

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

**COC Annual report 2022 - draft**

1. The draft COC Annual Report 2022 is attached at Annex A.
2. Members are asked whether they have any comments or suggested changes for the draft.

**Secretariat  
March 2023**

This is a background paper for discussion.  
It does not reflect the views of the Committee and should not be cited.

**CC/2023/04 Annex A**

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Draft report

**Secretariat  
March 2023**

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FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT**

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## Preface



The Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment (COC) evaluates chemicals for their potential to cause cancer in humans at the request of UK Government Departments and Agencies.

The membership of the Committee, agendas and minutes of meetings, and statements are all published on the internet (<https://www.gov.uk/government/groups/committee-on-carcinogenicity-of-chemicals-in-food-consumer-products-and-the-environment-coc>).

[To be updated]

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MD DSc FRCPath FRCPEd FRCSEd

## **COC Ongoing topics**

### **Hydroxyanthracene derivatives**

Following a request from UK-wide Nutrition Labelling Composition and Standards (NLCS) policy group, the UK Food Standards Agency (FSA) commissioned an independent view from the Committee on Mutagenicity (COM) on the mutagenicity of hydroxyanthracene derivatives (HADs) based on consideration of the European Food Safety Authority (EFSA) 2018 opinion on HADs and any additional new data that have become available. The genotoxicity of HADs used in foods had been discussed at the COM meeting in October 2021.

Overall, the COM agreed that the available evidence indicates that emodin, aloemodin, and dantron are genotoxic in vitro, namely from Ames tests. The COM agreed that the negative results from the in vivo bone marrow micronucleus assay are valid and concluded that there is reasonable evidence that there is no genotoxic effect or mechanism in vivo. Consequently, a new in vivo genotoxicity study would not be helpful. The COM considered that the reported carcinogenic effects of HADs, including those seen in the comet assay of colon cells, are caused by the high levels of irritation, inflammation, and diarrhoea.

In March 2022 a discussion paper on the safety of HADs for use in food was brought for review by the COC for its opinion on the carcinogenic potential of HADs. The FSA requested that the COC review the carcinogenicity studies provided in the paper and evaluate the risk of HADs and whether a health-based guidance value (HBGV) could be derived from the information provided.

The COC agreed with the COM that HADs are not a genotoxic carcinogen in vivo. The committee suggested that while theoretically it would be possible to set an ADI, the data available was insufficient as a dose response has not been described. The COC indicated that a dose response was required in order to be able to identify a threshold or point of departure. The COC concluded that more information on the characterisation of HADs would be required for the Committee to discuss a possible HBGV and it would not be possible to set a HBGV for HADs as a single group as they are complex mixtures of different compounds that may have differing mechanisms of action. Therefore, more data would be required to make a decision as a blanket value could be misinterpreted.

Following a call to industry for new information and data, CRN UK were able to provide the FSA with a record of relevant journal articles that had not been considered in the original EFSA opinion. Following an assessment of the information provided, the Secretariat determined that one of the articles might address some of the issues raised by the Committee at the March 2022 meeting.

In July 2022 this additional article, which suggested a potential HBGV for HADs, was presented to the COC. Members indicated that as this HBGV was not based upon any new data and therefore, the value presented in the paper was based upon many different variables including different strains of animals used, different dosing regimens and various endpoints. The COC agreed that there was still insufficient data to conclude

on an appropriate HBGV for HADs. It was noted that the likely levels of exposure seemed to be less than those that would be expected to cause a risk in humans, but this should be explored further with a detailed exposure analysis.

An interim position paper with the addition of dietary and dermal exposure assessment will be presented to the COC in 2023.

## **Joint ongoing topics**

### **Relevance and Reliability of Evidence**

The COT, COC and COM have continued to develop the joint non-technical statement on how the Committees evaluate the relevance and reliability of data when assessing a chemical of concern in 2022. An updated version was presented to the COC in July 2022. Further revisions are expected to be considered by correspondence across all three Committees in 2023.

## **COC Workshop**

The COC held a workshop in November 2022 which aimed to determine what definitive steps can be undertaken to make progress towards improvement of the chemical risk assessment process and regulatory requirements for carcinogenicity, based on research undertaken over the last 10-20 years. The workshop considered issues in the context of pesticides, with different regulatory areas to be covered in future workshops.

Dr Susy Brescia (UK HSE) presented an outline of the status quo of the cancer assessment of pesticide active substances, identifying the limitations of the current paradigm and exploring some of the new approaches that are being developed. A second presentation was given by Dr Phil Botham (Syngenta Product Safety) which outlined a project being carried out by a working group of (mainly US) experts called the Rethinking Carcinogenicity Assessment for Agrochemicals Project (ReCAAP). This aims to propose a weight of evidence approach for waiving rodent cancer bioassays for the registration of food-use pesticides. The final presentation from Dr Richard Haworth (COC member) explored new approaches being taken for pharmaceuticals which evaluate whether a 2-year rat study is likely to add value to a human carcinogenicity risk assessment, and whether the assessment of pesticides can learn from these.

A number of key questions were then addressed in breakout discussion groups to answer the main theme questions:

- What opportunities are there to improve carcinogenic risk assessment in the UK?
- What is the future of the 2 year / lifetime bioassay?

A draft summary of the workshop will be presented to COC at the meeting in March 2023. Further development of the summary is ongoing.

## **Joint session**

COC and COM held a joint discussion session in March 2022, to which COT members were also invited.

Dr John Doe gave a presentation summarising the key points from the recent paper by Harrison and Doe 'The modification of cancer risk by chemicals' (Toxicology Research, Volume 10, Issue 4, August 2021, Pages 800–809). There was agreement that the model proposed by Harrison and Doe articulated the development of cancer very clearly and there was desire to consider its use in chemical risk assessments. Future aspects to address included quantification, accounting for chemical concentration effects, and ensuring appropriate communication of uncertainty and ambiguity.

This was followed by a presentation by Dr Lesley Rushton on the evidence for shift work acting as a modifying risk factor for cancer. This was considered to exemplify why the impact of modifying factors for cancer risk should be evaluated, including considering other factors associated with them, for example obesity is associated with shift work and would also affect cancer risk/

The session continued to provide a number of updates to COC and COM on the COT work on microplastics, the COM guidance on nanomaterials, the work of the FSA Joint Expert Groups, the OPSS Scientific Advisory Group on Chemical Safety of Non-Food and Non-Medicinal Consumer Products and the FSA computational toxicology fellowship and LiDO PhD studentship.

## **Horizon scanning**

The COC undertakes horizon scanning exercises at regular intervals with the aim of identifying new and emerging issues which have potential to impact on public health.

In 2022, the Committee continued to have a standing agenda item for each meeting on horizon scanning topics and to update the COC on upcoming topics for UK and international scientific advisory groups. A full horizon scanning discussion was held in November 2021 and the COC will review the priority topics from the subsequent horizon scanning discussions in 2023.

At the end of discussion in 2021, it was agreed that the priority topics were:

- Maintain a watching brief on factors affecting cancer susceptibility including shift work, stress and other lifestyle factors and how that might affect assessment of chemicals and carcinogenicity

- Consider an update to guidance on assessment of nanomaterials, possibly as a joint activity across COC, COM and COT
- Gain awareness of the potential effects of antibiotics and antivirals on the microbiome
- Consider a joint discussion with COM on thresholds for in vivo mutagens and whether there is new information subsequent to the 2010 COM opinion
- Endocrine disruption and the link with carcinogenicity, acknowledging that endocrine disruption is also within the COT remit
- Impact of chemicals on potential for metastasis or progression of cancer, in particular with respect to the tumour microenvironment
- Communication of cancer risk and how COC should be involved with this, especially with the move away from a yes/no decision on whether a substance is a carcinogen, and ensuring consistency in describing risks, possibly starting with a landscape review of terminology across a number of Committees (FSA and UKHSA) and led by Lay Members
- Ensuring appropriate considerations are made to acknowledging diversity in the population especially where there might be differences in risk between different groups

## Working Groups

### **COT/COC subgroup on the synthesis and integration of epidemiological and toxicological evidence in risk assessment**

The COT and COC set up a subgroup to review the approaches to synthesising epidemiological and toxicological evidence that are used in chemical risk assessments. More information is provided in the COT section [1.XX-1.XX](#)<sub>[BGI]</sub>

## Guidance statements

The Committee continued development of the guidance statement series during 2022. Final revisions to the COC Guidance Statement (G04) 'Use of Biomarkers in Carcinogenic Risk Assessment' are ongoing and are expected to be completed in 2023.