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CC/07/18

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

### Horizon scanning exercise 2007

1. Members are asked to propose items for consideration by the Committee in 2008. Some suggestions from the secretariat are given below.

#### Review of the 2006 horizon scanning exercise

2. The topics identified for further work in the 2006 horizon scanning exercise and the outcome are given in the table below. Members are asked whether they would still support further work on the outstanding items (see CC/06/21: <http://www.advisorybodies.doh.gov.uk/pdfs/cc0621.pdf>) for more information on how these items arose).

Topic	Outcome
Trends in cancer incidence	Review of NHL currently underway  Members asked to see data on trends in breast cancer before deciding whether further work necessary – see below
Computational systems biology	To be considered as part of toxicogenomics review
Formaldehyde – leukaemia and occupational exposure	Considered by COM, and by COC in July 2007
Toxicogenomics - role in predicting carcinogenicity and in confirming or proposing a mechanism of action	Considered in July 2007; draft statement to be drawn up with COM and COT
Thresholds for genotoxic carcinogens	Outstanding
Dose-response modelling to assess mechanism of action	Outstanding
Methodological flaws in epidemiological studies linking carcinogen-DNA adduct levels with cancer risk	In progress
Carcinogenicity of mixtures	Outstanding
Nanomaterial carcinogenicity - update	Outstanding

#### Breast cancer

3. Members asked to see data on trends in breast cancer before deciding whether further work necessary. Annex 1 is a download from the ONS website

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which shows trends in breast cancer incidence in women from 1971 to 2004. Age-standardised rates have increased from approximately 70 per 100,000 to 120 per 100,000, although the rate of increase appears to have slowed since the end of the last century. However, the situation is complicated by the introduction of screening in 1988, which leads to the detection of smaller tumours (Aubard et al, 2002) and may account for the rapid rise in incidence in the subsequent few years. Members will wish also to note a new review of the epidemiological data on environmental pollutants and breast cancer by Green Brody et al (2007), attached at Annex 2. Are there any environmental pollutants for which Members consider that it would be useful to review the data on association with breast cancer?

## Human Relevance Framework/ Mode of Action

4. Members also agreed last year that the committee should take a new look at the Human Relevance Framework when an paper from IPCS with an update of its Mode of Action (MOA) framework was published, together with some case studies. These papers have now been published in Critical Reviews in Toxicology and this subject will be brought to the committee for further discussion next year. This could include a review of completed MOA assessments in the literature – do Members think this would be useful?

## Potential further topics

### *Mechanisms of transgenerational carcinogenesis*

5. The FSA is arranging a joint workshop on transgenerational epigenetics in February next year. This may identify work which the COC wishes to take forward on mechanisms of transgenerational carcinogenesis.

6. A few other items are suggested following a limited search of PUBMED for references during 2007 which used the terms 'carcinogen evaluation' and 'carcinogen epidemiology'. Titles and abstracts were briefly scanned to identify topics or papers which might be of interest to the Committee. A few suggestions are made below.

### *Suggestions from experimental studies*

7. A negative assay in transgenic mice for resveratrol has been published. A negative six-month study has been published in p53+/- transgenic mice to evaluate the possible oncogenicity of resveratrol (3,5,40-trihydroxy-trans-stilbene), a cancer chemopreventive agent present in grapes and other foods (Horn et al, 2007). The COC published a statement on transgenic mouse models in 2002. Is there scope for a review of studies published since this date? Would this help with risk assessment?

8. The consideration of toxicogenomics papers at the July meeting did not cover proteomics and/or metabonomics data. A paper by Gluckman et al (2007) used a classical proteomics approach, verified by a recently introduced protein

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quantitation method, for the evaluation of early protein biomarkers which are predictive for chemically induced hepatocarcinogenesis in rats. N-nitrosomorpholine was used as the chemical hepatocarcinogen. The authors claim that their results show the usefulness of the new method for biomarker prevalidation as well as for identification of further potential marker proteins, which are indicative for liver hepatocarcinogenicity. In a separate paper, the potential of quantitative proteomic analysis to predict carcinogenicity of chemical compounds was investigated (Yamanaka et al, 2007). The effects of 63 chemical compounds given for 28 days on protein expression in the rat liver was analysed using zoom gel imaging. The authors claim it was possible to distinguish between genotoxic carcinogens and non-genotoxic carcinogens. The authors report that transcriptomics could differentiate between the two types of animal carcinogen studied, but metabolomics was relatively poor at identifying endogenous biomarkers although the whole metabolite profile was altered.

9. An evaluation has been published of genetic alterations during rodent carcinogenesis of the brain and lung with butadiene and chloroprene (Ton et al, 2007). The COC and COM have previously indicated an interest in mutation spectra following chemical induced carcinogenicity. Should this area be subject to a detailed review?

## *Suggestions from human studies*

10. A recent review has been published of the susceptibility of children and adults to secondary or therapy-related acute myelogenous leukaemia resulting from treatment with certain cytostatic chemotherapeutic agents (Pyatt et al, 2007). The authors concluded there was no evidence to support the EPA proposal of an additional default factor of 10 for susceptibility of children to cancer. Would this be a useful paper for COC to review?

11. Some authors are promoting 'mutagen sensitivity' as a genetic susceptibility phenotype for various cancers. A case-control study by Wu et al (2007) evaluated mutagen sensitivity, as assessed by two separate assays, as a susceptibility marker for lung cancer and explored the interplay of the genetic marker and multiple epidemiologic risk factors in modulating lung cancer risk. The study included 977 patients and 977 controls. The authors claim that the outcome strongly supports mutagen sensitivity as a predisposition factor for lung cancer. Would members like to review this area in more detail?

## Comments

12. Do Members wish to take forward any of the above suggestions? Many are generic issues which impact on carcinogen risk assessment and would eventually be of value in any updating of the COC guidelines.

13. Do Members have any other topics or chemicals to suggest?

14. Do Government departments/agencies wish to raise any topics?

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15. What priority should be given to items identified for further work?

Secretariat  
October 2007

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Annex 2 to CC/07/18

Green Brody J, Moysich KB, Humblet O, Attfield KR, Beehler GP and Rudel RA (2007). Environmental pollutants and breast cancer. Cancer Supplement 109 (12). Published online 14 May 2007.

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