



voedsel en waren autoriteit

DUTCH REGULATORY FRAMEWORK FOR BOTANICALS with a focus on enforcement

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General

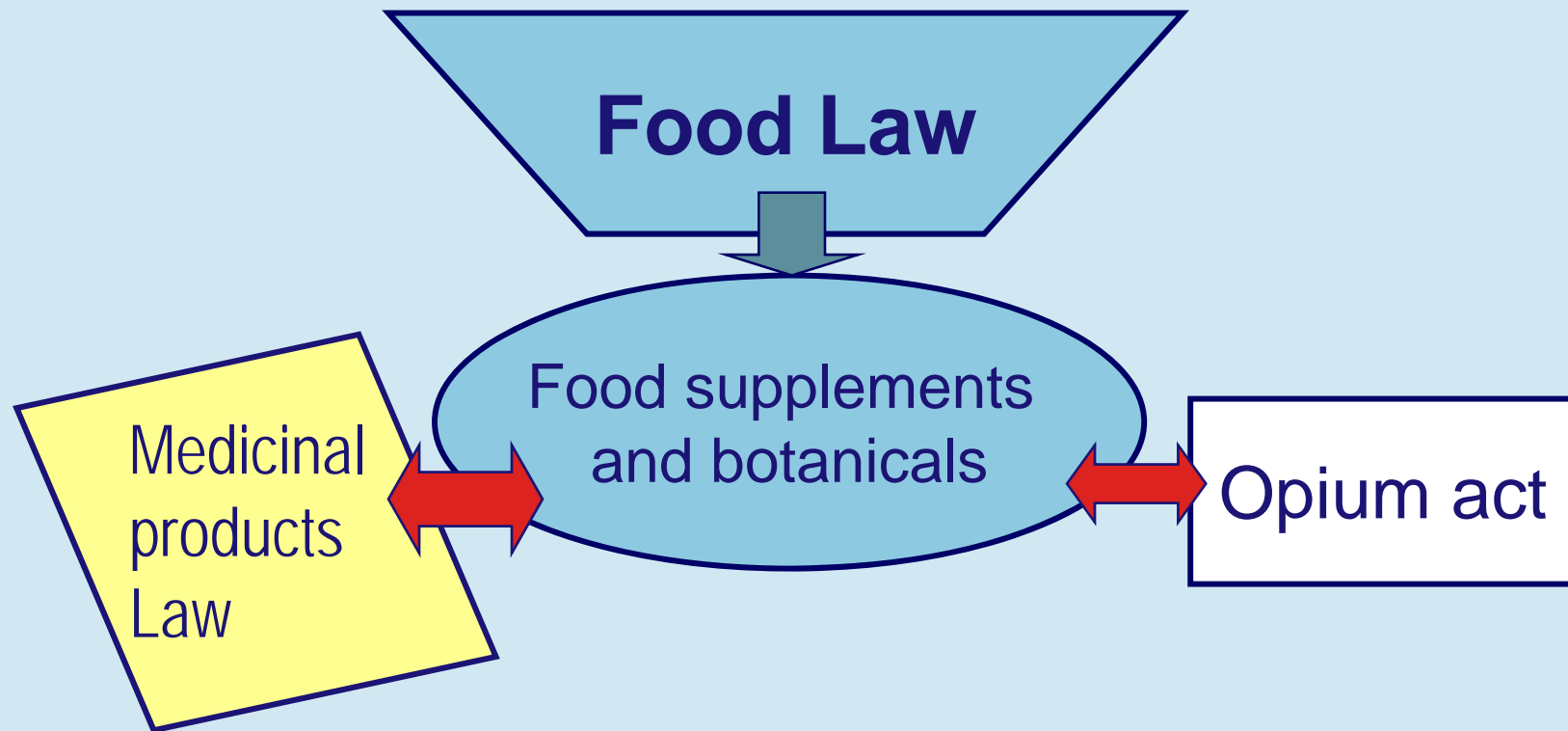
- focus on special foods, nutrition and food preparation and handling in small businesses and industry
- translation of policy to enforcement actions

Special foods

- food supplements, herbal preparations, claims and dietetic foods
- project management at R&D Department in Eindhoven (3 FTE)
- 10 specialised inspectors based throughout the Netherlands
- analytical investigations performed by VWA laboratories and the National Institute for Public Health and the Environment (RIVM)



Regulatory framework for food supplements and botanicals





National legislation for herbal preparations

Commodities act decree 'Herbal preparations'

- entered into force January 2001
- the decree only applies to foods including food supplements with herbal ingredients



National legislation for herbal preparations

Commodities act regulation 'Contaminants in foodstuffs'

contains a limit for benzo(a)pyrene specifically for:

- food supplements without botanical ingredients: 2 $\mu\text{g}/\text{kg}$
- herbal preparations: 10 $\mu\text{g}/\text{kg}$

B(a)P levels were regulated nationally when harmonised limits for food supplements were not feasible in 2005 due to a lack of data from other MS



Harmonised legislation for food supplements

Commodities act Decree 'Food supplements'

- general rules for labelling of food supplements

Commodities act Regulation 'Food supplements'

- positive lists of vitamins and minerals and chemical forms
- ⇒ both based on Directive 2002/46/EC

Commodities act decree 'Novel foods'

- based on Regulation (EC) No 258/97



Commodities act Decree 'Herbal preparations'

- herbal preparations are herbal substances, processed or not, for human use
- herbal preparations are products for oral or topical use or products intended to be inhaled
- the Decree does not apply to medicinal products, raw materials for medicinal products, cosmetics, spices for culinary uses, or flavourings



Commodities act Decree 'Herbal preparations'

- ban on herbal preparations containing hazardous quantities of herbs in general
- limit for toxic pyrrolizidine alkaloids (PAs) of 1 $\mu\text{g}/\text{kg}$ for plants in annex I and other plants suspected to contain toxic PAs
- ban on aristolochic acids and derivatives
- ban on yohimbe alkaloids and derivatives



comfrey (*Symphytum officinale*)

Commodities act Decree 'Herbal preparations'

- ban on 46 potent herbs and fungi in annex II, including botanicals with:
- cardiac glycosides (e.g. *Digitalis purpurea*, *D. lanata*, *Nerium oleander*, *Adonis vernalis*)
- belladonna alkaloids (e.g. *Datura stramonium*, *Hyoscamus niger*, *Mandragora officinarum*)
- other alkaloids (e.g. *Aconitum napellus*, *Claviceps purpurea*, *Strychnos nux-vomica*)
- thujone (*Artemisia cina*, *A. maritima*)



thornapple (*Datura stramonium*)



mandrake (*Mandragora officinarum*)



Commodities act Decree 'Herbal preparations'

Modifications since 2001 to the list of banned herbs and fungi by the Ministry of Health on advice by the VWA and RIVM:

Removed:

- *Stephania tetrandra*
- *Lycium barbarum*
- *Magnolia officinalis*

Added:

- *Piper methysticum* (kava kava)
- *Pausinystalia yohimbe* (yohimbe)



Asian traditional herbal preparations (THPs)





Aristolochic acids in Chinese THPs

- Aristolochic acids (AAs) found in *Aristolochia*, *Asarum* and *Bragantia* spp. (Aristolochiaceae)
- Preparations of *Aristolochia* spp. in use in Traditional Chinese Medicine (TCM): e.g. 'fang ji', 'mu xian', 'ma dou ling' and 'mu tong'
- IARC concluded that AAs are carcinogenic to humans
- AAs cause of 'Aristolochic Acid Nephropathy', characterised by rapidly progressing interstitial fibrosis



Survey AAs in Chinese THPs

Chinese THPs sampled between 2002 and 2007 (n=190)

- 68 Chinese of these identified as possibly containing AAs
 - 25 Chinese of these THPs positive for AAs
- ⇒ 37% of suspected THPs contained AAs in this study!

highest AA concentrations found in 'mu tong':

- 'mu tong' refers to the stem of *Aristolochia manshuriensis* (with AAs) or to 2 *Clematis* spp. or to 2 *Akebia* spp. (no AAs)
- 7 of 14 mu tong samples contained AAs up to 2.1 g/kg

Martena et al. Anal. Bioanal Chem. 389, 263-275



Metals and metalloids in Asian THPs

- traditional herbal preparations (THPs) in use in Ayurveda, Traditional Chinese Medicine (TCM) and other traditional Asian medicine systems can contain mercury, lead and arsenic compounds
- these compounds are deliberately used as ingredients of Asian THPs and have resulted in intoxications world wide
- after 2 severe lead poisonings with Ayurvedic THPs in 2004 the VWA intensified investigations

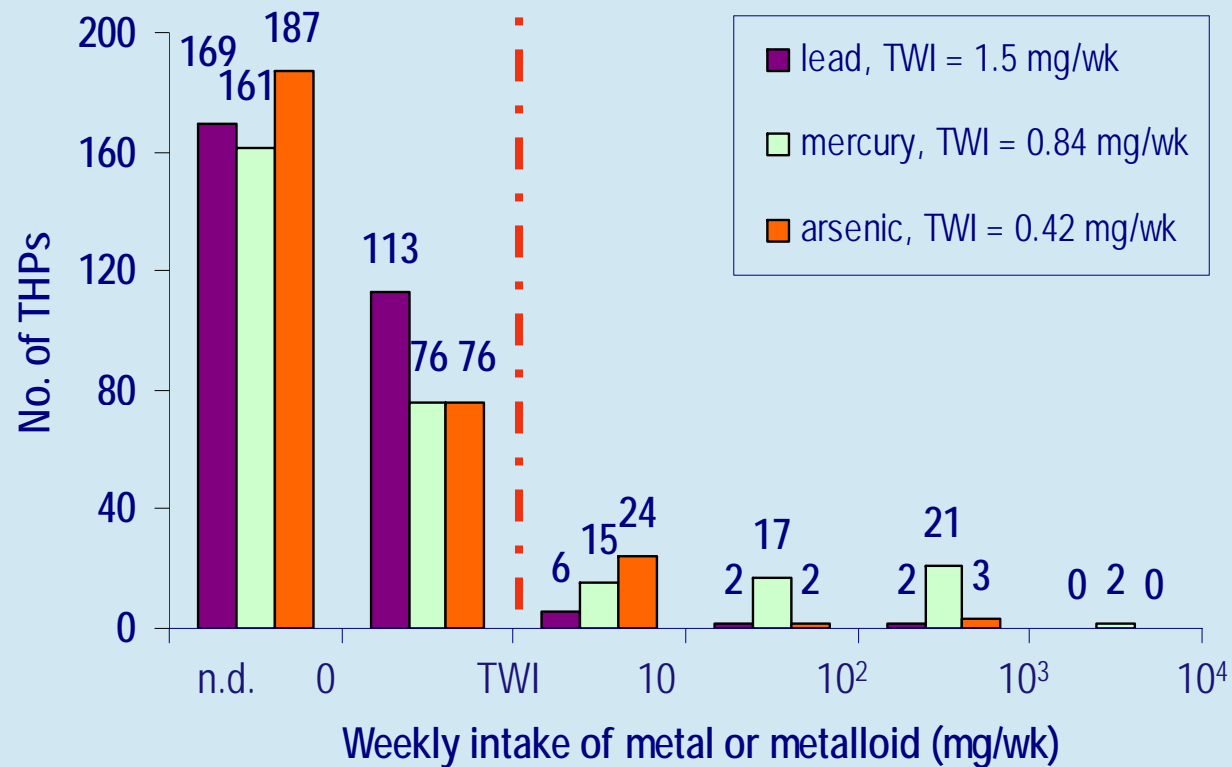


Survey metals and metalloids in Asian THPs 2004 - 2007

- 292 THPs from Ayurveda, TCM and Traditional Tibetan Medicine were sampled throughout the Netherlands in retail channels
- 186 THPs (64%) contained mercury, lead or arsenic
- estimated element intakes for 59 of these (in total 20%) exceeded established safety limits
- no maximum product levels for these elements existed at that time for food supplements



Estimated intake of metals and metalloids for Asian THPs in survey 2004-2007



Martena et al. Food Additives and Contaminants (accepted for publication)



Analytical parameters of VWA for botanicals

- metals and metalloids
- 13 PAHs, including benzo(a)pyrene
- mycotoxins
- pesticides
- pharmaceuticals, such as sildenafil analogues, fenfluramine
- phytotoxins, such as aristolochic acids, pyrrolizidine alkaloids, safrole, thujone, anisatine, glycyrrhizinic acid
- irradiation



Last slide: some medicinal products disguised as food supplements

Libido stimulating 'food supplements' with botanical ingredients found to contain undeclared sildenafil, tadalafil, vardenafil or derivatives



'Darling'



'Libidifit'



'Stamina Rx'



'Libido Forte'



Thank you for your attention