



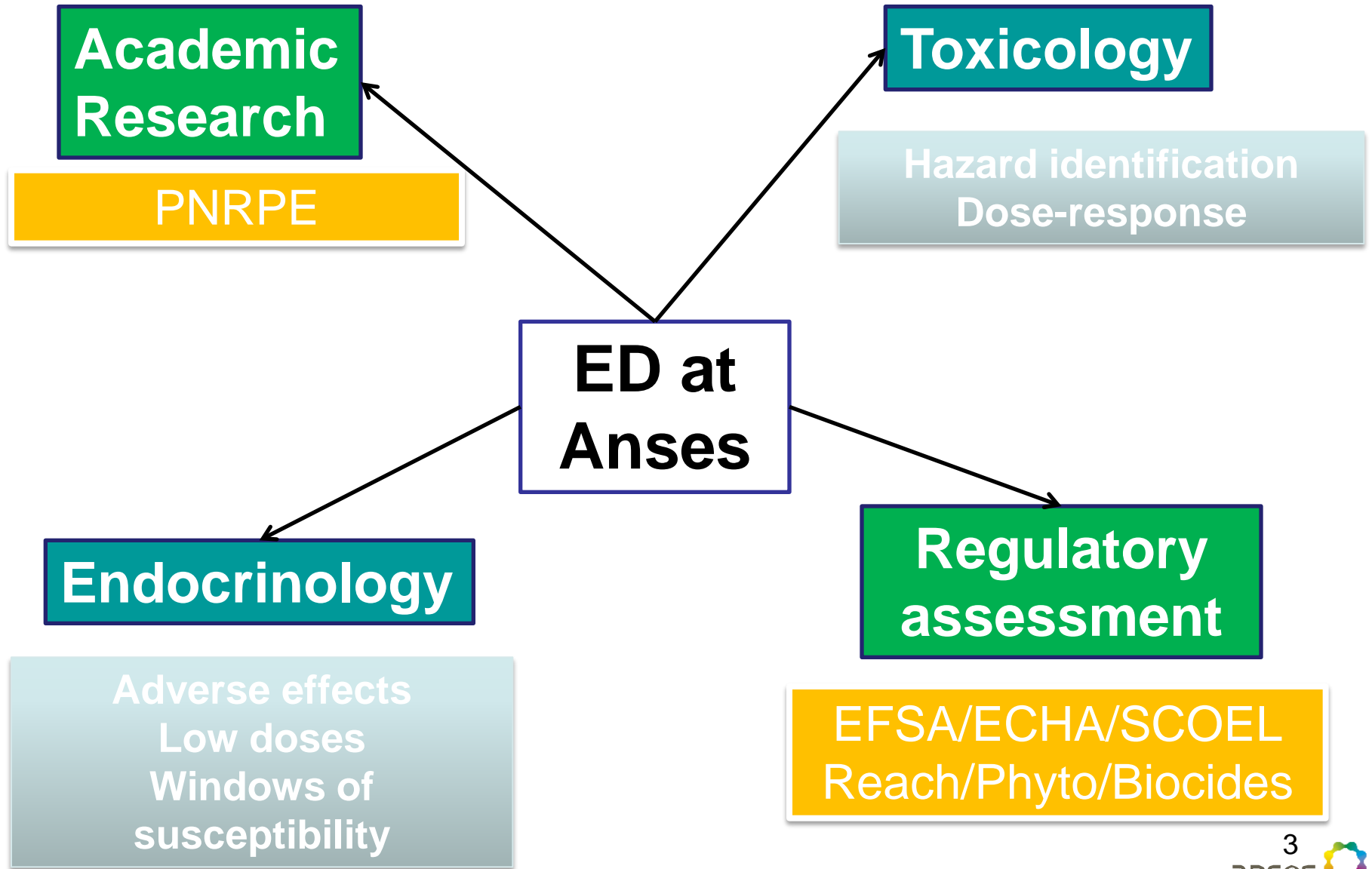
Endocrine Disrupters: Determination of OELs and Risk Assessment for workers

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Anses key challenges on EDs at work

- Introduction : EdDs at Anses
- Elaboration of OELs for 3 phthalates?
- Risk assessment of some specific compounds of interest for their reprotoxic and/or ED properties ?
- Risk assessment of nail workers?
- Conclusions-perspective



Risk Assessment of EDs: what has been already achieved

- **Individual compound approach:**
 - Proposal for Classification of BPA as a Reprotoxicant 1B
 - Restriction dossier on BPA in thermal paper (Echa, <http://echa.europa.eu/fr/>)
 - Risk Assessment of 12 Reprotoxic 2 and/or suspected EDs used in consumer products
 - French EDs Strategy: assessment of 5 compounds every year
- **Chemical family approach:**
 - State of the Art on **Phtalates** and on **Perfluorinated compounds** : **6 reports published in 2015** ,
 - State of the Art on **Brominated compounds** : **on going**

Risk Assessment of EDs: what has been already achieved

- **Ubiquitous massive exposure:**
 - Risk Assessment of flame retardants in furniture : *published in 2015*
<https://www.anses.fr/fr/content/perturbateurs-endocriniens-1>
- **Exposure of susceptible groups – children – workers**
 - Food : *to be published in 2016*
 - Toys *to be published in 2016*
 - Nail products *on going*

Setting Occupational Exposure Limits: the French Framework

A 3 stage process:

1- An independant scientific appraisal phase :

Health effects assesement (recommendation of atmospheric and biological values)
Assessment of the measurement methods for the recommended OELVs

- ▶ This is done at the Agency since 2005

2- Establishment of a draft regulation by the French Labour Ministry :

Setting of binding OELs by decrees or of indicative OELs by orders

- ▶ The binding or indicative nature of the OEL is established according to specific criteria which were discussed with social partners)

3- A stakeholder consultation phase :

Presentation of the draft regulation to the French Steering Committee on Working Conditions (COCT) for technical and economical feasibility discussions.

- ▶ Some application delays might be set according to the problems of technico-economic feasibility raised

Goal of ANSES expert committee on Occupational Exposure Limits



Recommending atmospheric values

- 8-hour Time Weighted Average values (8h-TWA)
- 15 min-Short Term Exposure Limit (STEL)
- Ceiling value

Recommending

- Skin Notation
- Ototoxic Notation
- Methods for measuring occupational exposure
- Biological Limit Values and Biological Reference Values

all the reports are available on the Anses website :

the methodological reference document is available at :

<https://www.anses.fr/en/system/files/VLEP2009sa0339RaEN.pdf>

Method for setting OELs for EDs

Toxicological Profile and Health effects Assessment:

- Key literature concerning **Health effects**
- Conditions of **Exposure- Target population**
- **Hazard** identification
- First priority is given to the **inhalation route**
- Identification of the **Dose-response** relationship
- Selection of a critical dose (POD) (NOAEL, LOAEL, Benchmark Dose)
- Elaboration of a numerical value for the 8h-TWA/STEL using adjustments factors

<https://www.anses.fr/fr/taxonomy/term/683>

OEL for Di-n-butylphthalate (DnBP)

DnBP is a phthalate used as a plasticiser for commonly used products. Phthalates are used in most rigid, semi-rigid and flexible articles made from polyvinyl chloride (PVC). Some products, such as plastic bags, window frames, food packaging, plastic raincoats, shower curtains, boots, garden hoses, certain medical devices and blood storage containers can contain up to 50% phthalates.

Critical effect	Critical dose	CF	8h-OEL
Reduction in testosterone concentrations in foetal testes (Lehman et al., 2004)	NOAEL = 10 mg.kg⁻¹.day⁻¹ <u>Route-to-route extrapolation</u> NOAEL_{inhaled HEC} = 17.6 mg. m⁻³	9 CF _A 3 CF _H 3	1.95 mg.m⁻³ rounded to an 8h-OEL of 2 mg.m⁻³

OEL for Butylbenzyl-phthalate (BBzP)

BBzP is a phthalate used primarily as a plasticiser in products containing polyvinyl chloride (PVC). It is also used for the production of other polymers found in sealants, glues, paints, coatings and inks.

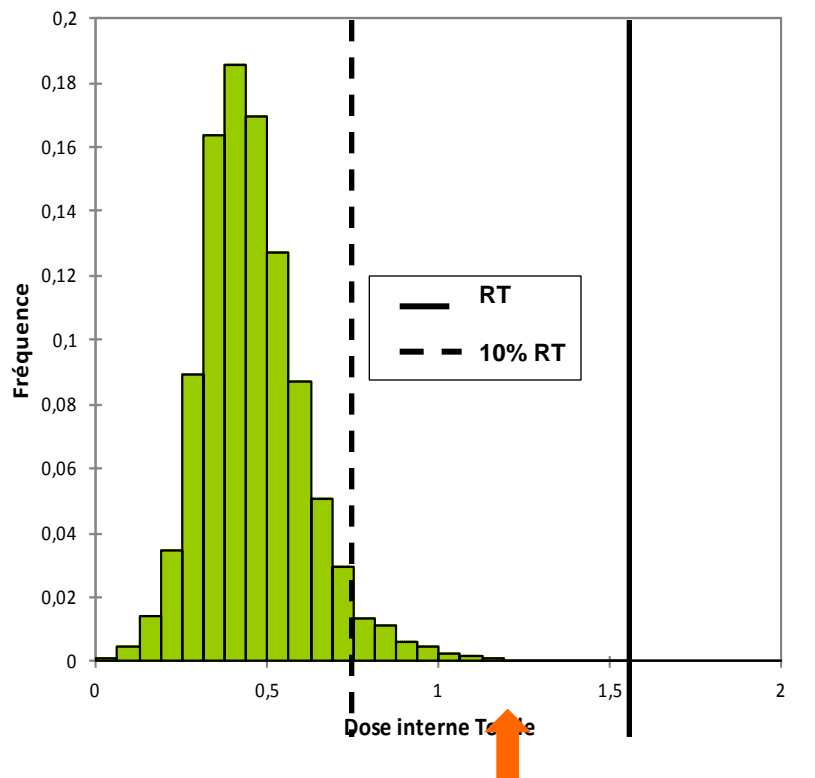
Critical effect	Critical dose	AF	8h-OEL
Impairment of reproductive organs and fertility (NTP, 1997)	NOAEL = 200 mg.kg⁻¹.day⁻¹ <u>Route-to-route extrapolation:</u> NOAEL_{inhaled HED} = 352.6 mg. m⁻³	27 AF _A 3 AF _H 3 AF _S 3	13 mg.m ⁻³

RA of Workers Exposure to EDs or R2 via consumer products

- In 2009, the French Health Ministry requested ANSES to assess the risks regarding exposure to suspected EDs and/or R2s in consumer products.
- 5 R2s and/or EDs: **n-hexane, toluene, cis-CTAC, orthophenylphenol (OPP) and methyl-tert-butylether (MTBE)** were identified based on national sector survey among manufacturers and available bibliographic data.
- For each product, **use patterns and exposure scenario** were defined for workers and general populations. Both **direct exposure** to EDs in consumer products and **indirect exposure** by the intake of contaminated air were considered. For each scenario, uptake doses were modelled through a **probabilistic approach** based on a one-dimensional Monte Carlo simulation
- A **scientific review of the effects on reproduction** (fertility/development) and **ED** potential was conducted in order to select critical doses for these target populations. **Toxicological benchmark doses** (TBs) were calculated as the ratio between critical doses and uncertainty factors.
- The **statistical distributions of doses** through direct and indirect exposure were compared to TBs to assess the risk.

<https://www.anses.fr/fr/system/files/CHIM2009sa0331Ra-01.pdf> <https://www.anses.fr/fr/system/files/CHIM2009sa0331Ra-04.pdf>
<https://www.anses.fr/fr/system/files/CHIM2009sa0331Ra-02.pdf> <https://www.anses.fr/fr/system/files/CHIM2009sa0331Ra-05.pdf>
<https://www.anses.fr/fr/system/files/CHIM2009sa0331Ra-03.pdf>

Exposure dose distribution and toxicological benchmark



P95

TB : Toxicological Benchmark doses.
P95 : The 95th percentile of the probabilistic distribution of exposure doses.

➤ Situations *at risk* or *presumed at risk* (*) of *in utero* developmental effects associated with the use of a product by pregnant women at work for:

- **Toluene** and liquid glues, liquid paints, varnishes, paint strippers for wood(*), spray degreasing agents/lubricants for metal(*), paint thinners, plastic renovators (*),
- **N-hexane** and liquid glues, liquid and spray paints(*), paint strippers for wood(*), spray degreasing agents/lubricants for metal(*), glue thinners, stain removers for textiles(*), textile waterproofing products(*), wood maintenance products (waxes, floor polishes..)(*).

➤ Situations *with significant exposure*:

- **Toluene** and spray paints, fuel in service stations
- **N-hexane** plastic renovators, car air freshener sprays, fuel in service stations
- **Cis-CTAC** and detergents, household liquid cleaners, liquid glues and varnishes, repellents for skin application (spray)
- **OPP** and household spray cleaners household spray cleaners, liquid degreasing agents/lubricants for metal
- **MTBE** and fuel in service stations

BPA in thermal paper: restriction proposal

Entry [#].

4,4'-isopropylidenediphenol (Bisphenol-A)

CAS No 80-05-7

EC No 201-245-8

1. Thermal paper shall not be placed on the market after [36 months after the entry into force] if it contains this substance in concentration equal or higher than 0.02% by weight
2. The existing standard analytical methods for BPA have to be used

➤ ≈ Ban of BPA in thermal paper

➤ Concentration limit based on:

- no safe concentration could be determined
- below 1%, thermal paper gets inefficient
- limit proposed is the lowest as possible= average of LoDs= 0.02%

➤ Transitional period of 3 years based on:

- Alternatives exist and some of them are already used
- No information about a longer period got from the STOs so far

BPA: Thermal receipts uses

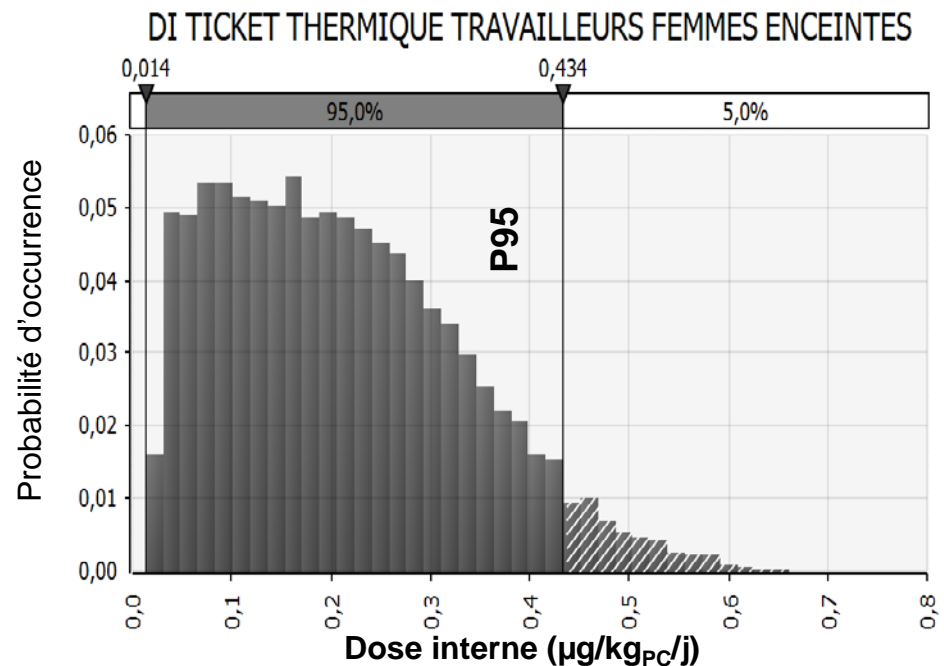
Occupationnal exposure – Pregnant women



$$DJE (\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{j}^{-1}) = \frac{F (\mu\text{g}\cdot\text{cm}^{-2}\cdot\text{h}^{-1}) \times D (\text{h}\cdot\text{j}^{-1}) \times S (\text{cm}^2)}{Pc (\text{kg})}$$

Dose interne ($\mu\text{g}/\text{kg}_{\text{PC}}/\text{j}$)

Minimum	0,01
P5	0,05
P25	0,11
P50	0,20
P75	0,29
P90	0,38
P95	0,43
Maximum	0,71
Moyenne	0,21



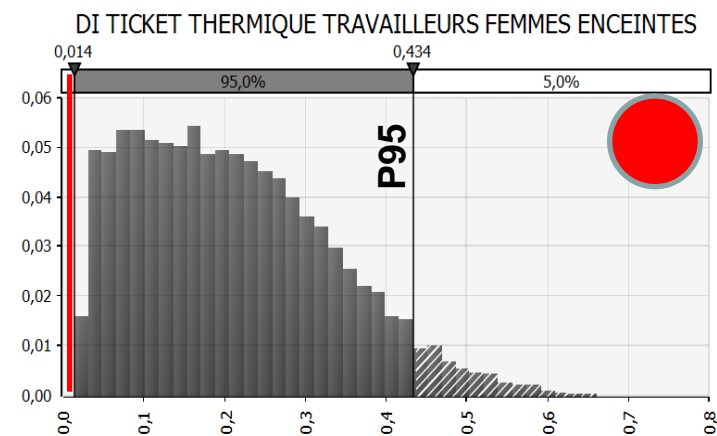
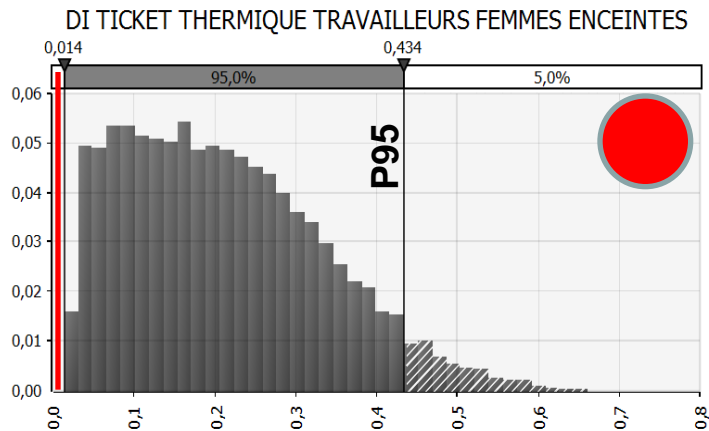
Brain and development

$RT_{final} = 0,005$
 $\mu\text{g}/\text{kg}/\text{j}$



Female reprotoxicity

$RT_{final} = 0,01$
 $\mu\text{g}/\text{kg}/\text{j}$

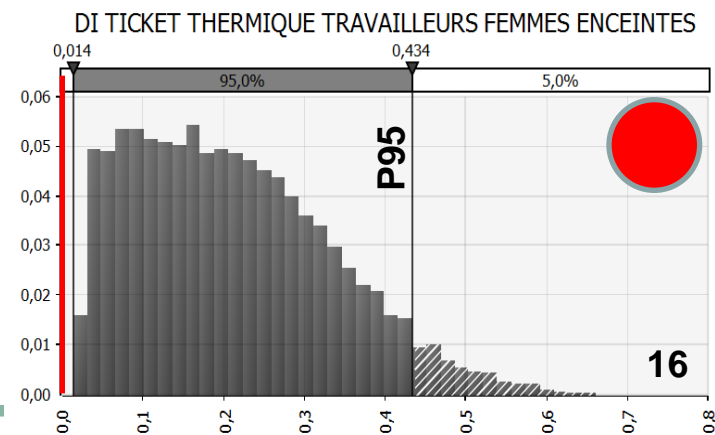
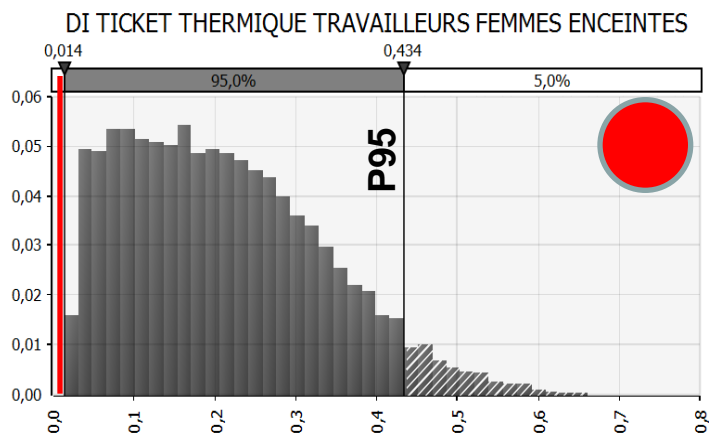


Metabolism and obesity

$RT_{final} = 0,009$
 $\mu\text{g}/\text{kg}/\text{j}$

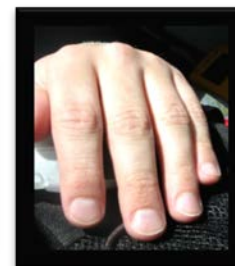
Mammary Gland

$RT_{final} = 0,0025$
 $\mu\text{g}/\text{kg}/\text{j}$



BPA in thermal paper: Forseen regulation

- The restriction is implementable, enforceable manageable and monitorable – *SEAC agrees*
- But for SEAC, the proposed restriction is considered unlikely to be proportionate. *However there may be favourable distributional and affordability considerations*
- Now it is up to the EC to decide on the risk management measure:



Risk Assessment for workers linked to nail products

Context and scope

- ❖ Request from the French National Agency for Medicines and Health Products Safety (ANSM) dated from 2014 May 23th

- ❖ **Context**

Assessment made by ANSM concerning health risk to consumers linked to toluene in cosmetic products and more particularly in varnishes



identification of Reprotoxic properties of Toluene

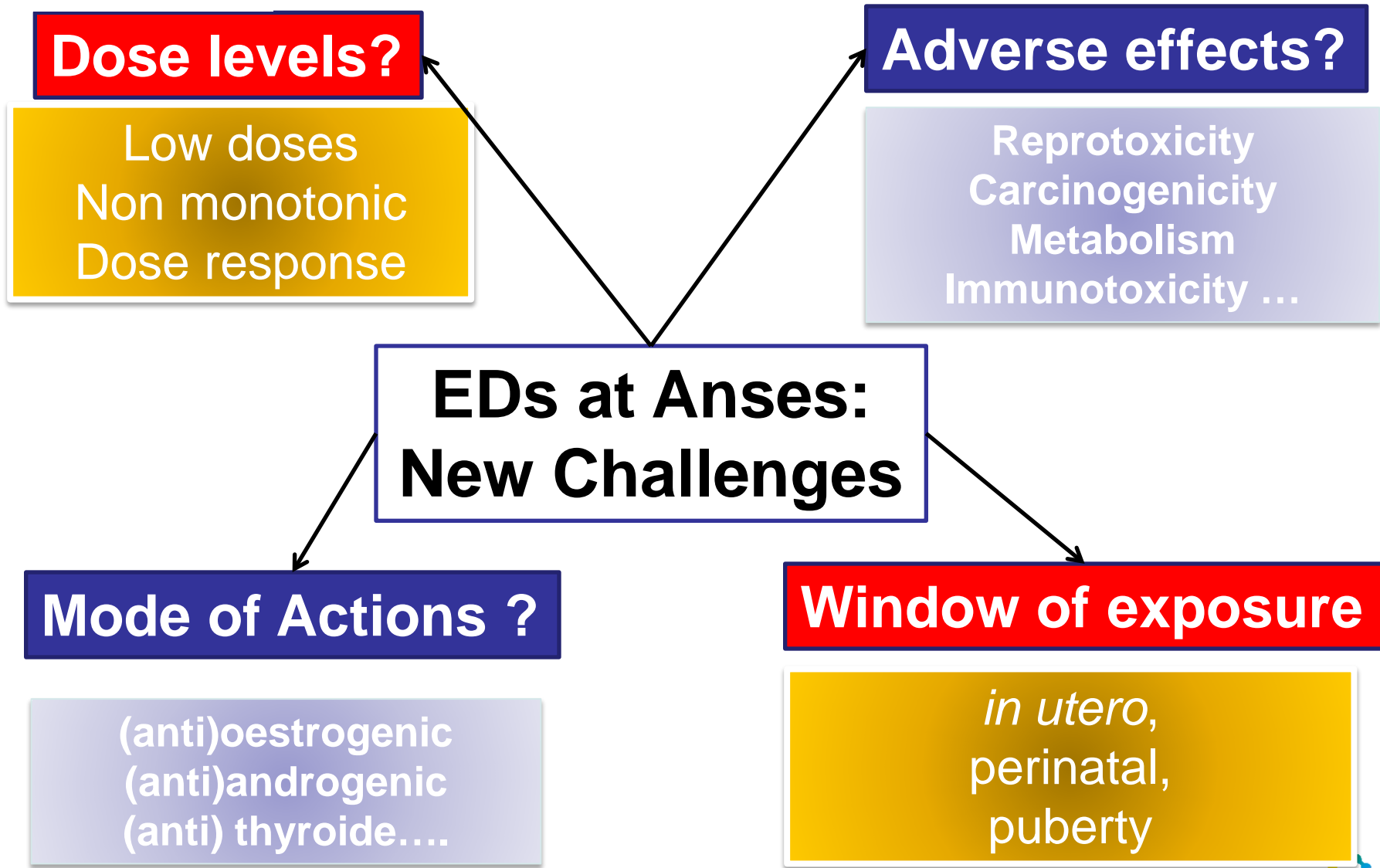
What about the workers who handle varnishes or other products linked to nails?

- ❖ **Request**

ANSM request an expert assessment on the risks for workers linked to products used in nails activities in aesthetic sector

Ongoing work

- ❖ Bibliographic review on nail care occupation, nail care techniques and occupational diseases
- ❖ Interviews of stakeholders of the aesthetic sector
- ❖ Extraction of databases to collect information on:
 - Occupational diseases - RNV3P/ REVIDAL
 - Occupational exposure to chemicals in workers area - COLCHIC
 - Composition of products - BNPC
- ❖ Ongoing study with INRS laboratory and the Occupational Health Department of Lille to screen VOCs and measure dust in the air of nail salons
- ❖ Prioritization of chemicals for regulation based on hazard classification, toxicological values and exposure data



Connaissances relatives
à la réglementation,
à l'identification,
aux propriétés chimiques,
à la production et aux usages
des composés de la famille
des Phtalates (Tome 1)

Note d'accompagnement
Rapport d'étude

Mars 2016 | 68 pages | 8 pages

Connaissances
relatives aux données
de contamination et aux

Mars 2016 | 68 pages | 8 pages

Merci pour votre attention!

Évaluation
des risques sanitaires
des substances
reprotoxiques
et/ou perturbatrices
endocriniennes
dans les produits
de consommation :
le cis-CTAC
(n° CAS 51229-78-8)

Avis de l'Anses
Rapport d'étude collective

Mars 2016 | 68 pages | 8 pages

Évaluation
des risques
du bisphéno A (BPA)
pour la santé
humaine

Tome 1

Avis de l'Anses
Rapport d'étude collective

Mars 2011 | 68 pages | 8 pages

