



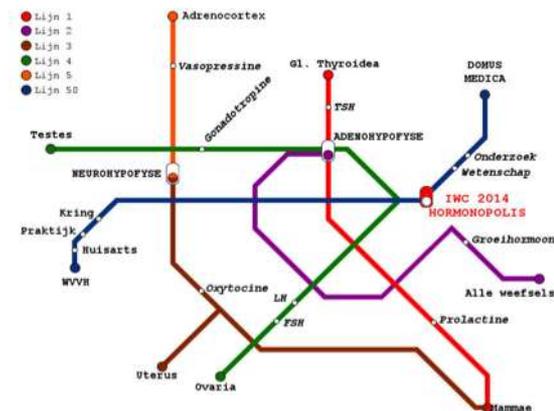
Help, ... hormonen op mijn bord?

Prof. L. Vanhaecke

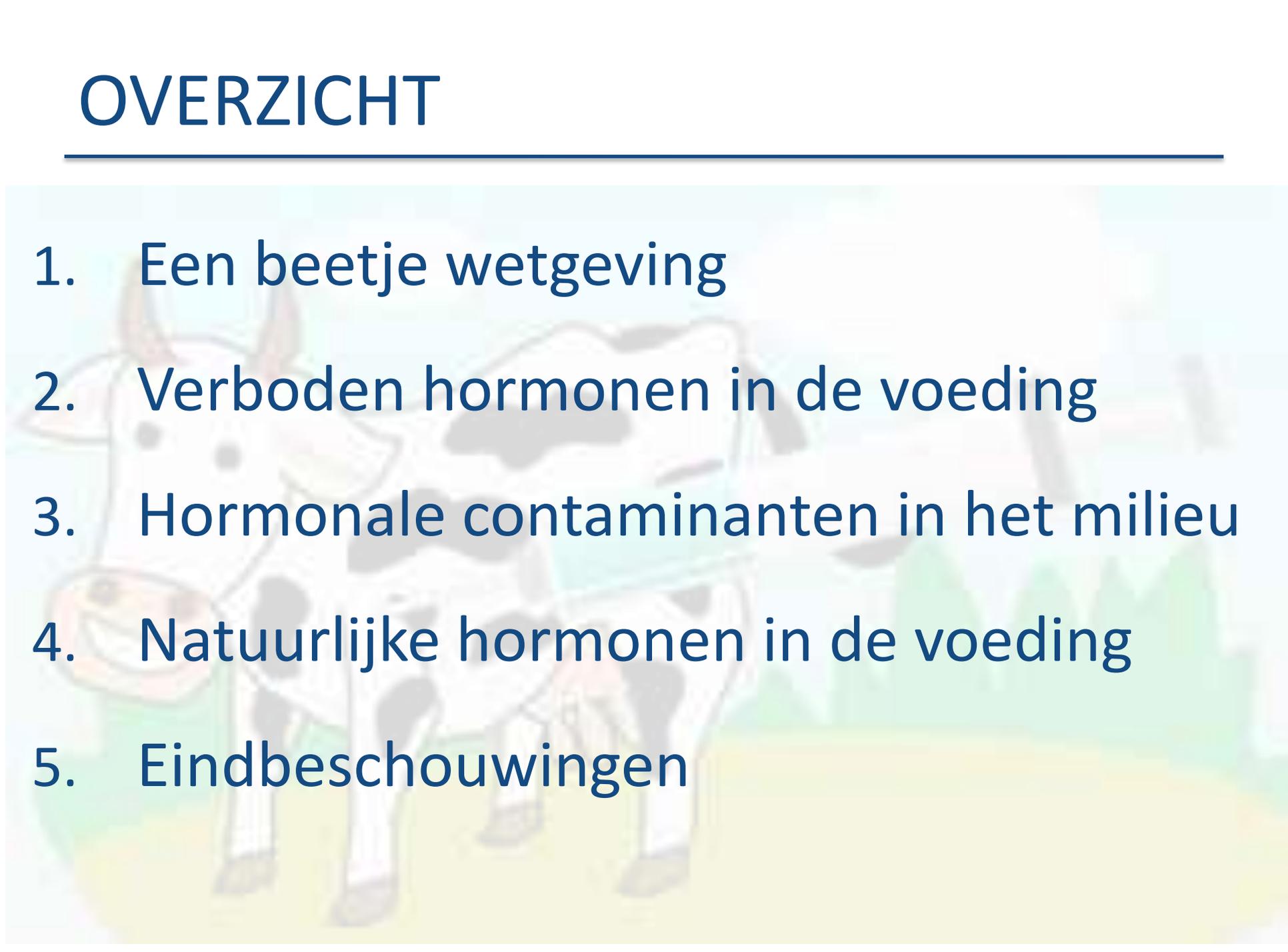
Vakgroep Veterinaire Volksgezondheid en Voedselveiligheid

Faculteit Diergeneeskunde

Universiteit Gent



OVERZICHT

1. Een beetje wetgeving
 2. Verboden hormonen in de voeding
 3. Hormonale contaminanten in het milieu
 4. Natuurlijke hormonen in de voeding
 5. Eindbeschouwingen
- 
- A faint, stylized illustration of two cows in a field. One cow is in the foreground, facing left, and another is behind it, facing right. The background shows a green field and some trees under a light sky.

Vraag 1:

Is het gebruik van hormonen in de dierlijke productie toegelaten in Europa?

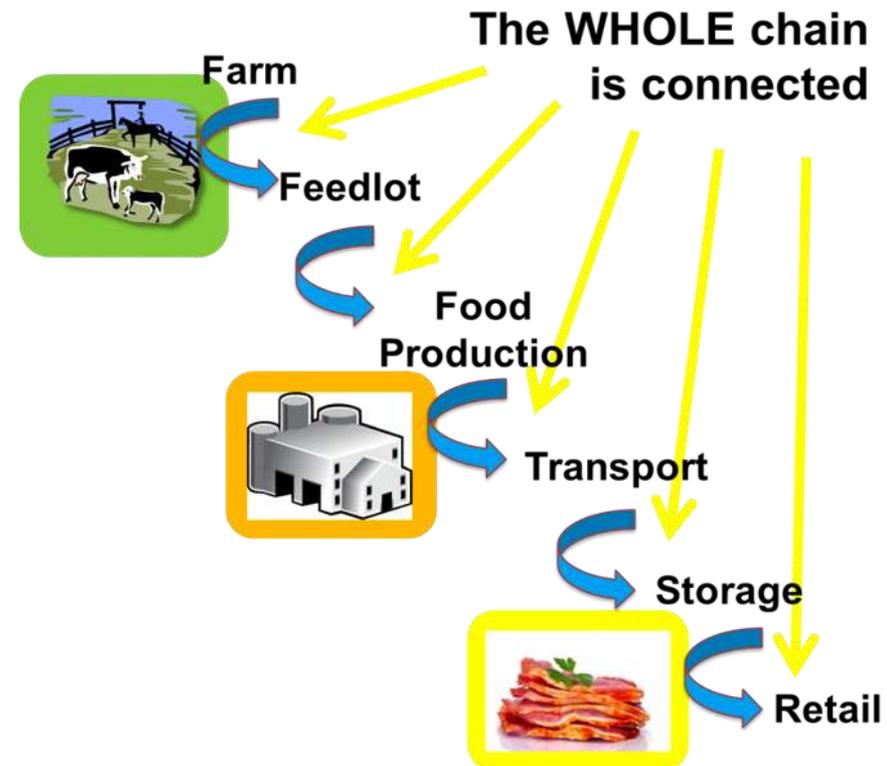
- A. Ja, maar tot aan bepaalde concentraties
- B. Neen, er heerst een absolute nultolerantie
- C. Enkel natuurlijke hormonen (estradiol, testosteron, ...) zijn toegelaten

Voedselveiligheid in Europa: *from farm to fork*

- 2002: General Food Law (EG) Nr. 178/2002
- DG SANCO met Food and Veterinary Office (FVO)
- RASSF (Rapid Alert System for Feed and Food)



- EFSA



Voedselveiligheid in België: *van riek tot vork*

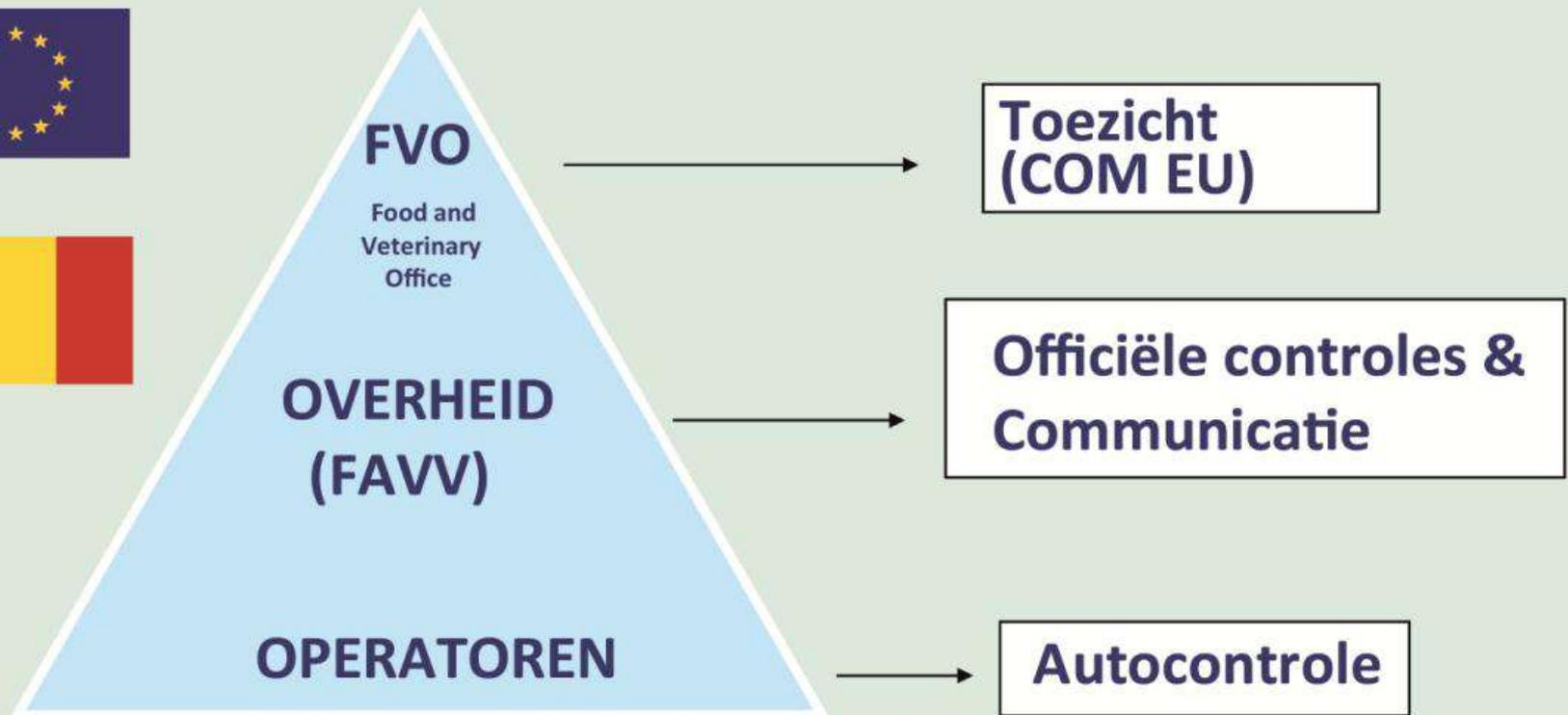
- FAVV: Federaal Agentschap voor de Veiligheid van de Voedselketen

FAVV in Europese context



Gen.FOOD.LAW Verord. (EG) 178/2002

ART. 17 : VERANTWOORDELIJKHEDEN



Wetgeving op residuen in dierlijke producten

COUNCIL DIRECTIVE 96/23/EC

of 29 April 1996



on measures to monitor certain substances and residues thereof in live animals and animal products and repealing Directives 85/358/EEC and 86/469/EEC and Decisions 89/187/EEC and 91/664/EEC

CHAPTER I

Scope and definitions

Article 1

This Directive lays down measures to monitor the substances and groups of residues listed in Annex I.

Group A: Substances with anabolic effects and unauthorized substances

- Stilbenes, stilbene derivatives, and their salts and esters
- Antithyroid agents
- Steroids
- Resorcylic acid lactones including zeranol
- β -agonists
- Compounds included in Annex IV to Council Regulation 96/23/EC²

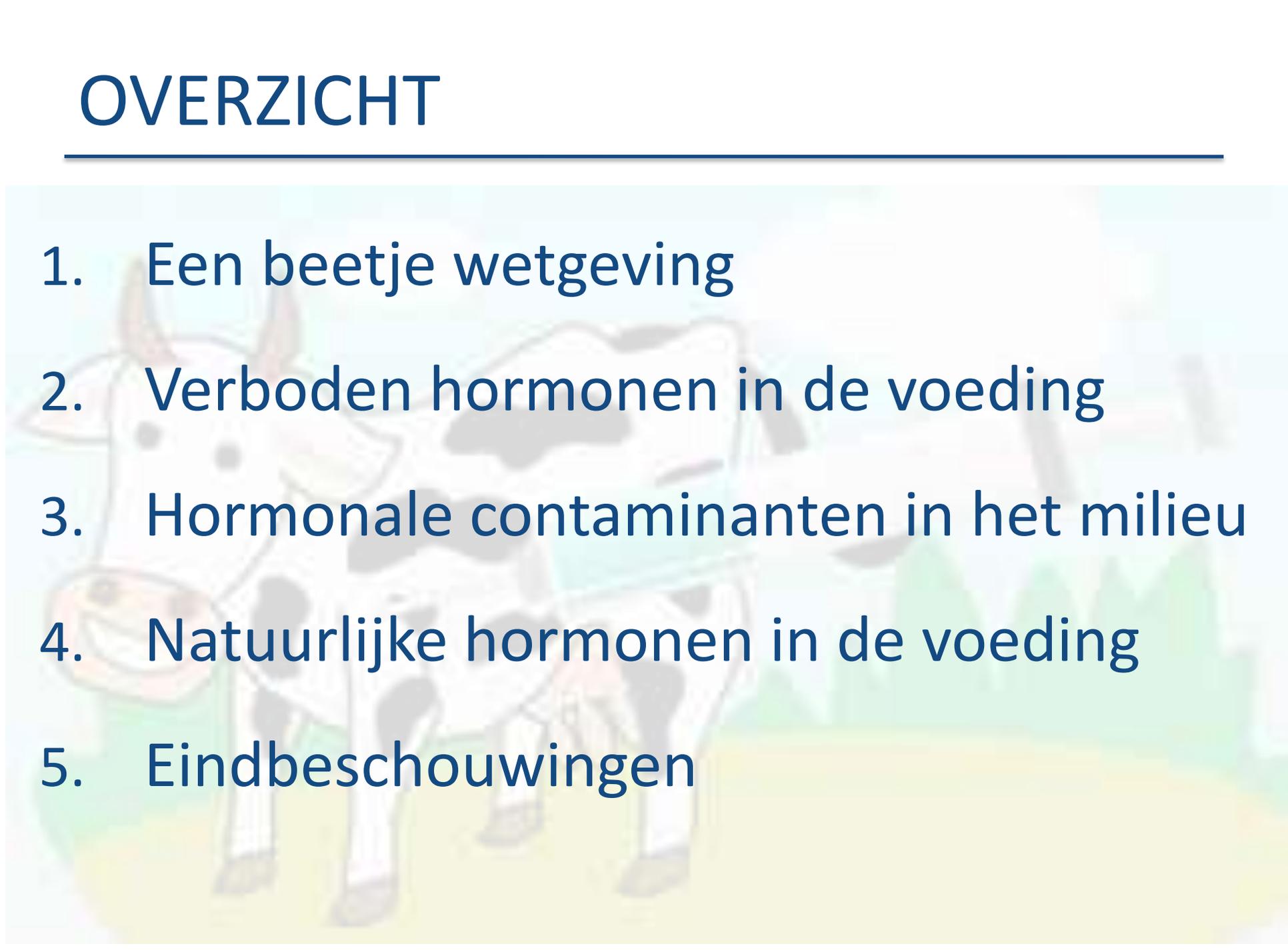


Group B: Veterinary drugs and contaminants

- Antibacterial substances, including sulphonamides and quinolones
- Other veterinary drugs
 - Anthelmintics
 - Anticoccidiostats, including nitroimidazoles
 - Carbamates and pyrethroids
 - Carbadox and olaquinox
 - Sedatives
 - Non-steroidal anti-inflammatory drugs (NSAIDs)
 - Other pharmacologically active substances
- Other substances and environmental contaminants
 - Organochlorine compounds including PCBs
 - Organophosphorus compounds
 - Chemical elements
 - Mycotoxins
 - Dyes
 - Others



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- A faint, stylized illustration of a cow with black and white spots, standing in a green field with trees in the background. The illustration is semi-transparent and serves as a background for the text.

Vraag 2:

Welk van volgende medische aandoeningen werd reeds vastgesteld bij personen die hamburgers aten met schildklier in verwerkt?

- A. Thyrotoxicose, een type hyperthyroïdisme
- B. Aplasia cutis congenita, een schedeldefect
- C. Papillaire schildklierkanker

HORMONEN: ... VERBODEN



1. THYREOSTATICA: *schildklierremmers*
→ waterretentie
2. BETA-AGONISTEN: *herverdelers*
→ meer spier, minder vet
3. CORTICOSTEROIDEN
→ waterretentie
4. ANABOLICA: *steroidhormonen*
→ betere karkaskwaliteit

1. THYREOSTATICA



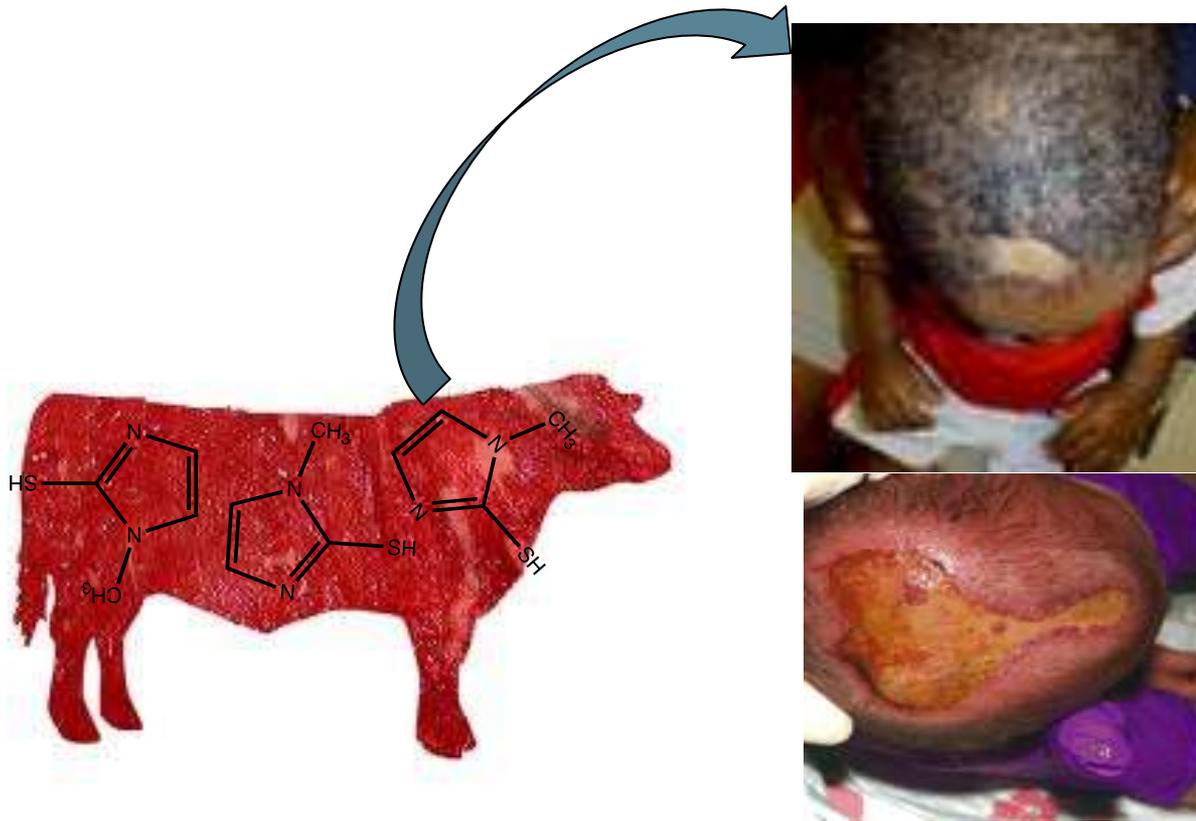
THY
→



- ✧ Inhibitie schildklier, ↓ L-thyroxine, T4 en L-tri-iodothyronine, T3
- ✧ Groeipromotor: ↑ waterretentie
- ✧ ↓ Vleeskwaliteit → Water voor de prijs van vlees!
- ✧ Gezondheidsrisico (groep 2b, IARC), teratogeen

Mogelijke gevolgen?

- ✧ International Agency for Research on Cancer (IARC): groep 2b
- ✧ Aplasia cutis (Spanje): tapazol besmet vlees



→ **HUIDAFWIJING (NEWBORNS)**

Thyrotoxicosis

Thyroid hormones are orally active, which means that consumption of thyroid gland tissue can cause thyrotoxicosis, a type of hyperthyroidism.

Several outbreaks of **thyrotoxicosis** have been attributed to a practice, now banned in the US, called "gullet trimming", where meat in the neck region of slaughtered animals is ground into hamburger. Because thyroid glands are reddish in color and located in the neck, it's not unusual for **gullet trimmers to get thyroid glands into hamburger or sausage.**

People, and presumably pets, that eat such hamburger can get dose of thyroid hormone sufficient to induce disease.

A report by Hedberg et al. (1987) on this topic is one of several in the literature. They described an outbreak of thyrotoxicosis in Minnesota and South Dakota that was traced to thyroid-contaminated hamburger. A total of **121 cases were identified in nine counties**, with the highest incidence in the county having the offending slaughter plant.

The patients complained of sleeplessness, nervousness, headache, fatigue, excessive sweating and weight loss.



2. BETA-AGONISTEN

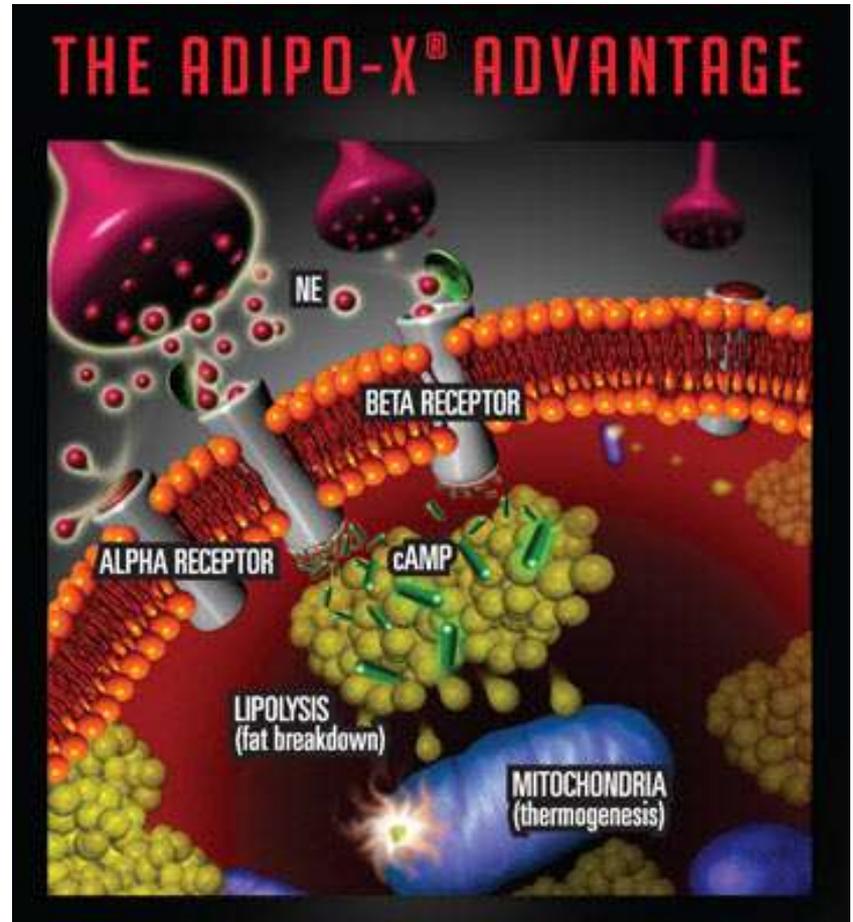
- ✧ Binden op beta-2-receptoren
- ✧ Spierontspanners
- ✧ Bronchodilatoren
- ✧ 5 – 10 x therapeutische dosis



Herverdelers:

↑ Spiermassa

↓ Vetmassa



Clenbuterol intoxicaties

Symptomen:

- Tremoren
- Palpaties of tachycardie
- Agitatie, hoofdpijn, spierpijn
- Duizeligheid
- Asthenie
- Misselijkheid, braken en koorts

30 min. tot 6u na ingestie,
duren 40u

Clenbuterol was found in pork and pork related products, including ham and sausage.

At least 70 people suffered food poisoning after eating pig organs.

Over 330 people were poisoned by eating pork contaminated with clenbuterol.

50 persons were poisoned by clenbuterol containing liver and pork.

A total of 35 reports of clenbuterol poisoning, affecting 82 persons, related to consumption of contaminated pork and pork offal were reported.

A total of 17 persons were affected by clenbuterol food poisoning.

At least 22 persons from France and 113 cases from Spain were reported. Veal liver was believed to be the source of intoxication.

3. CORTICOSTEROÏDEN

Bijnierschors hormonen en synthetische varianten:

- Therapeutisch
- Niet-therapeutisch: gewichtsaanzet, watergehalte vlees verhogen

Bijnierschors hormonen (natuurlijke corticosteroiden):

- Mineralocorticoiden: zout-water balans → bloeddruk
- Glucocorticoiden: stress, vet-, eiwit- en KHmetabolisme
- Anti-inflammatoir, anti-allergisch
- Immunosuppressief

Synthetische glucocorticoïden

vb: dexamethasone, betamethasone, prednisolone, methylprednisolone...

- veel sterkere anti-inflammatoire eigenschappen
- bevorderen gewichtstoename
- verminderen voederconversiesnelheid

Groeipromotoren in rundvee

Richtlijn 96/23/EC:

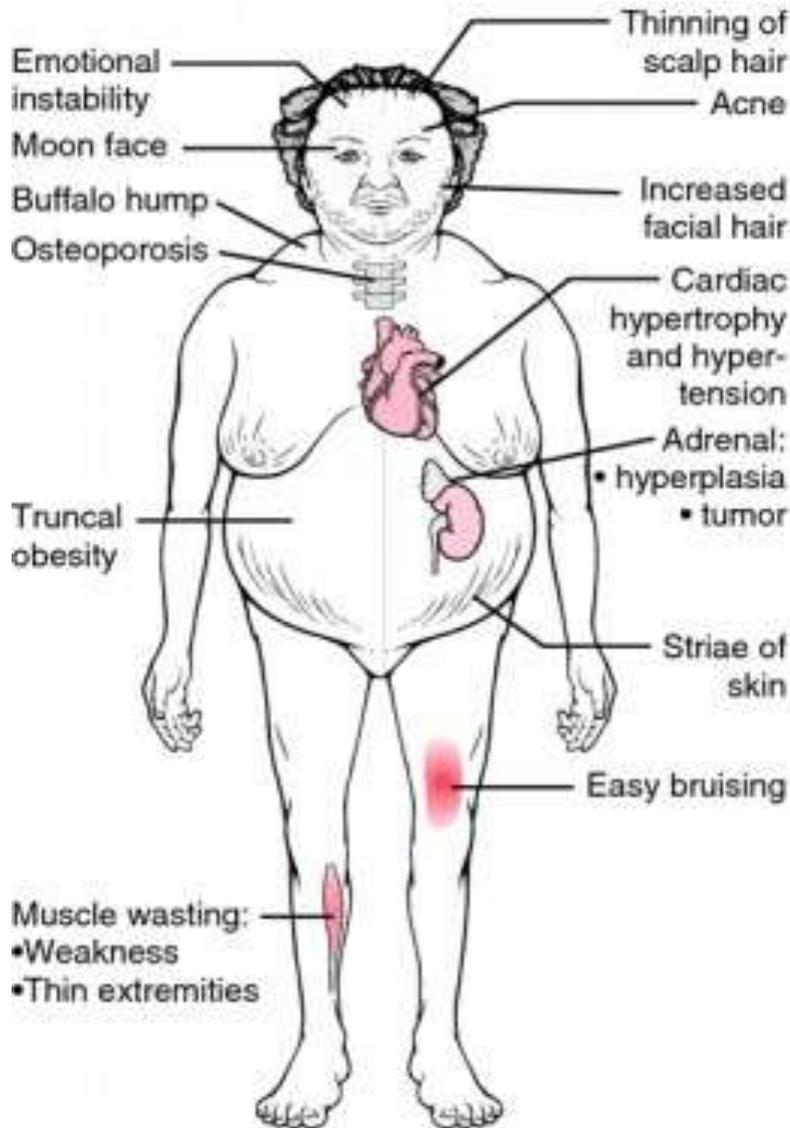
stoffen met hormonale werking

→ **verboden ('zero tolerance')**



→ **MAAR: voor therapeutische doeleinden dexamethasone, prednisolone, methylprednisolone toegelaten, residuen echter sterk gereguleerd.**

Mogelijke gevolgen?



Steroids in pharmacological doses over a prolonged period of time can **cause Cushing's syndrome** with associated **oedema** and **redistribution** of fat.

Fluid retention leads to a swelling of the face called **'mooning'** as the face becomes rounded like a full moon.

A central type of obesity develops with thin extremities, a fatty **'buffalo hump'** on the neck and enlargement of the supraclavicular area (above collar bone or clavicle).

These features are related to excessive **protein catabolism** (where breakdown of stored protein is used as fuel in times of stress) as well as **sodium and water retention**. The retention of sodium and water also leads to hypertension and **weight gain**.

4. ANABOLICA

ECHE TE HORMONEN



Groei (voedsel)



Performance (sport)

→ Meer **SPIERMASSA**

→ **BETERE VOEDSELCONVERSIE**

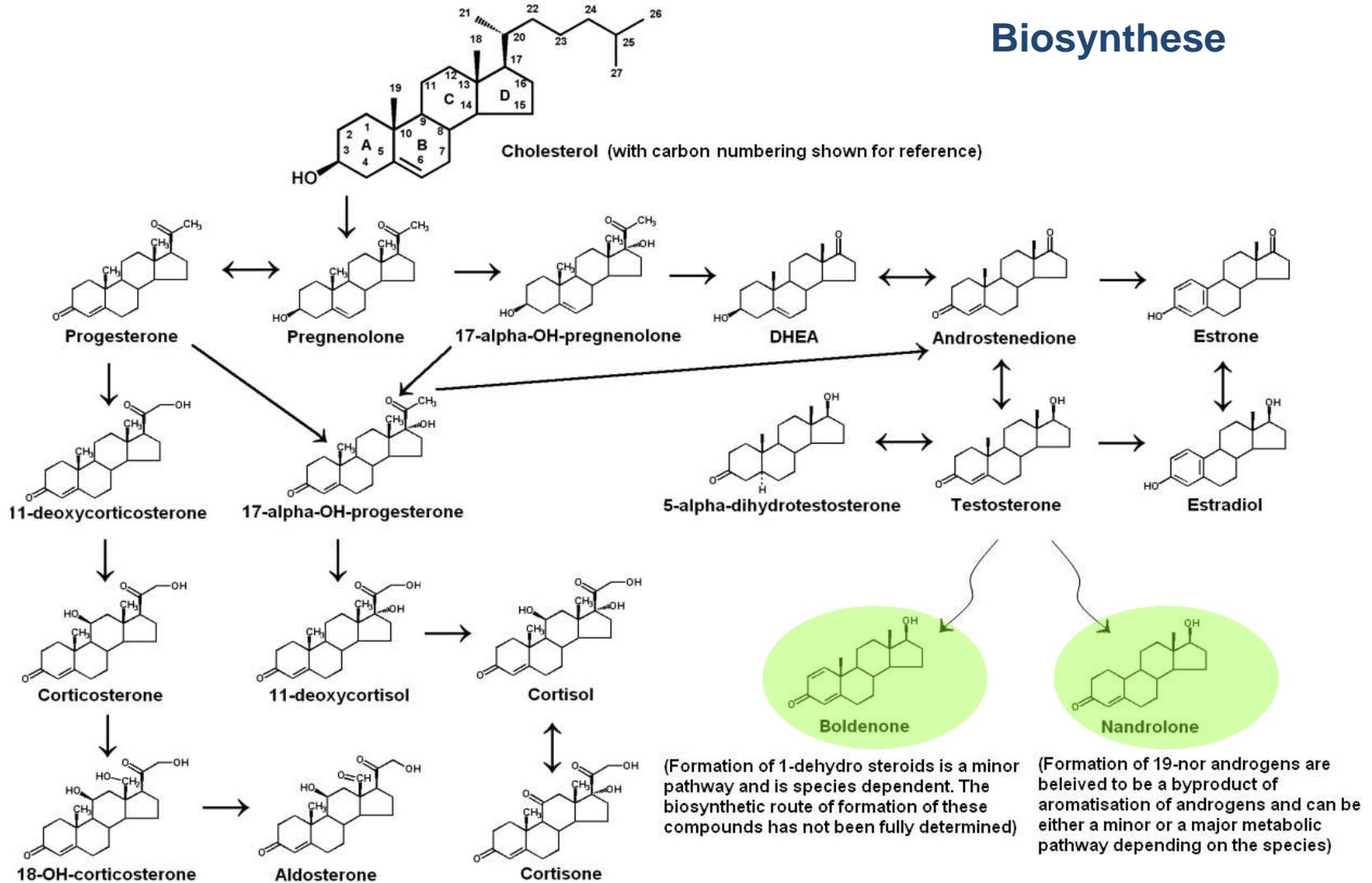
EGA's ?

→ **RENDEMENT** verhogen

→ **ESTROGENEN, GESTAGENEN, ANDROGENEN**

- Sommige steroïden komen **van nature** voor in zoogdieren (bvb. T, E2)
- Andere worden enkel in bepaalde species/sexes teruggevonden onder specifieke omstandigheden zoals zwangerschap, ziekte, ... (bvb. NT)

Biosynthese



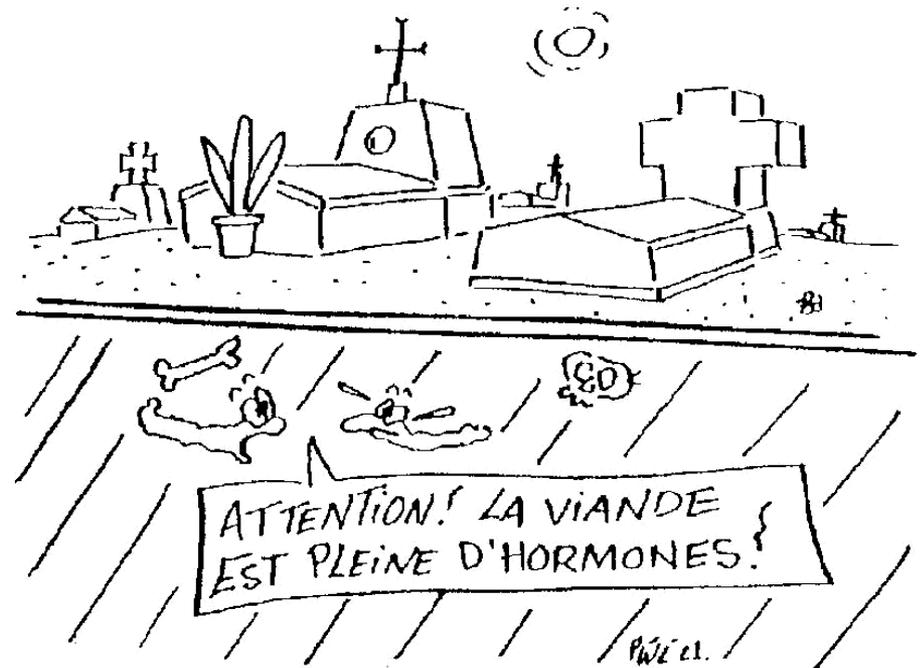
Risico's?

Hartaanval, leverfalen, agressiviteit, veranderd libido, verminderde vruchtbaarheid, groeivertraging bij kinderen, ...



CONSUMENT

ZORGEN



CASE: DIETHYLSTILBESTROL

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Yes...
desPLEX®
to prevent ABORTION, MISCARRIAGE and
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1947 - 1976

CLEAR-CELL ADENOCARCINOM

DES Daughters



DES

Diethylstilbestrol

I AM A DES DAUGHTER. ARE YOU?
YOUR LIFE MAY DEPEND
ON KNOWING THE ANSWER....

VERENIGDE STATEN: legaal!

5+1



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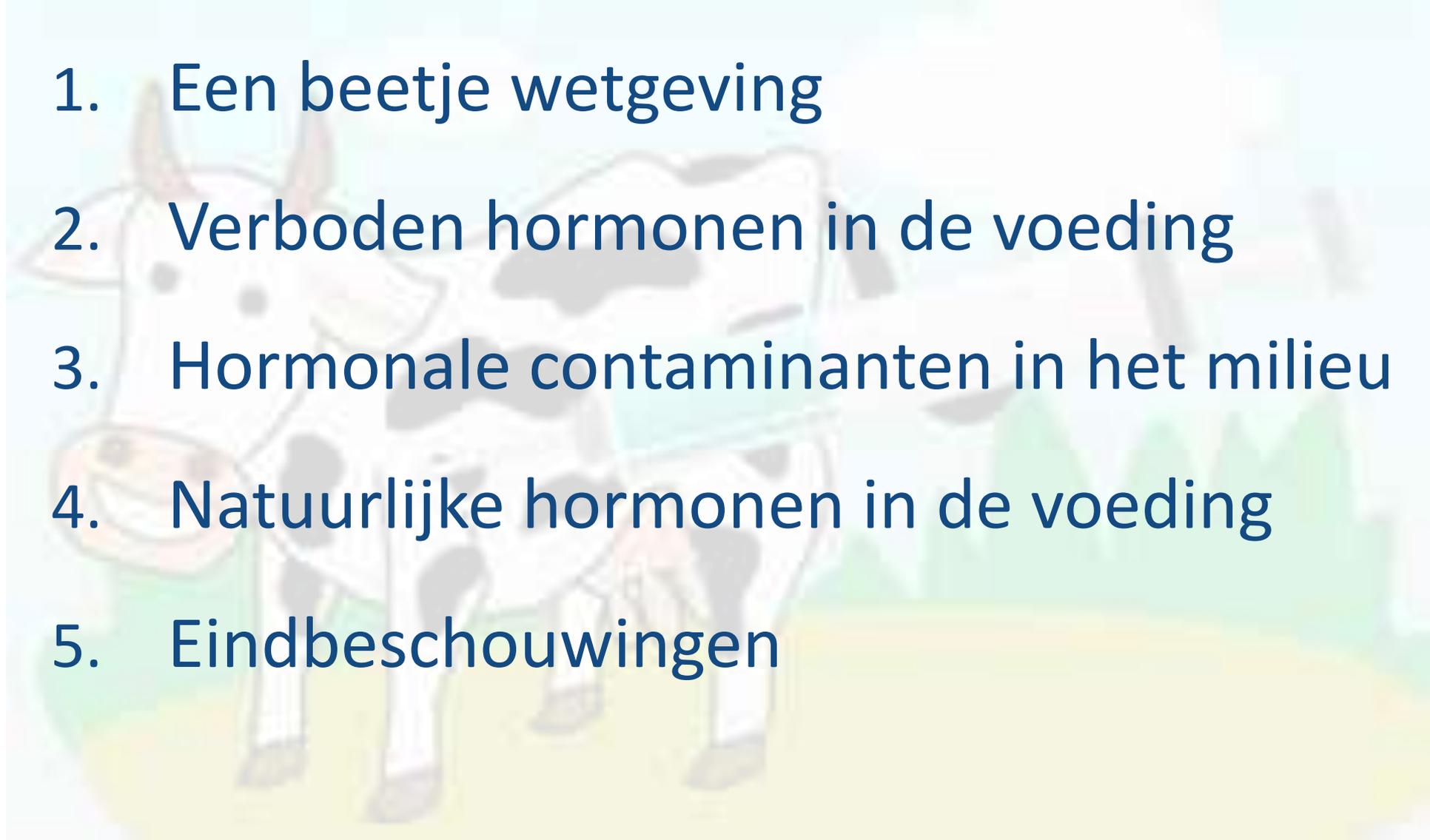


FINAPLIX-S
140 mg TBA



ook ILLEGAAL CIRCUIT ??

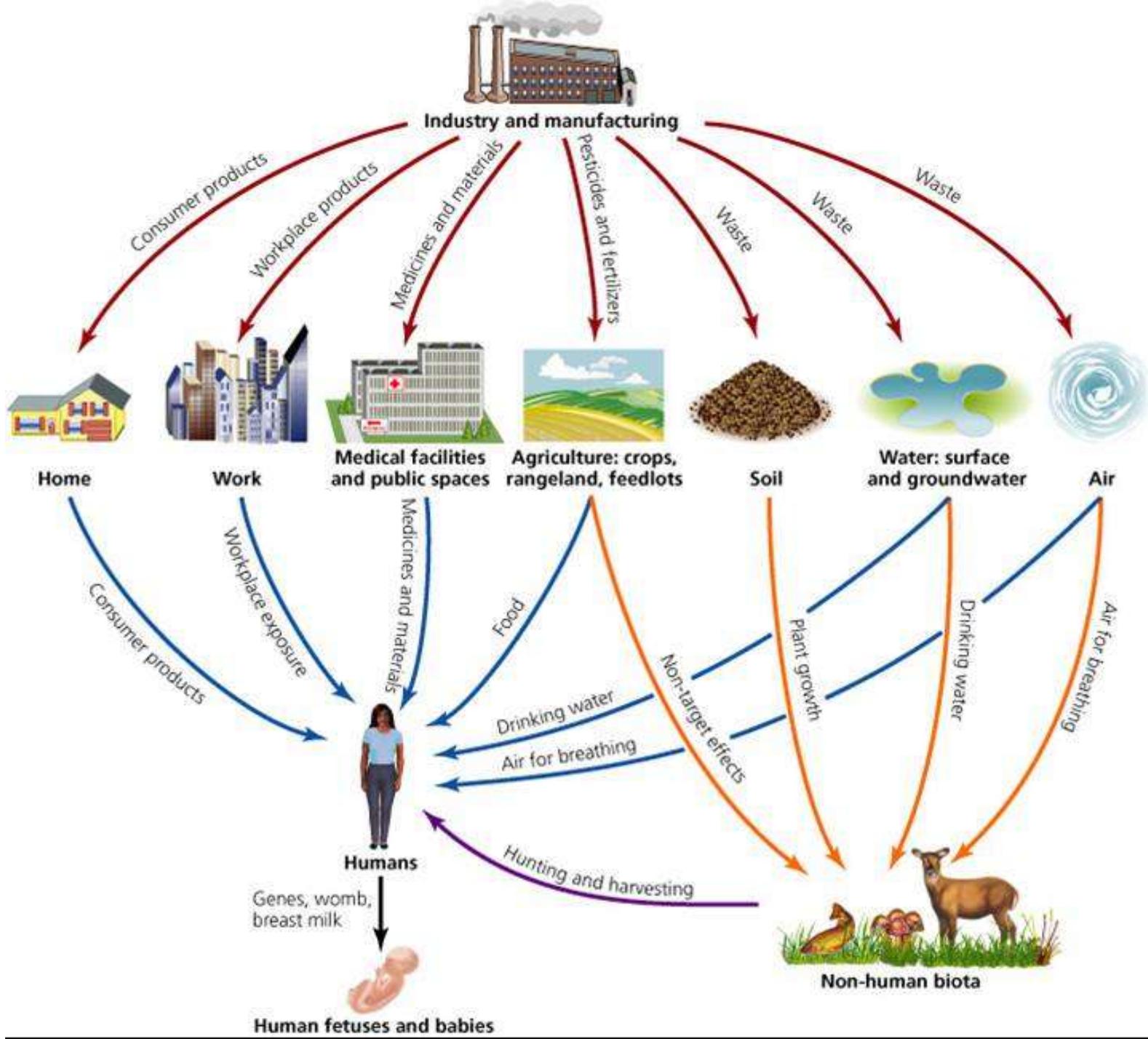
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Vraag 3:

Welk van volgende stoffen vertonen geen oestrogene activiteit?

- A. Ftalaten (weekmakers plastics)
- B. PCB's
- C. Perfluorcomponenten (teflon)
- D. Bisfenol A

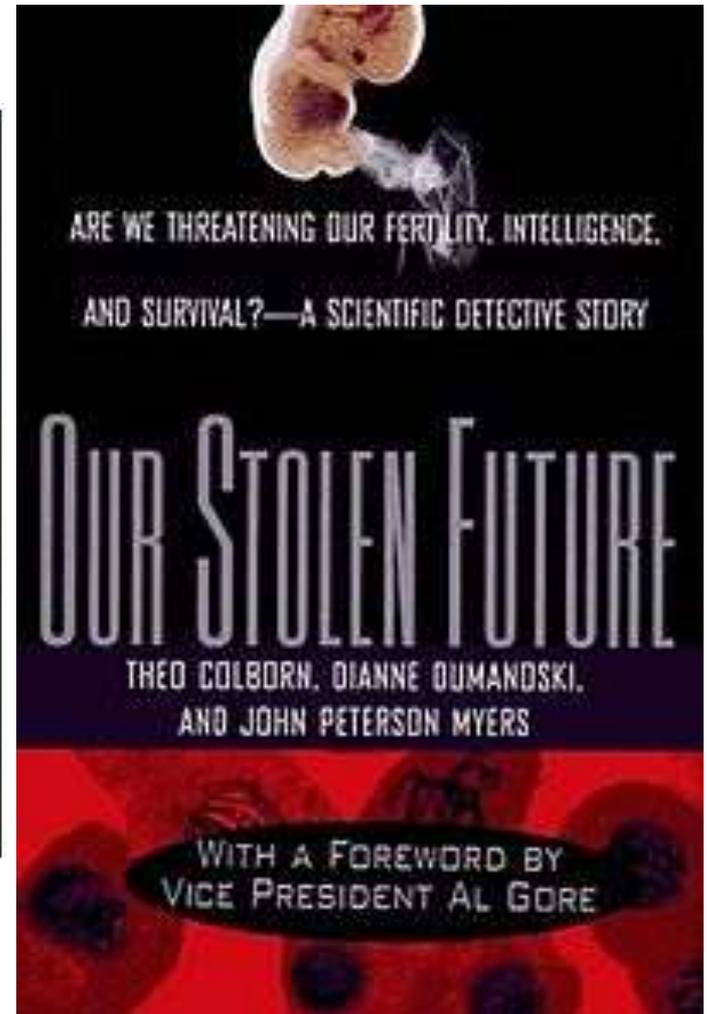
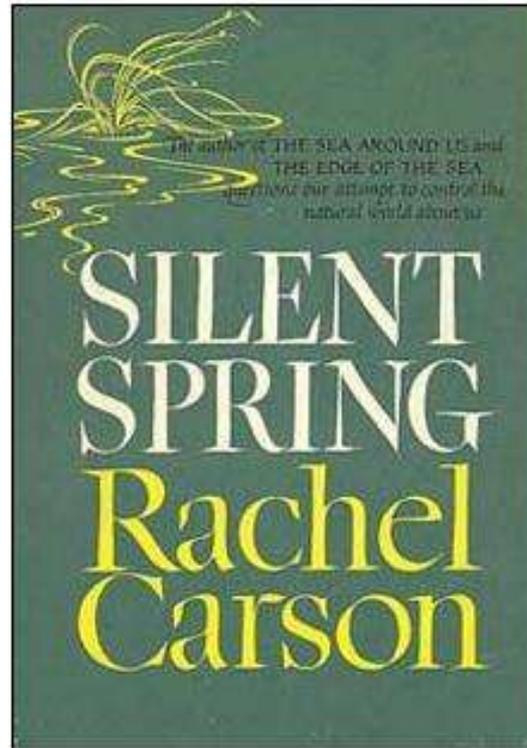


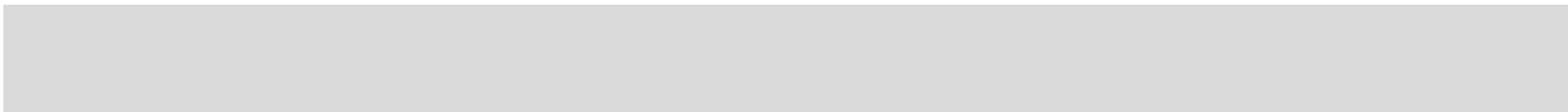
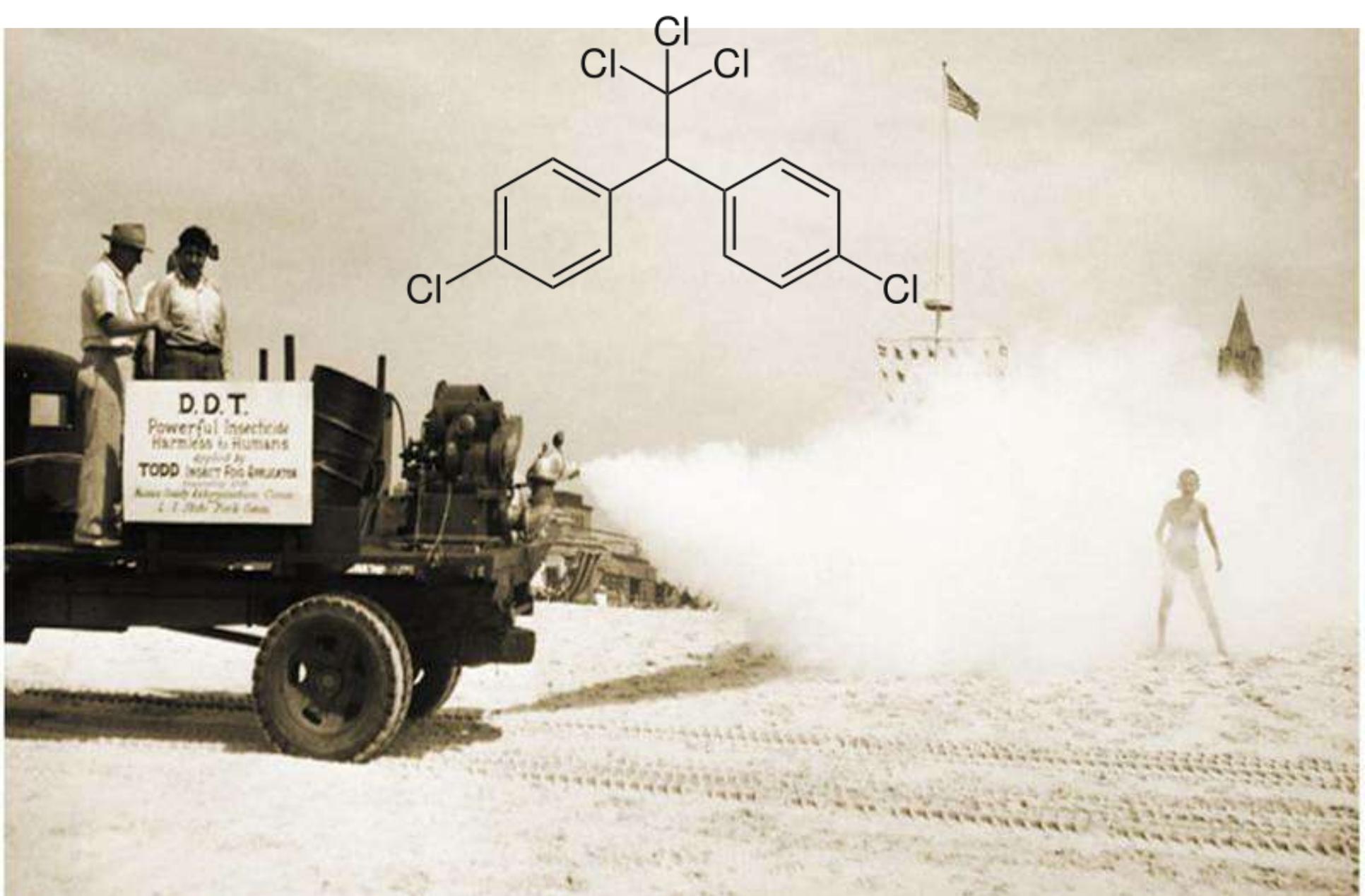
HORMOONVERSTORENDE CONTAMINANTEN

(Endocriene disruptoren)

1996

1962





- **Vaststelling van diverse reproductiestoornissen**
(bv. onvruchtbaarheid, geslachtsomkering):

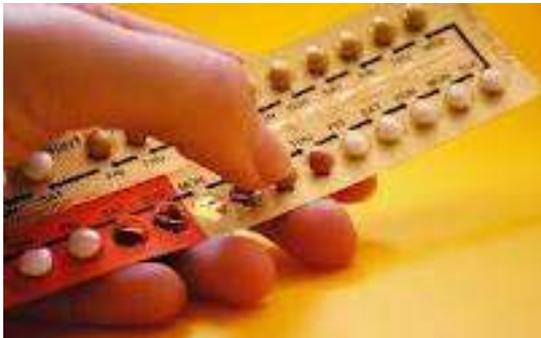
Op wildpopulaties bij vogels, vissen, amfibieën,
zeehonden, alligators, enz.



Great Crested Grebes

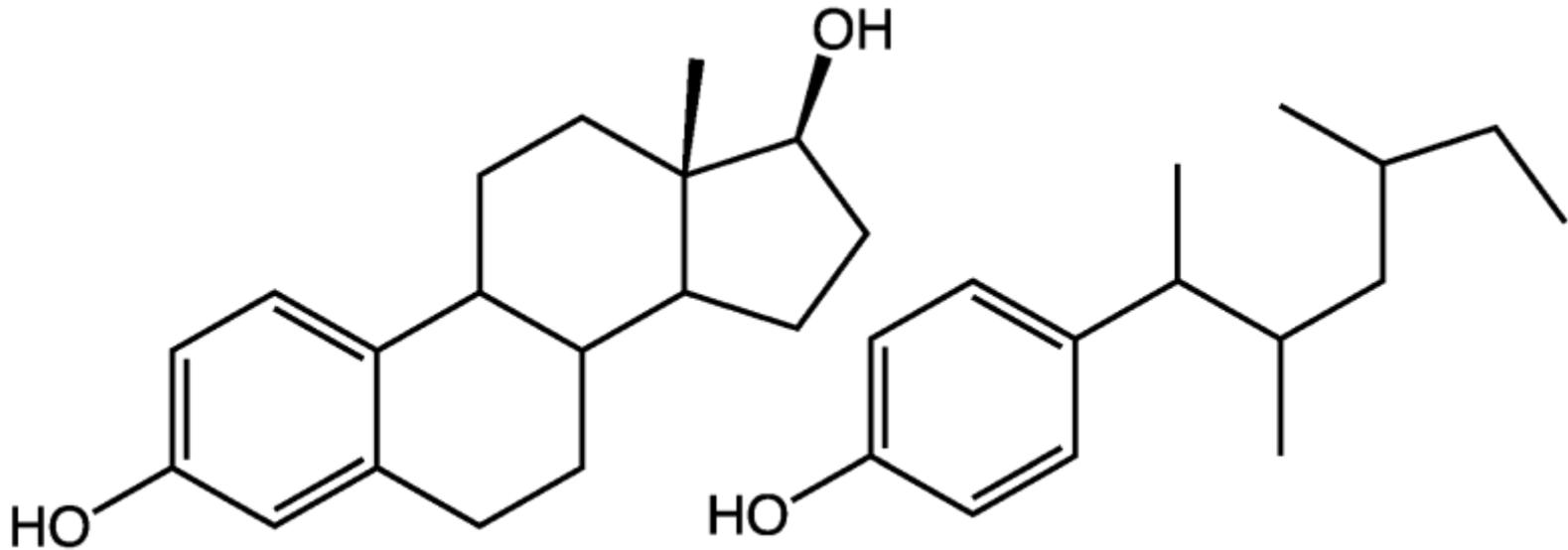
HORMOONVERSTORENDE STOFFEN

- Behoren tot een breed gamma van structureel verschillende stofgroepen:
 - Antropogene oorsprong → synthetische hormonen (bv. ethinylestradiol of EE2, diethylstilbestrol of DES), POP's, ftalaten en fenolen (bv. Bisfenol A of BPA)
 - Natuurlijke oorsprong → lichaamseigen hormonen (17 β -estradiol: E2, estron: E1 en estriol: E3), en de fyto-estrogenen (bv. genisteïne): zie eerder



XENO-OESTROGENEN

- Aandacht momenteel vooral gericht op de **meest bestudeerde groep 'xeno-oestrogenen'**: stoffen die de werking van het vrouwelijk geslachtshormoon 17β -oestradiol kunnen nabootsen of de werking ervan blokkeren.



17β -estradiol

nonylphenol

Table 2: Trends in human health effects potentially related to endocrine function

End point	Region	Trend	Degree of change
Hypospadias	Canada	Increasing incidence	4.3% per year
	US		3.3% per year
Cryptorchidism	Canada	Increasing incidence	3.5% per year
	US		1.6% per year
Sperm count	Canada	Decreasing	-0.7%/mL per year*
	US		-3%/mL per year
	Europe		-5.3%/mL per year
Testicular cancer	Canada	Increasing incidence	2.1% per year
	US		2.3% per year
	Europe		2.3%–5.2% per year†
Prostate cancer	Canada	Increasing incidence‡	3% per year
	US		5.3% per year
Breast cancer	Saskatchewan	Increasing incidence	3.3% per year
	US		1.9% per year
Sex ratio	Canada	Shift toward females	-1.0 males/10 000 per year
	US		-0.5 males/10 000 per year
Age at breast development	US	Shifting earlier	11.2–9.96 years in white population

The data linking exposures to EDCs and human diseases are much stronger now than in 2002. Since human studies can show associations only, not cause and effect, it is important to use both human and animal data to develop the evidence for a link between exposures to EDCs and

• Reproductive/endocrine

- Breast/prostate cancer
- Endometriosis
- Infertility
- Diabetes/metabolic syndrome
- Early puberty
- Obesity

• Immune/autoimmune

- Susceptibility to infections
- Autoimmune disease

Over the past 10 years, there has been a dramatic shift in focus from investigating associations between adult exposures to EDCs and disease outcomes to linking developmental exposures to disease outcomes later in life. This is now considered the most appropriate approach for most endocrine-related diseases and dysfunctions, based on data presented below (section 8). Children are the most vulnerable humans (**Figure 6**).

human disease. Even so, it may never be possible to be absolutely certain that a specific exposure causes a specific disease or dysfunction due to the complexity of both exposures and disease etiology across the lifespan (**Figure 5**).

• Cardiopulmonary

- Asthma
- Heart disease/hypertension
- Stroke

• Brain/nervous system

- Alzheimer disease
- Parkinson disease
- ADHD/learning disabilities

Figure 5. Diseases induced by exposure to EDCs during development in animal model and human studies.

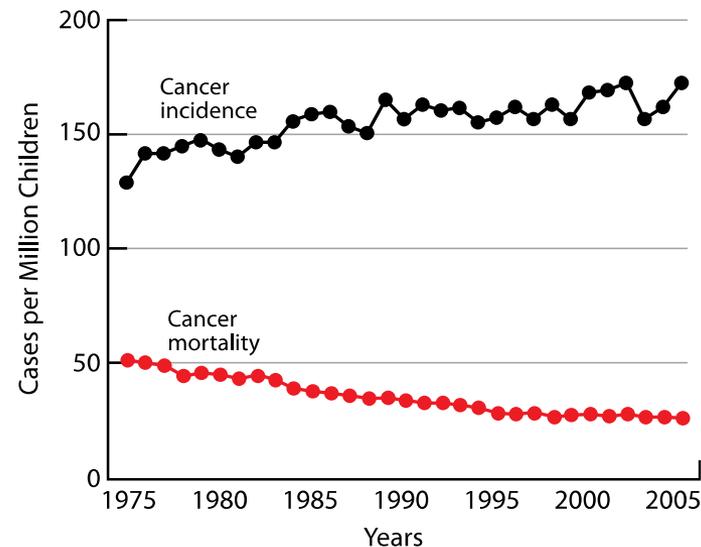
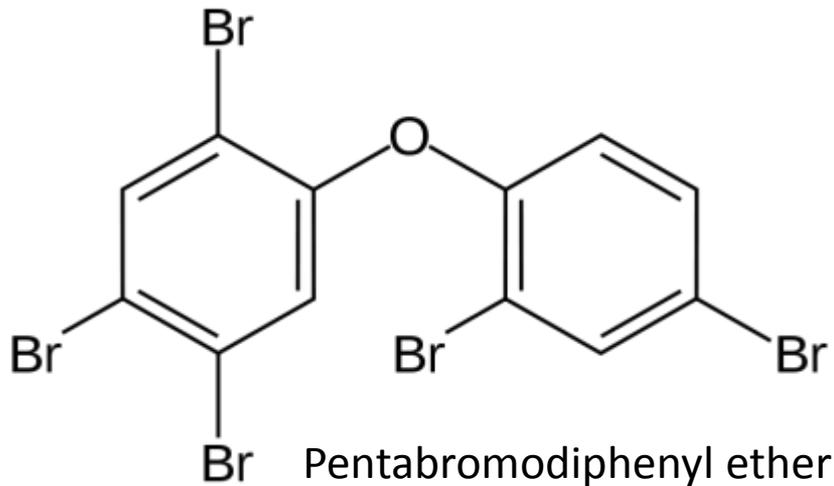


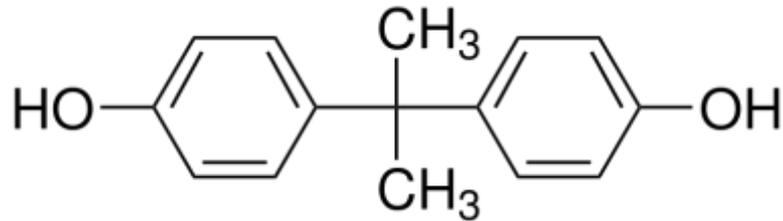
Figure 6. Children are among the most vulnerable humans. The figure shows cancer incidence and cancer mortality among children under 20 years of age in the USA (based on data from the United States National Cancer Institute's Surveillance, Epidemiology and End Results Program).

Br-vlamvertragers (PBDE's)

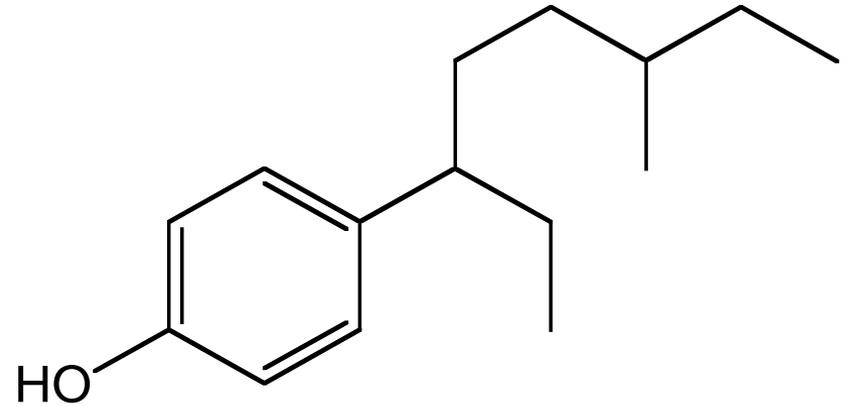


- Stoffen toegevoegd aan kunststoffen om de **brandbaarheid te verminderen** (gebruikt in bv. TV's, PC's, huishoudtoestellen, textiel en meubelbekleding, bedrading, verlichting, ...)
- Worden in **vetweefsels** opgeslagen en kunnen o.m. de normale ontwikkeling van het zenuwstelsel beïnvloeden en werking v/d schildklier verstoren en zijn toxisch voor de lever
- Ook in **zalm, vlees, boter een kaas** aangetroffen → Canada

Fenolen



Bisfenol-A (verboden sinds 2011 in babyflesjes)



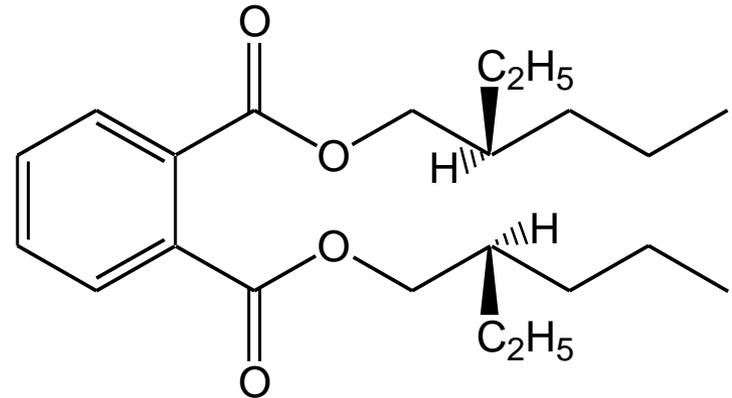
Nonylfenol

(1 isomeer: verboden sinds 2005)



- Gebruik als **surfactant** in o.m. commerciële **pesticiden**, als **adhesief** in de bandenindustrie, als **elektrische isolator**, ...; als **anti-oxidant** in PVC-plastics en als **monomeer** voor PC-plastics.
- Verschillende hebben **hormoonverstorende** werking.

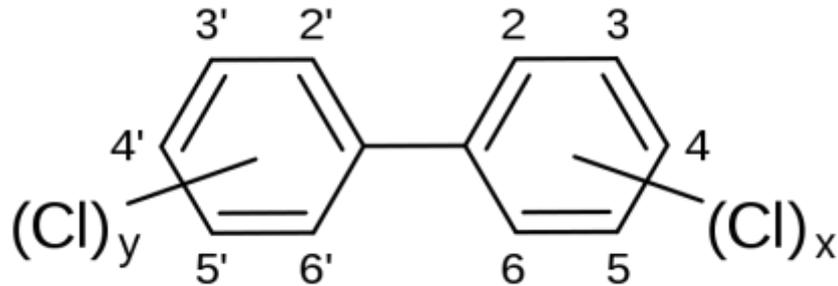
Ftalaten



Di(2-ethylhexyl)ftalaat (DEHP)

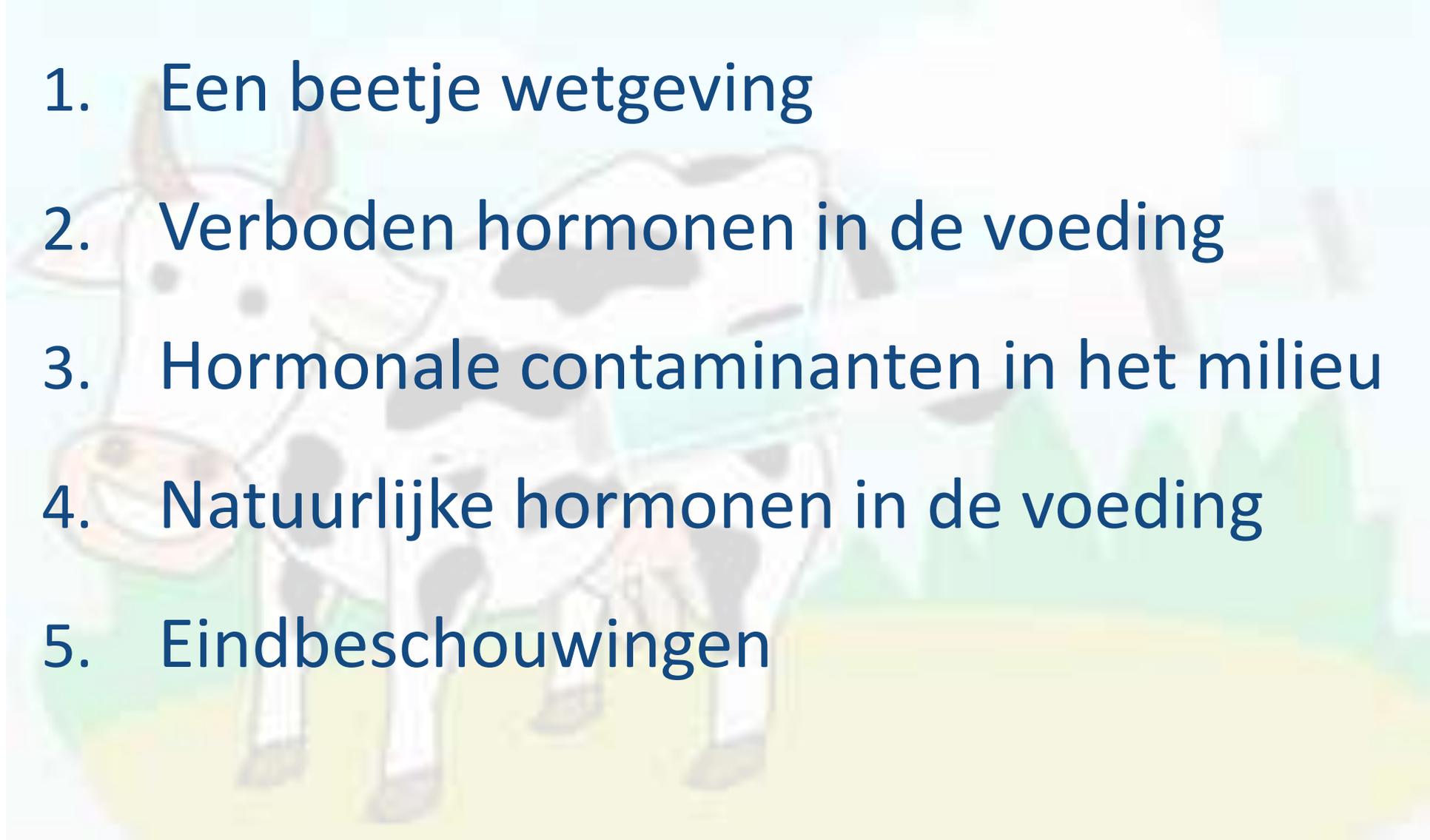
- Worden o.m. gebruikt bij het vervaardigen van **drukinkten en lijmen** en als **weekmakers** voor **plastics** (polymeren zoals PVC), maar ook in solventen, parfums en geparfumeerde producten, enz.
- Sommige hebben effecten op de **ontwikkeling en voortplanting** en worden daardoor in alle speelgoed en kinderverzorgingsartikelen verboden (0-3 jaar), migratie vanuit verpakking hier belangrijk probleem.

Polychloorbifenylen (PCB's)



- Uitgebreide familie (**209 congenere**) van giftige stoffen
→ worden opgeslagen in vet(weefsel)
→ bioaccumulatie doorheen voedselketen
- Productie en gebruik van PCB's **verboden sinds 1985**
- Verstoring ontwikkeling kinderen, leverschade, verstoring schildkliermetabolisme, carcinogeen, teratogeen, endocriene verstoring: verminderde vruchtbaarheid

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Vraag 4:

Dient men de consumptie van fyto-oestrogenen (bvb. soja) bij vrouwen met borstkanker te adviseren?

- A. Ja, in Azië consumeert men algemeen meer soja en worden minder borstkankers vastgesteld
- B. Neen, fyto-oestrogenen binden ook op de ER en zullen op deze wijze ook de celdeling helpen versnellen
- C. De wetenschappelijke resultaten over de consumptie van fyto-oestrogenen bij borstkanker zijn omstreden en zeer sterk afhankelijk van de situatie: gepersonaliseerd advies is beter

FYTO-OESTROGENEN

- *“Plant constituents which structurally or functionally mimic the female estrogen E2”*

Groep	Subgroep	Voorbeelden	Voedingsbron
17 β -Oestradiol	Endogeen oestrogeen	nvt	nvt
Polyfenolen		Resveratrol	Pel druiven, rode wijn
Flavonoïden	Flavanones	Eriodictyol, Hesperetine, Homoeriodictyol, Naringenine	Citrusvruchten en sappen
	Flavones	Apigenine, Luteoline, Tangeritine	Peterselie, Selder, Capsicumpeper
	Flavonolen	Fisetine, Kaempferol, Myricetine, Pachypodol, Quercetine, Rhamnazine	Boerenkool, broccoli, uien, tomaten, sla, appels, druiven, rode wijn
	Catechines	Proanthocyanides	Chocolade, groene thee, bonen, abrikozen, kersen, bessen
Isoflavonoïden	Isoflavonen	Biochanin A, Glyciteïne, Daidzeïne, Formononetine, Genisteïne	Sojabonen en andere peulvruchten
	Isoflavanen	Equol	Metaboliet van daidzeïne
	Coumestanen	Coumestrol	Klaver, luzerne, spinazie

Phytoestrogen sources	food	Phytoestrogen content (µg/100g)
Flax seed		379380
Soy beans		103920
Tofu		27150.1
Soy yogurt		10275
Sesame seed		8008.1
Flax bread		7540
Multigrain bread		4798.7
Soy milk		2957.2
Hummus		993
Garlic		603.6
Mung bean sprouts		495.1
Dried apricots		444.5
Alfalfa sprouts		441.4
Dried dates		329.5
Sunflower seed		216
Chestnuts		210.2
Olive oil		180.7
Almonds		131.1
Green bean		105.8
Peanuts		34.5
Onion		32
Blueberry		17.5
Corn		9
Coffee, regular		6.3
Watermelon		2.9
Milk, cow		1.2

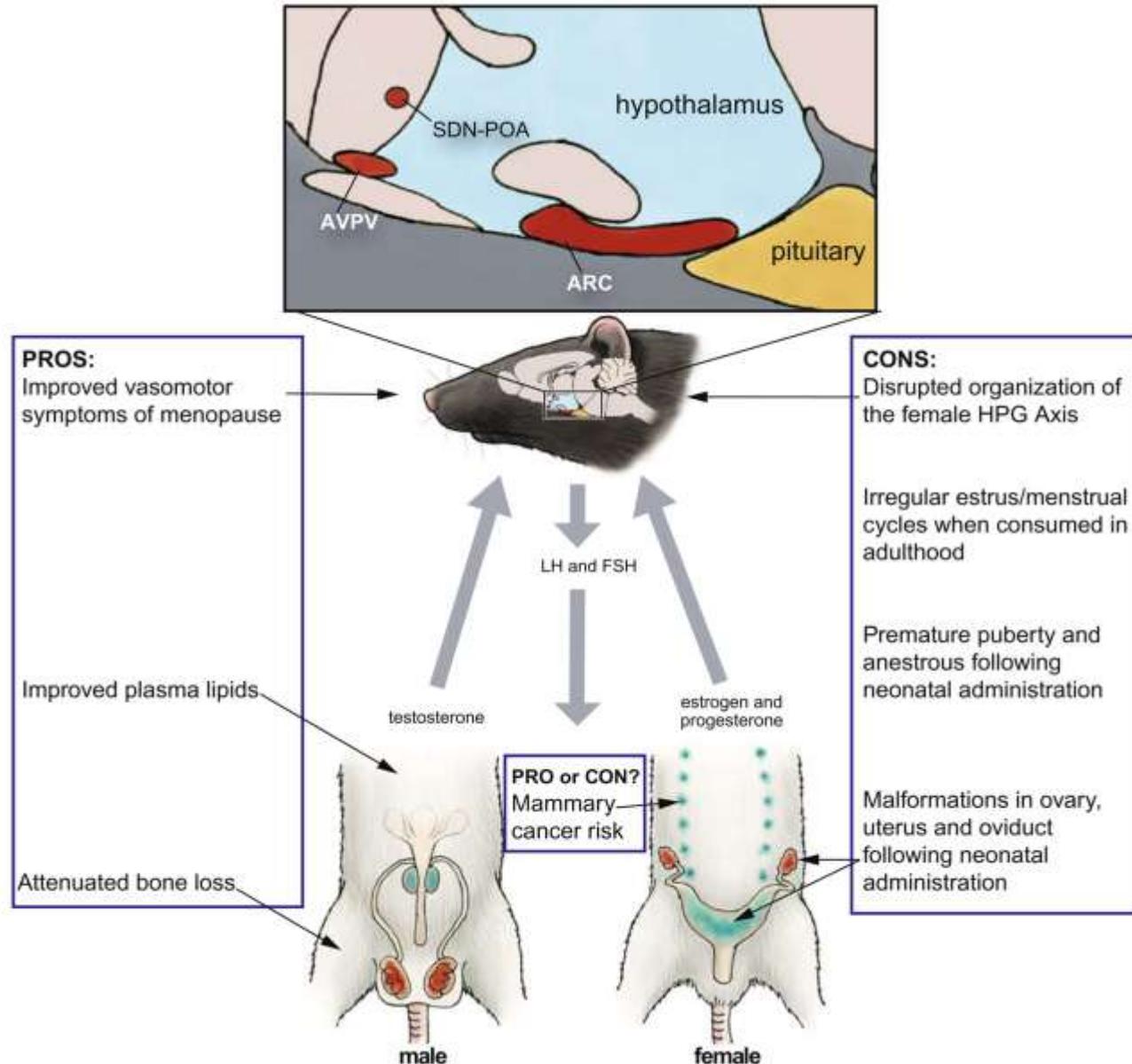
Food product	Genistein (mg/100g)	Daidzein (mg/100g)	Total isoflavones (mg/100 g)
Soy Infant Formula (powder)	13.5	6.32	26.3
Edamame (raw green soybeans)	22.6	20.3	48.9
Miso	23.2	16.4	41.5
Silken tofu	8.4	9.2	18.0
Raw tofu, regular	13	9	23
Textured soy flour	89.4	67.7	172.6
Soy protein isolate	57	31	91
Soy-based sliced cheese	6.5	5.1	14.5
Soy-based bacon bits	45.8	64.4	118.5
Soy-based burgers	5.0	2.4	6.4
Red clover	10	11	21
Multigrain bread	0.2	0.2	0.4
KASHI Go Lean cereal	7.7	8.4	17.4
Green tea, Japanese	0.02	0.01	0.02
Flaxseeds	0.04	0.02	0.07
Raw broccoli	0.00	0.04	0.25

Comparison of estradiol Bisphenol A (BPA) and genistein levels in newborns, infants, and adults. For all age groups and in all fluids listed, genistein levels are higher than BPA levels. Compiled values represent the range of those previously reported and do not take into account methodological differences or sample sizes.

	E2 (ng/mL)	Genistein (ng/mL)	Bisphenol A (BPA, ng/ml)
Plasma, Adult Western Woman (follicular phase)	0.25–1.8	1–2	0.3–5
Plasma, Adult Western Woman (preovulatory peak)	1.4–5.4	1–2	0.3–5
Amniotic Fluid, Western		0.4–1.7	
Cord blood, Western			1–3
Plasma, Adult Japanese Woman		7.2–83	1.4–2
Amniotic Fluid, Japan		15	1.1–8.3
Cord blood, Japan		19.4–45	2.2
Breast Milk		8–13.5	1.3
Plasma, Breast-Fed Infant	<0.04–0.08	2–4.7	
Plasma, Infant fed Bovine Formula	<0.04–0.08	9.4	
Plasma, Infant fed Soy Formula	<0.04–0.08	684–757	

→ Genesteïne voor alle categorieën veel hoger dan BPA!!!

Vb. genisteine



PROS & CONS FYTO-OESTROGENEN

Consumers should be aware that soy contains **endocrine disrupting compounds** and make dietary choices accordingly.

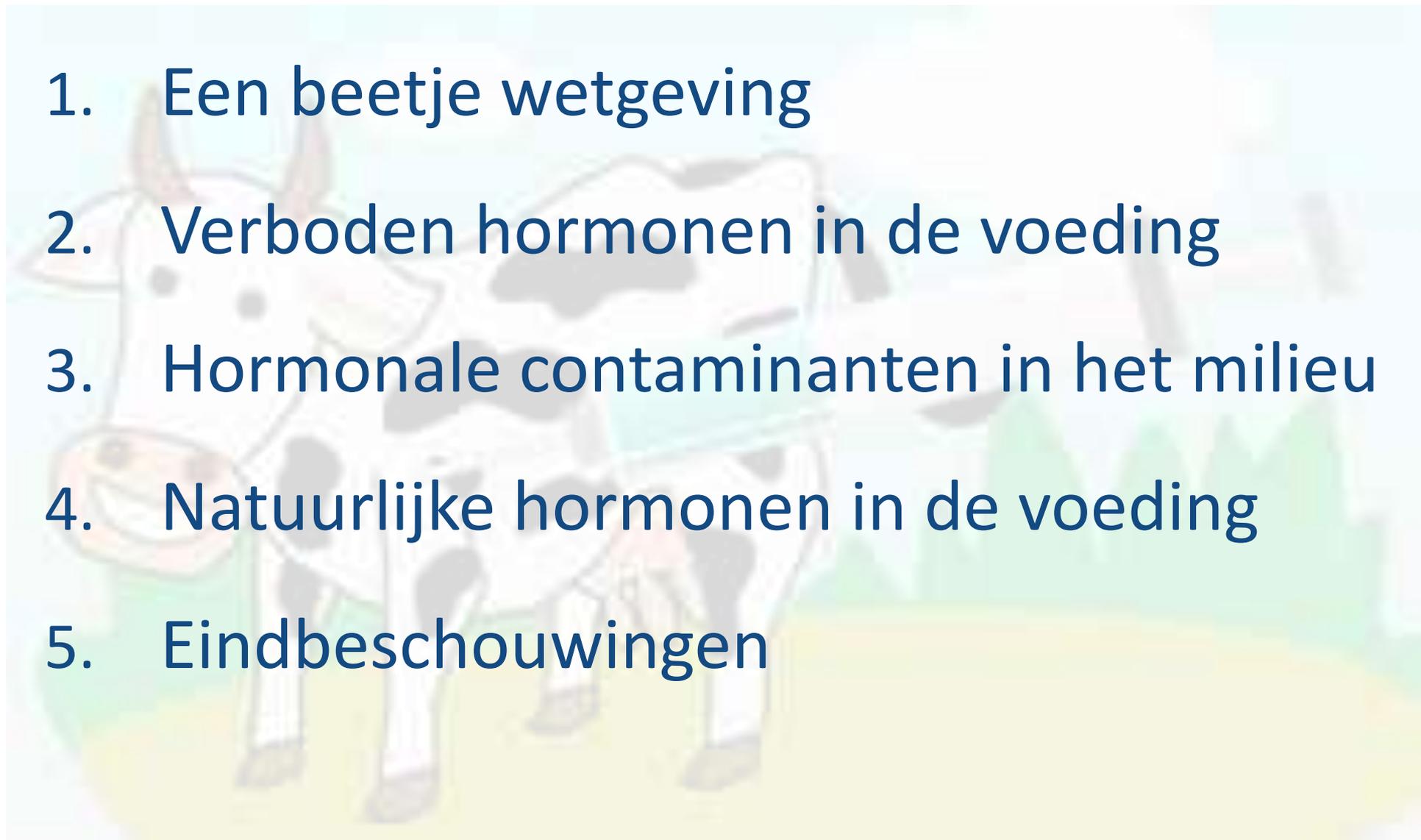
For a **typical consumer**, alarm over soy products is likely unnecessary but so is the belief that a soy-rich diet will alleviate all ills.

Women who are pregnant, nursing, or attempting to become pregnant should use soy with caution and be aware that soy formula may not be the best option for their babies. Main indications include severe lactose intolerance, galactosaemia and need to avoid foods of animal origin.

Older individuals, especially those with **high cholesterol**, may experience modest **benefits** including improved bone and cardiovascular health, and perhaps a decreased risk of carcinogenesis. Moderation is likely key and the incorporation of real foods, as opposed to supplements or processed foods to which soy protein is added, is probably essential for maximizing health benefits.

Finally, the **relative importance of the soy protein itself**, compared to the isoflavones, on health outcomes such as lipid levels, reduced risk of carcinogenesis, and fracture risk must be resolved. If something other than the **isoflavone phytoestrogens** is producing the mild but measurable health benefits of soy foods, this would considerably help shape the development of dietary guidelines for both **adults and children**.

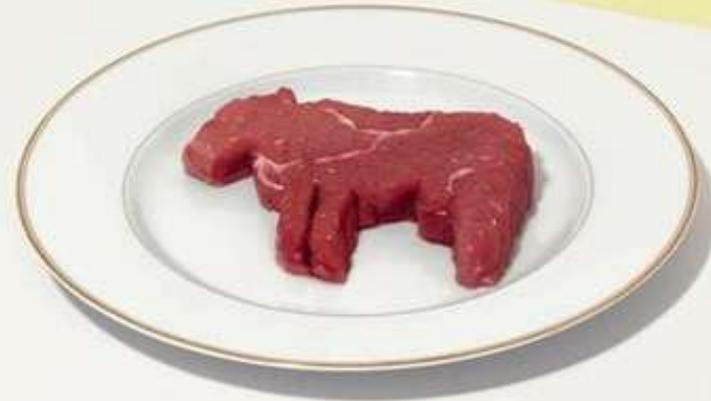
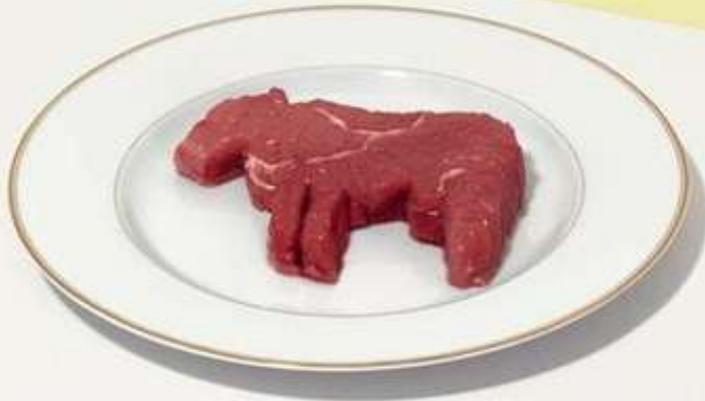
OVERZICHT

1. Een beetje wetgeving
 2. Verboden hormonen in de voeding
 3. Hormonale contaminanten in het milieu
 4. Natuurlijke hormonen in de voeding
 5. Eindbeschouwingen
- 
- A faint, stylized illustration of a cow with black and white spots, standing in a green field with trees in the background. The illustration is positioned behind the list of items.

En om te besluiten...

- **Illegale groeipromotoren (hormonen) in de voeding?**
 - Kans zeer klein (0,3%)
- Vormen **xeno-oestrogenen** uit de **voeding**, maar ook het **milieu** een probleem?
 - Op basis van tal van wetenschappelijke studies zijn heel wat trends gelinkt met **EDCs**, maar duidelijke correlaties tussen specifieke stoffen en effecten niet altijd voorhanden.
 - Opgelet met soja, bevat meer oestrogenen dan bvb. plastics uit papflessen en zeker bij zwangere vrouwen en baby's onder 6 maand, te beperken.

Dank voor uw aandacht!



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