CC/2021/08

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

COC Annual report 2020 - draft

1. The draft COC Annual Report 2020 is attached at Annex A.

2. Members are asked whether they have any comments or suggested changes for the draft.

Secretariat
March 2021

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

COC Annual report 2020 - draft

Draft report

Secretariat
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COMMITTEE ON THE CARCINOGENCITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT

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

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).

Further detail to be added by the Chair

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COC Evaluations

The Microbiome

The microbiome had been on the COC horizon scan list and Professor Tim Gant (PHE) joined the meeting to give an overview of the area and describe some of the specific aspects of relevance to chemicals and carcinogenicity.

The microbiome represents the community of microorganisms that are resident on or in the human body and includes bacteria, viruses and fungi. The term also encompasses the environmental microbiome however the focus of the presentation and subsequent discussions was the internal one. Sequencing methods have indicated a large diversity with the total microbiome being around 30 trillion similar to the number of cells in the human body. The gene pool was estimated to be far larger than that of the human host. The ratio of bacterial to human cells though previously reported at more than 10:1 was considered to be 1:1

The microbiome has been found on any surface of the body that has a connection with the environment and in particular, where conditions favour microbial growth. Humans are thought to be born sterile with the microbiome then immediately establishing, with initial seeding reflecting that of the route of delivery.

Influences on the microbiome have been shown to be both genetic and environmental. Age is an important parameter in driving diversity of the gut microbiome, as are diet and degree of exercise. The gut microbiome provides around 70% of the energy for the gut and is particularly important for the metabolism of small molecules, including environmental chemicals. Thus, changes to the microbiome may lead to changes in host phenotype. Changes to the gut microbiome diversity may alter the types of reactions occurring both for endogenous and exogenous chemicals which may also impact on any toxicological response. Differences in toxicological response have also been reported within animal strains that were housed together and commonly used for chemical testing, which was attributed, at least in part, to differences in the gut microbiome. Such differences allowed metabolism prior to absorption from the gut to occur in some animals, and in others no metabolism occurred, resulting in a difference in the outcome following exposure which could not be predicted.

In terms of therapeutics and disease, treatment with antibiotics may adversely affect the microbiome and the reestablishment of the microbiome can be slow, following the end of a treatment regimen. Evidence is emerging suggesting an adverse effect of antibiotics on the microbiome having a role in in disease processes particularly respiratory diseases. There was some uncertainty in the epidemiology due and more evidence was required to establish the association and in particular causality. Although the microbiome may be involved in modulating toxicity it was not generally taken into account in toxicity or carcinogenicity testing.

A role for the microbiome in the development of cancer was not less established at present, though it was plausible given the role of the microbiome in metabolism of exogenous molecules. An important aspect of microbiome research that was considered missing, and which might impact on its use in risk assessment, was the lack of an agreed definition of

what is considered ‘normal’ in both humans and animals. Also linked to this was the uncertainty around how to predict what proportion of intra-individual variability in response is due to differences in the microbiome.

The COC recognised that the microbiome was an area of concern to the general public who were aware of its potential involvement in the underpinning of a number of diseases. It was agreed that going forward, the Committee should assess how this may impact COC guidelines and opinions. This would best be achieved by establishing a baseline of what is currently known and what further work needs to be carried out to fill critical gaps in knowledge.

Ongoing topics

The Tumour Microenvironment

The COC has been developing a watching brief document on the tumour microenvironment in recognition of the awareness of its role in cancer development. Many of the key events associated with the interaction of neoplastic cells with the microenvironment are not considered in current risk assessment methodologies. This is an area that the Committee will be keeping awareness of in the coming years

Joint meetings

In November 2020, the COC and COM held a joint online meeting over two half days, to which COT Members were also invited. The purpose of this meeting was to allow committee members to meet and discuss issues of joint interest and decide how to take such issues forward. In addition, the meeting allowed for discussion of recent developments in COC and COM guidance and other activities.

The discussion topics for the meeting were: updates on Committees guidance, discussion of the implications of EU exit and the end of the transition period, review of the amendments to the COT Terms of Reference and Code of Practice, joint horizon scanning, and biological relevance and statistical significance (see section below 3.XX-3.XX).

3. From the joint horizon scanning, the following topics were agreed and the Secretariats will consider how to progress these either as joint topics or which Committee might lead on these:

- Use of toxicogenomics/omics technologies in toxicity testing
- PBPK modelling – a COT workshop was held the following week; COC members participating may wish to feed back on this.
- Next generation sequencing
- Further exploration of microplastics/microparticles and their composition – also linking with COMEAP
- Development of a dynamic cancer risk model, including consideration that pre-cancer effects are assessed as ‘general’ toxicity pathways, and other influencers on cancer/toxicity risk (e.g. shift work)

- Knowledge sharing across the three Committees, including impacts of EU Exit
- Consideration of uncertainty, use of uncertainty factors and margins of exposure – noting this also links with other activities.

Biological Relevance and Statistical Significance

A scoping paper outlining current literature concerning assessment of biological relevance and statistical significance was presented at the November joint meeting. During the discussion, the importance of considering statistics as more than statistical significance was emphasised, with consideration of all aspects of the study being crucial for interpretation. The recommendation to move away from the use of p-values and their specific interpretation to an estimation of effect using confidence intervals (CIs) has been discussed over many years. It was considered that there is a need to encourage scientists to apply the term significance only to statistical results and not to biological meaning. In addition, in the wider scientific community, statistical significance is considered to be the primary factor, when in fact this needs to be framed within the context of biological relevance.

It was agreed that although this issue had been recognised for many years, there remained a problem when trying to implement changes in practice. One contributing factor may be that the limitations of 'p-values' had not been effectively communicated to the general public. To address this, a short non-technical paper on how the committees evaluate data, including use of WoE and meta-analysis tools would be written, and this will be taken forward in 2021 as a joint effort by all three Committees.

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.

At the end of discussion in 2020, 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

The Committee continues to have a standing agenda item for each meeting on horizon scanning topics and to update the COC on upcoming topics for IARC and the EU Scientific Committees.

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

Guidance statements

The Committee continued to develop the guidance statement series during 2020. This included finalising revisions to the overarching strategy for risk assessment of carcinogenicity (G01), defining points of departure and potency estimates in carcinogenic dose response (G05), and effects of combined exposures to chemical carcinogens (G08).

Updates to the cancer risk characterisation methods (G06) statements are ongoing and it is expected to be finalised in 2021.

The Committee also reviewed the guidance on hazard identification and characterisation (G03) and alternatives to the two-year bioassay (G07) and considered these should be combined. A draft scope of such a document has been presented and will be further developed in 2021.