Draft Minutes of Joint Committees on Carcinogenicity and Mutagenicity of Chemicals in Food, Consumer Products and the Environment (COC and COM) discussion session held on Wednesday 2 March 2022 at 10am via Teams

Chairs: Prof Gareth Jenkins (COM Chair) and Prof David Harrison (COC Chair)

COC Members:	Dr G Clare
	Dr M Cush
	Dr J Doe
	Dr R Haworth
	Dr R Kemp
	Dr L Rushton
	Dr L Stanley
	Prof H Wallace
COM Members:	Dr C Beevers
	Mr A Bhagwat
	Prof S Doak
	Dr P Fowler
	Dr G Johnson
	Ms J Kenny
	Dr A Povey
COT Members:	Prof A Boobis (COT Chair)
	Prof T Halldorsson
	Dr C Harris
	Prof G Hutchison
	Dr D Lovell
	Prof S Price
	Dr M Provan
	Ms J Rix
	Dr C Scudamore
	Prof M Wright
Secretariat:	Ms B Gadeberg (UKHSA Scientific Secretary COC & COT)
	Ms C Mulholland (FSA Scientific Secretary COC, COM & COT)
	Dr O Sepai (UKHSA Scientific Secretary COM)
	Dr D Gott (FSA)
	Ms C Potter (FSA)
	Mr S Robjohns (UKHSA)
	Ms S Wells (FSA)
Contractors:	Dr R Bevan (IEH Consulting)
	Dr P Rumsby (IEH Consulting)

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Assessors and Officials	Prof T Gant (UKHSA)
	Ms F Hill (BEIS)
	Ms J Little (HSE)
	Dr J O'Brien (FSA Science Council)
	Mr N O'Brien (VMD)
	Ms S Peters (DHSC)
	Mr M Symington (UKHSA)
Observers	Dr P Braun (PETA Science Consortium International)
	Dr L Levy (IEH Consulting)

Item 1. Welcome

Participants were welcomed to the joint meeting of COC and COM, to which COT Members had also been invited.

Apologies were received from: COC: Mr D Bodey, Dr R Dempsey; COM: Ms M Wang; and COT; Ms J Case, Prof P Wilson, and Prof M Younes

Item 2. Discussion of Cancer Risk Modification with Introduction from Dr John Doe (CC/MUT/2022/01)

Dr Doe (COC) gave a presentation summarising the key points from the recent paper by Harrison & Doe[1], 'The modification of cancer risk by chemicals'.

The paper is based on the premise that advances in understanding the carcinogenic process have led to an undermining of the binary view that chemicals can be classed as either carcinogens or non-carcinogens. Although a proportion of cancers cannot be prevented, of those that can, a number of risk factors have been identified which are grouped into those which are intrinsic factors that cannot be modified, and endogenous and exogenous factors that may be controlled or modified. Chemicals are generally classed as exogenous factors that could be modified e.g. by introduction of risk management measures.

Harrison & Doe propose a 'dynamic cancer risk model' which takes the form of a generic adverse outcome pathway for carcinogenesis, to which the risk modification rates can be applied. In this way, chemicals are not evaluated as either carcinogens or non-carcinogens but assessed for their ability to modify cancer risk. The approach can use data from a range of sources and can incorporate some of the challenging concepts considered by COC in recent years, such as the effect of less than lifetime exposures and the effect of exposures to more than one chemical on overall cancer risk.

[1] David J Harrison, John E Doe, The modification of cancer risk by chemicals, *Toxicology Research*, Volume 10, Issue 4, August 2021, Pages 800–809,

During the follow up discussion, it was emphasised that not all mutations are equal in their potential effect in terms of promotion of a cell towards cancer and this would need to be factored into the model. Members considered that the model articulates the development of cancer very clearly and wondered whether and how it could best be used by the UK Expert Committees dealing with chemical risk assessments. It was noted that cancer is just one endpoint of chronic toxicity, and that classification and labelling of chemicals was seen as a problem in general, but it was recognised that these are required by some regulations.

Quantification of the model was seen to be a significant issue with application of population genetics being considered as a possible way forward. The importance of considering chemical concentration effects was highlighted and the inclusion of cell replication effects and epigenetic changes as a modifying factor. From a public communication point of view, the importance of including communication of uncertainty and ambiguity was flagged.

Agenda Item 3. Discussion of Shift Work as a Risk Modifier with Introduction from Dr Lesley Rushton (CC/MUT/2022/02)

Dr Rushton (COC) gave an introductory presentation on the evidence on shift work as a modifying risk factor for cancer, including discussion of the latest IARC evaluation[2] on night shift work, as well as describing other health endpoints associated with shift work.

The literature base looking at adverse effects of shift work is extensive and shift work has been linked to some effects such as sleep disturbances and accidents, and non-cancer endpoints such as cardiovascular disease and diabetes. A major challenge is defining what is meant by shift work with definitions being around 'non-standard hours', although, even standard hours may vary considerably in the modern workplace. Much of the health-related outcomes are linked particularly with night work but there is also no standard definition of what a night's work is, and this can vary over different countries.

Considering cancer and shift work and cancer, the most recent evaluation of night shift work by IARC had concluded this was in category 2A. Breast cancer and prostate cancer, in particular, have been linked to night shift work with, for example, around 5% of female breast cancer cases in Britain being attributable to night shift work. There are a large number of potential risk factors for breast cancer and it is difficult to tease out the effects of night shift work on each of these. Other factors to also take into account are the risk from exposure to certain chemicals that have been linked with an increased risk of breast cancer. For the three expert Committees, the three important considerations were, what is meant by shift work, how do you evaluate the dynamics of exposure and, the impact of confounding factors.

[2] Night Shift Work. IARC Monographs on the Identification of Carcinogenic Hazards to Humans Volume 124. https://publications.iarc.fr/593

The Committees considered that the example of shift work exemplified why the impact of modifying factors on cancer risk should be evaluated. Discussion around potential mechanisms included whether the DNA signatures from, for example, breast cancer would be different in night shift and non-night shift workers. It was recognised that additional risk factors associated with shift work such as obesity would also impact on carcinogenic risk. As different health outcomes may be due to different modifying factors, for example cardiovascular and cancer outcomes, teasing these out would be difficult. It was also recognised that a number of aspects are interlinked, and collecting good data on the many variables at play is important in epidemiological studies on the topic. From a risk reduction point of view, it was recognised that shift work was integrated in the current lifestyle, and there may be many reasons why individuals undertake shift work, such that there are challenges to reducing risks across the population.

Agenda Item 4. Update on COT work on Microplastics (CC/MUT/2022/03)

The recent COT papers on microplastics (including nanoplastics) were provided as an update for the COC and COM and for discussion of aspects of relevance and awareness. The overarching COT statement on the potential risks from exposure to microplastics was presented along with its lay summary and a sub-statement on the potential risk(s) from exposure to microplastics via the oral route.

The COT evaluation concluded that a complete assessment for the potential risks to humans from exposure to micro and nanoplastics via the oral and inhalation routes was not possible with currently available data. Significant data gaps were identified as, a lack of appropriate and harmonised analytical methods for the detection of micro- and nanoplastics (together with suitable reference standards), as well as information on their toxicokinetic and toxicity profiles in/relevant for humans. Additional information was also needed regarding levels of exposure from different sources including food, indoor and outdoor air, dust and soil and particle types.

During the discussion, Members were informed that the European Commission is supporting projects on micro/nano particles which include the development of tools to improve current detection of these particles in biological and environmental samples. This will help to better understand exposure levels. With regards to the papers presented, it was suggested that the addition of a ‘decision tree’ may help with application of the guidance when assessing whether there is a hazard. It was highlighted that these materials may not be suitable for standard hazard testing e.g. in submerged assays as they may float. Some adaptation of the assays may be required, and it is important that the method of particle administration is physiologically relevant. COC and COM members concurred with the conclusions reached by COT.

As a wider topic, it was agreed that a joint paper to emphasise the critical role that exposure considerations play in risk assessments across all three Committees should be developed, particularly in light of other countries taking a hazard-based approach.

Agenda Item 5. Update on revised COM guidance on Nanomaterials (CC/MUT/2022/04)

For awareness purposes, members were provided with the revised COM guidance on the genotoxicity texting of nanomaterials. No comments were received.

Agenda Item 6. Updates from Government Departments and Advisory Groups

Update on the work of the FSA Joint Expert Groups (CC/MUT/2022/05)

Three Joint Expert Groups (JEGs) have been established by the FSA to cover the authorisation of regulated products which are over seen by the COT and, where applicable, the Advisory Committee on the Microbiological Safety of Food (ACMSF) who will provide challenge, comment and assurance of their work. The JEGs are comprised: AFFA JEG – the Joint Expert Group on Animal Feed and Feed Additives; FCM JEG - the Joint Expert Group on Food Contact Materials; AE JEG - the Joint Expert Group on Additives, Enzymes and other Regulated Products. Members of JEGs are independent scientific experts with expertise necessary to cover the, wide-ranging, aspects of the dossiers. The JEGs have been active since January 2021 and have reviewed or are currently reviewing a number of applications for new authorisations, and renewals of authorisation.

Update on the work of the OPSS Scientific Advisory Group on Chemical Safety of Non-Food and Non-Medicinal Consumer Products (CC/MUT/2022/06)

The SAG-CS have carried out or are currently carrying out a number of risk assessments feeding into regulatory changes on toys and cosmetics.

Update on the FSA computational toxicology fellowship and LiDO PhD studentship (CC/MUT/2022/07)

COT has been exploring the novel approach methodologies and aligned to that FSA has established a fellowship based at the University of Birmingham and a PhD studentship at Kings College London. The aim of these projects is to develop in silico tools such as artificial intelligence machine learning to predict the toxicity of chemicals in food. They will collaborate with other government departments to get an understanding of how these tools can be used in the regulatory space.

Closing remarks

Members were asked to provide feedback to the secretariat on whether the joint meetings are useful and what topics could be included in future sessions.

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