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Regulation of Endocrine Disruptors:

REACH may change, but will the science evolve?

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Who we are

Cruelty Free Europe: a new network of animal protection groups

Brussels based with a presence at the heart of EU decision-making

Working to bring animal testing to an end across Europe and beyond

Putting animals used in experiments firmly on the European political agenda

Campaigning for humane modern science and progressive legislation

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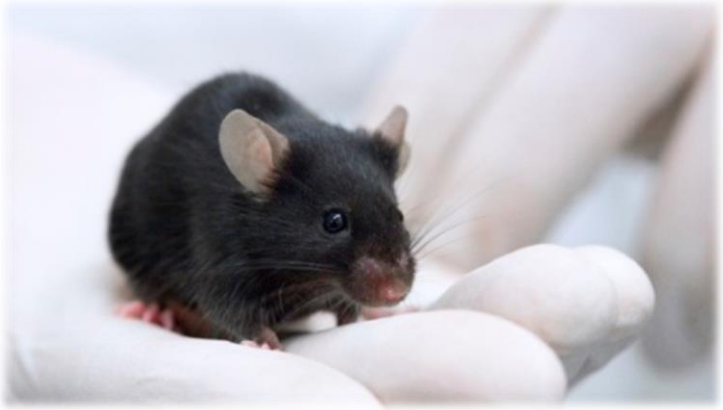
Today's presentation

- What are endocrine disruptors
- Changes to REACH?
- Testing strategies
- Problems with *in vivo* testing methods
- Animal-free methods
- Our recommendations



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Endocrine disruptors

Endocrine active substances

- hormone mimics
- hormone blockers
- changing hormone production and circulation

Mechanisms

- estrogen
- androgen
- thyroid
- steroidogenesis …and more

Endocrine Disruptors cause an
adverse health outcome

Identifying EDs for humans and wildlife - not easy!

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Changes to REACH?

- Calls for REACH to more fully address ED concerns
- REACH already requires a lot of test data, is more needed?
- Attempts to evaluate all substances for ED potential may **rely very heavily on studies on animals**
- Doubtful that animal data is suitable for protecting human and wildlife populations at risk

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Testing strategies

- Focus on high tonnage substances?
  … no, exposure is key
- Address substances one by one?
  … no, mixture effects may be key

- Screen all substances, then test further if endocrine effects observed?
  … no, most substances will have some degree of effect, may be no effect-free level
- Use *in vivo* tests to screen, and predict adverse health outcomes
  … no, animal models may not be relevant or reliable

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Testing strategies - a better approach

Testing directed by real-world **exposure**, not import and manufacture tonnages

Exposure can be:

- Predicted – accounting for tonnage, intrinsic properties and environmental fate (persistence, spread, accumulation)
- Measured - by ecological monitoring and biomonitoring. *For example*: the HMB4EU project

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Problems with *in vivo* methods

- Uncertain effects relevance
- Unreliable prediction of **adverse** outcomes
- Tests not designed for endocrine disruptors
- Little or no validation

In vivo **screening** methods:

- Uterotrophic bioassay
- Hershberger bioassay

… reliability for detecting human-relevant effects is not well characterised

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Problems with *in vivo* methods

In vivo tests for predicting **adverse health outcomes**:

- Repeat dose oral tox 28 day + 90 day
- Combined toxicity and carcinogenicity studies
- Reproduction and developmental studies

} new or repeat studies under REACH?

Some tests updated to address endocrine disruptors
e.g. thyroid hormone measurements added

But there are concerns tests are "… ***not providing the specific information needed to assess endocrine disruption. … at present this approach is failing.***" (CRO quoted in ChemWatch)

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Non-animal methods

- *In silico* approaches and in vivo assays
- Validation work underway at ECVAM
- Advantages of NAMs:
  - Human and wildlife – relevant
  - Lower cost in the long-term
  - Faster, and amenable to high-throughput and automation
  - Ideal for addressing mixtures
- The only option for cosmetics ingredients

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A testing strategy for REACH

REACH may change, but will it follow the latest science?

A solid testing strategy will be **adverse effect-driven** and will:

- Use real-world exposures to identify vulnerable populations and prioritise substances for evaluation
- Link exposure to adverse effects using epidemiological and monitoring data
- Use species-relevant non-animal methods to reveal how substances interact with the endocrine system

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Our recommendations

No routine use of studies on animals to address ED concerns

yet more animal studies under REACH is not the answer

Consider real-world exposures, predicted and measured - not import and manufacture tonnages

Use non-animal methods for human-relevant assessment of endocrine activity

Link exposure and real-world adverse health outcomes using biomonitoring and epidemiological data

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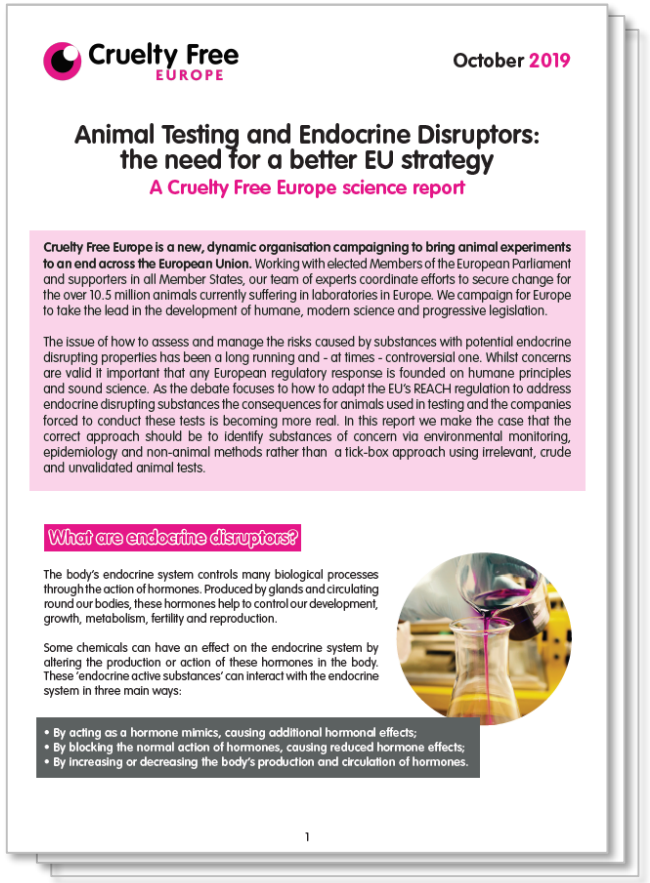
Find out more:

Animal Testing and Endocrine Disruptors: the need for a better EU strategy

Cruelty Free Europe Science report



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Animal Testing and Endocrine Disruptors: the need for a better EU strategy

A Cruelty Free Europe science report

Cruelty Free Europe is a new, dynamic organisation campaigning to bring animal experiments to an end across the European Union. Working with elected Members of the European Parliament and supporters in all Member States, our team of experts coordinate efforts to secure change for the over 10.5 million animals currently suffering in laboratories in Europe. We campaign for Europe to take the lead in the development of humane, modern science and progressive legislation.

The issue of how to assess and manage the risks caused by substances with potential endocrine disrupting properties has been a long running and - at times - controversial one. Whilst concerns are valid it important that any European regulatory response is founded on humane principles and sound science. As the debate focuses to how to adapt the EU's REACH regulation to address endocrine disrupting substances the consequences for animals used in testing and the companies forced to conduct these tests is becoming more real. In this report we make the case that the correct approach should be to identify substances of concern via environmental monitoring, epidemiology and non-animal methods rather than a tick-box approach using irrelevant, crude and unvalidated animal tests.

What are endocrine disruptors?

The body's endocrine system controls many biological processes through the action of hormones. Produced by glands and circulating round our bodies, these hormones help to control our development, growth, metabolism, fertility and reproduction.

Some chemicals can have an effect on the endocrine system by altering the production or action of these hormones in the body. These 'endocrine active substances' can interact with the endocrine system in three main ways:

- By acting as a hormone mimics, causing additional hormonal effects;
- By blocking the normal action of hormones, causing reduced hormone effects;
- By increasing or decreasing the body's production and circulation of hormones.

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