

No scientific basis for conclusions on DINP and reproductive health

The European Council for Plasticisers and Intermediates (ECPI) is committed to the safety and sustainability of plasticisers, human health being of paramount importance for the European plasticisers producers. For this reason, ECPI experts wish to address the misconceptions related to the conclusions of a study presented in the recent publication by Bornehag (2014)ⁱ on pre-natal phthalate exposure and anogenital distance in Swedish boys and broadly alarmingly reported by several European media.

The conclusions made by Bornehag and his coworkers are not justified and do not provide any scientific evidence of the reduction of the anogenital distance (AGD) in boys associated with urinary concentrations of DINP metabolites.

The authors already admitted that their data would only “suggest an effect” and it is in fact evident that Bornehag’s conclusions are not supported by the actual data included in the published paper. Furthermore the data are inconsistent with the results published in 2005 by Swan, a co-author of the current studyⁱⁱ.

Bornehag (2014) was not able to reproduce the findings as published by Swan (2008), i.e. the correlation of reduced AGD with urinary DEHP metabolite levels. This is remarkable as his study, included 196 boys instead of only 106 – which significantly increases the statistical power to detect effects if they are occurring- could not confirm the previous results of Swan (2008). The inability to detect an association between DEHP and the anti-androgenic endpoint of AGD calls into question the methodological approach used by Bornehag and questions any biological significance of the results reported. Regarding the reported very small reduction in AGD in association with levels of DINP metabolites, it is to be noted that comprehensive animal studies on DINP have shown no adverse effects on reproduction, as acknowledged in the publication by Bornehag et al.

Moreover, while AGD measurements on rats can routinely be done by experienced technicians, the difficulties associated with the measurement of AGD in humans have been described in detail by Salazar-Martinez (2004)^{iv}.

Furthermore, Bornehag did not provide any evidence for the claimed association between reduced anogenital distance and male genital birth defects and impaired reproductive function in adult males. In our view this hypothesis is not supported by any data. It should be noted that the children examined were in the normal range of health for children of their age, and there were no genital defects as reported in the media.

Epidemiological studies in the general population are observational and are subject to unavoidable uncertainty arising from various sources including exposure assessments. To date, the scientific community has not developed a set of systematic guidelines for implementing and interpreting biomonitoring exposure data for chemicals that, like phthalates, are quickly eliminated from the body. Nonetheless, a single urine sample taken during the first trimester of pregnancy does not provide enough information to draw conclusions on longer term exposures.

Therefore, data presented by Bornehag are not suitable to correlate exposure of the mothers during pregnancy with any effect on the offspring.

Extensive human biomonitoring studies have shown that exposures to DINP are well within conservative safe limits.

The European Chemicals Agency has recently reviewed all relevant data for DINP including the Swan et al studies and the biomonitoring data with the conclusion of no further risks for adults or children from the use of DINP in current applications.

ⁱ Prenatal Phthalate Exposures and Anogenital Distance in Swedish Boys. Carl-Gustaf Bornehag, Fredrik Carlstedt, Bo AG. Jonsson, Christian H. Lindh, Tina K. Jensen, Anna Bodin, Carin Jonsson, Staffan Janson and Shanna H. Swan. *Environmental Health Perspectives*. Advance Publication: 29 October 2014.

ⁱⁱ Swan (*Environ Health Perspectives* 113(2005), 1056-1061) reported urinary concentrations of the metabolites of Di-(ethyl)phthalate (DEP), Benzylbutylphthalate (BBP), Di-(isobutyl)phthalate (DIBP) were associated with reduced anogenital index (AGI=the anogenital distance (AGD)/body weight). No correlation was identified for three metabolites of Di(2-ethylhexyl)phthalate (DEHP), which reduces the AGD in male rats. Decreased AGD was found to be associated with 3 metabolites of DEHP in a subsequent publication by Swan (*Environ Research* 108 (2008), 177-184). Here, the data from 2005 were updated and analyzed by improved statistical methods and by increasing the number of observations (106 boys observed as compared to 85 in the previous study).

ⁱⁱⁱ Swan *Environ Research* 108 (2008), 177-184

^{iv} Salazar-Martinez, *Environmental Health: A Global Access Science Source* 2004, 3:8 doi:10.1186/1476-069X-3-8