Reviewer’s report

Title: Exposure to Hazardous Air Pollutants and Risk of Incident Breast Cancer in the Nurses' Health Study II

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Reviewer: Zorana Andersen

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In article 'Exposure to Hazardous Air Pollutants and Risk of Incident Breast Cancer in the Nurses' Health Study II' authors aim to reproduce results from two studies based on California Teacher's Study (CTS) where associations between several HAPS and estrogen disruptors with breast cancer incidence was reported. Authors find little agreement with CTS study, and generally weak support for increased risk of breast cancer with any HAPs, with associations being weak positive, and going in both directions (positive and negative). Study is well designed and clearly written and presented, based on a well-established NHSII cohort, with excellent data on breast cancer incidence, subtypes by ER status, risk factors, and good data on HAPs. However, authors need to discuss several issues which may help elucidate differences between CTS and NHSII study, before study can be accepted. My specific comments can be seen bellow:

Comment 1: My main concern in the study design is the choice of exposure matrix for HAPs for year 2002, the reason being that earlier studies in CTS based their funding on HAPs data from the same year. The NATA had data available from HAPs assessment in 1996, 1999, 2002 and 2005. Authors write that EPA cautions against comparing concentrations against NATA due to differences in methodology. Did author's consider different criteria to choose which NATA data to use, for example based on the quality of data, if there are any validation studies of HAPs predictions for different years available? Although methods are different, I would argue that there is added benefit in trying different windows of exposure. Perhaps focusing on the earliest data from 1996 would have been more optimal, since easiest exposures are probably the most relevant for breast cancer development, as authors do point out in discussion. Can authors discuss a bit further?

Comment 2: Page 11, line 9: Authors state that 'Women in the CTS were also likely to be parous (26% versus 18%)?' This seems to be mistake, it should be nulliparous, according to statistics in Table 1.

Comment 3: Author point out the differences between CTS and NHSII cohorts, one being number of postmenopausal women in two cohorts, which is much higher in CTS. They speculate that HAPs may be more relevant for postmenopausal women, but could have they tested this (effect modification analyses) in their data, for selected HAPs and estrogen disruptors?

Comment 4: Can author discuss in little more detail geographical differences between the two studies, CTS based on California and NHSII, being a nationwide study, as this is an important possible explanation for different findings in two studies. Are concentrations of HAPs
higher/lower in California then rest of the country/states represented in NHSII? Is NATA data assessment for HAPS possibly better for California (number of measurements, etc.), if there are any validation studies possible?

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