

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

DRAFT SACN REPORT ON IRON AND HEALTH

Introduction

1. In their report, *Nutritional Aspects of the Development of Cancer* (Department of Health, 1998), the Committee on Medical Aspects of Food Policy (COMA) highlighted possible links between red and processed meat and colorectal cancer and recommended that “*higher consumers should consider a reduction*” in red and processed meat consumption.

2. However, it is known that red meat is a rich source of dietary iron. Any general recommendation to reduce meat consumption might compromise dietary sources of iron, as well as other micronutrients. This concern was recognised by COMA which recommended that “*the possible associated adverse implications of a reduction in meat consumption on other aspects of health, particularly iron status*” should be the subject of review.

3. The Scientific Advisory Committee on Nutrition (SACN) Working Group on Iron was established in 2001, with the following terms of reference:

To review the dietary intakes of iron in its various forms and the impact of different dietary patterns on the nutritional and health status of the population and to make proposals.

It was agreed that consideration of both beneficial and adverse effects of increasing iron intakes was required, including the:

- Effect of dietary components on iron absorption and utilisation in the body;
- interaction of infections and inflammation, with iron metabolism and the possibility that this may affect the apparent incidence of iron deficiency.
- effect of iron deficiency on health and well-being, for example mental and physical development;
- potential adverse effects of excess iron, including free radical damage and the risk of cardiovascular disease and cancer.

The draft SACN report on Iron and Health was published for consultation on the 17th June and is attached at Annex A.

Meat and cancer

4. The relationship between meat and cancer was reviewed by COMA in 1998, they concluded that “evidence from cohort studies was: inconsistent for an effect of total meat consumption on risk of colorectal cancer; moderately consistent for a positive association between consumption of red or processed meat and risk of colorectal cancer; moderately consistent that poultry (white meat) and fish were not associated with colorectal cancer risk”. Subsequent meta- analyses (Sandhu *et al*, 2001; Norat *et al*, 2002; Larsson *et al*, 2006) indicate that red meat and processed meat are associated with a small increase in CRC risk, but not total meat. The relationship between meat and cancer is also discussed by the World Cancer Research Fund (1997) who concluded that red and processed meat was a “convincing” cause of colorectal cancer and recommended that the population average consumption should be no more than 300g per week and very little, if any, should be processed. See paragraphs 435-440 of the SACN report for more detail

5. For the current draft report, SACN reviewed prospective cohort studies published since 1996 (when the COMA review was completed). These studies are tabulated and briefly described in Annex B. The relevant extracts from the main report are given below. The main focus of the SACN review was the human epidemiology data, particularly the prospective studies and whilst some animal and mechanistic studies were considered, this was as background to the subsequent work on modelling. This mechanistic data (discussing heterocyclic amines, *N*-nitroso compounds and polycyclic aromatic hydrocarbons (PAHs)) is contained in Annex 5 (pp 211-131) of the draft SACN report which is attached as Annex A to this paper.

Extract from the draft SACN report

6. The following extracts discussing meat and cancer are taken from the SACN report; they discuss the available information and the limitations of that data particularly with regard to classification of red and processed meat:

Meat and colorectal cancer

432. There are a number of plausible biological mechanisms for an association between meat and colorectal cancer. Meat, particularly red meat, contains high levels of haem iron, which is proposed to catalyse the production of free radicals. Consumption of red and processed meat, but not white meat or fish, is associated with increased endogenous production of potentially carcinogenic N-nitroso compounds (Bingham et al, 2002). Heterocyclic amines (HCAs) and

polycyclic aromatic hydrocarbons, which are formed when foods are cooked at very high temperatures have also been proposed to increase the risk of colon cancer (Sugimura, 2000). The fat contained in meat may also affect colorectal cancer risk by increasing production of secondary bile acids which have been associated with promoting colon cancer (Narisawa et al, 1978). The potential mechanisms are considered further in Annex 5. In addition, people eating diets high in meat may eat less fruit and vegetables, foods which might be protective against cancer risk (WCRF, 2007).

433. Several studies have examined the association between red and processed meat intake and colorectal cancer risk. There are a number of difficulties in interpreting the results from these studies including lack of consistency in definitions of red and processed meat, adequacy of dietary assessment methods, and variability in quantification of intakes. These limitations are discussed in further detail in paragraphs 446-454.

Prospective studies of red and processed meat intake and colorectal cancer risk

441. In this report prospective studies published after August 1996²⁵, on the association between red meat and processed meat intake and colorectal cancer, are considered in more detail (Annex 4, Tables 7.5-7.6).

Red meat intake and colorectal cancer risk (Table 7.5)

442. Twenty-one prospective studies have been published since 1996 (including some updated analyses from previously published cohorts). Two of these studies (Balder et al, 2006; Sato et al, 2006) considered the risk of colorectal cancer with total meat consumption rather than only red meat. Twenty-one out of the 25 relative risks reported were greater than one, 3 significantly so; the median relative risk for highest vs lowest red meat intake was 1.17. The increased relative risk was statistically significant in 1 out of the 4 largest studies (Wei et al, 2004; Chao et al, 2005; Norat et al, 2005; Cross et al, 2007); the trend was statistically significant in 2 of the 4 studies and close to significance in 1 study.

²⁴ Defined as beef, pork, lamb, goat, including that contained in processed foods

²⁵ The COMA report, 'Nutritional Aspects of the Development of Cancer' considered cohort studies up to August 1996.

443. Significantly increased colorectal cancer risk was associated with red meat intakes of: ≥ 114 g/d for men, ≥ 80 g/d for women (Chao et al, 2005); ≥ 94 g/day (Larsson et al, 2005); and 62.7 g per 1000 kcal (equivalent to 145 g/d for men and 102 g/d for women²⁶) (Cross et al, 2007). In all the studies which reported a significantly increased risk of colorectal cancer, processed meat was included under the category of red meat.

Processed meat intake and colorectal cancer risk (Table 7.6)

444. Fourteen prospective studies have been published since 1996 (including some updated analyses from previously published cohorts). Thirteen out of the 18 relative risks for highest compared to lowest processed meat intake were greater than one, 5 significantly so; the median relative risk was 1.16. The relative risk was statistically significant in 3 out of the 4 largest studies (Wei et al, 2004; Chao et al, 2005; Norat et al, 2005; Cross et al, 2007) and the trend was statistically significant in all the studies.

445. Significantly increased colorectal cancer risk was associated with processed meat intakes of: ≥ 20.3 g/day (Oba et al, 2006); ≥ 29 g/d (English et al, 2004), ≥ 80 g/day (Norat et al, 2005); 22.6 g per 1000 kcal (equivalent to 52.3 g/d for men and 36.9 g/d for women²⁷) (Cross et al, 2007) and 5 times per week or more (Wei et al, 2004).

Limitations in interpreting the results from prospective studies on red and processed meat intake and colorectal cancer risk

446. The majority of prospective studies published after 1996, suggest that high intakes of red and processed meat are associated with an increased risk for colorectal cancer. Although the increased risk was not statistically significant in most studies, this would be expected if the studies were not adequately powered to detect a significant association.

447. There are a number of methodological inconsistencies between the different studies which make comparisons difficult. These include: adequacy of the dietary assessment methods to obtain reliable estimates of red and processed meat intake; lack of consistency in the categorisation of red and processed meat; and variability in the reporting of quantities of red and processed meat intake.

448. In most studies red meat and processed meat intake is based on a single dietary assessment at the start of the study. This does not take account of changes in dietary patterns over a number of years and could therefore be an unreliable estimate of intake over the specified follow-up period. The relevant period between dietary intake and development of cancer is also uncertain and dietary intakes estimated at baseline may not be the relevant period for dietary assessment in relation to cancer risk.

449. There are also considerable inconsistencies between studies in categorisation and definition of red and processed meat. Some studies have collected detailed information of the foods included under the red and processed meat categories, while others have used very broad classifications (e.g., beef, pork, lamb). In addition, some studies have separated red and processed meat categories and have only included fresh or untreated red meat in the red meat category while other studies have also included processed meat under the red meat category.

450. Another difficulty is the variability in reporting quantities of red and processed meat intake. While most studies compared highest versus lowest red and processed meat intake in grams per day/week/month, some studies reported intake as g/1000 kcal, frequency of intake per week/month or servings/day. There are also large differences in the quantiles of intake between different studies so that the amounts in lowest quantiles described in some studies are higher than the top quantiles in other studies: for red meat, intakes in the highest quantiles ranged from more than 40-158 g/d and in the lowest quantile from 10-61 g/d; for processed meat, intakes in the top quantiles ranged from 16.3 g/d to 80 g/d or more and intakes in the lowest quantiles ranged from 0-12 g/day.

451. Some studies also analysed the association between colorectal cancer risk and red/processed meat intake for men and women combined although intake in the highest and lowest quantiles differed by sex (Brink et al, 2005; Chao et al, 2005). In the study by Chao et al (2005), a significant association was found for men and women combined in the highest compared to the lowest quintile of red meat intake, however intakes of men in the highest quintile were above 114 g/d whilst for women they were above 80 g/d.

452. Although results from prospective studies of dietary fibre and colorectal cancer are inconsistent, it has been suggested that higher intakes of foods containing fibre may protect against colorectal cancer risk (WCRF, 2007; Bingham et al, 2003). However only 8 out of the 21 studies on red meat intake and colorectal cancer risk and 5 out of the 14 studies on processed meat intake and colorectal cancer risk adjusted for fibre intake.

453. There are also a number of other factors that have been associated with colorectal cancer risk. These include genetic predisposition, high total fat intake, low fruit and vegetable intake, low fibre intake, low physical activity, and meat preparation and cooking methods. Studies have varied in the adjustments made for all these factors, so the effects of confounding cannot be excluded.

454. All these factors make it difficult to quantify a level of red or processed meat intake that may be associated with colorectal cancer risk. The effect of a recommendation to reduce the consumption of red meat and processed meat intake on iron and zinc intakes in the UK is considered in section 10.

455. Toxicological data examining whether differences in colorectal cancer risk between white, red, and processed meat can be explained on the basis of heterocyclic amines, N-nitroso compounds, or haem iron can be found in Annex 5.

Conclusions

6. Taking this information into account, SACN drew the following draft conclusion:

The available epidemiological evidence suggests that red and processed meat intake is probably associated with increased colorectal cancer risk. However, as the available evidence is based on prospective observational studies, the effects of confounding by other factors associated with increased colorectal cancer risk cannot be excluded. It is not possible to identify if there is a dose-response or threshold level of red and processed meat which may be associated with an increased colorectal cancer risk because of a number of limitations in the data.

Advice required from COC

7. COC are asked to comment on:

a) whether the prospective data support the draft SACN conclusion that consumption of red and processed meat is probably associated with an increased colorectal cancer risk?

b) whether there is any additional information that should be considered?

Secretariat
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Annexes A and B

These annexes contain information from the draft SACN report on iron and health. It does not necessarily represent the final views of the committee nor the policy of the Food Standards Agency.