Reviewer's report

Title: Cadmium Burden and the Risk and Phenotype of Prostate Cancer

Version: 1 Date: 28 November 2008

Reviewer: Marco Vinceti

Reviewer's report:

- Major revisions

Overall, the study results offer very little if any evidence to support a role of cadmium in prostate cancer etiology, though limitations of the study might explain this. In particular, I would strongly emphasize (both in the abstract and in the discussion) the possibility that progression of the disease could lead to a decrease in body Cd content, due to a concentration of the metal in the prostate itself or due disturbances in nutrition and metabolism, and this is particularly true for short-term markers of exposure (such as blood and, to some extent, urine). The sentence in the Discussion section "We conclude that body burden of cadmium is associated with the risk of prostate cancer.." is incorrect, due to the study results. Finally, the possibility that the (interesting) relation between prostate cancer phenotype and Cd levels is due to and effect of the specific tumor type and not to an etiologic role of the metal must also be considered, in my opinion.

The Statistical analysis section does not (correctly) mention statistical significance testing, but unfortunately this concept is present in the Results section. The approach based on statistical significance, i.e. for example on cutoff of P-values at 0.05 o 0.001, is incorrect and might led to inadequate evaluation of study results (particularly of those defined as 'non-significant'..).

The possibility of selection bias should be carefully considered at least for controls (and possibly also for cases), since no information about causes of referral to the hospital are reported in the manuscript. Selection bias might particularly have occurred in admittance to services of urology and family medicine. Were cases with other malignancies and with hormonal disorders also excluded from the study, as the authors did for controls?

- Minor points

Relevant recent PubMed-indexed papers concerning the cadmium-prostate cancer relation have not been cited by the authors.

Conclusions of the abstract do not mention a (or 'the') major finding of the study, i.e. the observation that the study results yielded very weak evidence supporting a role of cadmium in prostate cancer etiology.

The last sentence in the Background ("We found, for the first time,...") is inappropriate in this section.
**Level of interest:** An article of importance in its field

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests