

# Endocrine Disrupting Pesticides

A number of chemicals such as pesticides are known to interfere with the endocrine system and thereby impair fertility and the development of animals and possibly of humans. There have been a number of attempts to formulate a definition of endocrine disrupting or modulating substances. WWF prefers the definition of the US EPA document from the 1997 Special Report on Environmental Endocrine Disruption: An Effects Assessment and Analysis:

*“An environmental endocrine or hormone disruptor may be defined as an exogenous agent that interferes with the synthesis, secretion, transport, binding, action, or elimination of natural hormones in the body that are responsible for the maintenance of homeostasis, reproduction, development, and/or behaviour.”*

Chemicals may bind to sex hormone receptors, activate them and thus lead to responses similar to endogenous oestrogens and androgens. They may also bind to hormone receptors without activating them. However, by this they block binding of endogenous hormones, which therefore cannot be active.

Beside such receptor-mediated direct actions a number of indirect (anti)oestrogenic and (anti)androgenic reactions are possible. Those include changes in

## An Evaluation of Pesticides Disrupting the Hormone and Reproductive System

the concentration of hormone receptors in the target organs, interference with the biosynthesis of hormones in the endocrine organs, or effects on the biotransformation in the liver. Furthermore, binding of hormones to proteins in the blood plasma as well as the endocrine activity of pituitary and hypothalamus may be influenced.

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In a recent study, utilising in vivo and in vitro assay systems, the following pesticides (licensed in Germany, see Table 1) showed oestrogenic activity in different assay systems: amitraz, lindane, parathion-methyl, permethrin, triadimefon and s-triazines (simazine, atrazine). No anti-oestrogenic or androgenic properties were observed with licensed pesticides. Atrazine, lindane, linuron, procymidon, pyrethroids, vinclozolin and its metabolites showed anti-androgenic activity.



Some pesticides may also disrupt steroid metabolism. Atrazine, for example, induces aromatase, an enzyme that transforms androgens to oestrogens. Conazole fungicides also interfere with the steroid hormone biosynthesis by inhibiting necessary enzymes. This can lead to a reduction in steroid hormone level. Carbofuran and lindane also influence steroid metabolism.

Amitrole, metribuzin, some dithiocarbamates such as maneb, mancozeb and zineb as well as some pyrethroids can disturb thyroid function. Usually the synthesis of thyroid hormones is inhibited. This leads to an enlargement of the thyroid.

It is assumed that some pesticides such as amitraz, some organophosphate pesticides and dithiocarbamates have an influence on the gonadotrophic hormones. For example, interferences with the release of luteinizing hormone (LH) have been observed. The disturbances of the hormone balance may then lead to changes in the gonads, eg. to a lower weight of the testes or the ovaries.

Many pesticides also influence spermatogenesis and the number and quality of sperms, for example organophosphate compounds, dithiocarbamates, copper fungicides and some pyrethroids.

**Table 1: Pesticides Disrupting the Hormone and Reproductive System - Examples from Germany**

Oestrogenic activity	Anti-androgenic activity	Disrupt steroid metabolism	Disturb thyroid function
amitraz lindane parathion-methyl permethrin triadimefon s-triazines	atrazine*) lindane linuron procymidon vinclozolin (metabolites) pyrethroids	atrazine*) carbofuran conazole (epoxiconazole, propiconazole) lindane	amitrole some dithiocarbamates (e.g. maneb, zineb, mancozeb) ioxynil metribuzin certain pyrethroids trifluralin
Influence on gonadotrophic hormones	Influence on spermatogenesis	Reproductive toxicity	*) not licenced by Germany in 1998
amitraz atrazine*) certain organophosphates some dithiocarbamates	copper fungicides certain pyrethroids some dithiocarbamates glyphosate some organophosphates	2,4-D some dithiocarbamates some organophosphates	

Some pesticides have been reported to impair female reproduction and the development of offspring, respectively. Among those pesticides are 2,4-D and some dithiocarbamates. Organophosphate pesticides probably lead to reproductive effects by interfering with hormones of the pituitary-gonad-axis. Furthermore, pesticides can influence the nervous and immune system as well as behaviour.

### Recommendations

Different in vivo and in vitro assay systems are currently used by regulatory authorities for the evaluation of reproductive and developmental toxicity. These assays may not be competent in detecting endocrine disrupting activity.

- Some of the assays should be improved in that regard by adding new endpoints such as determination of sex hormone concentrations, induction of vitellogenin, gonad histology, vaginal cytology, etc.

- For some applications and organisms, however, new assays have to be developed and validated, respectively.

- General monitoring programmes for the determination of wild populations should be extended and contain parameters for the evaluation of potential endocrine disruption, eg. vitellogenin measurements in fish.

- Already licensed pesticides should be reassessed for their potential endocrine activity. There is especially need to investigate the endocrine effects of pesticides in the same group as those substances already identified as endocrine disruptors, for example other triazines or diuron.

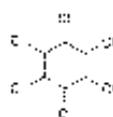
- For the registration of new compounds assays to evaluate endocrine activity should be included in the approval requirements of the EC Directive 91/414. The process to select and validate assay systems has to be speeded up.

- More data on tissue concentrations of the target organs are needed. The bioavailability of endocrine active chemicals should be investigated and more emphasis has to be laid on the investigation of the effect of mixtures.

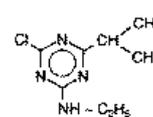
- It should also be assessed whether important metabolites of pesticides that themselves show no hormonal activity have an endocrine disrupting effect.

- There is a need to reassess adjuvants used in pesticide formulations for their endocrine activity. Compounds showing effects on the endocrine system or reproduction, such as alkylphenolic surfactants, should be phased out.

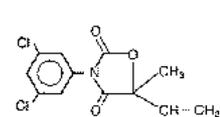
Text prepared by Ulf Jacob



Lindane



Atrazine



Vinclozolin

### References / Further Reading

This briefing is a summary of the case study: Evaluation of Pesticides Disrupting the Hormone and Reproductive System by Dr. Andrea Dankwardt, Technical University of Munich, for WWF-Germany, 1998.

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