

# The EURISKED Project: Multi-organic risk assessment of selected endocrine disruptors

*Experiments indicate that endocrine disrupting chemicals (EDCs) with oestrogenic actions exist. It is not clear whether these substances interact with other steroid receptors or act in non-reproductive organs such as the neuroendocrine brain, the cardiovascular, skeletal or urogenital system during development and in adult life. Hence, risk assessment for organs known to be oestrogen-, androgen-, progesterin-, glucocorticoid- or thyroid hormone-receptive following exposure to the aforementioned endocrine disruptors cannot yet be made.*

## Objectives

- The ultimate goal of the EURISKED project was to determine multi-organic effects of a variety of EDCs. These were: octylmethoxycinnamate (OMC), nonylphenol, 4-methylbenzylidene-camphor (4-MBC), bisphenol A, dibutylphtalate, benzophenone-2, procymidon, linuron, resveratrol, 8-prenylnaringenin, genistein, estradiol-benzoate and androstandioli;
- The plant-derived substances and the plasticisers have been shown to be uterotrophic, i.e. to have oestrogenic effect in the uterus, while the 2 pesticides prevent androgen-stimulated prostate growth. Since these steroids, but also thyroid hormones and glucocorticoids, have profound effects in many other organs outside the reproductive tract, the goal of this project was to

study these effects outside the reproductive tract. As a control, targets within the reproductive tract were incorporated in the study design as well.

## Key findings and conclusions

- Experiments yielded clear indications that EDCs act within the reproductive tract, but also in literally all organs of the organism. In addition immune functions are also compromised by many of the EDCs;
- Many of the EDCs exert effects in the hypothalamo-pituitary-thyroid axis, which renders the human hypothyroid, in cases of iodide deficient food supply;
- Oestrogenicity of isoflavones may endanger the mammary gland and uterus of postmenopausal women and these fears are substantiated by findings of the EURISKED consortium. However, the isoflavones appear to have protective effects in male accessory sex organs like the prostate;
- The well known anti-androgenic effects of procymidone and linuron were confirmed and effects of anti-androgens in intact male animals were also demonstrable. Such effects may be potentially harmful also to humans. Of particular sensitivity may be the exposure of male foetuses, newborns or babies to these anti-androgenic substances, because it is known that androgens play an important role in imprinting brain structures at this early time of life;
- It was observed that UV-screens had oestrogenic effects and had profound inhibitory effects within the thyroid gland to reduce thyroid hormone production by inhibiting iodide uptake into the thyroid follicles as well as by inhibition of thyroid peroxidase activity. Similarly, several isoflavones,

which are freely available as food additives had clear oestrogenic effects and inhibitory effects in the thyroid gland. Thus both groups of these EDCs may endanger a large group of persons living in iodide deficient areas in Europe to develop goiters;

- Some of the EDCs were also active in the liver to modulate the production of high- and low-density lipoproteins, storage pools for cholesterol and tryglycerides. This is another alarming signal, which may indicate that the substances have profound effects on a variety of metabolic parameters;
- In several *in vitro* and *in vivo* test systems, the pesticides procymidone and linuron proved to be pure anti-androgens.

## Relevance and contribution to EU policy

While oestrogenic and anti-androgenic effects of some of the studied EDCs have been intensively investigated internationally. However, the effects in the thyroid gland and in the adrenal open totally new perspectives, which clearly deserve further investigation.

Food additives on the market to replace hormone replacement therapy or used for cosmetic purposes such as bust enhancement or as anti-ageing compounds need further attention. Since genistein and 8-prenylnaringenin not only interfere with thyroid hormones but also have strong oestrogenic effects, their safety concerning the uterus and mammary gland should be thoroughly investigated. It should thus be a political goal to make European food safer and to sponsor research addressing the safety of isoflavone-containing foods, particularly in view of the potency of their oestrogenic effects in the mammary gland and uterus, which may endanger these organs and increase the risk for the development of cancers. EURISKED was part of the CREDO cluster of projects ([www.credocluster.info](http://www.credocluster.info))



## Multi-organic risk assessment of selected endocrine disruptors

### Project acronym

EURISKED

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### FP5 Thematic Programme

Energy, Environment and Sustainable Development

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### EC contribution

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### Website

<http://www.eurisked.org>

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