

The EDEN Project: Endocrine disruptors: exploring novel endpoints, exposure, low-dose and mixture-effects in humans, aquatic wildlife and laboratory animals

Within the European Union and throughout the industrialised world there are significant human and wildlife problems relating to male reproductive health. Since the early 1990s, there has been considerable scientific and media attention concerning this issue, but more work is required to clarify the role of endocrine disrupting chemicals (EDCs) on reproductive health.



Objectives

EDEN was a multidisciplinary effort designed to address the key issues that currently hamper hazard- and risk-assessment for EDCs in the European Union, with the following specific objectives:

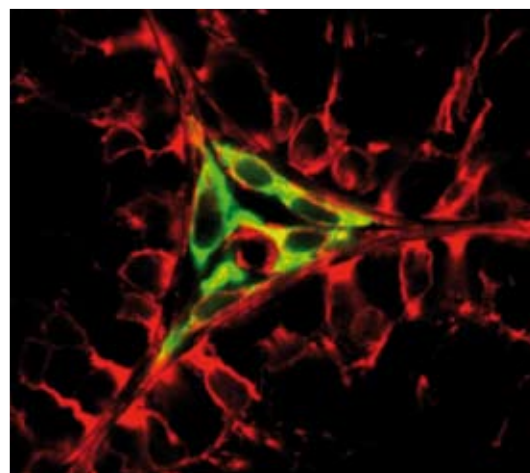
- To gather data about the composition of complex mixtures of EDCs in human and fish tissues from within the European Union;
- To investigate the mechanisms underlying the action of EDCs to evaluate current experimental models for wildlife and human hazard assessment

and to develop novel endpoints and biomarkers for the early detection of effects;

- To provide new insights into indicators of impaired reproductive function and to extend and improve existing European databases;
- To gather data about low-dose effects of EDCs and to develop criteria for low-dose studies by evaluating various bio-statistical approaches for estimating low responses;
- To assess the effects of multi-component mixtures of EDCs and to investigate whether EDCs produce joint effects when combined at doses below their individual effect thresholds.

Key findings and conclusions

- Initial results from chemical analyses have revealed the presence of multiple EDCs in human and fish tissue specimens. Further data



are expected in 2007. Mechanistic investigations have established that the effects of EDCs are not restricted to the reproductive system, but involve multiple targets, including cell signalling and the nervous system. Phthalates, widely used as plasticizers, are capable of inducing many effects *in vivo* that characterise the testicular dysgenesis syndrome observed in humans. It has become clear that these effects arise early in foetal life;

- Analyses of semen quality were extended to Central Europe. New data indicate that poor semen quality is widespread in young men. In some areas of Europe, semen quality has approached crisis levels that may impair human reproduction;
- Experiments designed to assess the effects of low doses of EDCs in cultured cells, fish and rodents are completed. Unusually-shaped dose-response curves were not observed, but the work highlighted the weakness of customary approaches for estimating low dose effects;
- Significant progress has been made with mixture studies. The effects of a four-component mixture on zebra fish and of a three-component mixture on male sexual differentiation in the rat could be successfully predicted by using the concept of dose addition. The mixture led to disruption of male sexual differentiation at doses of the components that individually did not induce observable effects. These observations are of great importance for the regulation of EDCs in the EU.

Relevance and contribution to EU policy

New assays have been developed and molecular tools utilised by research scientists to allow the clinicians and epidemiologists to test for novel biomarkers in human population studies. The relationship between EDCs and their effects in a range of test systems are being explored, which will feed into risk assessment strategies. A database of information pertaining to human male reproductive health in European countries will allow further investigation into the relationship between issues currently affecting human health and causative compounds.

EDEN will strive to determine whether the current hazard and risk assessment strategies currently in place in the European Union are sufficient to deal with the issues of EDCs or require revising. The results of exposure assessment and mixture studies undertaken will help EDEN to assess how this data can be taken into consideration in testing guidelines and risk assessment procedures for wildlife and humans.

All of the information gained from this study is of direct relevance to the research community, the citizens of the European Community and the industry.

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Project acronym

EDEN

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