Karolinska Institutet

Institutet för Miljömedicin

Risk Assessment of Endocrine Disrupting Compounds

AKADEMISK AVHANDLING
som för avläggande av medicine doktorsexamen vid Karolinska Institutet offentligen försvaras i Samuelssonsalen.

Fredagen den 31 maj, 2013, kl 09:00

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Stockholm 2013

ABSTRACT

During the past decade a growing number of chemicals have been identified as having endocrine disrupting properties in laboratory studies. Also, associations between exposure to such substances and endocrine-related health effects in the general population, as well as in wildlife, have been increasingly reported. This implies that past chemical regulation has failed to adequately protect human health and the environment. Endocrine disrupting compounds (EDCs) have lately been identified as substances of very high concern that should be phased out in new European (EU) legislations for e.g. industrial chemicals, plant protection products and biocides. There is thus an increased pressure on regulatory agencies to be able to efficiently and reliably identify, characterize and risk assess EDCs.

However, risk assessment of EDCs has proven complicated, in part due to the complex toxicity exhibited by substances that can interact with the endocrine system, and also because there are currently no generally agreed upon criteria within the EU or internationally that direct how to specifically identify compounds with endocrine disrupting properties.

The aim of this thesis project has been to identify how scientific uncertainties concerning the toxicity of EDCs can be reduced or handled to make health risk assessments of EDCs more transparent, systematic, and reliable. To that end literature studies were conducted that investigated the risk assessment process for EDCs within different regulatory frameworks in the EU, as well as the underlying toxicity data available to risk assessors and how the use of all available toxicity data can be improved. The much debated EDC bisphenol A (BPA) was used for a case study in a large part of this work.

A comparison of different regulatory frameworks within the EU showed that the regulatory risk assessment process, including underlying policies, criteria and requirements may differ for EDCs belonging to different regulatory groups, e.g. industrial chemicals, plant protection products or pharmaceuticals. The investigations within this project also showed that non-standard research studies, i.e. studies not conducted according to standardized regulatory test guidelines, fill data gaps and contribute information that could be particularly important for the identification and risk assessment of EDCs. However, non-standard studies were often criticized for having methodological limitations or being insufficiently reported, limiting their use in regulatory risk assessment. Regulatory agencies commonly gave more weight to standard than non-standard studies in risk assessment of BPA, despite the growing amount of research indicating that toxic effects at low doses were being overlooked.

A framework of criteria and guidelines intended to enable transparent and systematic evaluation of non-standard research studies, as well as guidance for how to report in vivo research to meet the requirements for regulatory risk assessment, was proposed. These tools are intended to facilitate the use of non-standard research studies in regulatory risk assessment and hopefully improve the reliability of risk assessment conclusions for EDCs.

ISBN: 978-91-7549-144-8