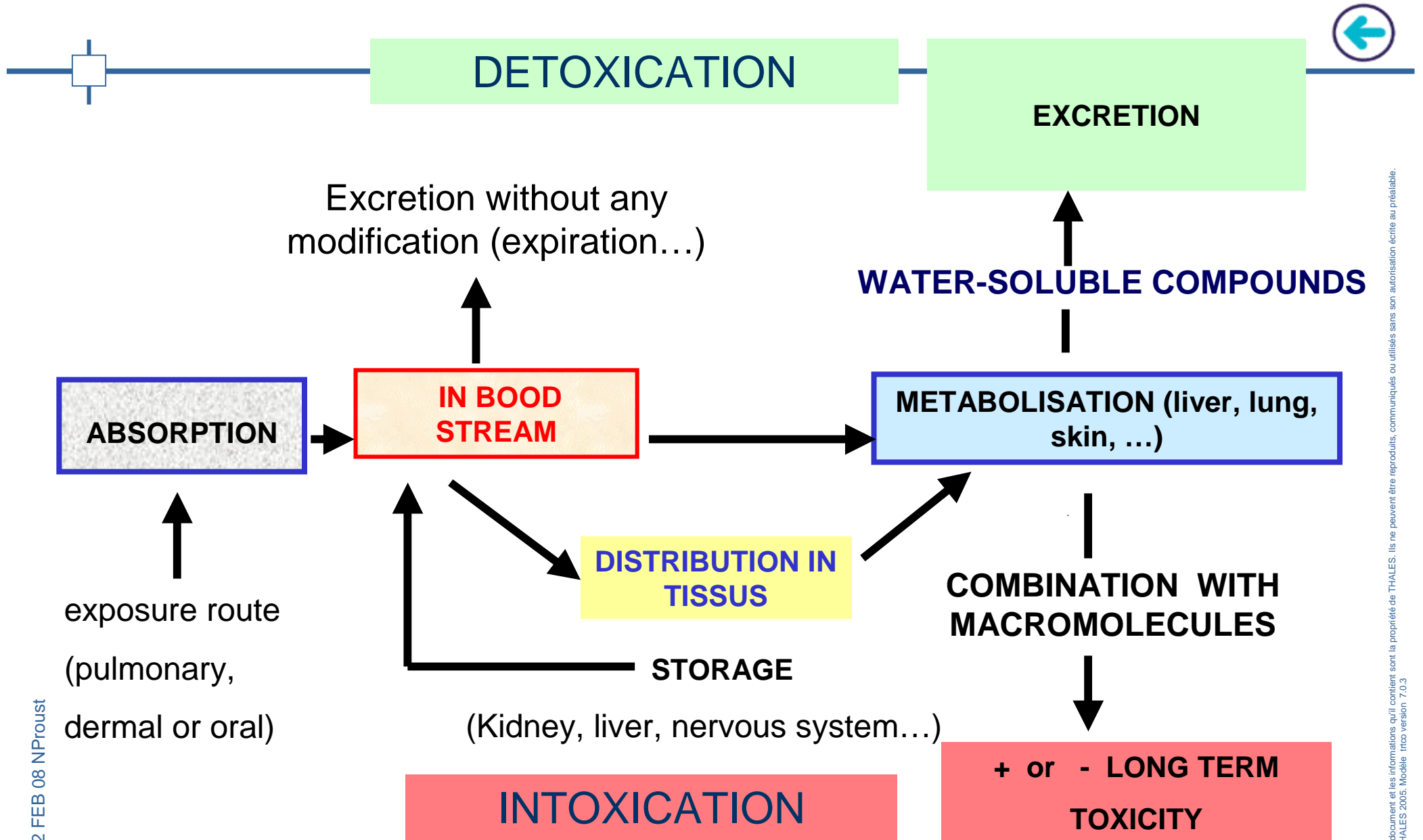


**Active transport**

**Exocytosis  
Endocytosis**

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**Speciation** is a very important parameter

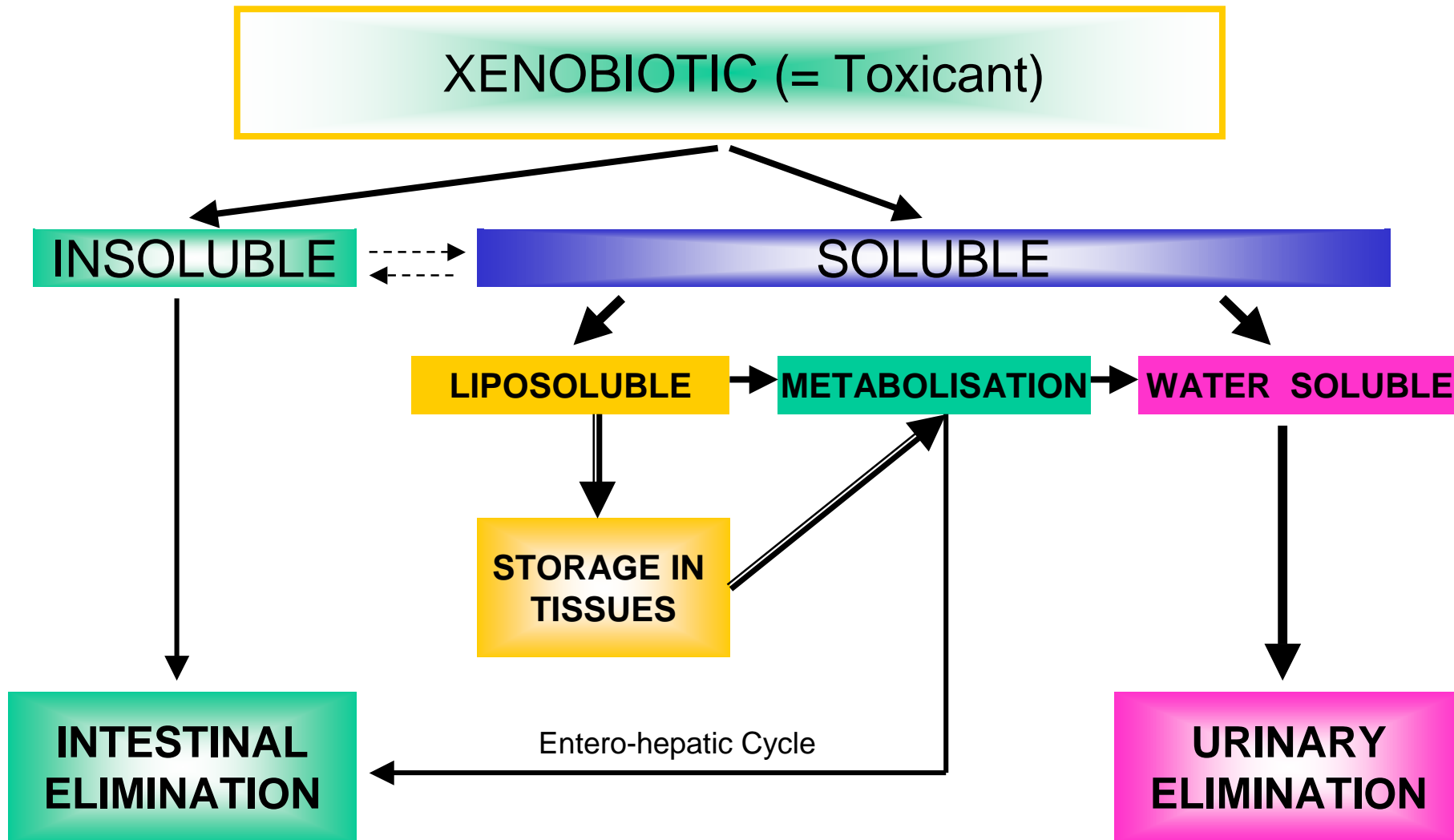
**Each compound** of a same family has specific properties

There are differences in term of:

- chemical, physical... properties
- solubility (insoluble, lipid soluble, water soluble)
- reactivity with water, oxygen...

**→ Toxicity will be also different!**





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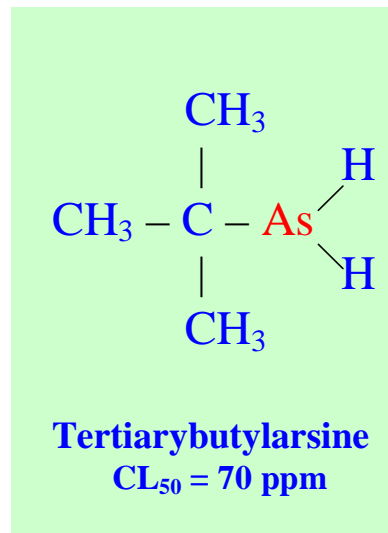
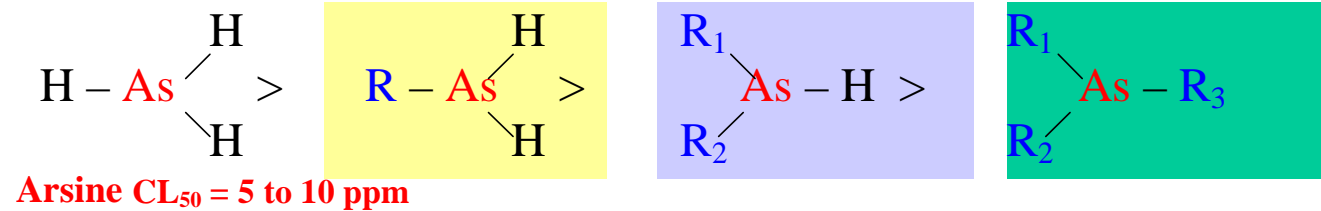
## DL<sub>50</sub> arsenic compounds

Arsenic compounds	DL <sub>50</sub> (mg/kg)	Animal / Administration mode
<b>Arsenite : arsenic trioxide</b>	<b>34,5</b>	<b>mice / oral</b>
<b>Arsenite : sodium arsenite</b>	<b>4,5</b>	<b>rat / intraperitoneal</b>
<b>Arsenate : sodium arsenate</b>	<b>14 - 18</b>	<b>rat / intraperitoneal</b>
MMA : monomethylarsonic acid	1 800	mice / oral
DMA : dimethylarsinic acid	1 200	mice / oral
<b>Arsenobetaine</b>	<b>10 000</b>	<b>mice / oral</b>
<b>Trimethylarsine oxide</b>	<b>10 600</b>	<b>mice / oral</b>
<b>Trimethylarsine</b>	<b>8 000</b>	<b>mice / subcutaneous</b>
<b>Trisdimethylaminoarsine</b>	<b>15</b>	<b>mice / subcutaneous</b>

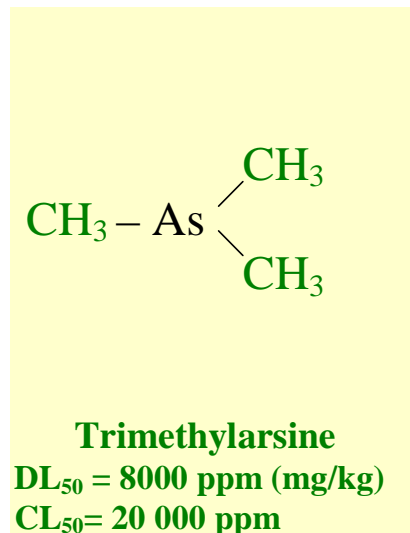


3 HYDROGEN CAN BE SUBSTITUTED AND REPLACED BY ORGANIC GROUPS TO DECREASE TOXICITY

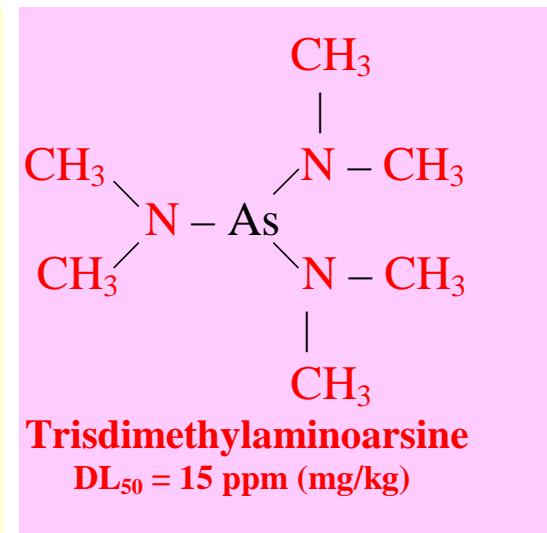
Decreasing toxicity (not always true!)



TBA



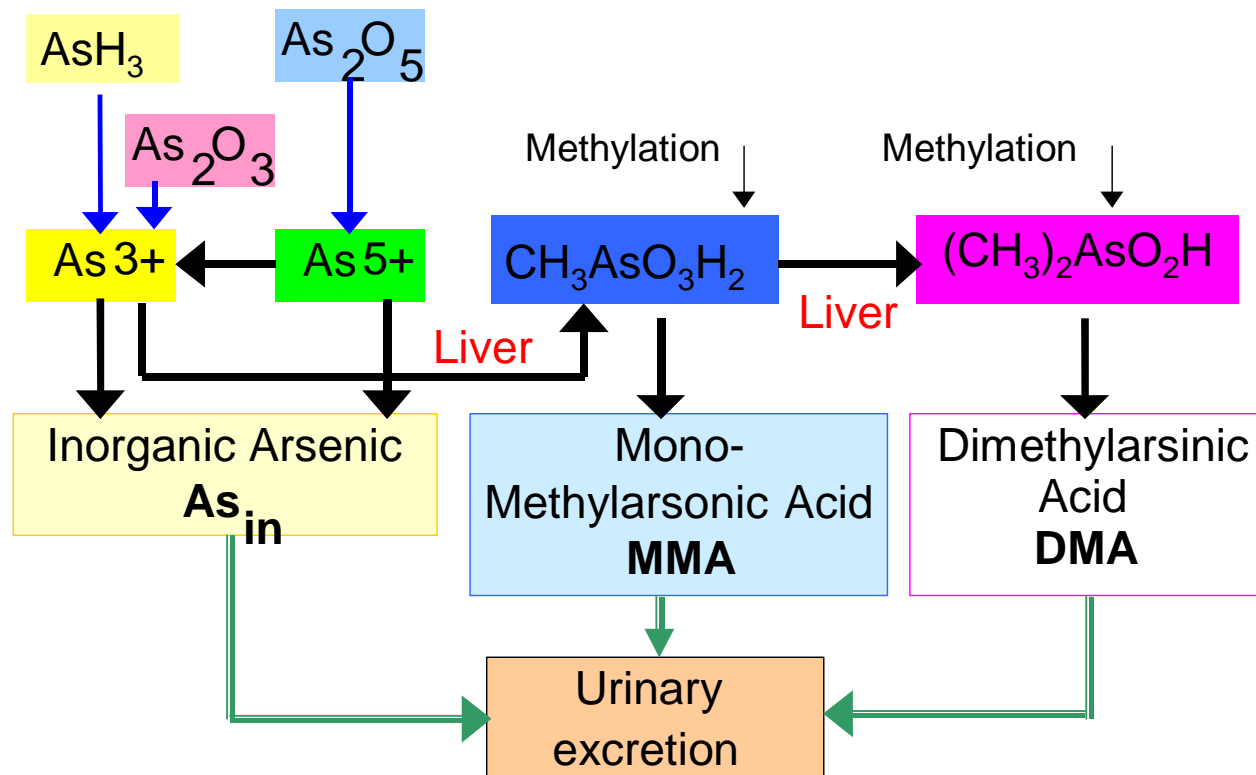
TMA

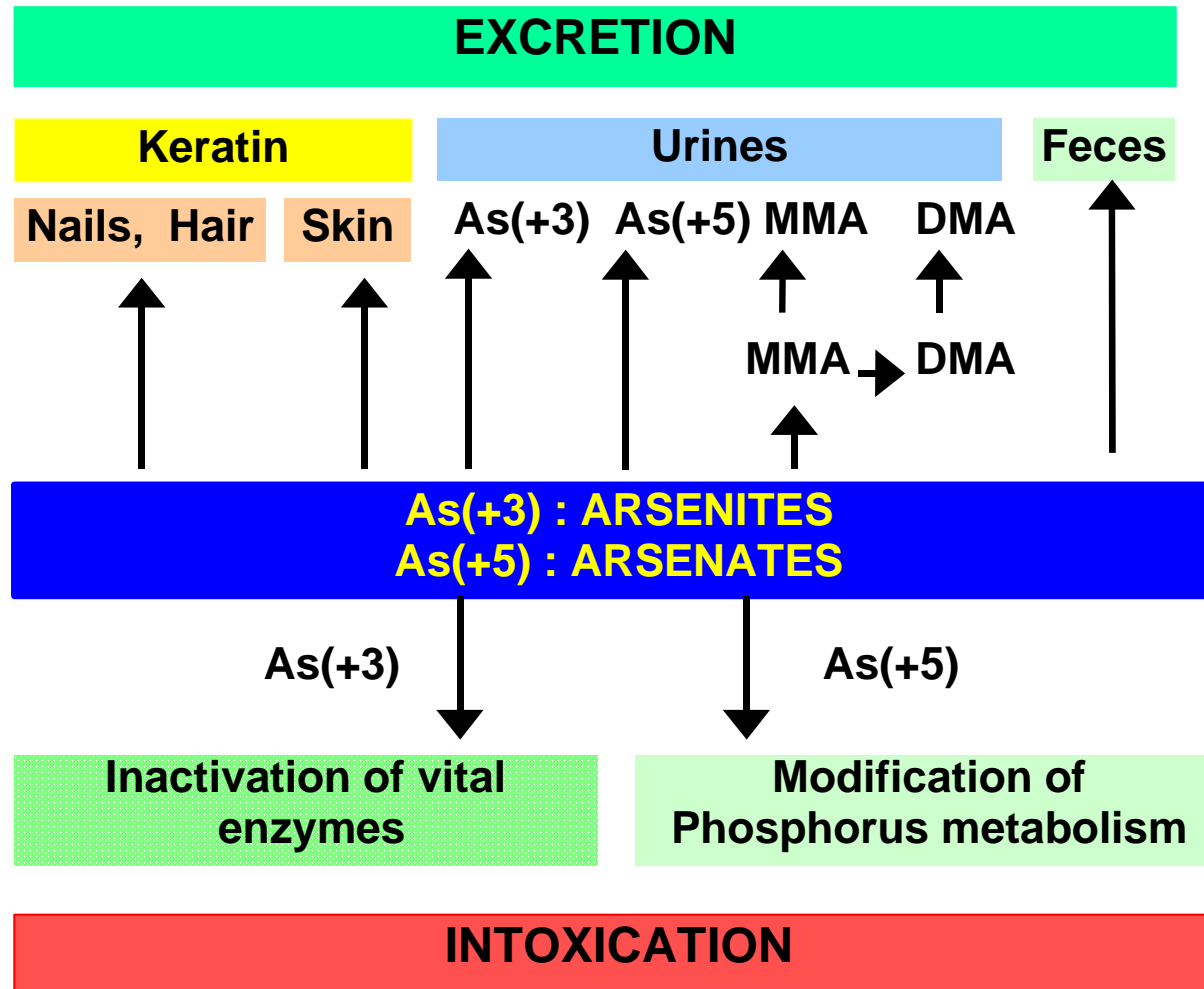


DMAAs



**Arsine:** the most toxic As compound causing hemolysis (destruction of red blood cells) + long term toxicity mineral As







## Ingestion of one Arsenic orale dose

### 1 -**INORGANIC** As : $\text{NaAsO}_2$

46% dose excreted in 4 days

1/2 excretion (23%) in 28h (1/2 biological lifetime)

excretion of 3 métabolites : Asi + MMA + DMA

on 96 h, are excreted : 25% Asi + 21% MMA + 54% DMA

### 2 - **DIMETHYLE** As : $(\text{CH}_3)_2\text{AsO}_2\text{Na}$

75% dose excreted in 4 days

1/2 excretion en 11h (1/2 biological lifetime)

excretion : only DMA

### 3- **TRIMETHYLED** commonly excreted **without any transformation** (arsenocholine, arsenobetaine, ...) 78 % dose in 1,5 day



**Arsine:** the most toxic As compound causing hemolysis (destruction of red blood cells) + long term toxicity mineral As

**Arsenates:** As(+5) modification of P metabolism (P replaced by As in ATP)

**Arsenites:** As(+3) Inactivation of vital enzymes. Proteins with S-H groups.

## IARC CLASSIFICATION

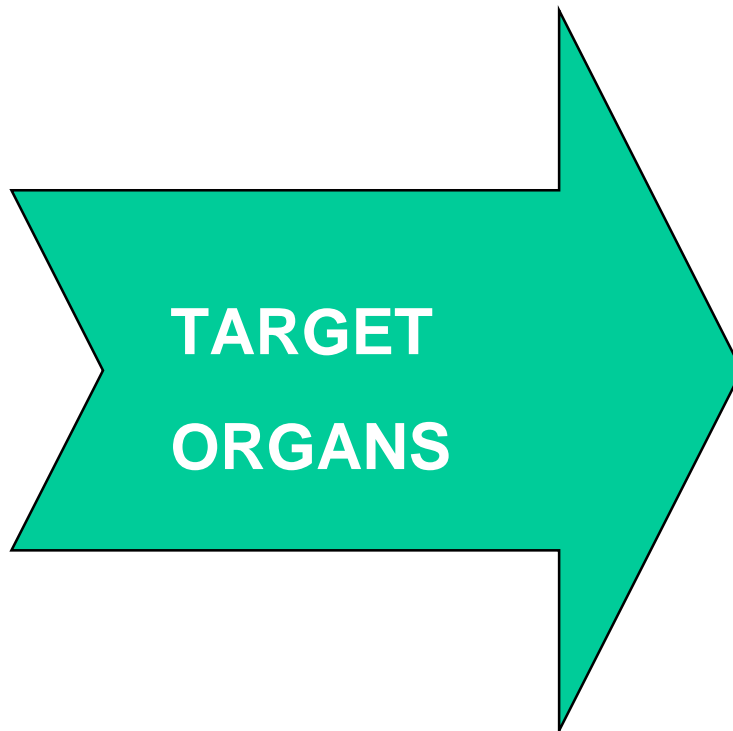
Arsenic and arsenic compounds

Gallium arsenide

**Group 1 : carcinogen for human**



## ACUTE, LONG TERM TOXICITY



Skin, Kidney, Liver

Blood

Respiratory system

Gastrointestinal tract

Nervous system

Cardiovascular system





- **Many industrial applications for Al and its compounds:** urban construction, transportation (cars, planes, trains, satellites...), electrical and mechanical industries, medicine, implants, cosmetics, water treatment (floculent), food industry ...
- EXPOSURE: *Foodstuffs and water are said to be the major sources of exposure* (EC regulation: max Al in water: **200 µg/L**)
- **Al in black tea**, 1 cup ~ **0.5 mg of Al** (**5µg Al/cm<sup>3</sup>**). *Digestive absorption of Al from a black tea cup **enhanced by lemon addition** (formation of soluble Al citrate complexes) or **decreased by milk addition** (formation of aluminium-phosphato species).*
- Others plants with high Al content: basil, thyme.
- Cooking: avoid **Al foils to cook fish “en papillote”** with lemon.
- Al in **drugs (antacid)**, in **vaccines**.
- Al in **antiperspirants (Al chloride)**, especially for women, are suspected to contribute to **breast cancer (EC regulation)**



→ Inhalation can result in a **direct transfer** of the Al particulates to brain tissue via the olfactory system.

→ Long term exposure to Al fumes and fine dusts can lead to accumulation.

→ The most important target organs are **lung (fibrosis), bones (osteomalacia) and brain (neurotoxicity)**.

→ **IARC Classification:** “Aluminium production industry” as a carcinogen process (Group 1) to Humans (risk of lung and bladder cancer).

→ **EC regulation:** Aluminium, Aluminium chloride, and Aluminium phosphide not classified as carcinogenic compounds.

→ **“Link” between Aluminium and Alzheimer disease ???**



→ Beryllium has important and specific uses in: nuclear, aerospace and electronics industries.

→ **Be and its compounds are very toxic** to mammalian cells. Interference with the **immune system**, after inhalation (dust, particules) to **lung disease** and possibly **cancer**.

→ **IARC classification:**

**Be and its compounds are placed in the group 1 (Carcinogen for Humans)**

→ **EC legislation:**

**Be and its compounds (except the Si, Al, Be oxide) are in the category 2 (possibly carcinogen by inhalation).**

→ **Be toxicity not well understood and rather speculative.**



## TARGET ORGANS

*Damage or perturbation on a lot of organs or systems*

**Immune system:** GaAs, Ga, As or both.

**Reproductive system:** Ga, In (different effects)

**Hematopoietic system:** Ga and As from GaAs and InAs particles (effect on heme biosynthetic pathway, Cytochrome P 450, some enzymes inhibited)

**Kidney:** Major target organ for metals such as In and Ga.

Alterations are different for Ga, In, GaAs, InAs)

**Liver:** In (inhibition of enzymatic activity)

**Bones:** accumulation of Ga



## Toxicology

- Many information on **Arsenic compounds** and their toxicity.
- Data on **Aluminium compounds** because of Alzheimer disease.
- Data on **Beryllium**.
- Few data on **Gallium and Indium**.
- Nothing on the metalorganics used in MOCVD.

## Safety

- **Maintenance is the most critical operation**, operators to be adequately protected, gases and particulates measurements, biometrology mandatory. Toxic waste to be handle.
- **Take care to burns** with metaloragnics, dermal entry for the chemical into the body.
- **Take care to fire** → particules of oxides → respiratory entry.