IRIS AperTO

UNIVERSITÀ DEGLI STUDI DI TORINO

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IRIS AperTO

UNIVERSITÀ DEGLI STUDI DI TORINO

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Letter to The Lancet DE

EU regulation of endocrine disruptors: a missed opportunity

A. Kortenkamp, J.P. Bourguignon, R. Slama, A. Bergman, B. Demeneix, R. Ivell, G.C. Panzica, L. Trasande and R.T. Zoeller

The European Commission (EC) has missed a unique opportunity of developing a regulatory system that sets new standards in the protection against endocrine disrupting chemicals. The proposed amendments to the EU pesticide law and the criteria for the identification of Endocrine Disruptors (EDs) which the EC published on 15 June 2016, after a delay of almost 3 years [1], ensure that hardly any EDs used as pesticides will be barred from commerce.

European Union (EU) legislation requires that all chemicals used as pesticides and biocides are approved through a risk assessment procedure that estimates a safe level of exposure. However, by a hazard-based exclusion clause, substances identified as carcinogens, mutagens, reproductive toxicants and EDs do not enter this complex risk assessment process. To minimize exposure to these hazardous substances via food, they are generally refused approval, but specific derogations exist. For pesticides, approval can still be granted if *exposure* is negligible. Since there is no exposure via food, this rule is somewhat relaxed for biocides, where approval can be given if the *risk* is judged negligible.

In violation of the hazard-based exclusion philosophy of the pesticide law, the EC has now proposed an amendment that extends the biocide relaxation to EDs in pesticides. They will be treated less restrictively than carcinogens, mutagens and reproductive toxicants, and exactly like other pesticide substances that have less hazardous properties. In practice, this ensures that exposures via food continue to occur. This is of concern because some pesticides can produce irreversible endocrine disrupting effects. An example is the organophosphate chlorpyrifos which can affect maternal thyroid hormone signalling [2] which may significantly impact children's IQ and brain structure [3]. Similarly, some widely used pesticides can antagonise the androgen receptor and suppress prostaglandin synthesis, with potentially irreversible consequences for male sexual development in fetal life [4].

Previously, the EC had listed four options for defining regulatory ED criteria of which two (labelled 2 and 3) rely on the WHO definition of EDs. Earlier, we favoured option 3 which allows differentiation between known, presumed and suspected EDs [5]. The EC now supports option 2 with a single category for EDs, but with a twist that will raise the level of proof required for identifying a chemical as ED. The proposed option 2 differs from the way in which carcinogens, mutagens and reproductive toxicants are currently categorised in EU law. The strictest hazard category 1 differentiates between known (1a) and presumed (1b) carcinogens, mutagens or reproductive toxicants. The evidence required for category 1a is normally based on human studies, while category 1b relies on data from animal studies, but categorisation as 1a or 1b triggers the same regulatory restrictions. The draft EDC criteria depart from this distinction and replace the requirement for a presumption with the much stronger demand that a chemical must be *known* to cause an endocrine disrupting adverse effect relevant for human health.

Should these proposals be adopted, many EDs with human exposure will escape identification, thus eroding the high level of protection enshrined in the EU pesticide and biocide laws, and violating the demand for scientifically-based ED criteria.

[1] http://europa.eu/rapid/press-release_IP-16-2152_en.htm (accessed 18 June 2016)

[2] EFSA, Scientific Opinion on the identification of pesticides to be included in cumulative assessment groups on the basis of their toxicological profile1. *EFSA Journal 2013; **11**(7):3293*-2013.

[3] Korevaar TI et al., Association of maternal thyroid function during early pregnancy with offspring IQ and brain morphology in childhood: a population-based prospective cohort study. *Lancet Diabetes Endocrinol*, 2016; **4**(1): 35-43

[4] Kugathas S, Audouze K, Ermler S, Orton F, Rosivatz E, Scholze M, Kortenkamp A, Effects of Common Pesticides on Prostaglandin D2 (PGD2) Inhibition in SC5 Mouse Sertoli Cells, Evidence of Binding at the COX2 Active Site, and Implications for Endocrine Disruption. *Environ Health Perspect* 2016; **124**(4): 452-459

[5] Bourguignon, JP, Slama R, Bergman A, Ivell R, Kortenkamp A, Panzica GC, Trasande L, Zoeller RT, Science-based regulation of endocrine disrupting chemicals in Europe: which approach? Lancet Diabetes Endocrinol 2016; Published Online June 13, 2016 http://dx.doi.org/10.1016/ S2213-8587(16)30121-8

andreas.kortenkamp@brunel.ac.uk

Brunel University London, Institute of Environment, Health and Societies, Uxbridge UB8 3PH, UK (AK); Pediatric Endocrinology, CHU Liège and Neuroendocrinology Unit, GIGA Neurosciences, University of Liège, Liège, Belgium (J-PB); Inserm, CNRS and University Grenoble Alpes, IAB Joint Research Center, Team of Environmental Epidemiology, Grenoble, France (RS); Swedish Toxicology Sciences Research Center, Södertälje, Sweden (ÅB); UMR CNRS/MNHN 7221, Department RDDM, Muséum National d›Histoire Naturelle, Paris, France (BD); School of Biosciences & School of Veterinary Medicine and Science, University of Nottingham, UK (RI); Department of Neuroscience, University of Torino, and Neuroscience Institute Cavalieri Ottolenghi, Orbassano, Italy (GP); Departments of Pediatrics, Environmental Medicine and Population health, New York University School of Medicine, New York, NewYork,USA(LT);andUniversityof Massachusetts, Biology Department, Amherst, MA, USA (RTZ)