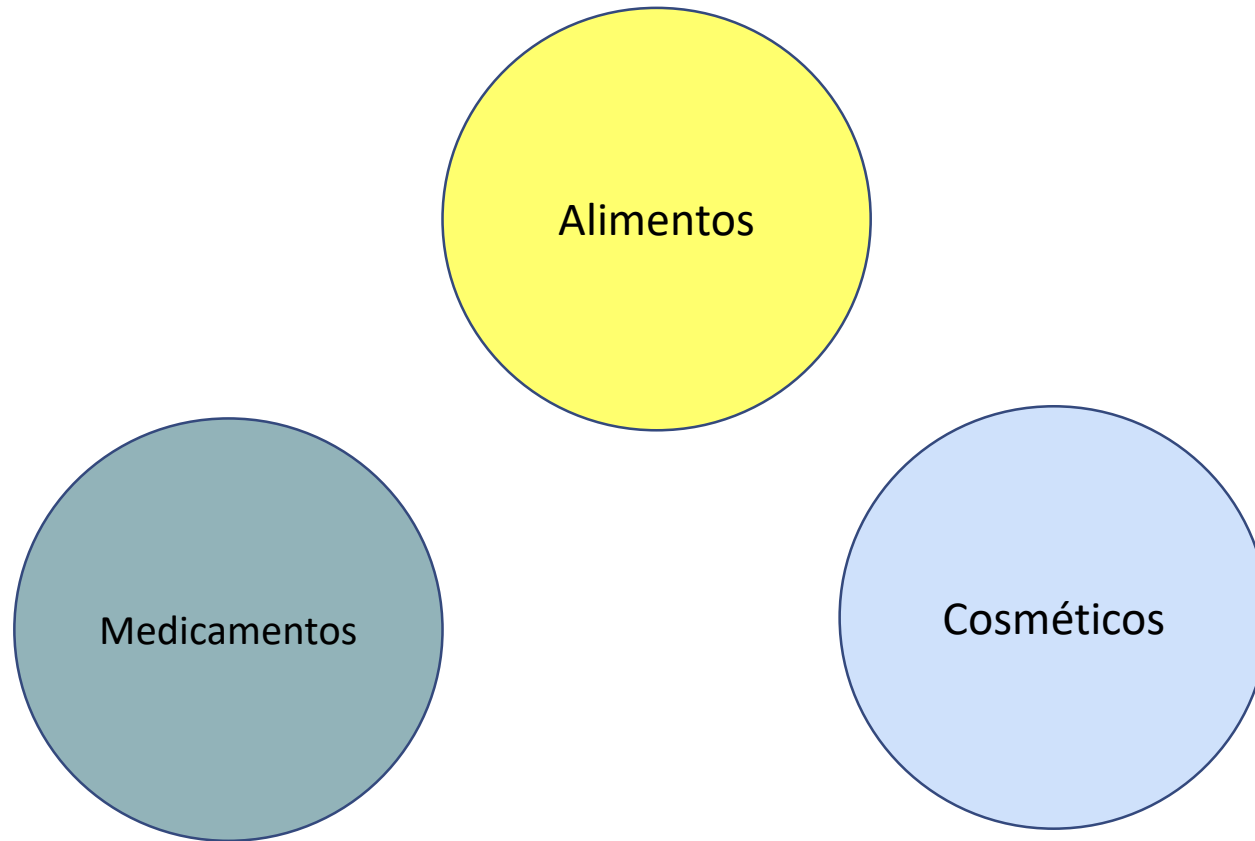


Inovação e Segurança do consumidor:  
Desenvolvimento de novos ingredientes

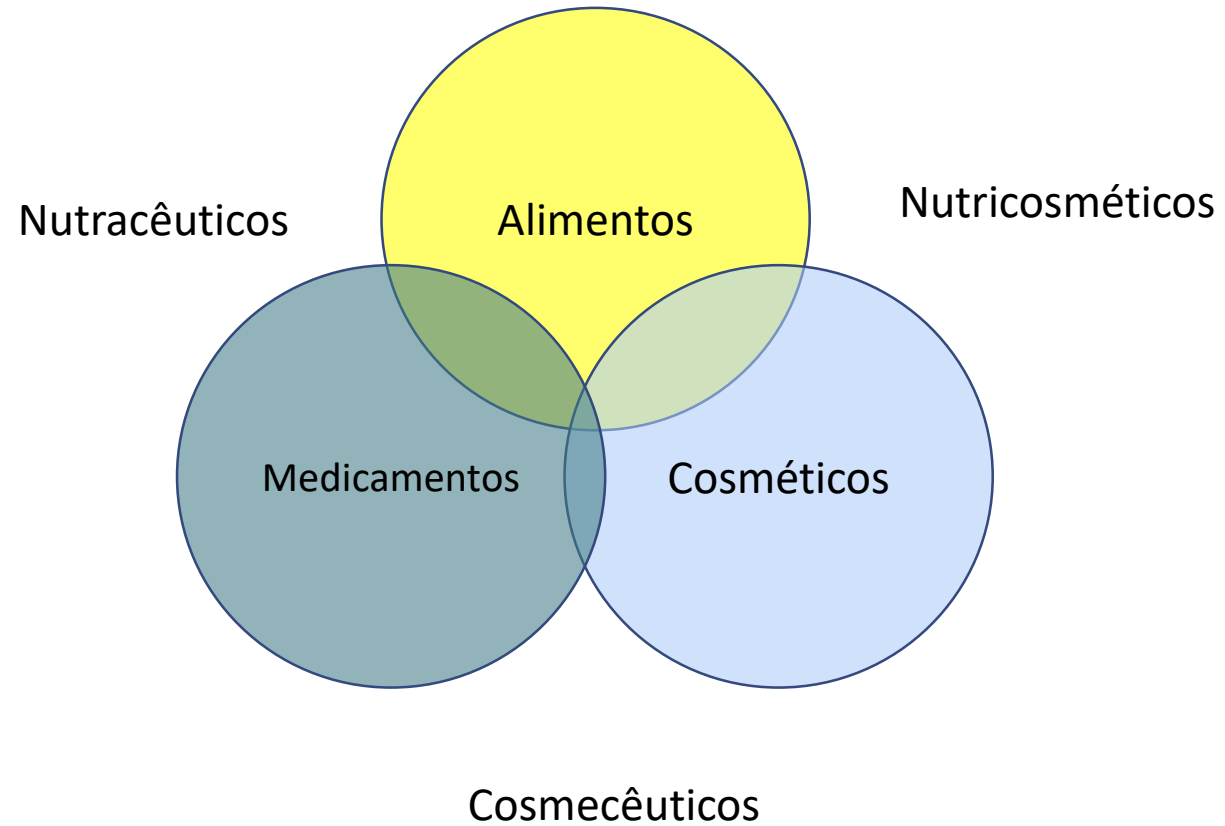


# FRONTEIRAS





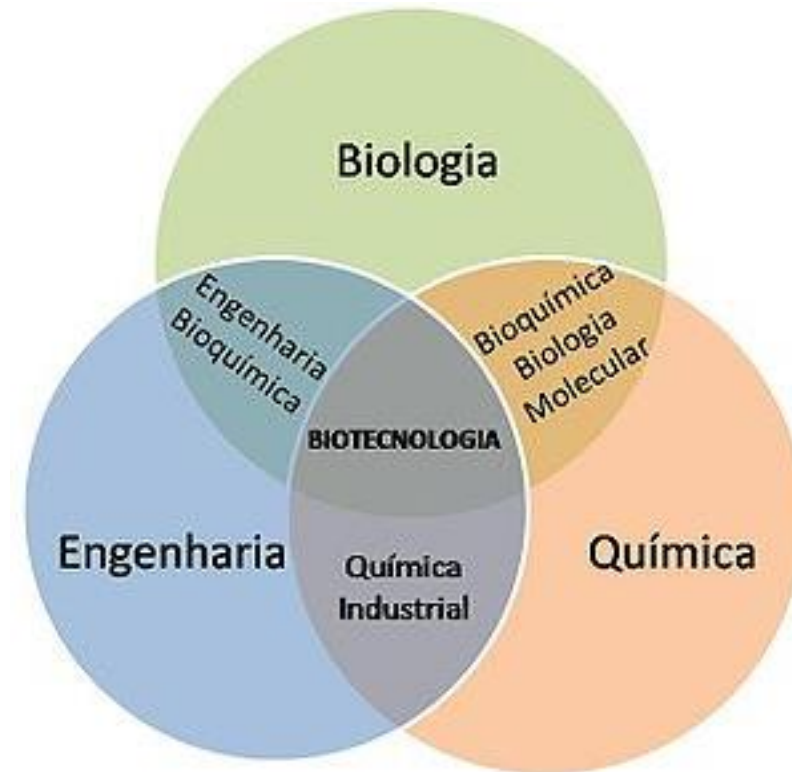
# FRONTEIRAS





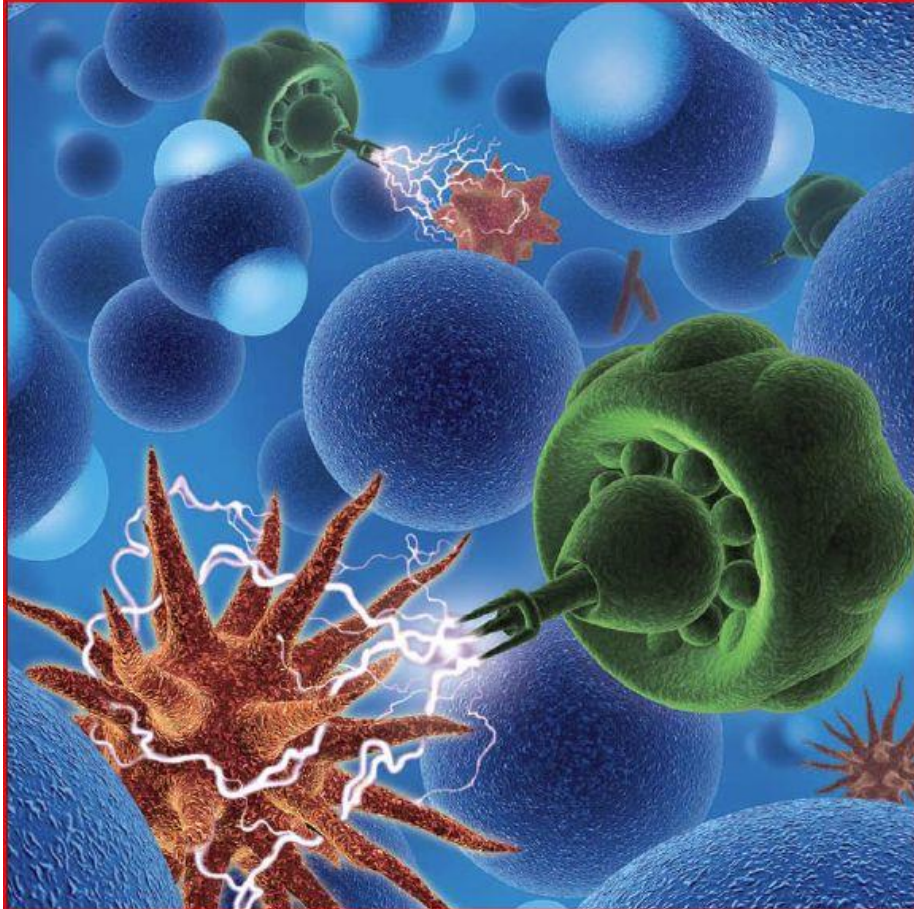
# Biotecnologia

- Uso de organismos pelo homem
  - **Tradicional:** uso dos processos e produtos dos organismos vivos, como a fermentação
  - **Moderna:** manipulação genética de organismos e inserção desses genes modificados nos mesmos para alcançar as características desejadas





# Nanotecnologia



football opinion culture business lifestyle fashion environment tech travel

law scotland wales northern ireland education media

## Toxic air pollution particles found in human brains

Detection of 'abundant' magnetite particles raises concerns because of suggested links to Alzheimer's disease



The new study examined brain tissue from people in the UK and Mexico and found abundant particles of magnetite, an iron oxide. Photograph: Manuel Velasquez/Getty Images



# Cosméticos

- Kosmein = Adornar
- Cosméticos:
  - Composto por substâncias naturais ou sintéticas
  - Partes externas e Mucosa oral
  - Limpar, perfumar, corrigir odores, melhorar aparência e proteger/preservar





# Pulvis Antimony Crudis

- Final do séc. XVIII
- Indicado pelos médicos para
  - Sífilis
  - Herpes
  - Lepra
  - Manias
  - Epilepsia
- Usado como cosmético





# Lash Lure vs Ms. Brown, 1936

Anilina em delineadores  
> 20 eventos adversos reportados  
1 caso confirmado de cegueira e  
possivelmente 1 morte







# Maquilagem permanente e tatuagens

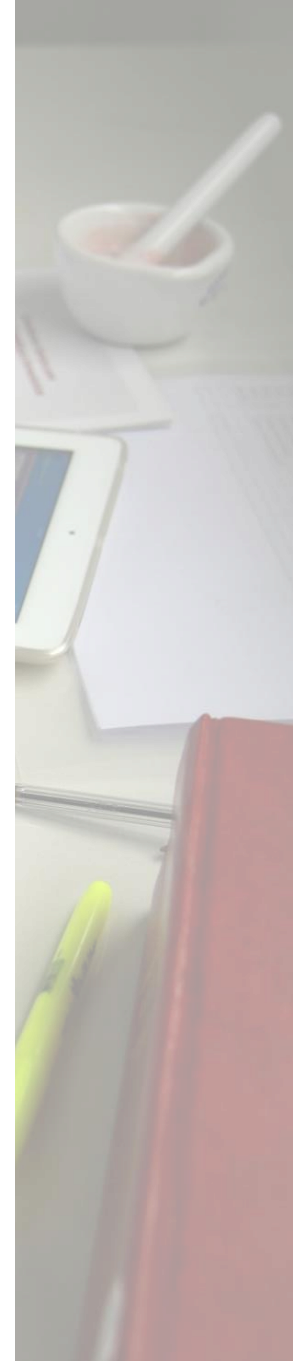
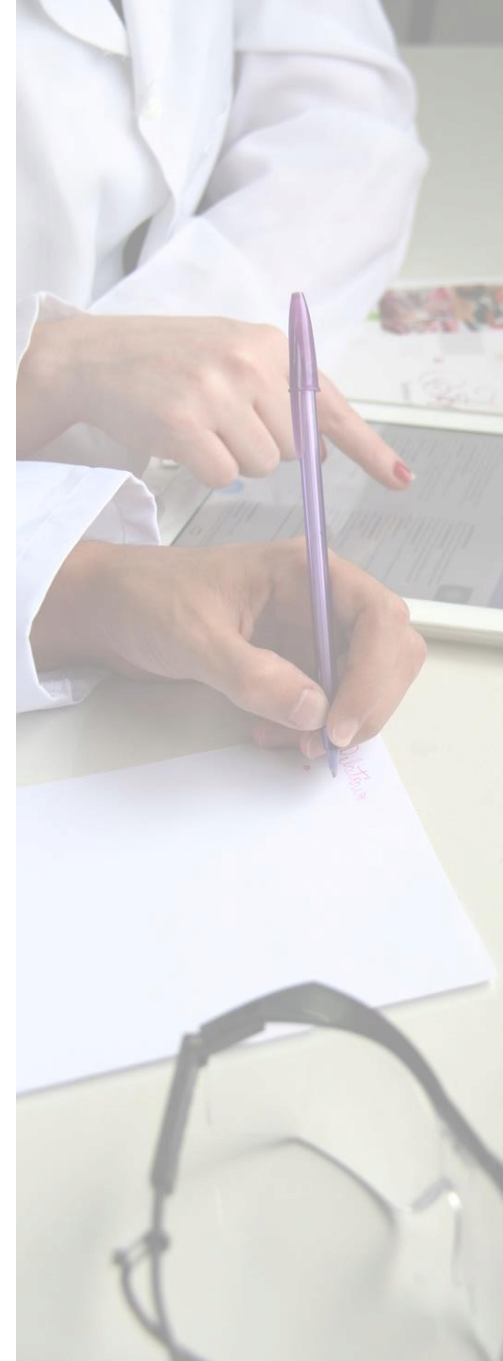
- 2003
- 150 casos de alergia a pigmento permanente
- Recall nos EUA





# Segurança de Cosméticos

- Os produtos de higiene pessoal, cosméticos e perfumes devem ser seguros nas condições normais ou previsíveis de uso
- Incidência de Eventos sérios: Média  $\cong 1,5$  ppm
- Reações suaves acometem cerca de 12% da população





# SEGURANÇA

## Uma fronteira importante





# Gestantes

Taxa de respiração aumenta cerca de 30%

Volume líquido de ar aumenta 50%

Maior absorção de compostos pelas vias aéreas





## Pré- Concepção até Implantação

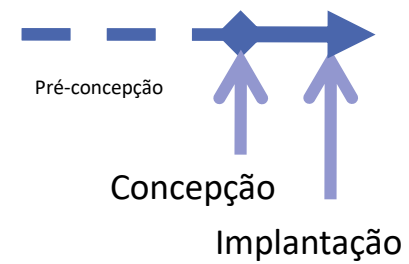
Funções reprodutivas dos adultos machos e fêmeas

Desenvolvimento de gametas

Fertilidade

Estágios na pré-implantação

implantação





# Clareamento de pele em gestantes

## Tendências observadas na análise sistemática de diversos estudos

- Redução do peso do recém-nascido
- Defeitos oro-faciais

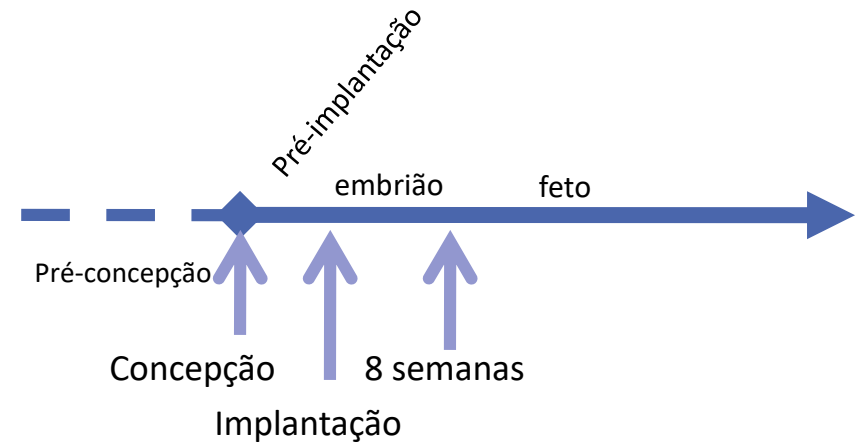
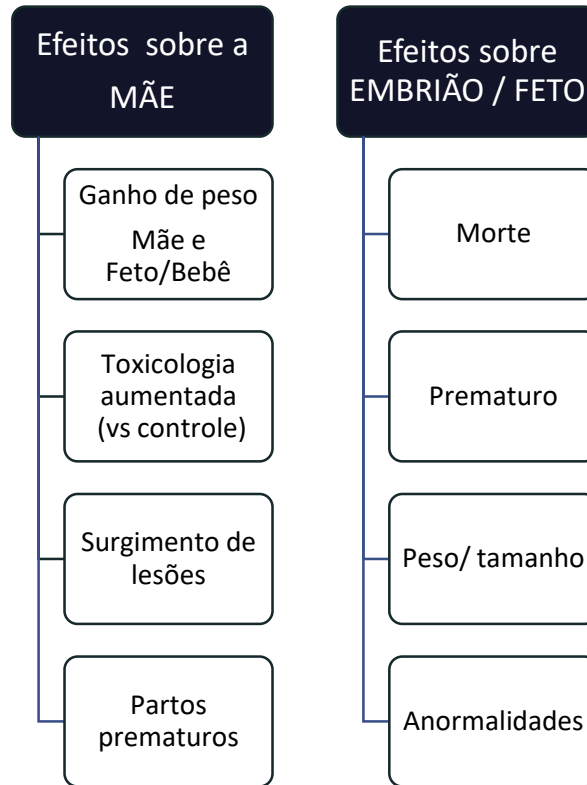
## Observações com uso de esteróides potentes

- Sangramento vaginal leve durante a gestação
- menor cortisol plasmático
- Menor placenta
- Menor peso do recém nascido



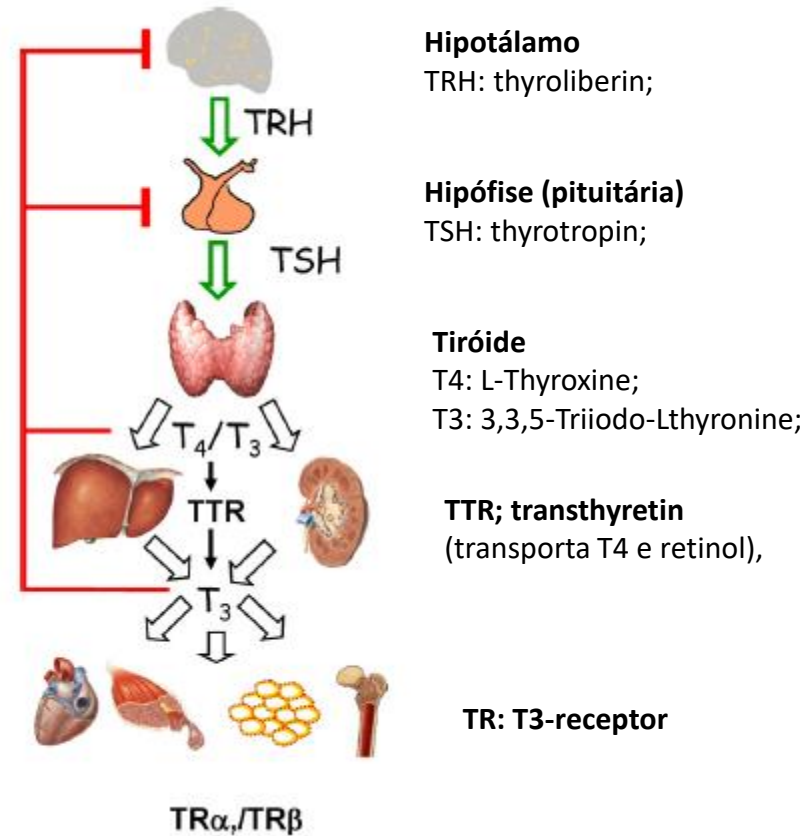
**Farmácia na Thailandia**

Mahé e col. *Trans R Soc Trop Med Hyg.*; 101(2):183-7, 2007  
Chi e col., *J Am Acad Dermatol* 2010;62:694-705.)





# Alvos para modulação ambiental do eixo dos hormônios da tireoide

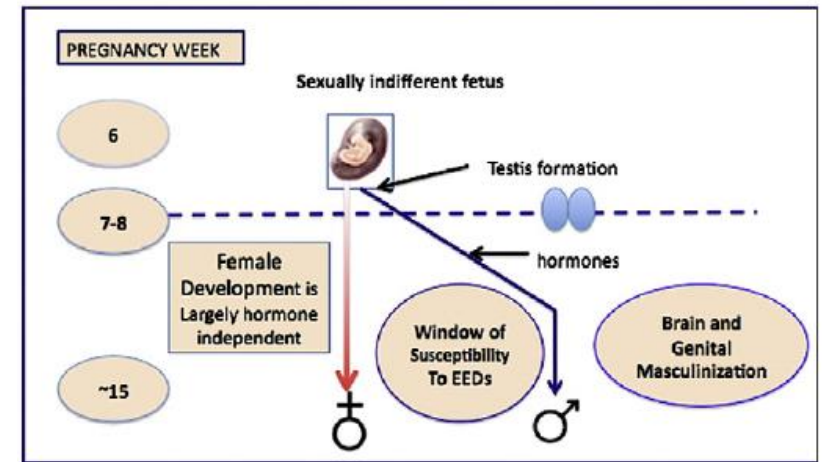


*J. Köhrle / Annales d'Endocrinologie 69: 116–122, 2008*



# Disruptores endócrinos

- Conjunto de ameaças à saúde reprodutiva masculina
  - Anomalias no desenvolvimento das gonadas
  - Hypospadia
  - Alterações de comportamento
  - Câncer de próstata
  - Infertilidade masculina na vida adulta
    - espermatozóides mal formados e em pequeno número
    - Pode ser transmitida para próximas gerações
  - Diminuição da memória na velhice
- Provocada por Disruptores Endócrinos



Weiss. Journal of the Neurological Sciences 305 (2011) 11–21



# Surfactantes

- APEs: alkylphenol polyethoxylates
  - Produto de degradação → 4-octylphenol
    - Estrogênico
    - Encontrado em águas de superfície
    - peixes machos feminizados encontrados à jusante das estações de tratamento de esgoto
  - Desenvolvimento testicular prejudicado





On the right, eggs can be seen in the abnormal male fish taken from the Grand River near the sewage treatment plant in Kitchener, Ont.

Image 2 of 3

<http://kitchener.ctvnews.ca/male-fish-in-grand-river-show-female-traits-1.985586>



# Cabeleireiras & gestação/fertilidade

- Environ Health Perspect. 2009; 117(2):303-7
- Hypospadias
  - Deformação urogenital em meninos
  - 4 a 24 casos em 10.000 nascimentos (Europa)
- Correlação positiva para exposição ocupacional a
  - Hair spray
  - Ftalatos
- Uso de folato no 1º trimestre diminui risco
- J Occup Health 2003; 45 (6): 400-4.
- Profissionais expostos a ácido tioglicólico
  - Comparados com grupos controle
    - Professores
    - Estudantes de medicina
- Observações
  - alterações na menstruação
  - maior atividade mutagênica (urina)
  - Voluntários recebendo permanente: micronúcleos nas células do folículo
- Dados sugerem redução da fertilidade

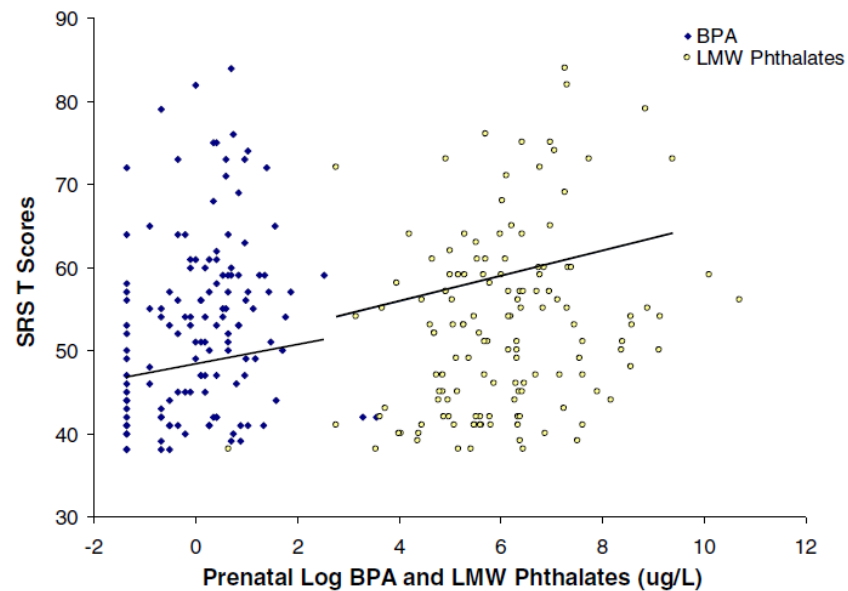


# Esteticistas & Gestação

- Am J Perinatol. 2009; 26(9):625-31
- Matern Child Health J. 2009; 13(1):90-7
- **Período investigado:**
  - 1997 to 2003
- **Local:** Nova York
- **Grupos comparados:**
  - Esteticistas (15.003)
  - Corretores imobiliários (4.246)
  - População geral (12.171)
- **Aumento de incidência de:**
  - Hemorragia pós-parto
  - Falha na indução do trabalho de parto
  - Necessidade de intubação do recém-nascido
  - Baixo-peso da criança
    - Durante a gestação
    - No nascimento
- **Diferenças mais acentuadas em não-brancos**



# Exposição pré-natal a ftalatos



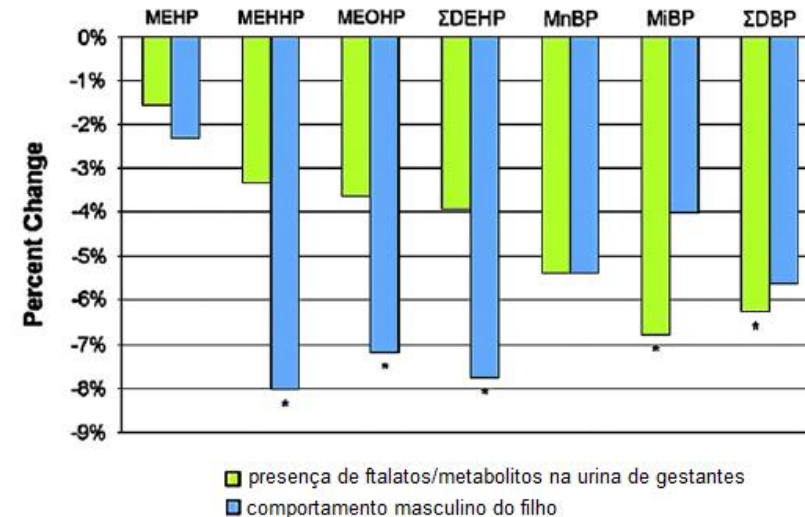
**Alterações de habilidades sociais**  
(comunicação, fala, motivação,  
cognição, maneirismos)

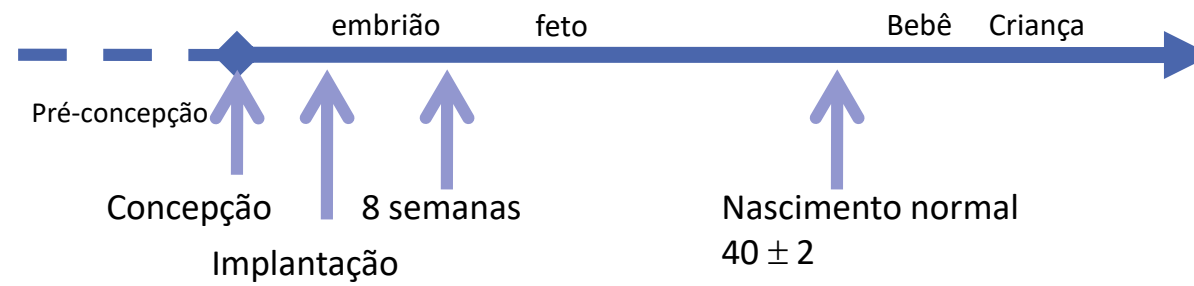
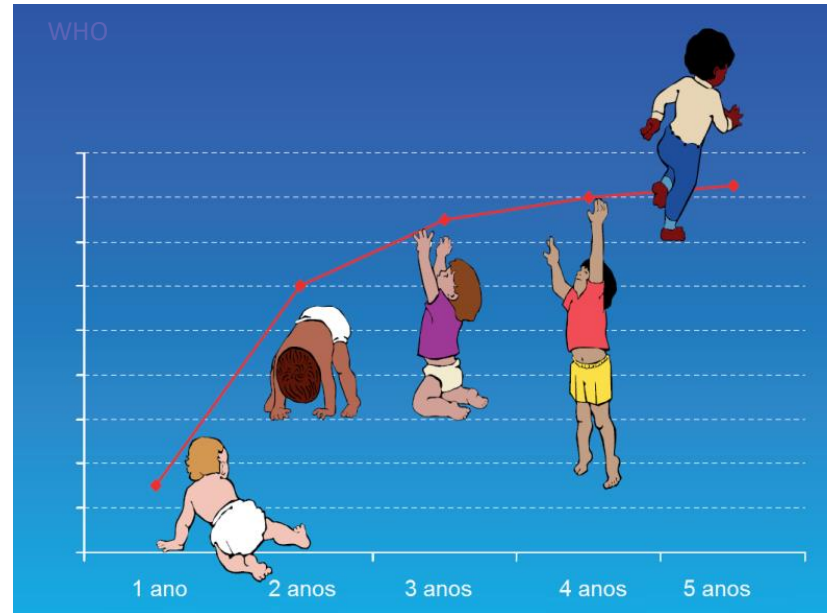
Miodovnick e col., *NeuroToxicology* **32**: 261–267, 2011

# Exposição pré-natal a ftalatos

- MEHP, Mono(2-ethylhexyl) phthalate;
- MEHHP, Mono(2-ethyl-5-hydroxyhexyl)-phthalate;
- MEOHP, Mono(2-ethyl-5-oxohexyl) phthalate;
- DEHP, Di(2-ethylhexyl) phthalate;
- MnBP Mono-butyl Phtalate
- MiBP, Mono-iso-butyl phthalate;
- DBP, Dibutyl phthalate

## Alterações de comportamento (comportamento feminino)



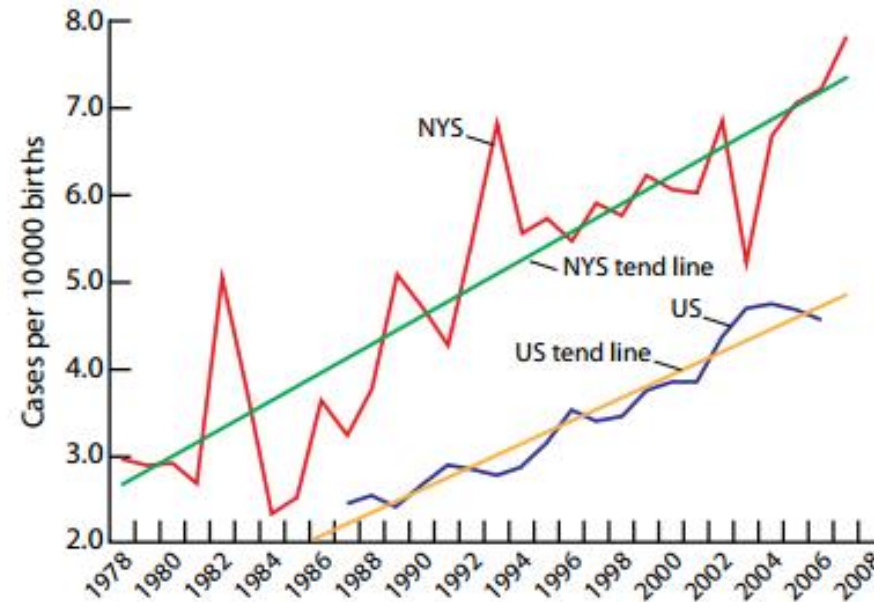


Coppoletta-Wolbach , Am J Pathol. 1933 January; 9(1): 55–70.





# Incidência de hipospadia congênita



**Figure 2.10.** Incidence rate of CH in New York State (NYS), 1987–2007, and in the United States (excluding NYS), 1987–2006. (Figure from Hinton et al. (2010), redrawn; Used with publisher’s permission).

# Bisphenol A



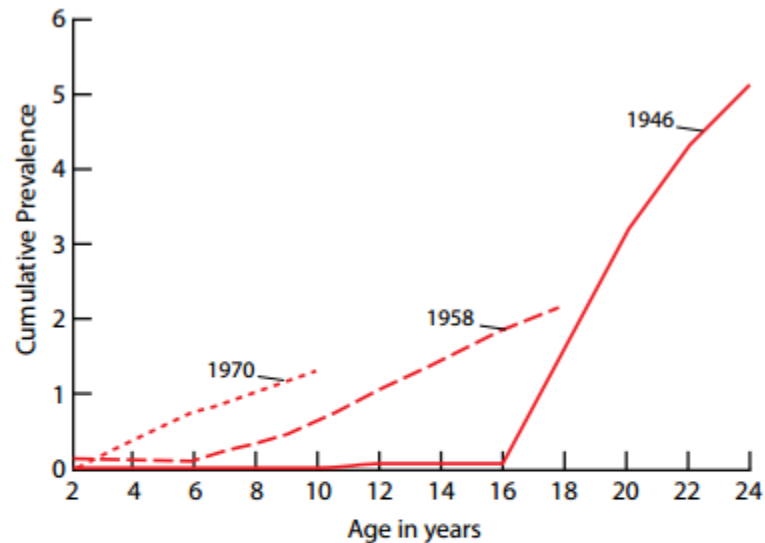
The screenshot shows a website with a header featuring a baby icon and the text "DIGA NÃO AO BISFENOL A A VIDA NÃO TEM PLANO B" and "CAMPANHA CONTRA OS DESREGULADORES ENDÓCRINOS". Below the header is a navigation menu with "HOME", "QUEM SOMOS", "CAMPANHA", "O QUE SÃO EDC'S", and "BIS". A date bar indicates "agosto 11, 2011". The main content area has the title "Projeto de Lei proíbe o bisfenol A no Estado de São Paulo" and "Posted by blogbisfenol". It includes a "5" icon and a "Curtir" button. A photograph of a fountain pen is shown. The text reads: "Foi publicado nesta quinta-feira o Projeto de Lei no. 737, que proíbe a comercialização de mamadeiras, chupetas e outros produtos utilizados para acondicionar alimentos e/ ou bebidas destinados ao consumo de crianças, adultos e animais, que contenham na sua composição o produto químico Bisfenol A (BPA), no Estado de São Paulo. O Projeto de Lei de no. 737, de autoria do Deputado José Bittencourt, do PDT, apresenta os riscos da substância à saúde humana e, a exemplo de outros países, sugere a suspensão do componente químico, tendo como base o princípio de precaução. Leia o Projeto de Lei na íntegra:"

[http://www.imprensaoficial.com.br/PortalIO/DO/BuscaDO2001Documento\\_11\\_4.aspx?link=%2F2011%2Flegislativo%2Fagosto%2F11%2Fpag\\_0025\\_AURVMEH1DEI5MeAPLJB79S48FRC.pdf&pagina=25&data=11%2F08%2F2011&caderno=Legislativo&paginaordenacao=100025](http://www.imprensaoficial.com.br/PortalIO/DO/BuscaDO2001Documento_11_4.aspx?link=%2F2011%2Flegislativo%2Fagosto%2F11%2Fpag_0025_AURVMEH1DEI5MeAPLJB79S48FRC.pdf&pagina=25&data=11%2F08%2F2011&caderno=Legislativo&paginaordenacao=100025)

- Bisphenol A (estrogenic)**
- Children's tooth sealant**
- Baby bottles**
- Can linings**
- Nail polish**
- Polycarbonate water bottles**
- Microwave ovenware**
- Flame retardants**
- PVC stabilizers**
- Artificial teeth**
- Adhesives**
- Enamels and varnishes**
- Returnable containers**



# Diabetes em crianças



**Figure 2.25.** A progressive leftward shift in age of onset of childhood type 1 diabetes has been and continues to be observed in the United Kingdom. This trend in a progressively earlier onset of diabetes is consistent with data from other countries. In 1946 no diabetes was shown in children until 16 years of age; in 1970, at 2 years of age. Source: Diabetes, 2002 American Diabetes Association, Inc. [www.medscape.com](http://www.medscape.com) (Used with publisher's permission).

WHO- UNEPE. State of the Science of Endocrine Disrupting Chemicals - 2012



# Crianças: exposição

## Taxa de respiração é o dobro em crianças que em adultos

O dobro de exposição a poluentes atmosféricos em relação ao peso corporal

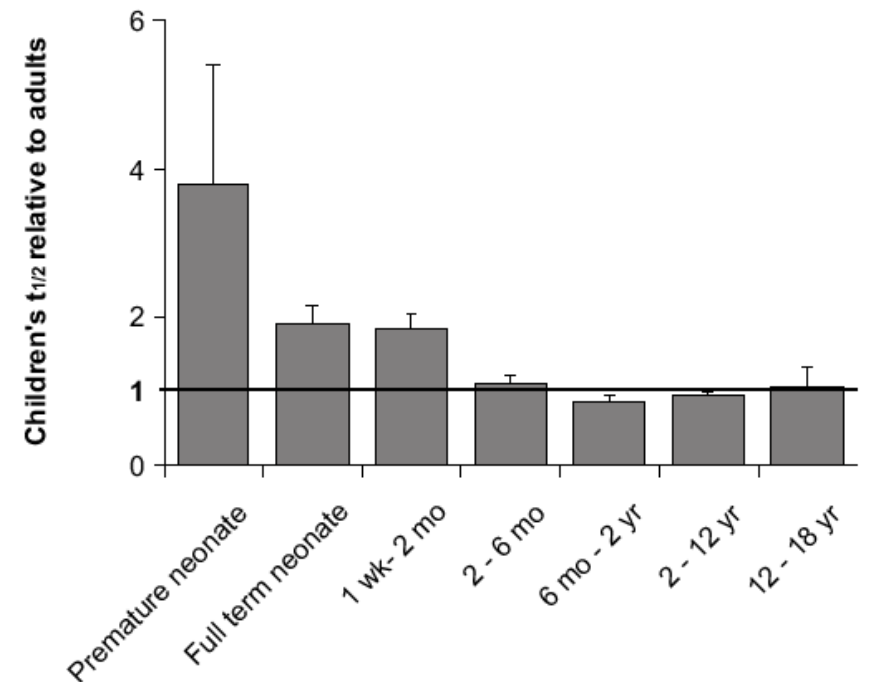
## Excreção renal de xenobióticos é menor

Plasma pobre em albumina

Maturidade renal ocorre apenas por volta de 2 anos

## Taxas de metabolismo e eliminação lentas

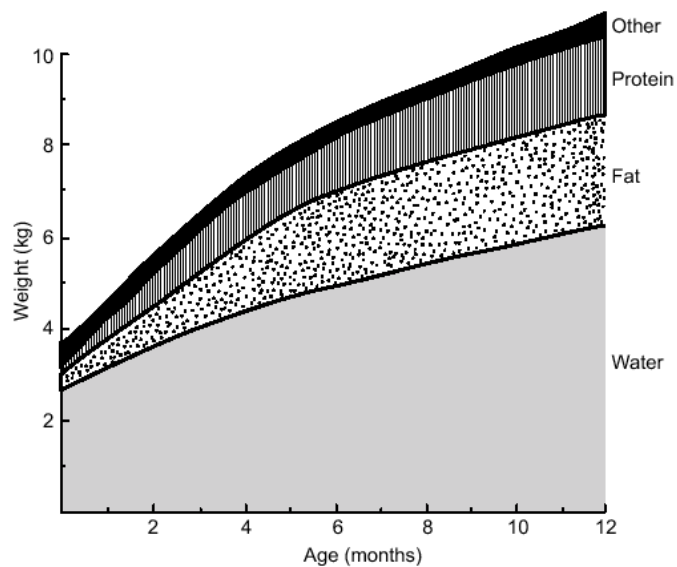
Aumenta a exposição, quando comparada a um adulto



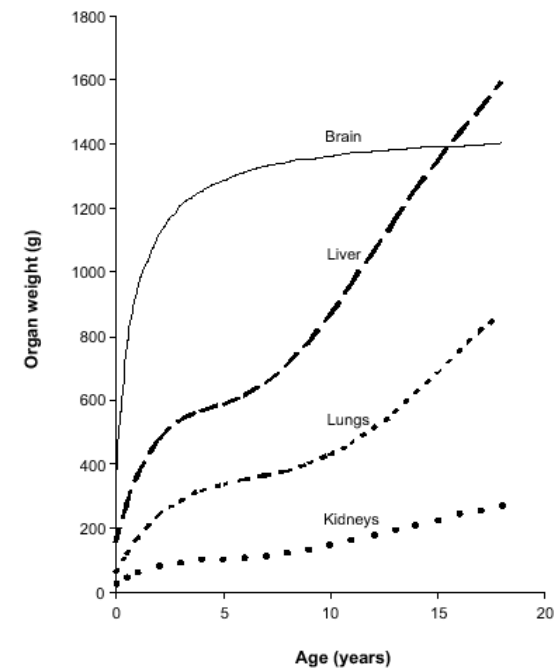


# Bebês e Crianças

- Alterações corporais



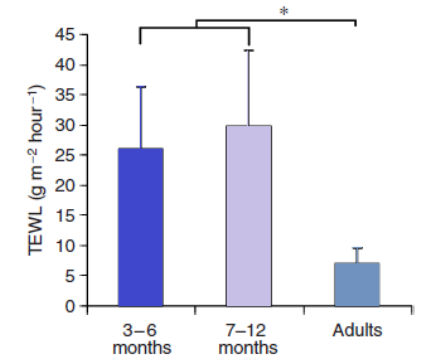
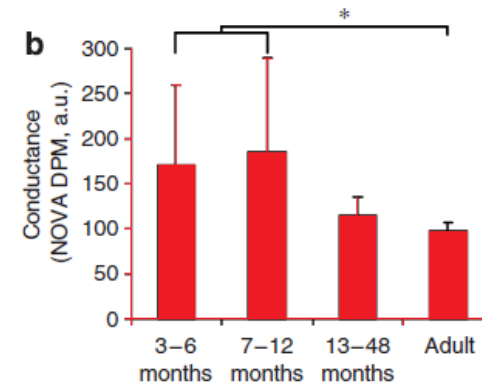
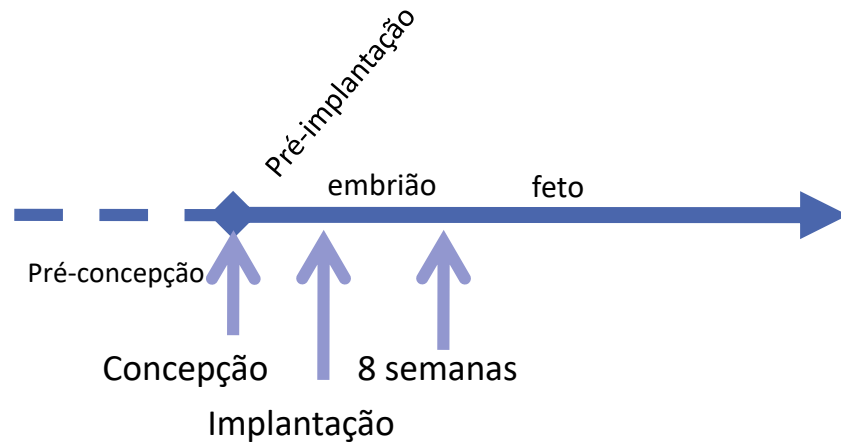
- Desenvolvimento físico





# A pele do bebê neonato a termo

- Membrana basal menos estruturada
- Glând. Sudoríparas écrinas
  - Resfriamento
- Renovação e síntese de manto hidrolipídico ajustadas



Adam. Pediatric Dermatology 25 (4): 427-433, 2008



# Dermatite atópica e Alergias

- Atinge cerca de 15% das crianças
- Usualmente desaparece após os 3 anos
  
- Marcha atópica
  - Dematite atópica
  - Rinite alérgica
  - Asma
  
- 60% crianças têm crises de bronquite antes dos 3 anos, mas poucas desenvolvem asma
  
- Adultos asmático
  - + 50% 1º surto antes dos 3 anos
  - + 80% antes dos 6 anos

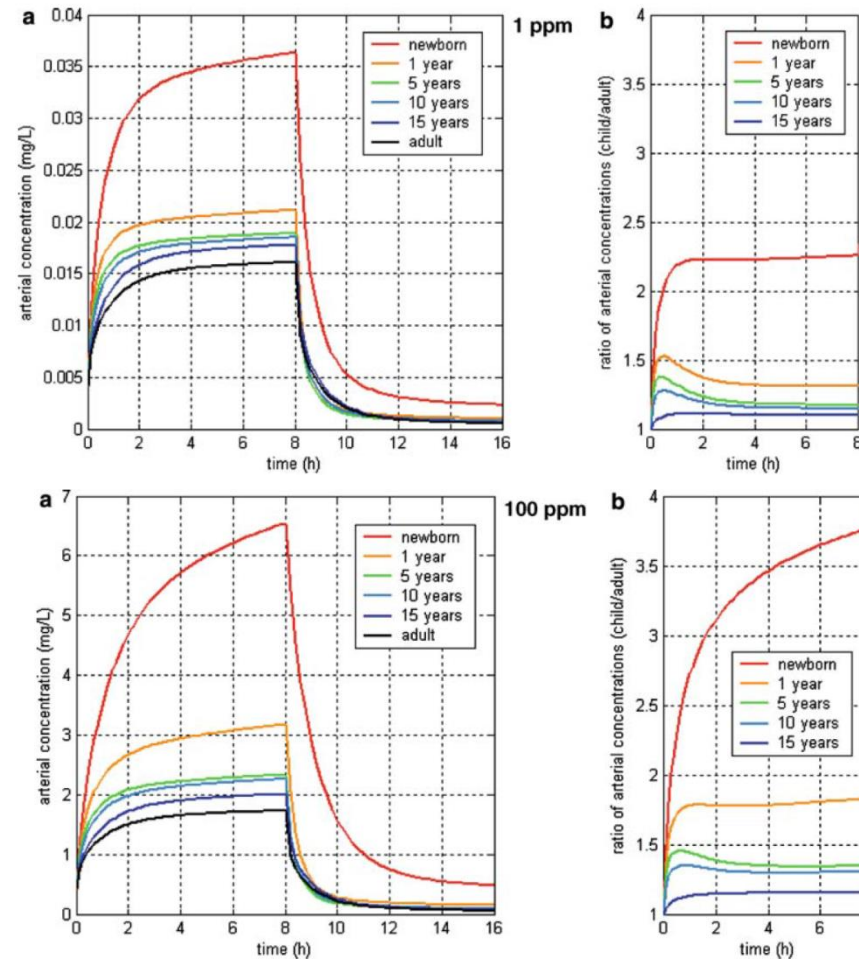




# Superexposição de crianças

## Arch Toxicol (2005) 79: 63–73

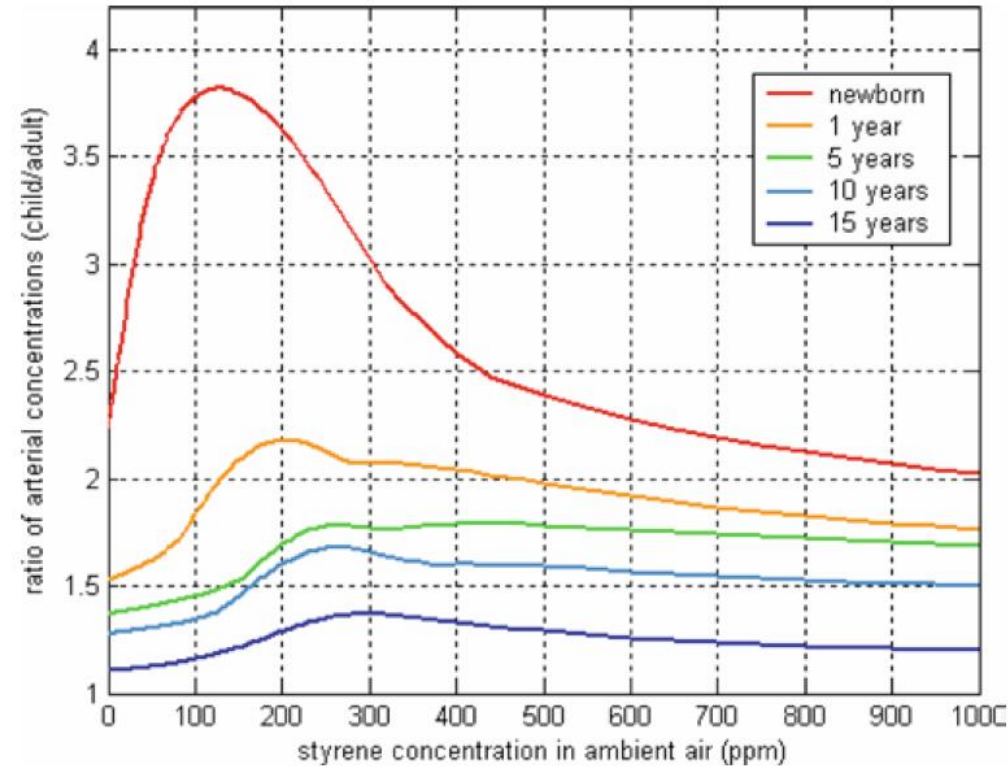
**Fig. 2** Model calculations for the inhalation exposure to styrene, with concentrations in ambient air of 1 ppm.  
**a** Concentration–time profile in arterial blood during styrene exposure for 8 h and the following 8 h in children (newborn, 1-, 5-, 10-, and 15-year-old) and the adult.  
**b** Corresponding ratios of arterial concentrations (child/adult) during the 8-h exposure






# Superexposição de crianças

Arch Toxicol (2005) 79: 63–73



**Fig. 5** Ratios of arterial concentrations (child/adult) after a styrene exposure duration of 8 h, depending on the concentration in ambient air, in children of different ages (newborn, 1-, 5-, 10-, and 15-year-old)



# Estudo com brinquedos aromatizados

## Indoor Air 21: 501–511, 2011

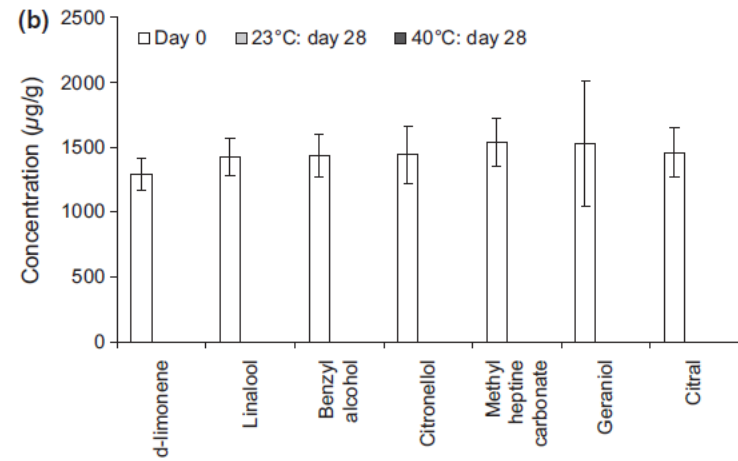
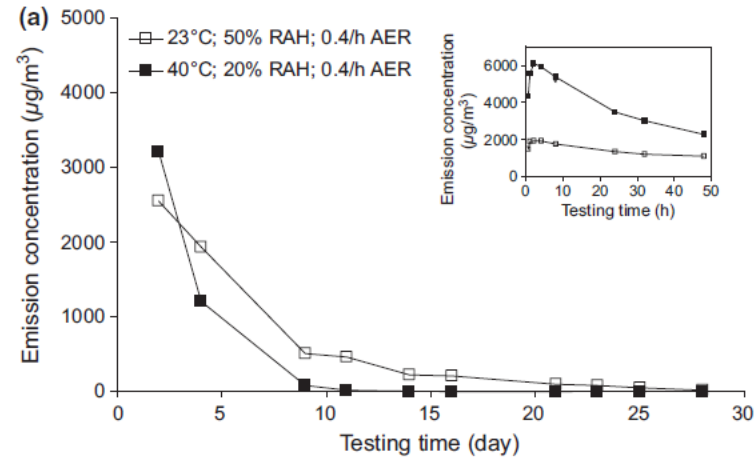
**Table 1** Retention times, quantifier, linearity, limit of detection (LOD), limit of quantitation (LOQ), precision, and suppliers of all fragrances under consideration

No.	Retention time (min)	Fragrance	CAS	Boiling point (°C)	Quantifier (m/z)	R <sup>2</sup>	LOD (ng)	LOQ (ng)	Precision (n = 6) (%)
1	12.20	d-Limonene <sup>a,1</sup>	5989-27-5	177	68	0.997	8.03	10.6	0.88
2	18.68	Linalool <sup>a,2</sup>	78-70-6	198	71	0.997	7.16	9.45	3.22
3	19.16	Benzyl alcohol <sup>b,3</sup>	100-51-6	205	108	0.997	10.2	13.2	2.85
4	23.83	Methyl heptine carbonate <sup>a,2</sup>	111-12-6	219	123	0.997	7.41	9.16	1.34
5	25.19	Citronellol <sup>a,3</sup>	106-22-9	225	81	0.997	8.13	10.8	5.23
6	26.41	Geraniol <sup>b,3</sup>	106-24-1	229	93	0.994	7.25	8.93	5.77
7	26.20/27.60	Citral <sup>b,3</sup>	5392-40-5 (mixture of <i>E/Z</i> isomers)	229	69	0.996	11.4	15.2	4.33
8	29.39	Cinnamal <sup>b,3</sup>	104-55-2	240	131	0.996	14.1	18.8	1.43
9	30.56	Hydroxy citronella <sup>b,1</sup>	107-75-5	252	59	0.991	9.03	11.1	6.29
10	30.90	Anisyl alcohol <sup>a,1</sup>	105-13-5	259	138	0.992	11.2	12.4	1.19
11	31.59	Cinnamyl alcohol <sup>b,1</sup>	104-54-1	250	134	0.999	9.08	12.3	1.24
12	31.79	Eugenol <sup>b,3</sup>	97-53-0	256	164	0.994	9.39	12.4	1.58
13	35.15	Isomethyl- $\alpha$ -ionone <sup>a,1</sup>	127-51-5	266	150	0.995	4.23	5.54	0.84
14	36.11	Isoeugenol <sup>b,2</sup>	97-54-1	267	164	0.999	6.89	9.06	2.44
15	37.62	Lilial <sup>a,4</sup>	80-54-6	279	189	0.995	12.4	16.6	11.7
16	38.06	Coumarin <sup>b,3</sup>	91-64-5	301	118	0.999	11.5	15.4	2.17
17	42.24	Amyl cinnamal <sup>b,2</sup>	122-40-7	289	145	0.999	0.67	0.86	3.51
18	44.23	Famesol <sup>a,2</sup>	4602-84-0 (mixture of isomers)	283	69	0.999	1.40	1.78	4.55
19	44.59	Amyl cinnamyl alcohol <sup>b,1</sup>	101-85-9	>200	91	0.999	0.88	1.15	3.34
20	44.88	Lyral <sup>b,3</sup>	31906-04-4	319	136	0.996	0.81	1.07	1.52
21	45.64	Hexyl cinnamaldehyde <sup>a,2</sup>	101-86-0	308	145	0.999	0.59	0.63	2.35
22	46.86	Benzyl benzoate <sup>a,3</sup>	120-51-4	324	105	0.999	0.88	1.14	3.78
23	50.27	Benzyl salicylate <sup>b,2</sup>	118-58-1	320	91	0.999	0.87	1.14	2.01
24	57.81	Benzyl cinnamate <sup>a,2</sup>	103-41-3	370	131	0.998	0.53	0.68	11.0
25	18.93	Benzyl-d7 alcohol	71258-23-6		85				
26	37.90	Coumarin-5,6,7,8-d4	185056-83-1		122				

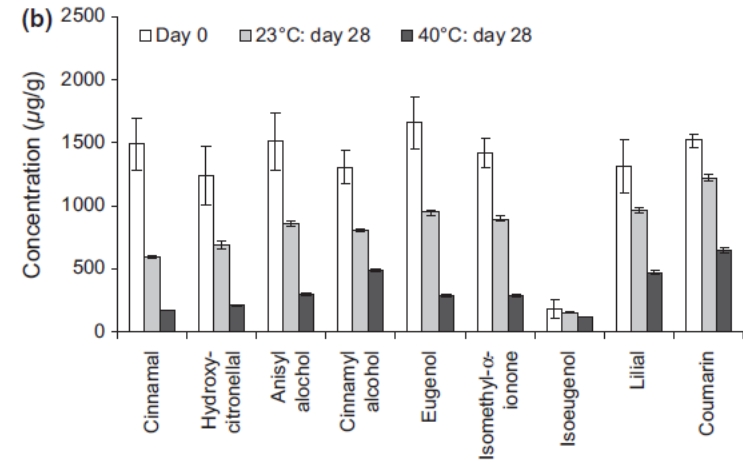
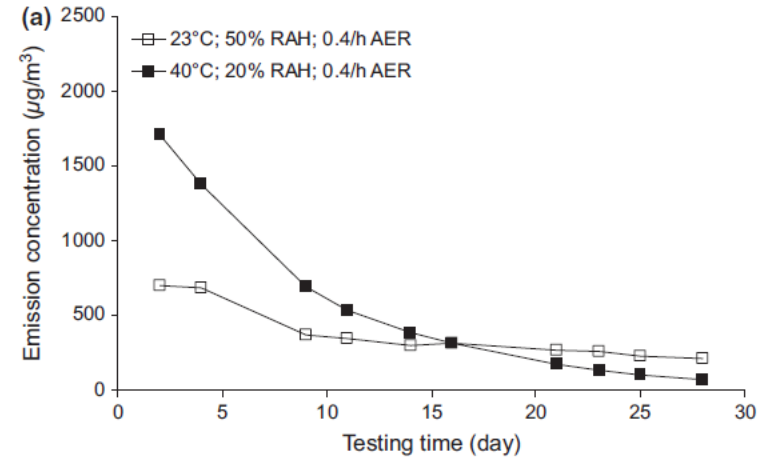
<sup>a</sup>According to Directive 2009/48/EC, 2009, compound requires declaration when contents of 100  $\mu$ g/g in the material are exceeded.

<sup>b</sup>Banned compound according to the Toy Safety Directive 2009/48/EC, 2009.

Suppliers: <sup>1</sup>Fluka Chemie (Steinheim, Germany). <sup>2</sup>SAFC Supply Solutions (St. Louis, MO, USA). <sup>3</sup>Sigma-Aldrich Chemie (Steinheim, Germany). <sup>4</sup>BASF Chemtrade GmbH (Burgbernheim, Germany).



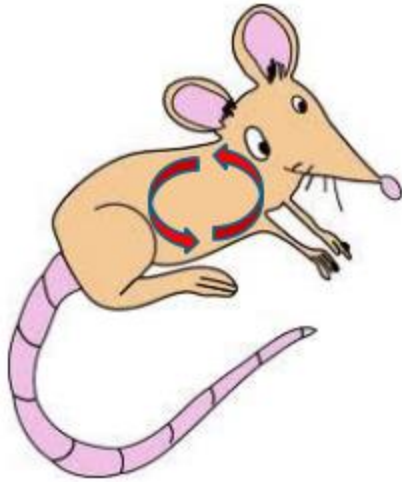
**Fig. 1** (a) Emission profiles of benzyl alcohol measured at two different conditions over a testing period of 28 days or during the first 48 h (inset). (b) Contents of highly volatile fragrances in the material at the start of monitoring (day 0) and the remaining amounts after 28 days at 23°C or 40°C



**Fig. 2** (a) Emission profiles of cinnamal measured at two different conditions over a testing period of 28 days. (b) Contents of semivolatile fragrances in the material at the start of monitoring (day 0) and the remaining amounts after 28 days at 23°C or 40°C



# LOW DOSE



Reference  
Dose

NOAEL

LOAEL

Max  
Tolerated  
Intake



# Exposição a baixas-doses e Toxicidade não monotônica

Definição de LOW DOSE???

**Table 1.**

Low-dose definitions and cutoff doses: BPA and DEHP as examples

Chemical	Estimated range of human exposures	Doses below the NOAEL	Doses below the LOAEL	Administered doses (to animals) that produce blood levels in typical humans
BPA	0.4–5 µg/kg · d ( <a href="#">679</a> )	No NOAEL was ever established in toxicological studies ( <a href="#">38</a> )	<50 mg/kg · d ( <a href="#">38</a> )	~400 µg/kg · d to rodents and nonhuman primates ( <a href="#">4</a> , <a href="#">253</a> )
DEHP	0.5–25 µg/kg · d ( <a href="#">680</a> )	<5.8 mg/kg · d ( <a href="#">681</a> , <a href="#">682</a> )	<29 mg/kg · d ( <a href="#">681</a> , <a href="#">682</a> )	Unknown

Estimates of human exposure are made from consumer product consumption data but do not take into account that there are unknown sources of these chemicals. DEHP, Bis(2-ethylhexyl) phthalate.

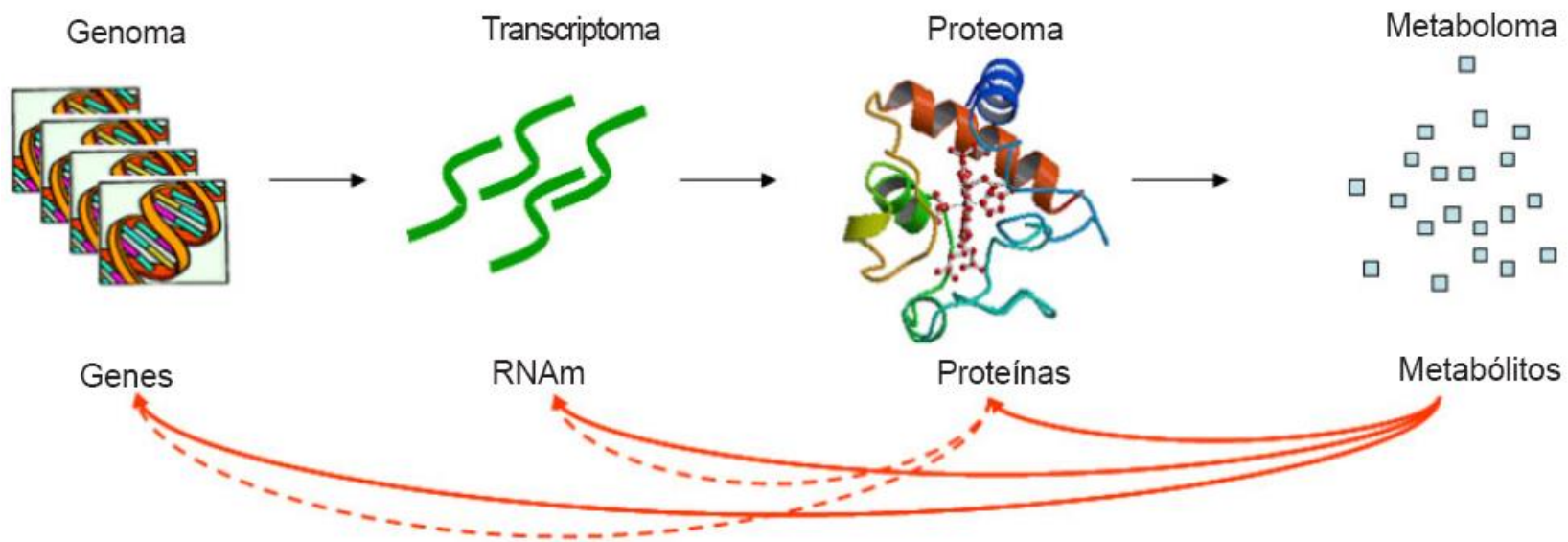


# DES e obesidade



- 1000 ppb exposures cause weight loss (not shown here)
- 1 ppb exposures cause extreme obesity

# Progressos importantes

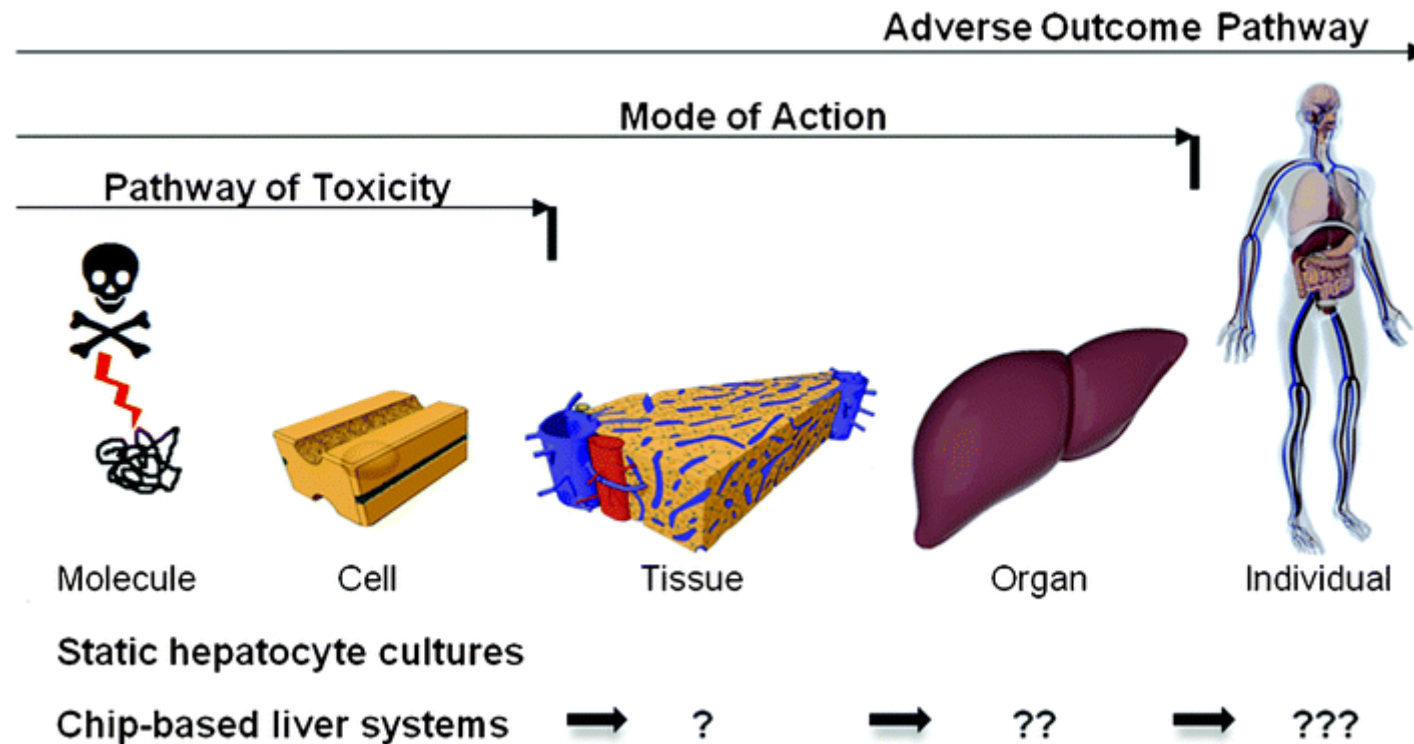


Villas-Boas, S. e Gombert, A.K. *Biotecnologia, Ciência e Desenvolvimento*, 36, 2006





# Adverse Outcome Pathway

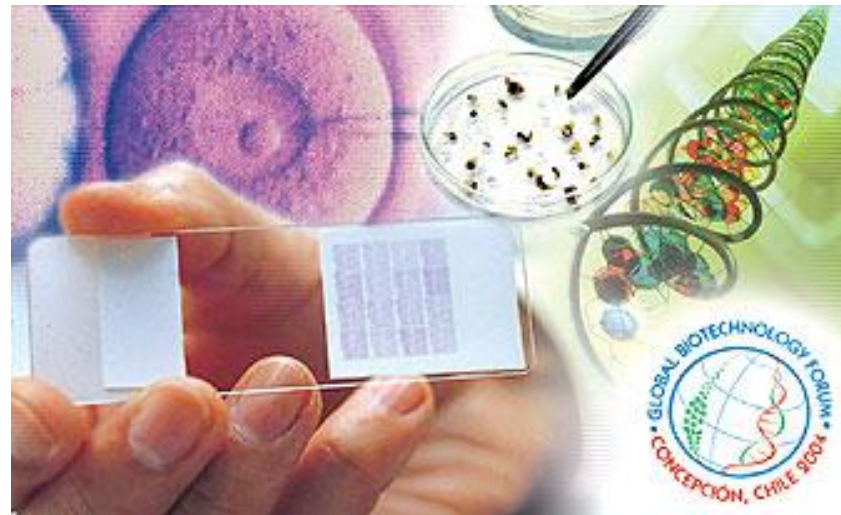


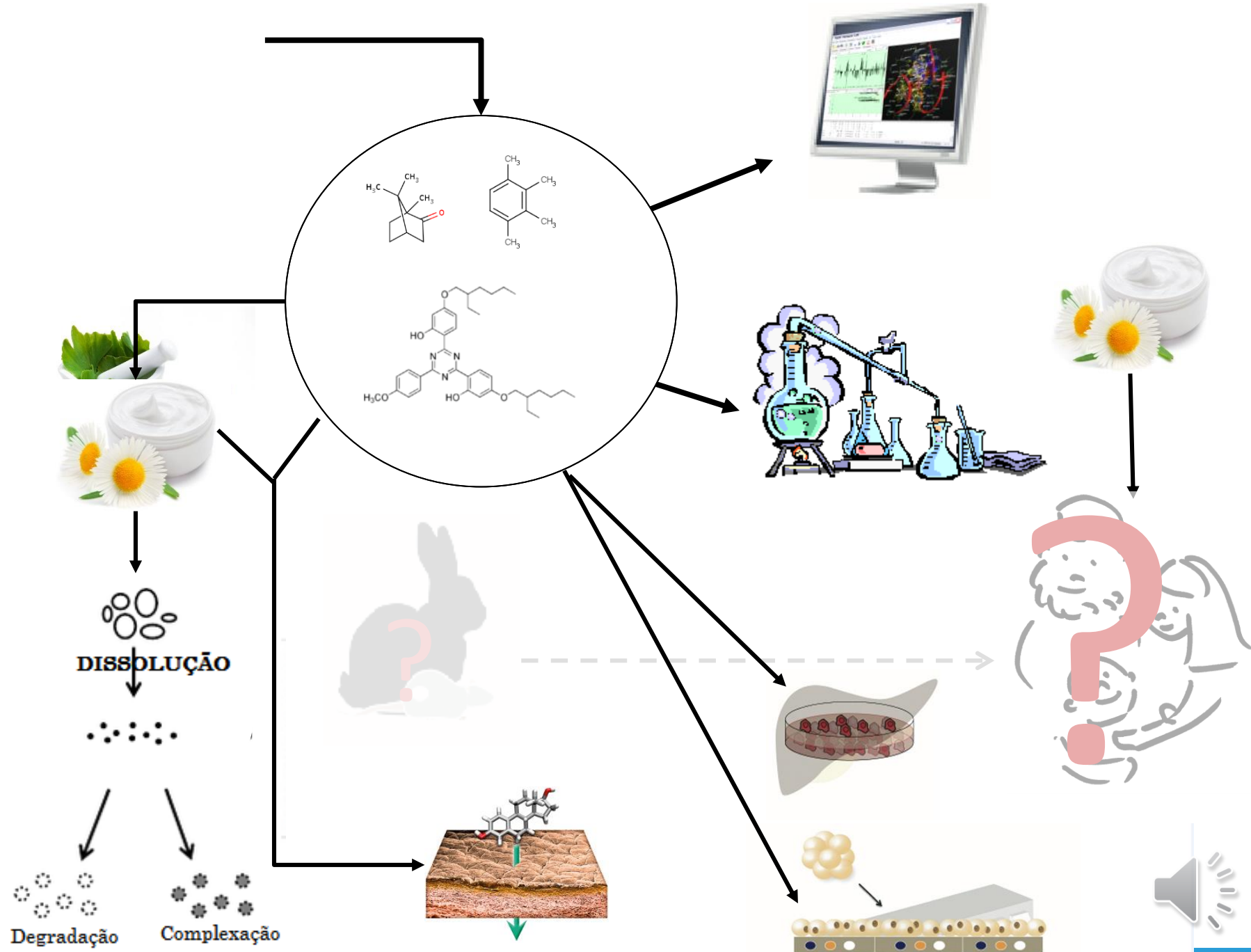
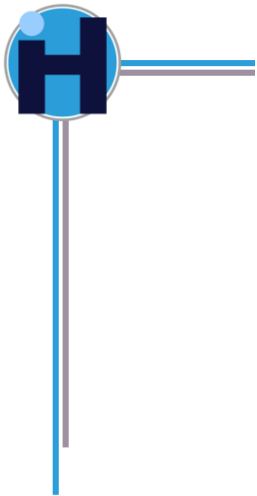




# Ganhos indiretos

- Desenvolvimento de métodos analíticos
- Aprimoramento das técnicas de ensaio *in vitro*
- Compreensão dos processos





DISSOLUÇÃO

Degradação

Complexação



# Problemas com a segurança de produtos



# VEGF (Fator de Crescimento Endotelial Vascular)





# Nem sempre faz tão bem assim....



CHEMICAL EXPOSURES

## The Ugly Side of Beauty Products

In recent decades reproductive and developmental problems have become more prevalent—for example, data from the Centers for Disease Control and Prevention (CDC) show that male reproductive problems, including undescended testicles and hypospadias, doubled between 1970 and 1993. Environmental chemicals are strongly suspected to be contributing factors. Several recent reports highlight the presence of low-level concentrations of potential reproductive or developmental toxicants, particularly phthalates, in cosmetics and personal care products. A key question is whether these exposures are significant enough to cause harm.

In June 2004, Environment California issued *Growing Up Toxic: Chemical Exposures and Increases in Developmental Diseases*, which details chemicals found in consumer products and their potential health impacts. Other reports released around the same time by the Environmental Working Group (*Skin Deep: A Safety Assessment of Ingredients in Personal Care Products*) and Friends of the Earth (*Shop Till You Drop? Survey of High Street Retailers on Risky Chemicals in Products 2003–2004*) support Environment California's publication.

According to these three reports, makeup, shampoo, skin lotion, nail polish, and other personal care products contain chemical ingredients that lack safety data. Moreover, some of these chemicals have been linked in animal studies to male genital birth defects, decreased sperm counts, and altered pregnancy outcomes. There is no definitive evidence for the same effects in humans, but widespread exposure, primarily to phthalates, has been shown to occur.

Phthalates, as key components in plastics, appear in many consumer products. The main phthalates in cosmetics and personal care products are dibutyl phthalate in nail polish, diethyl phthalate in perfumes and lotions, and dimethyl phthalate in hair spray. Often, their presence is not noted on labels.

"The concerns that are focused around this particular chemical [class] have arisen from a series of tests and

studies that have been released recently that point to significant potential health concerns," says Sujatha Jahagirdar, an environmental advocate with Environment California. For example, a population study conducted by the CDC and published in the March 2004 issue of *EHP* demonstrated that 97% of 2,540 individuals tested had been exposed to one or more phthalates. Another preliminary study conducted at the Harvard School of Public Health and published in the July 2003 issue of *EHP* showed a correlation between urinary phthalate metabolite concentrations and DNA damage in human sperm. However, exposure sources in this study were unknown.

The personal care industry remains confident about phthalate safety, however. The Cosmetic Ingredient Review panel, an independent research group sponsored by the Cosmetic, Toiletry, and Fragrance Association, published a detailed literature review in February 2003 that unequivocally states that current use of phthalates in cosmetics and personal care products is safe. Marian

Favor me with silence.  
Horace (65–8 B.C.)

Stanley, manager of the Phthalate Esters Panel of the American Chemistry Council, says, "Some of these concerns [from environmental groups] are based on high-dose animal testing. The exposure that we really see in people—and we have the CDC numbers to back that up—is remarkably low. To us, why bother getting rid of a highly useful product when there should be no concern?"

Therein lies the controversy—environmental groups view the CDC data as evidence of widespread exposure, whereas industry groups view it as evidence of low-level exposure that falls well below amounts shown to cause problems in animal studies. The environmental groups respond that although it may be low-level exposure, it is *chronic* low-level exposure. Says Elizabeth Sword, executive director of the nonprofit Children's Health Environmental Coalition: "In my view there is sufficient evidence to pique my concern, not only as a parent but as the executive director of this organization, to circulate this information directly to parents in a way that they can then make the healthiest decisions."

However, consumers cannot make such judgments without knowing the ingredients contained in the products they use. "There are industry trade secrets and formulations that for industry reasons are kept from the consumer," says Sword. "This prevents the consumer from making fully informed decisions."

Environment California and the other environmental organizations hope to change that through consumer education and policy reform at the state and federal levels. "Environment California is pushing for a common-sense chemical policy that requires chemical manufacturers to test . . . their chemicals before they are released into the market and also provide the public with the tools that it needs to protect itself from potential dangerous impacts," says Jahagirdar. "Labeling is an extremely important and ethical thing for manufacturers to be doing."

"I think a lot of this comes down to an individual's acceptance of risk," says Sword. "[Each person's] personal risk tolerance is different. I think what we as a society need to feel confident about is that adults will at least make better decisions if you give them a way to do so, particularly when the health of a child may be at risk from making a bad decision." —Julia R. Barrett



Starting too young? Concern is mounting over the effects of long-term exposures to chemicals—such as phthalates—found in cosmetics and personal care products.

VOX/RENY

# Uso cada vez mais precoce...



# Desafios

- Coexistência sustentável entre biodiversidade, biotecnologia e saúde
- Relação e a integração da natureza com a sociedade
- Regulamentação internacional

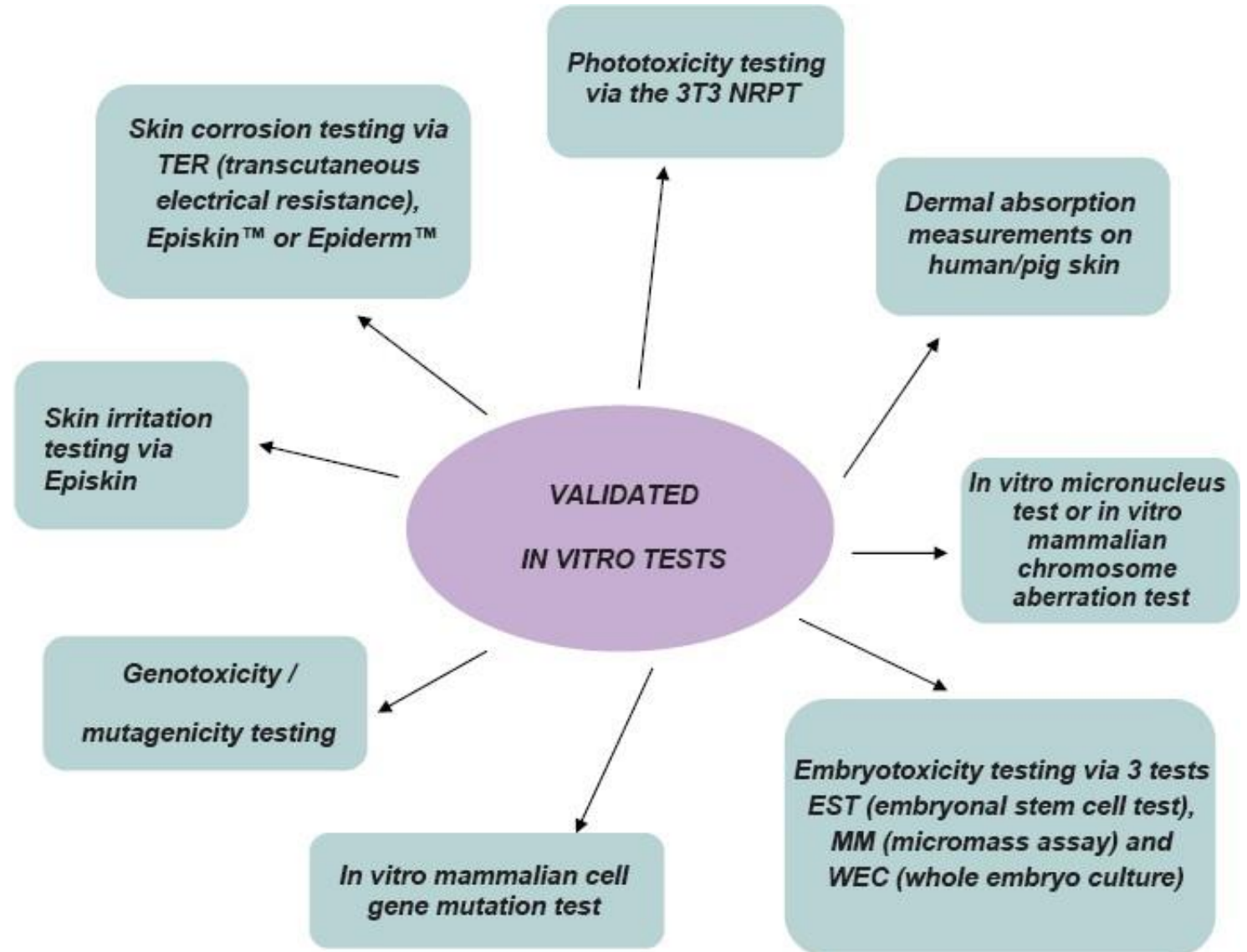


Garcia, E. *Cad. Saúde Públ.*, **11 (3)**: 491-494,1995.

Noury e Chiba, *Nature biotechnology*, **27 (3)**: 234-236, 2009.



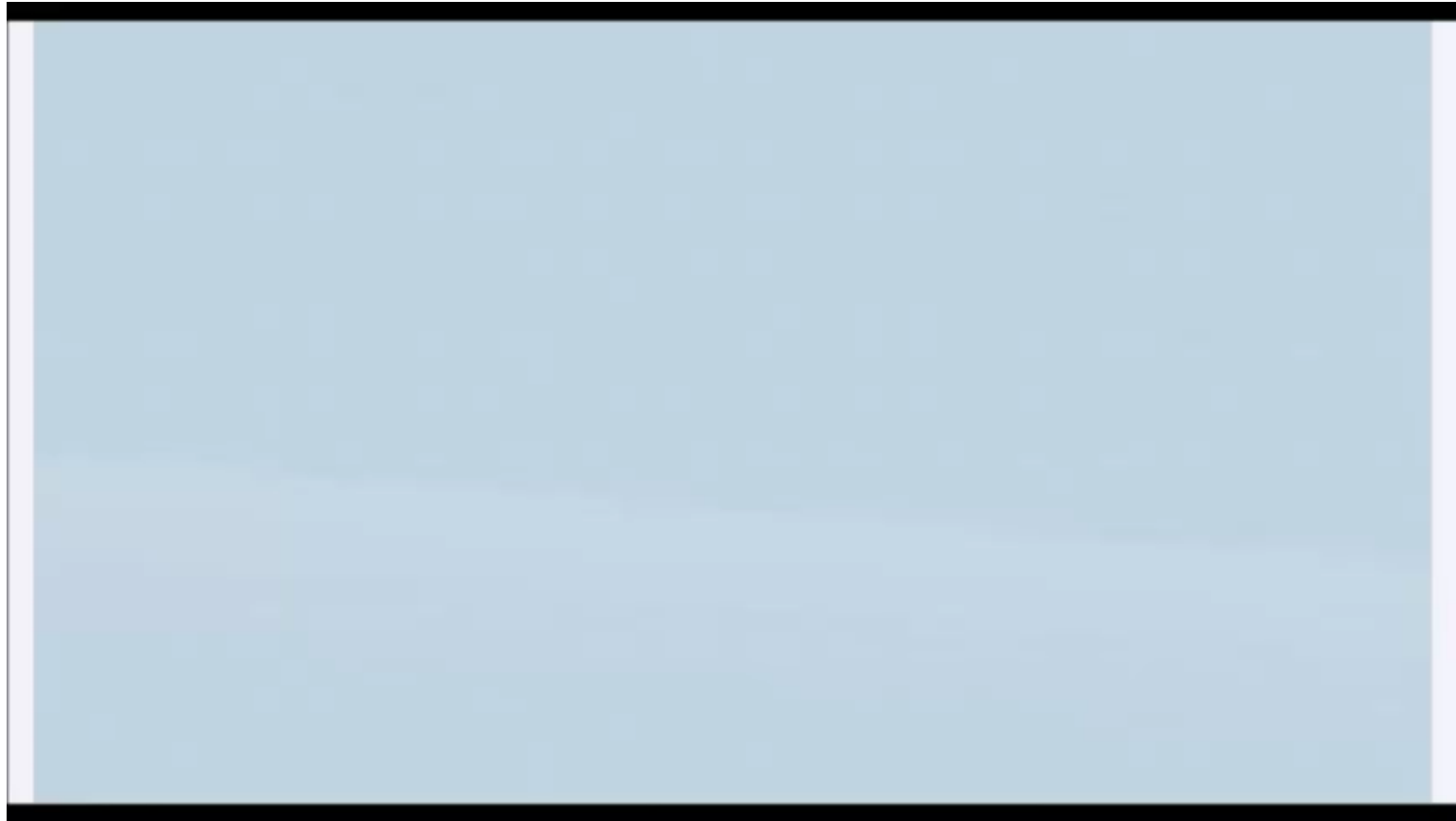
# Oportunidades







# Importante...





# Obrigada

