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WHO's Assessment of the Link between Exposure to Endocrine Disruptures and the Impact on Human Health

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' The threat of impairment of human reproductive function and the impact on wildlife as a result of exposure to environmental pollutants was a topic of growing scientific and public concern over the last years. A biologically plausible hypothesis has been advanced to explain these adverse health outcomes in terms of endocrine disruption by exposure to environmental pollutants. Numerous scientific papers have been published and concern was expressed by national authorities as well as by several international organizations.

As its 2nd session held in February 1997, the Intergovernmental Forum on Chemical Safety (IFCS) expressed concern regarding the potential health and ecological effects of endocrine disrupting chemicals (EDCs). In the same year the 50th World Health Assembly called upon the Director General of WHO to *take the necessary, steps to reinforce WHO leadership in undertaking risk assessment as a basis for tackling high priority problems as they emerge, and in promoting and coordinating related research, for example, on potential endocrine-related health effects of exposure to chemicals.* As a result of this the International Programme on Chemical Safety (IPCS) has taken the initiative on the Global Assessment of Endocrine Disrupters (GAED).

This state of the science assessment is intended to summarise what we know, identify what we do not know and help to direct future research emphases areas on endocrine disrupters. The assessment will be approached from three directions: (a) chemicals, (b) process/mechanisms (e.g., receptors, signal transduction); (c) health trends and ecological outcomes and their potential linkage to environmental exposures. The assessment document will provide a peer-reviewed scientific report, which reviews and summarize global research on the health and ecological effects of EDCs, building on recent international and national assessments supplemented by new published data.

One of the first actions of IPCS in this field was to agree on a working definition of endocrine disrupters.

An endocrine disrupter is an exogenous substance or mixture that alters function(s) of the endocrine system and consequently causes adverse health effects in an intact organism, or its progeny, or (sub)populations.

The assessment report will summarize and evaluate data on the potential associations between exposure to EDCs and a number of health effects in human populations such as decreased sperm counts and semen quality, change in sex ratio, developmental abnormalities of the male

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reproductive tract, testes and prostate cancer, breast cancer and endometriosis. The strength of evidence in the global literature relating to human reproduction and the endocrine disrupter hypothesis will be reviewed. Consideration will be given to both the general population as well as potentially sensitive sub-populations. It is expected that the first draft will be subject to a peer review will be available by the end of this year.

At this intermediary stage of the IPCS GAED process the current presentation will try to shed some light on a number of questions:

- Is there a general trend or are there geographical differences in human sperm counts and quality?
- Is there an increase of male reproductive tract abnormalities?
- What is the evidence and plausibility that testis dysfunction and male reproductive tract abnormalities may be linked to endocrine disrupters?

Some epidemiological, toxicological and clinical data supporting the hypothesis of endocrine-mediated dysfunction will be presented taking in account the other hypotheses, which may explain human testis function and semen quality variations. Strengths and weaknesses of the published data will be addressed according to various possible bias as the characteristics of the studied populations the methodological and laboratory procedures and the methods used to analyse the data.

In addition, the biological plausibility of a possible link between human cancers and endocrine-active compounds will be addressed. Given the hypothesis that exposure to chemicals with potential hormonal activity has increased over recent decades, age-adjusted incidence trends for some main types of tumours that are potentially hormone-related (breast, prostate and testis) will be presented as an example.

It should be recognized that still the major problem with regard to human health risk assessment of EDCs is the question whether the presence of endocrine disrupters in the environmental could lead to actual exposure of the general population to such an extent that human reproductive function could be adversely affected. Particularly for human health effects a causal link with exposure to environmental pollutants is often difficult to establish. Assessment of human exposure to endocrine disrupters is complicated by the wide range *of* compounds having endocrine disrupting properties. Many of them are persistent in the environment, accumulation in the food chain and will finally reach humans were they will sequester in the body. Others, however, are in the body for only short period of time. In the current presentation some examples will be given of methodological problems and the question how to assess human exposure during critical periods in our development.