COMMITTEE ON CARCINOGENICITY OF CHEMICALS IN FOOD CONSUMER PRODUCTS AND THE ENVIRONMENT

Organochlorine Insecticides and Breast Cancer: Additional information and first draft statement.

Introduction

1. The COC considered a review paper at its September 2003 meeting and tabulated and graphical summaries of the epidemiological data at the November 2003 meting. Members also considered a review of the additional data on oestrogenicity of organochlorine insecticides at the November 2003 meeting.

2. The Committee agreed that sufficient information had been provided to allow the secretariat to draft a first draft statement subject to consideration of a number of editorial comments on the tabulated summaries of epidemiological studies. Members asked for the graphs to be revised using a log scale for Odds/risk ratio and to incorporate a footnote regarding interpretation of the data.

3. The Committee agreed that the available data were consistent with the conclusion reached in 1999, namely that it is most unlikely that current exposures to organochlorine compounds would represent a significant risk for breast cancer.

4. It was suggested that a cut off date for the statements be proposed for the statements. January 2004 has been proposed.

Additional information since November 2003 meeting

Epidemiology (Annex 1)

5. The Committee discussed the suggestion that a meta-analysis study would assist in resolving whether there was an association between organochlorine insecticides and risk of breast cancer. Overall, members felt any such study was likely to show no overall association. Members will be interested to note the appended meta-analysis undertaken by Lopez-Cervantes M and colleagues (published in Environmental Health Perspectives volume 112, 207-214, 2004, and online on 22 October 2003. Annex 1) The authors identified 22 published studies from the literature which met a number of pre set criteria (at least 50 cases, reported measures of association and confidence intervals, a measure of ppDDE in biological samples and published in journals listed by Journal Citation Reports-Science Edition). All of the 22 studies identified were case-control design

although 9 were nested analyses from prospective studies. The summary risk ratio was 0.97 (95% CI 0.87-1.09). There was no clear evidence for heterogeneity (borderline effect for retrospective population based due to one study Van't Veer et al 1997,BMJ vol 315, 81-85). There was no apparent effect for a number of factors which might affect the association including whether biological analyses were based on serum or adipose tissue or breastfeeding. Overall there was no evidence for an association between p'p'DDE and risk of breast cancer.

6. In a separate study analysis of adipose tissue for a range of organochlorine chemicals was undertaken using a hospital based case-control of 224 newly diagnosed breast cancer patients at the Long Island Medical Center, Ny, U.S.A. and North Shore University Hospital, Manhasset NY, U.S.A. (between 1994-1996) (Muscat et al Cancer Epidemiology Biomarkers prevention, 12, 1474-78,2003). There was no evidence of an association between adipose tissue levels of DDE, DDT, â-HCH and other organochlorine chemicals and risk of breast cancer (based on highest versus lowest tertile levels). The data from this study will be entered onto the table.

7. A small case-control study of serum levels of DDE, total serum DDT and â-HCH was undertaken using 69 newly diagnosed premenopausal breast cancer cases and 53 controls recruited from three cancer hospitals in Egypt (Soliman et al Environmental Research, 92, 110-117, 2003). There was no association between OCIs and risk of breast cancer. The authors noted that breast feeding for a period of up to 18 months was associated with low levels of OCIs in serum. The data from this study will be entered onto the table.

8. A further small case-control study published in 2002, has recently been retrieved. The authors (Mathur V et al Environmental International, 28, 331-336, 2002) reported elevated levels of a range of OCIs in blood of breast cancer cases. Members are asked to comment on this paper. The paper will need to be added to the draft statement.

Studies of potential mechanisms (Annex 2)

9. MCF-7 cells were continuously exposed to â-HCH (at 100 nM and 0.1 ìM) for 13 months (Zou E and Matsumura F. Biochem Pharmacol, 66, 831-840, 2003). The authors reported increased proliferation in an anchorage-independent growth assay and changes in gene expression (as determined by Western blotting investigations) which were interpreted to indicate that the treatment had promoted cell transformation and invasiveness of these cells. These changes are of interest to note but their relevance to the assessment of the association between â-HCH and breast cancer is limited.

10. An unpublished (accepted for publication in EHP) paper from Tinwell and Ashby shows that effects of mixtures of potential xeno-oestrogens is likely to be less than additive. Although, not conducted with organochlorine compounds, the information may be appropriate to cite in the draft statement.

Revised tables and graphs (Annex 3)

11. These are presented for members information. The objective of publishing the tables is to provide publicly available summaries of the information used by COC in its evaluation. Members had discussed whether the presentation of the data in the graphs might be considered misleading as the reported odds/risk ratios were not presented in terms of unit increases in exposure. It is suggested that the tables do form a valuable and succinct pictorial presentation of the data and are acceptable provided the footnote is clear.

Draft statement and non-technical summary.

12. The draft statement and non-technical summary are appended as Annex 4. Members are asked to consider and comment on the draft conclusions.

Secretariat February 2004.