Re: The study of the relation between maternal occupational exposure to solvents and birth defects should include oxygenated solvents (authors' response)

We appreciate the interest of Dr Garlantézec *et al* in our article on the association between maternal occupational exposure to organic solvents (chlorinated, aromatic and Stoddard) and birth defects.[1] We reported a positive association between chlorinated solvents and neural tube defects, particularly spina bifida; we did not observe an association between solvent exposure and orofacial clefts.[2]

As noted in their comment, our exposure assessment did not include oxygenated solvents such as glycol ethers, which have been previously linked with an increased prevalence of some birth defects, including both oral clefts and neural tube defects. Garlantézec *et al* suggest that our exclusion of oxygenated solvents may explain our null findings for oral clefts because women exposed to such solvents may be included in our reference group, thereby introducing bias. Although potentially a plausible explanation for our findings, we believe that bias due to the lack of assessment for oxygenated solvents is unlikely. Based on preliminary, unpublished data from an expert industrial hygienist review-based assessment for the National Birth Defects Prevention Study, only 0.4% of working women in our study population had any exposure to glycol ethers during pregnancy or the 3 months before conception. Because the prevalence of occupational exposure to glycol ethers in our study population is exceedingly rare, its omission would not result in a meaningful underestimate of our effect measure estimates. However, estimated exposure to other oxygenated solvents such as aliphatic alcohols, ketones, esters and aldehydes, in our study population is unknown.

We agree with Garlantézec and colleagues that differences in the definition of exposure (characterised by solvent type, formulation or mixture, frequency and intensity, etc, as noted in our Discussion section) may explain apparent 'inconsistencies' in reported results across studies. We encourage further dialogue and research aimed at elucidating the true underlying relation

between exposure to distinct classes of organic solvents and birth defects.

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