COT/COM/COC Annual Report 2023

COT/COM/COC Annual Report 2023

About the Committees - 2023

In this guide

In this guide

1. About the Committees - 2023
2. COT Preface - 2023
3. COT evaluations - 2023
4. COT Assurance - 2023
5. Committee Procedures - 2023
6. Ongoing Work - COT 2023
7. Other Committee Activities: Joint Expert Groups, Presentations and Workshop -2023
8. 2023 Membership of the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment
9. Declaration of COT members' interests during the period of this report -2023
10. Sub-groups active in 2023
11. Committee on Mutagenicity of chemicals in Food, Consumer Products and the Environment Annual Report 2023
12. Ongoing work - COM 2023
13. Discussion Items -2023
14. 2023 Membership of the Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment
15. Declaration of COM members' interests during the period of this report -2023
16. Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment Annual Report 2023
17. COC Ongoing Topics - 2023
18. COC Workshop - 2023
19. Joint session Horizon scanning
20. COC input to COT work

21. 2023 Membership of the Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment
22. Declaration of COC members' interests during the period of this report -2023
23. Annex 1 - 2023 - Terms of Reference
24. Annex 2 - 2023 - Code of Conduct for members of the COC/COM/COT
25. Annex 3 – 2023 - Openness
26. Annex 4 – 2023 - Good Practice Agreement for Scientific Advisory Committees
27. Annex 5 – 2023 - Glossary of Terms
28. Annex 6 – 2023 - Previous Publications

Committee on Toxicity

Committee on Carcinogenicity

Committee on Mutagenicity

Annual Report

2023

An image of the front cover of the annual report. The image shows the name of each committee in a list form, in blue text, the year of the report (20213) and solid hexagonal decorative shapes in bright turquoise. The top hexagonal solid shape has small scientific pictograms in dark blue.

PDF
View COT/COM/COC Annual Report 2023 as PDF (791.31 KB)
PDF
View Annex 1 - Terms of Reference as PDF (66.9 KB)
PDF
View Annex 2 - 2023 Code of Conduct for members of the COC/COM/COT as PDF (234.42 KB)
PDF
View Annex 3 – 2023 - Openness as PDF (118.24 KB)
PDF
View Annex 4 - Good Practice Agreement for Scientific Advisory Committees as PDF (112.44 KB)
PDF
View Annex 5 - Glossary of Terms as PDF (250.01 KB)
PDF
View Annex 6 – Previous Publications as PDF (107.72 KB)

PDF documents on this page are not in a fully accessible format, if you require it to be fully accessible, please see the HTML page for that document.

About the Committees

This is the 33rd joint annual report of the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT), the Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment (COM) and the Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment (COC).

The aim of these reports is to provide a brief background to the Committees' decisions. Those seeking further information on a particular subject can obtain details from the Committee’s statements and minutes, available from the websites listed below or from the Committee’s administrative Secretary.

In common with other independent advisory committees, Committee members are required to follow a Code of Conduct which also gives guidance on how commercial interests should be declared. Members are required to declare any commercial interests on appointment and, again during meetings if a topic arises in which they have an interest. If a member declares a specific interest in a topic under discussion, and it is considered to be a conflict of interest, he or she may, at the Chair's discretion be allowed to take part in the discussion but is excluded from decision-making. Annex 1 contains the terms of reference under which the Committees were set up. The Code of Conduct is at Annex 2 and Annex 3 describes the Committees' policy on openness.

Annex 4 is the Good Practice Agreement for Scientific Advisory Committees. Annex 5 contains a glossary of technical terms used in the text. Previous publications of the Committees are listed at Annex 6. An alphabetical index to subjects and substances considered in previous reports is available on the COT website.

These three Committees also provide expert advice to other advisory committees, such as the Scientific Advisory Committee on Nutrition and the Advisory Committee on Novel Foods and Processes, and there are links with the FSA Science Council, Veterinary Products Committee and the Expert Committee on Pesticides (formerly the Advisory Committee on Pesticides), among others.

The Committees' procedures for openness include the publication of agendas, finalised minutes, agreed conclusions and statements. These are published on the internet at the following links:

Committee on Toxicity

Committee on Carcinogenicity

Committee on Mutagenicity

This report contains summaries of the discussions and links to the Committees' published statements. Paper copies are available upon request to the Secretariats.

COT/COM/COC Annual Report 2023

COT Preface - 2023

In this guide

In this guide

1. About the Committees - 2023
2. COT Preface - 2023
3. COT evaluations - 2023
4. COT Assurance - 2023
5. Committee Procedures - 2023
6. Ongoing Work - COT 2023
7. Other Committee Activities: Joint Expert Groups, Presentations and Workshop -2023
8. 2023 Membership of the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment
9. Declaration of COT members' interests during the period of this report -2023
10. Sub-groups active in 2023
11. Committee on Mutagenicity of chemicals in Food, Consumer Products and the Environment Annual Report 2023
12. Ongoing work - COM 2023
13. Discussion Items -2023
14. 2023 Membership of the Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment
15. Declaration of COM members' interests during the period of this report -2023
16. Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment Annual Report 2023
17. COC Ongoing Topics - 2023
18. COC Workshop - 2023
19. Joint session Horizon scanning
20. COC input to COT work
21. 2023 Membership of the Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment
22. Declaration of COC members' interests during the period of this report -2023
23. Annex 1 - 2023 - Terms of Reference
24. Annex 2 - 2023 - Code of Conduct for members of the COC/COM/COT
25. Annex 3 – 2023 - Openness
26. Annex 4 – 2023 - Good Practice Agreement for Scientific Advisory Committees
27. Annex 5 – 2023 - Glossary of Terms
28. Annex 6 – 2023 - Previous Publications

Preface

Head and shoulders Image of Prof Alan Boobis, standing in front of a patterned background. Prof Boobis is wearing half framed glasses and a light-coloured striped shirt.

The Committee continues to have a full and varied programme of work throughout the year, considering both new topics but also continuing to work on larger, longer standing items. The Committee met on seven occasions in 2023.

Amongst the range of topics discussed by the Committee were titanium dioxide, bisphenol A, per and poly-fluoroalkyl substances (PFAS), the mycotoxins T2 and HT2, the aircraft cabin air environment, the potential effects of microplastics by the inhalation route, and emerging marine biotoxins.

The Committee continued its review of components and contaminants in the maternal diet in support of the risk assessment currently being undertaken by the Scientific Advisory Committee on Nutrition (SACN), considering both ergot alkaloids and inorganic arsenic, a review which also took a detailed look at the epigenetics of inorganic arsenic. The Committee also reviewed pica as a potential route of exposure during pregnancy.

In 2023, the Committee continued to oversee and assure the risk assessment of regulated products that were previously assessed in Europe, considering a number of Joint Expert Group (JEG) opinions on food additives, food contact materials, and recycling processes.

The Committee are now also being tasked with requests for advice from the Nutrition Labelling Composition and Standards Policy Group, who co-ordinate the policy approach in this area across the UK. The Committee continued to work on fortificants in bread and flour and green tea catechins.

The Committee also contributed comments to a number of public consultations from European Food Safety Authority (EFSA), including those on vitamin B6, mineral oil hydrocarbons and polybrominated diphenyl ethers.

The joint COT and SACN Working Group continued to work on a benefit- risk assessment of plant-based drinks consumed as an alternative to cows' milk. It is expected that this WG will report in 2025 following a period of public consultation. Committee Members have been involved in several other working groups and joint working groups, covering areas as diverse as cannabidiol (CBD), PFAS and allergenicity thresholds in food. The Committee has also worked closely with their sister Committee on Mutagenicity on the review of titanium dioxide and with the Committee on the Medical Effects of Air Pollutants on the risk from exposure to microplastics via inhalation.

The Committee held a workshop "Evolving our assessment and future guiding principles", which took place in May 2023. The purpose of the workshop was to start the process of updating the Committee's guidance on toxicity testing and risk assessment, which it is hoped will begin later in 2024.

In 2023, the Committee welcomed new Members Professor Peter Barlow from Edinburgh Napier University and Dr Steven Enoch from Liverpool John Moores University. Along with the other FSA Scientific Advisory Committees, the COT has been trialing an Associate Members scheme, where early career researchers can join the Committee for a one year period to obtain experience of advisory Committee work with a view to applying for full Membership in due course. We were pleased to welcome Professor Jeanette Rotchell, Dr Samantha Donnellan, Dr Ben Amies-Cull, Ms Eimear O' Rourke, Dr Charlotte Mills and Dr Tarek Abdelghany as Associate COT Members. This has been an interesting and valuable initiative, and it is hoped that it will continue in the future.

As Chair, I would like to express my sincere thanks to my fellow Committee Members for all of their hard work and commitment to the COT and its sub-groups over the last year. I am particularly grateful to the deputy chair, Dr Sarah Judge, for taking on the additional task of chairing the Committee's discussions on titanium dioxide. The Committee could not function without its joint scientific secretariat, and on behalf of all Members I would like to express our great appreciation to the joint Scientific Secretaries and their respective staffs for their support of the Committee.

Professor Alan Boobis (Chair)

OBE PhD FBTS FBPhS

COT evaluations - 2023

In this guide

In this guide

1. About the Committees - 2023
2. COT Preface - 2023
3. COT evaluations - 2023
4. COT Assurance - 2023
5. Committee Procedures - 2023
6. Ongoing Work - COT 2023
7. Other Committee Activities: Joint Expert Groups, Presentations and Workshop -2023
8. 2023 Membership of the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment
9. Declaration of COT members' interests during the period of this report -2023
10. Sub-groups active in 2023
11. Committee on Mutagenicity of chemicals in Food, Consumer Products and the Environment Annual Report 2023
12. Ongoing work - COM 2023
13. Discussion Items -2023
14. 2023 Membership of the Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment
15. Declaration of COM members' interests during the period of this report -2023
16. Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment Annual Report 2023
17. COC Ongoing Topics - 2023
18. COC Workshop - 2023
19. Joint session Horizon scanning
20. COC input to COT work
21. 2023 Membership of the Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment
22. Declaration of COC members' interests during the period of this report -2023
23. Annex 1 - 2023 - Terms of Reference
24. Annex 2 - 2023 - Code of Conduct for members of the COC/COM/COT

25. Annex 3 – 2023 - Openness
26. Annex 4 – 2023 - Good Practice Agreement for Scientific Advisory Committees
27. Annex 5 – 2023 - Glossary of Terms
28. Annex 6 – 2023 - Previous Publications

Oral nicotine pouches

1.1 The COT was requested by the Office of Health Improvement and Disparities (OHID) Tobacco team to consider the toxicological risks from the use of oral nicotine pouches that do not contain tobacco, including ones that may contain up to approximately 120 mg nicotine per pouch.

1.2 Oral nicotine pouches contain tobacco-derived nicotine and food grade ingredients and are placed between the lip and gum to release the nicotine into the saliva so it can be absorbed within the mouth before entering the blood stream.

1.3 The Committee considered the available information on ingredients present in the products and reviewed the oral bioavailability of nicotine to assess any potential risks associated with use of oral nicotine pouches.

1.4 The COT noted that oral nicotine pouches provide a pharmacologically active dose of nicotine in both conventional cigarette (CC) smokers and nicotine-naïve users and, as such, they are not ‘harmless’ products. However, use of oral nicotine pouches could be considered as part of a harm-reduction strategy if their use is of lower risk than that of CC smoking and if concurrent use of other nicotine-containing products is avoided.

1.5 It was anticipated that nicotine-related ill-effects on health could occur with long-term use of oral nicotine pouches. Risks include effects on a range of endpoints in users and their offspring.

1.6 Experienced users may self-titrate nicotine intake. Systemic exposure levels of nicotine equivalent to those from CC smoking can be achieved from use of oral nicotine pouches. Factors influencing the level of nicotine exposure and retention include the type of pouch used, user profile, usage parameters, nicotine concentration, and the overall formulation of the pouch contents. However, there is potential for the use of oral nicotine pouches by adults in excess of that recommended by the manufacturers, which could be of concern due to the

potential for increased and prolonged nicotine exposure.

1.7 The health risks from other constituents of CC smoke or oral nicotine pouches have not been fully assessed. However, it is plausible that use of oral nicotine pouches, produced according to appropriate manufacturing standards and used as recommended, as a replacement for CC smoking, would be associated with a reduction in overall risk of adverse health effects, although the magnitude of the decrease will depend on the effect in question.

1.8 Individuals who have never been exposed to nicotine and who take up the use of oral nicotine pouches would be at risk from effects of nicotine to which they would not otherwise be exposed. This includes the risk of addiction.

1.9 Use of oral nicotine pouches in parallel with other nicotine-containing products (e.g., CC, ENDS) could potentially lead to increased nicotine exposure compared with that from use of a single product-type and may increase the overall risk of nicotine-related toxicity.

1.10 While there are limited data on which exposure estimates can be made, the estimated exposure to nicotine from 10 mg pouches as outlined by Azzopardi et al (2021) exceeds the COT reference value. It is very likely that exposures from pouches containing higher levels of nicotine as reported to the Committee by DHSC would be significantly higher, and as such the potential risks would be greater, both for people using these pouches and from accidental ingestion.

1.11 The Committee considered that accidental exposure of children to oral nicotine pouches is possible, and that appropriate (i.e., childproof) packaging and labelling is a key safety issue. The appeal and ease of availability of oral nicotine pouches to individuals under 18 years of age was also highlighted as of potential concern for uptake in this age group.

1.12 There is an absence of data on the potential influence of co-exposure to food and drink (hot and cold) or the effects of mechanical manipulation (e.g., sucking or chewing) on absorption of nicotine from oral nicotine pouches. Additionally, it was considered that prolonged buccal membrane exposure to food-grade ingredients within the pouches would result in a high local exposure which has not been addressed from a food safety perspective.

1.13 The Committee expressed concerns over the current regulatory framework for oral nicotine pouch products as they did not fall under specific regulations. It was noted that the different regulatory frameworks for different potential harm-reduction products also made it difficult to compare such

products, as the data requirements varied.

1.14 The Committee commented on the variation in how manufacturers present nicotine content and strength across different products, which may be confusing for the consumer. In addition, use of the description ‘tobacco-free’ may be misleading as the nicotine may be derived from tobacco, which raises concerns regarding carry over of toxicologically relevant contaminants (e.g., metals and nitrosamines).

1.15 An absence of independent data on use/exposure to oral nicotine pouches was identified, with currently available data being largely industry sponsored.

1.16 Overall, the COT considered that the use of oral nicotine pouches, as recommended by the manufacturer, as a replacement for CC smoking was likely to be associated with a reduction in overall risk of adverse health effects, although the magnitude of the decrease will depend on the effect in question. Use of oral nicotine pouches by nicotine-naïve users was likely to be associated with some adverse health effects to which the user would not otherwise have been subject, as a pharmacologically active dose of nicotine is delivered. Concurrent use of oral nicotine pouches with CC smoking or other nicotine-containing products could increase and prolong nicotine exposure compared to a single source.

1.17 The use of oral nicotine pouches could result in prolonged exposure of the buccal membrane to the flavouring products and other constituents used in the pouches. The effect of this had not been investigated and is an important data gap. There are large gaps in nicotine exposure data for the use of oral nicotine pouches in humans, which prevent detailed comparison with CC smoking or the use of other smokeless products. It is not currently possible to predict the adverse health effects that could be associated with use of oral nicotine pouches in the long term, particularly at higher nicotine content levels. As the information and science relating to oral nicotine pouches is changing rapidly, the COT will keep this area under review.

1.18 The full COT statement can be found at: Statement on the bioavailability of nicotine from the use of oral nicotine pouches and assessment of the potential toxicological risk to users .

Interim position on per- and polyfluoroalkyl substances

1.19 The COT had considered per- and poly-fluoroalkyl substances (PFAS) on a number of previous occasions and published a statement in 2022 on the European Food Safety Authority (EFSA) opinion in which the scientific basis of their new tolerable weekly intake (TWI) for the sum of four PFAS was reviewed. The Committee was subsequently asked to consider what further guidance can be provided to support human health risk assessments undertaken by UK Government Departments and Agencies.

1.20 The Committee considered there were a number of uncertainties with regards to the critical endpoint of decreased vaccine response in children, used as a basis for the EFSA TWI and draft US EPA RfDs for PFOA and PFOS, with respect to the biological significance of the response and reservations concerning the critical studies (Abraham et al. (2020) and Grandjean et al. (2012)). In the statement on the EFSA TWI the COT expressed a number of reservations with respect to some of the modelling undertaken to determine the TWI.

1.21 In considering the wider evidence base, the Committee noted that a number of different approaches had been adopted by other authoritative bodies in deriving their HBGVs due to differences in the critical study and endpoint selected, resulting in a range of available HBGVs for a number of different PFAS.

1.22 The Committee noted other challenges regarding the risk assessment of PFAS including the lack of data for most PFAS and consequently HBGVs only being established for a small number and the uncertainty over how best to assess all detected PFAS, such as by summing all PFAS present or grouping similar substances.

1.23 Due to the uncertainties noted and the need for more guidance to support UK Government Departments and Agencies undertaking risk assessments for PFAS, the COT decided to undertake its own consideration of the evidence base and risk assessment.

1.24 Future COT work to be undertaken by a subgroup of Members would include:

- An independent review of toxicological and epidemiological data, focusing on a number of critical endpoints, and considering the biological relevance of

the endpoints assessed.

- Consideration of the toxicokinetics of PFAS.
- Whether and how different PFAS can be grouped for assessment.
- Establishing a HBGV or a number of HBGVs as the data allow.

1.25 The Committee acknowledged that a further review of PFAS would be an extensive and lengthy undertaking. In the meantime, consideration should be given to the available HBGVs for the specific compounds identified, recognising the uncertainties with respect to the critical effects and modelling approaches adopted.

1.26 The full COT position paper can be found at: Interim Position Paper on Per- and Polyfluoroalkyl Substances.

Statement paper on the guidance levels for the fortificants in the Bread and Flour Regulations

1.27 The Bread and Flour Regulations (BFR) stipulate the levels of calcium carbonate, iron, thiamin (also known as vitamin B1) and nicotinic acid that must be present in flour. In 2022, the Department for Environment, Food and Rural Affairs (Defra) held a consultation on the BFR 1998 review and asked whether the consultees agreed with the proposal to raise the minimum levels of calcium carbonate, iron and niacin added in non-wholemeal wheat flour to 15% of the nutrient reference values (NRV) supplied by 100g of flour as stated in point 1 of Part A of Annex XIII of regulation EC No. 1169/2011. NRVs are established guidelines for the recommended daily energy and nutrient consumption. The minimum amount of thiamin required to be present in non-wholemeal wheat flour will remain the same at 19% of the NRV.

1.28 The COT were asked by DHSC to provide a risk assessment on the dietary exposure of calcium carbonate, iron, nicotinic acid and thiamin at the current and proposed fortification levels to identify whether there were any potential adverse health effects.

1.29 High calcium intakes (around 4 g per day) can cause milk-alkali syndrome in people with peptic ulcers. Milk-alkali syndrome is characterised by hypercalcemia (a condition where calcium blood levels are above normal), alkalosis (a condition where the blood becomes too alkaline, i.e., has a PH >7) and impaired kidney function, symptoms of high blood pressure, problems

affecting the brain, abdominal pain, and a build-up of calcium in tissues of the body. In individuals at risk of colonic polyps, calcium at levels of 1.6 g or greater per day can lead to ill-health effects that include problems in the gastrointestinal system (i.e., mouth, throat, oesophagus, stomach, small intestine, large intestine, rectum, and anus). Hight calcium diets can also affect how other minerals such as iron, zinc, magnesium, and phosphorus can be absorbed by the body (via the intestine).

1.30 High intakes of iron in infants of around 20 mg per kg of body weight can result in irritation to the gastrointestinal system. Lethal doses in children are between 200 and 300 mg per kg bodyweight. High intakes of iron in adults between 50 and 220 mg per day can cause constipation, nausea, and vomiting. It can also cause inflammation and perforation (formation of holes) of the gastrointestinal tract, has effects on the metabolism of cells, central nervous system, liver, and heart. For adults the lethal dose is 1.4 g per kg bodyweight. Excessive levels of iron can also result in increased levels of bilirubin and enzymes indicative of damage to the liver (alkaline phosphates and aminotransferase) in the blood. Other side effects may include anorexia, ophthalmological effects (effects on the eye), darkening of the skin and incipient psychosis.

1.31 High intakes of niacin can cause flushing (redness of the skin), itchy skin, nausea, vomiting, diarrhoea, and constipation. Long term intakes of 3 g per kg of body weight or more can cause jaundice, hyperglycaemia (high blood sugar levels) and abdominal pain.

1.32 Thiamin is generally of very low toxicity, with symptoms such as headache, nausea, irritability, insomnia, rapid pulse and weakness being seen at high oral doses of ≥7,000 mg thiamin hydrochloride per day. There have been a small number of reports of effects such as muscle tremors, rapid pulse and nerve hyperirritability at daily doses as low as of 17 mg per day and there have been one or two cases indicative on allergic reaction at doses as low as 100 mg per day.

1.33 A tolerable upper level (TUL) or safe upper level has not been established for calcium, iron, nicotinic acid and thamin by the UK Expert Group on Vitamins and Minerals although they did provide levels for guidance, below which the risk of adverse effects was considered low (EVM, 2003). The EVM reported that intakes of 1,500 mg per day of calcium in supplemental form were not expected to result in any adverse effects. For iron, intakes of 17 mg per day would not be expected to produce any adverse effects. However, this level does

not apply to individuals with increased susceptibility (i.e. genetic predisposition) to iron overload. For nicotinic acid in supplemental form, the EVM reported intakes of 17 mg per day would not be expected to produce any adverse effects. This level does not apply to sustained release preparations of nicotinic acid. Whilst the EVM did not set an UL for nicotinic acid, the Scientific Committee on Food (SCF, 2003) did set an UL of 10 mg per day. For thamin, the EVM proposed a guidance level of 100 mg per day.

1.34 Exposure assessments were performed using data from the Diet and Nutrition Survey of Infants and Young Children (DNSIYC) and National Diet and Nutrition Survey (NDNS) to estimate intakes of these minerals to the UK population from food sources. In the absence of any published data, various online sources were used to estimate the intakes of these minerals from supplements. The assessment determined how much exposure there was to the above minerals from:

a) non-wholemeal flour (i.e., wheat flour without grain wheat),

b) all food groups in the entire diet,

c) supplements.

1.35 Acute (short-term) intakes for all nutrients (calcium, iron niacin and thamin) at the current and proposed fortification level in food did not exceed levels considered to be acutely toxic and are therefore not a health concern.

1.36 Chronic (long term) intakes of calcium, iron, niacin, and thiamin at the current and proposed fortification levels in food did not exceed their guidance levels. Therefore, chronic intakes of calcium, iron, niacin, and thiamin from fortified non-wholemeal flour are not of concern to health.

1.37 Intakes of calcium from supplements alone did not exceed the guidance level. However, daily intakes of iron, niacin and thamin from supplements alone may result in exceedance of their guidance levels when higher dosage supplements are consumed. However, it is important to note that not all of the population consume supplements. Therefore, potential risks to health apply only to members of the population who consume high dosage iron, niacin, and thiamin supplements.

1.38 Intakes of calcium from both food and supplements will not result in exceedance of the guidance level of calcium. However, intakes of iron, niacin and thamin from food and supplements combined can lead to exceedances of their

guidance levels. Given that the exceedance of the guidance levels is evident from supplement consumption alone, the exceedances of iron, niacin and thiamin here would only be of toxicological concern to individuals that consume high dosage of iron, niacin, and thiamin through supplements.

1.39 The COT concluded that the proposed increase in the fortification level of calcium, iron and niacin in non-wholemeal flour would not result in any excess risk. However, there would be a possible exceedance in individuals that consume supplemental iron, niacin and thiamin alongside food containing and/or fortified with these minerals.

1.40 The full statement can be accessed at Statement on the guidance levels for the fortificants in the Bread and Flour Regulations.

COT Assurance - 2023

In this guide

In this guide

1. About the Committees - 2023
2. COT Preface - 2023
3. COT evaluations - 2023
4. COT Assurance - 2023
5. Committee Procedures - 2023
6. Ongoing Work - COT 2023
7. Other Committee Activities: Joint Expert Groups, Presentations and Workshop -2023
8. 2023 Membership of the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment
9. Declaration of COT members' interests during the period of this report -2023
10. Sub-groups active in 2023
11. Committee on Mutagenicity of chemicals in Food, Consumer Products and the Environment Annual Report 2023
12. Ongoing work - COM 2023
13. Discussion Items -2023
14. 2023 Membership of the Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment

15. Declaration of COM members' interests during the period of this report -2023
16. Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment Annual Report 2023
17. COC Ongoing Topics - 2023
18. COC Workshop - 2023
19. Joint session Horizon scanning
20. COC input to COT work
21. 2023 Membership of the Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment
22. Declaration of COC members' interests during the period of this report -2023
23. Annex 1 - 2023 - Terms of Reference
24. Annex 2 - 2023 - Code of Conduct for members of the COC/COM/COT
25. Annex 3 – 2023 - Openness
26. Annex 4 – 2023 - Good Practice Agreement for Scientific Advisory Committees
27. Annex 5 – 2023 - Glossary of Terms
28. Annex 6 – 2023 - Previous Publications

Assessment of the risk of allergic reaction from fortification of non-wholemeal wheat flour with folic acid

1.41 The FSA and Food Standards Scotland undertook a risk assessment to consider the risk in terms of hypersensitivity to UK consumers if folic acid were used to fortify non-wholewheat wheat flour at a level of 250 µg per 100 g without its presence being labelled on the packaging or not conveyed by other means during a 3-month derogation period. The Committee were asked to review and assure the draft risk assessment.

1.42 The UK prevalence of hypersensitivity to folic acid is not known. Leading UK allergy specialists and the UK wide charity operating for people at risk from severe allergic reactions and anaphylaxis were contacted to inform the risk assessment and were not aware of evidence of hypersensitivity to folic acid in the UK. A small number of cases have been reported in the literature although these were linked to the use of food supplements rather than the consumption of food.

1.43 An allergen reference dose for folic acid has not been established and so the usual approach for assessing hypersensitivity risk could not be followed.

Instead, the 75th and 97.5th percentile amount of folic acid that would be consumed if non-wholemeal flour is fortified at the proposed level was estimated and found to be lower than the amount reported to have caused adverse reactions from supplements described in the published literature, with the exception of two cases.

1.44 This suggests that while it may be possible for the proposed amount of folic acid in fortified non-wholemeal wheat flour to trigger reactions, this is only likely to occur very rarely in highly sensitive individuals and is not significant on a population basis.

1.45 Symptoms of the reported adverse reactions to folic acid supplements range from mild to severe (including anaphylaxis) although no deaths have been reported in the literature. There are currently no reports of hypersensitivity to folic acid in food.

1.46 Overall, if non-wholemeal wheat flour is fortified with folic acid at 250 µg per 100 g without its presence being labelled on the packaging of the final food or, in the case of food sold loose, not conveyed by other means during a 3-month derogation period, then the risk of hypersensitivity to folic acid in UK consumers is estimated to be as follows:

- The **frequency of adverse reactions to folic acid in food** to be **very low** (i.e., very rare but cannot be excluded).
- The **severity of illness in relation to adverse reactions to folic acid in food** to be **medium** (i.e., moderate illness: not usually life-threatening, sequelae rare, moderate duration).
- The **level of uncertainty** to be **medium** (i.e., there are some but not complete data available; evidence is provided in small number of references).

1.47 This risk assessment was published in 2023: Assessment of the risk of allergic reaction from fortification of non-wholemeal wheat flour with folic acid.

COT/COM/COC Annual Report 2023

Committee Procedures - 2023

In this guide

In this guide

1. About the Committees - 2023
2. COT Preface - 2023
3. COT evaluations - 2023
4. COT Assurance - 2023
5. Committee Procedures - 2023
6. Ongoing Work - COT 2023
7. Other Committee Activities: Joint Expert Groups, Presentations and Workshop -2023
8. 2023 Membership of the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment
9. Declaration of COT members' interests during the period of this report -2023
10. Sub-groups active in 2023
11. Committee on Mutagenicity of chemicals in Food, Consumer Products and the Environment Annual Report 2023
12. Ongoing work - COM 2023
13. Discussion Items -2023
14. 2023 Membership of the Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment
15. Declaration of COM members' interests during the period of this report -2023
16. Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment Annual Report 2023
17. COC Ongoing Topics - 2023
18. COC Workshop - 2023
19. Joint session Horizon scanning
20. COC input to COT work
21. 2023 Membership of the Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment
22. Declaration of COC members' interests during the period of this report -2023
23. Annex 1 - 2023 - Terms of Reference
24. Annex 2 - 2023 - Code of Conduct for members of the COC/COM/COT
25. Annex 3 – 2023 - Openness
26. Annex 4 – 2023 - Good Practice Agreement for Scientific Advisory Committees
27. Annex 5 – 2023 - Glossary of Terms
28. Annex 6 – 2023 - Previous Publications

Public consultation on draft EFSA opinion on polybrominated diphenyl ethers (PBDEs)

1.48 In June 2023, EFSA released for public consultation a draft update of its risk assessment of polybrominated diphenyl ethers (PBDEs) in food; PBDEs were previously used as flame retardants in construction materials, furniture, and electric and electronic equipment and are widespread environmental contaminants.

1.49 EFSA had previously published a risk assessment of PBDEs in 2011. In the new assessment, two additional congeners were considered, and a total margin of exposure approach was used. The draft updated assessment concluded that the dietary exposures estimated raised a potential health concern for toddlers, with >70% certainty at mean exposure and >95% certainty at 95th percentile exposure. The Committee were asked to provide comments on the draft opinion to be submitted to EFSA as part of their consultation process.

1.50 The Committee considered the animal data to be generally robust but noted that some significant assumptions had been made. They agreed that neurodevelopmental effects and reproductive toxicity were the critical endpoints. The available epidemiological studies, though robust, were difficult to assess, and the epidemiological evidence was considered to provide less of a signal than the toxicological data.

1.51 The Committee considered that some of the evidence from animal studies for a substance-related effect was questionable, and this should have been considered in the uncertainty analysis. Some of the neurobehavioral changes were very minor and there were major inconsistencies in the neurobehavioral changes reported, which lacked biological plausibility. In a developmental neurotoxicity study conducted according to OECD test guideline 426, a technical PBDE product showed no adverse effects at any dose level, which contrasted greatly with the point of departure identified for its major constituent congener, but there did not appear to be any discussion of this. The Committee considered that findings in single studies, in particular those without clear dose-response relationships, should be treated with caution, especially when an adequate OECD guideline study identifies no adverse effects.

1.52 Animal studies showed effects on the thyroid and the draft opinion appeared to be trying to link this to thyroid disease in humans, but the

Committee considered this a step too far. The effects observed in studies in rats were typical of a liver-thyroid effect seen in rats, with microsomal enzyme induction causing increased clearance of thyroid hormones. The draft opinion did not appear to discuss direct versus indirect effects on the thyroid.

1.53 The Committee found the uncertainty analysis difficult to interpret. It was not considered useful without a rationale being provided and without further information on how the numbers for percent certainty were generated and what they mean. Risks may be overestimated by the body burden approach used when considering the endpoints and susceptible populations and the very long half-lives in humans, which were up to 8 years, and it was unclear how this had been taken into account in the uncertainty analysis.

1.54 The recommendations made in the draft appeared largely pertinent. However, the Committee questioned the objective of some of the recommendations for those PBDEs that are no longer used, e.g., the development of Adverse Outcome Pathways (AOPs), when there was already a significant amount of toxicology and exposure data available, and a risk had been identified.

1.55 The comments agreed by the Committee were submitted to EFSA as part of their public consultation process. The final EFSA opinion is expected to be published in early 2024.

Public consultation on draft EFSA opinion on polychlorinated naphthalenes (PCNs) in food and feed

1.56 EFSA released for public consultation a draft opinion on polychlorinated naphthalenes (PCNs) in food and feed in November 2023. PCN mixtures were used in the past in dielectrics, lubricants, electric cable insulation, preservatives of wood, paper and fabric, cutting and grinding fluids, and plasticisers and can also be formed as unintentional byproducts in the production of other industrial chemicals. They are formed by combustion processes including incineration, forest fires and burning of coal. They are lipophilic, bioaccumulative and occur widely in food and feed. They are considered persistent organic pollutants (POPs) under the Stockholm Convention.

1.57 EFSA’s evaluation focused on hexaCNs as there were only very limited data on other PCN congeners. No suitable epidemiological data were identified. The toxicological data were considered insufficient to establish an HBGV and a

margin of exposure (MOE) approach was used, based on a BMDL20 for decreased platelet count in a subchronic toxicity study in rats which tested a hexaCN mixture. MOEs for the exposure to hexaCNs were all much greater than 2000, and the draft opinion concluded that these did not raise a health concern. No risk characterisation was performed for animals exposed via feed because suitable points of departure could not be identified for each species. The Committee were asked to provide comments on the draft opinion to be submitted to EFSA as part of their consultation process.

1.58 The Committee largely agreed with the opinion and with the recommendations made and agreed that dietary exposures to hexaCNs are not a concern. Any information on production, environmental persistence, and trends in occurrence levels over the last 10-20 years would be useful. One of the recommendations, on the use of non-animal methods in order to assess risks from feed, was open ended, and clarity would be welcome.

1.59 While the Committee agreed that dietary exposures to hexaCNs are not a concern, it was not clear how the conclusion of 99% certainty of no health concern had been arrived at from the uncertainty analysis conducted. The Committee considered that some clarity and explanation would be useful.

1.60 The Committee could not see why the toxicology data in laboratory animals could not also be used to characterise the risks to animals exposed via feed, allowing for uncertainties as had been done for the human health risk characterisation.

1.61 The comments agreed by the Committee were submitted to EFSA as part of their public consultation process. The final EFSA opinion is expected to be published in mid-2024.

Draft EFSA opinion on the Tolerable Upper Level for vitamin B

1.62 The EFSA Food and Nutrition Innovation Unit held a public consultation on their draft opinion on a proposed tolerable upper intake level (TUL) for vitamin B6. The COT were asked to provide comments on the draft opinion to be fed back to EFSA. The TUL was based on the observation of peripheral neuropathy in a study in women being treated for premenstrual syndrome. The Committee agreed that this was the most relevant toxicological endpoint noting that it had been observed in both humans and animals. However, the Lowest Observed Adverse

Effect Level (LOAEL) used to derive the TUL and the rationale for the accompanying uncertainty factors needed additional clarification as they might not reflect the full variability of the human pharmacokinetics; additional discussion of the suitability of the TUL for pregnant women would be useful.

1.63 The Committee considered that further clarification of the section on Absorption, Distribution, Metabolism and Excretion (ADME) was needed, as this suggested binding was to the lysine residues of albumin in some parts of the section but noted binding to lysine residues in other proteins in addition to albumin elsewhere in the section.

1.64 The Committee discussed biomarkers of vitamin B6 intake and status, stating it would provide greater context if commentary on the implications of genetic variability, for example in alkaline phosphatase activity, were provided. A recently published paper by Jarett et al (Am J Clin Nutr, 116, 1767-1778, 2022) was cited which showed an interaction between vitamin B6 status and genotype which affected the dose-response. It was agreed that this study should be brought to the attention of EFSA.

1.65 Members commented on the case reports reviewed by EFSA. In particular, the accuracy of the summary for the Dalton and Dalton (1987) study was questioned; the participant was not positively re-challenged but rather symptoms recurred when consumption of the vitamin was resumed.

1.66 It was noted that the recommended range of the health-based guidance value (HBGV) for vitamin B6 was wide; 10-100 mg for adults. This reflected variability, but also choices made in the selection of LOAELs and UFs. A paragraph introducing or providing an explanation of the broad range of HBGVs would be beneficial for context setting and transparency.

1.67 The Committee expressed concern regarding the interpretation of the LOAEL identified in the dog studies which was outlined in the animal data section of the opinion. Members stated that while pathological changes had been observed, there was uncertainty around the measurement of the neurological endpoints, and it was questioned how sensitive these clinical signs would be.

1.68 It was also highlighted that there seemed to be a mismatch between human and animal data and the comparability of the reproductive toxicity endpoints since the available human data related to effects on women rather than their offspring.

1.69 Members supported the proposed recommendations for further research made by EFSA, in particular those for further studies on toxicogenetics.

1.70 The Committee were of the opinion that further detail on the reason behind EFSA's selection of 50 mg/day Vitamin B6 as the threshold at which peripheral neuropathy occurs was needed, given that the available nutrivigilance data indicted effects at lower doses.

1.71 The Committee made a number of minor editorial comments and suggestions which were also submitted to the consultation.

1.72 The final EFSA opinion is expected to be published later in 2023.

Public consultation on EFSA'S 2023 re-evaluation of the risk to public health from inorganic arsenic in food

1.73 In July 2023, the EFSA Panel on Contaminants in the Food Chain (CONTAM) published a draft opinion re-evaluating the health risks arising from the presence of inorganic arsenic (iAs) in food. EFSA had considered it appropriate to update their assessment as new studies had become available on the toxic effects of iAs, as well as new information on occurrence and exposures. The COT were asked to comment on the draft opinion as part of the EFSA public consultation process.

1.74 The draft opinion was also circulated to Members of the Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment (COC) who provided comments which were combined with those of COT.

1.75 Members agreed that the draft opinion was comprehensive and clearly laid out.

1.76 The Committee noted that a relationship between arsenic and skin lesions is well established, though the mechanism is unclear, and further information was needed in this area. It was noted that the paper by Diamond-Gilbert (Environ Health Perspectives, 121, 1154-60, 2013) which was discussed by EFSA in this context referred specifically to invasive squamous cell carcinoma. A lot of the data came from human studies in Bangladesh where there were high levels of arsenic in drinking water. It was possible that UV radiation was a co-carcinogen.

1.77 EFSA used a margin of exposure (MOE) approach in their assessment as iAs is considered a genotoxic carcinogen with additional epigenetic effects. While the calculated MOEs raised potential health concerns with respect to skin cancer, supported by the uncertainty analysis, EFSA concluded that they were unable to derive a level of low concern for iAs as the endpoint used was human cancer and there was no EFSA guidance on the use of such an endpoint. The Committee did not accept this view, noting that human data had been used in this way by EFSA for other compounds with a presumed linear dose-response relationship, such as lead.

1.78 The final EFSA opinion is now published.

EFSA public consultation on “Update of the risk assessment of mineral oil hydrocarbons (MOH) in food”

1.79 The EFSA were asked by the European Commission (EC) to assess any toxicity studies on mineral oil hydrocarbons (MOH), that had become available since the 2012 EFSA evaluation and to update their scientific opinion, if necessary. EFSA were also asked to update their exposure assessment and to update the risk characterisation, if necessary. The COT were asked to comment on the draft opinion.

1.80 The Committee noted that the datasets for mineral oil saturated hydrocarbons (MOSH) and mineral oil aromatic hydrocarbons (MOAH) differed significantly and hence the current opinion should really be considered as two different assessments, one for MOSH and one for MOAH.

1.81 Following the publication of the 2012 opinion, EFSA commissioned toxicology studies on MOSH, which were available for the current evaluation. The rat study provided additional data on the Fischer rat and hence allowed for a clear conclusion on strain sensitivity, which had previously been suggested but not confirmed. The study used to establish the Health Based Guidance Value (HBGV) proposed in the EFSA opinion was a well-defined study, with the No Observed Adverse Effect Level (NOAEL) being at the highest dose tested. Overall, the Committee agreed with EFSA’s approach to the assessment of MOSH.

1.82 Members also agreed with the overall approach taken by EFSA for the assessment of MOAH, utilising the BMDL10 for PAH8 in the absence of studies to define a reference point (RP) for 3- or more ring MOAH.

1.83 However, Members would have liked to have seen additional detail on the derivation of the uncertainty factors, in particular the application of an additional uncertainty factor of 6. While the Committee did not disagree with the use of the additional factor, the discussion and underlying reasoning was complicated, and a clearer definition/explanation would have been useful.

1.84 Overall, the Committee agreed that the 2023 EFSA draft opinion was a good compilation and discussion of the available data and agreed with EFSA's approach and conclusions.

1.85 Members noted that setting standards for MOH was difficult, especially as MOH was a mixture of compounds, often not well defined. Hence it was difficult to conclude on a representative chemical, and the assessment was further complicated by the fact that there was incidental exposure to other MOHs.

1.86 The Committee would have liked to have seen further details covered within EFSA's recommendations, especially with regard to the specifications of food grade MOH, and other sources of MOAH in food.

1.87 The comments agreed by the Committee were submitted to EFSA as part of their public consultation process.

1.88 The final EFSA opinion is now published.

Ongoing Work - COT 2023

In this guide

In this guide

1. About the Committees - 2023
2. COT Preface - 2023
3. COT evaluations - 2023
4. COT Assurance - 2023
5. Committee Procedures - 2023
6. Ongoing Work - COT 2023
7. Other Committee Activities: Joint Expert Groups, Presentations and Workshop -2023

8. 2023 Membership of the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment
9. Declaration of COT members' interests during the period of this report -2023
10. Sub-groups active in 2023
11. Committee on Mutagenicity of chemicals in Food, Consumer Products and the Environment Annual Report 2023
12. Ongoing work - COM 2023
13. Discussion Items -2023
14. 2023 Membership of the Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment
15. Declaration of COM members' interests during the period of this report -2023
16. Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment Annual Report 2023
17. COC Ongoing Topics - 2023
18. COC Workshop - 2023
19. Joint session Horizon scanning
20. COC input to COT work
21. 2023 Membership of the Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment
22. Declaration of COC members' interests during the period of this report -2023
23. Annex 1 - 2023 - Terms of Reference
24. Annex 2 - 2023 - Code of Conduct for members of the COC/COM/COT
25. Annex 3 – 2023 - Openness
26. Annex 4 – 2023 - Good Practice Agreement for Scientific Advisory Committees
27. Annex 5 – 2023 - Glossary of Terms
28. Annex 6 – 2023 - Previous Publications

Existing health-based guidance values (HBGVs) for T2 & HT2 mycotoxins

1.89 T2 and HT2 are mycotoxins which are produced by Fusarium fungi and found in cereal grains and their products. The COT last assessed T2 and HT2 mycotoxins in 2018 when reviewing the diet of infants aged 0 to 12 months and young children aged 1 to 5 years. At the time, the COT agreed with the group Acute Reference Dose (ARfD) and group Tolerable Daily Intake (TDI) for T2 and HT2 established by the EFSA in 2017.

1.90 Commission Recommendation 2013/165/EU sets out indicative levels for T2/HT2 in a number of food commodities. However, the European Commission has now proposed replacing these current indicative values with legislative limits for T2/HT2 in the EU. These draft legislative limits are much lower that the pre-existing indicative values and may have an impact on UK industry, especially on cereals. Currently there is no retained EU law covering T2 and/or HT2. However, the FSA has had extensive dialogue with industry, and has previously been involved in EU working groups on the development of appropriate maximum levels.

1.91 The COT were asked to consider the existing HBGVs for T2/ HT2 published by EFSA and by the Joint FAO/WHO Expert Committee on Food Additives (JECFA), and to confirm an appropriate HBGV for FSA risk assessments. The Committee reviewed the available data on the absorption, distribution, metabolism, and excretion of T2 and HT2 in animals and humans, as well as their toxic effects, such as haematotoxicity, immunotoxicity, emesis, and reduced body weight used in the establishment of the HBGVs along with the mode of action, species sensitivity, and dose-response relationships of T2 and HT2.

1.92 The Committee noted that it was unclear why JECFA did not include an uncertainty factor to account for interspecies differences; this could be because JECFA had considered emesis to be a direct effect rather than a central effect, and therefore no variability would be expected in the kinetics. The COT did not necessarily disagree, but clarification on this would be helpful when the full toxicological monograph was available.

1.93 Overall, the Committee was content with the use of EFSA's HBGVs for future risk assessments.

1.94 The FSA intends to assess the level of risk arising from dietary exposure to T2/HT2 for UK consumers through a call for UK occurrence data. Once completed, this will be presented to the Committee for their consideration.

Position paper on chitosan in bio-based food contact materials

1.95 As part of an ongoing programme of work on bio-based food contact materials (BBFCMs), the Committee discussed the potential allergenicity and environmental impacts of chitosan, a biodegradable polysaccharide derived from chitin.

1.96 Chitin is obtained mainly from crustacean shells but can also be derived from certain fungal species. Chitosan is produced by deacetylating chitin. Both chitin and chitosan have applications in food, medicine, and biotechnology. BBFCMs containing chitin or chitosan are used in applications such as films, coatings, and drinking straws.

1.97 The Committee considered information on the prevalence, causes, and symptoms of shellfish allergy, which is mainly triggered by tropomyosin, a muscle protein found in crustaceans and molluscs. The possibility of cross-reactivity between shellfish and other sources of chitin or chitosan, such as insects and fungi was also considered.

1.98 The Committee further considered the challenges and uncertainties regarding the migration, degradation, and allergenicity of these materials.

1.99 A position paper setting out the views of the Committee will be published in 2024.

Hepatotoxicity of green tea catechins

1.100 In 2017, following a series of reports of adverse effects on the liver following the consumption of green tea supplements, the European Commission requested the EFSA to assess the available information on the safety of green tea catechins (principally - epigallocatechin-3-gallate (EGCG)) from all dietary sources including preparations such as food supplements and traditional infusions, with a focus on liver toxicity. At that time, and at the request of the Department of Health and Social Care (DHSC), who have the policy lead for food supplements in England, the FSA Chemical Risk Assessment Unit team reviewed the EFSA opinion informally and agreed with its conclusions.

1.101 Following a request to the Food Standards Agency from the Nutrition Labelling Composition and Standards (NLCS) Common Framework on behalf of the UK, the COT have been asked to evaluate whether the conclusions of the 2018 EFSA opinion are still applicable (EFSA, 2018), in view of any new data that have become available since its adoption, to enable them to consider the next steps.

1.102 The 2018 EFSA opinion itself and its evaluation by the COT, focus on green tea catechins and the associated cases of probably idiosyncratic hepatotoxicity, rather than being a safety assessment of either green tea catechins or green tea infusions and extracts more generally.

1.103 A discussion paper was presented to the Committee in September 2021, since which drafts of the statement have been reviewed, with the final substantive discussion being held in May 2023.

1.104 The statement will be finalised by the COT in 2024.

Review of titanium dioxide as a food additive

1.105 Following the publication of the EFSA opinion on titanium dioxide in 2021, which concluded that titanium dioxide could no longer be considered ‘safe’ for use in food, the Food Standards Agency (FSA) initiated a review of the EFSA opinion. The EFSA opinion was presented to the COM in June 2021 (MUT/2021/03) and to the COT in July 2021 (TOX/2021/36). The COM had several concerns over the EFSA opinion on the genotoxicity of titanium dioxide. Due to this and following the advice of the COT the FSA initiated an independent evaluation of the safety of the use of titanium dioxide as a food additive.

1.106 In October 2021, paper MUT/2021/08 was presented to the COM, which summarised the available genotoxicity data on titanium dioxide. Members considered that it was not possible to evaluate the genotoxicity of titanium dioxide at that stage. The COM suggested a sifting approach to the available genotoxicity studies should be adopted as a first step before evaluation. The Chair of the COM, a subgroup of the COM and the secretariat subsequently attended meetings to discuss and agree the criteria and methodology for sifting to identify suitable papers for the evaluation of titanium dioxide.

1.107 At the COM June 2022 meeting, paper MUT/2022/05 provided information and papers on approaches relating to the sifting and evaluation of the quality genotoxicity studies and evaluating data on nanomaterials. As an update since that meeting, members were informed that a sub-group of the COM had met to discuss the process to select relevant and appropriate studies to be reviewed by the committee. A proforma had been produced, which would be shared with members. This considered two levels, namely, whether the characteristics of the test material had been sufficiently described (e.g., micro or nano sized particles) and the quality and reliability of how the genotoxicity studies had been conducted.

1.108 In March, July, September and October 2023, papers TOX/2023/16, TOX/2023/32, TOX/2023/44 and TOX/2023/56 were presented to the COT, respectively. These papers summarised the following topics and endpoints: Absorption, Distribution, Metabolism, Excretion (ADME), Aberrant Crypt Foci,

Reproductive and Developmental Toxicity, immunotoxicity, neurotoxicity and the establishment of a Health-Based Guidance Value for titanium dioxide, dependent on the outcome of the review by the COM.

1.109 In the October 2023 meeting, COT members were updated on the progress of the COM sub-group review. It was noted that a third draft statement, along with the concluding statement on the genotoxic potential of titanium dioxide, would be finalised by May 2024. The COM sub-group would be considering potential mechanisms and whether the effects were linked to the nanoparticle fraction.

1.110 The COT would publish a statement on its conclusions on the safety of titanium dioxide as a food additive in 2024, and simultaneously the COM would publish its final conclusion and supporting documentation.

Discussion paper on the effects of pica during pregnancy

1.111 As part of its discussions regarding the contribution of soil and dust to lead exposure in the maternal diet, the Committee requested further information on the practice of pica, the consumption of non-food substances, in pregnant women.

1.112 Members noted that the main concern with respect to pica was geophagia (the consumption of earth, soil, or clay), primarily of soil of ancestral origin, due to the presence of contaminants, notably heavy metals. Geophagia (and pica more generally), was not a practice uniformly distributed across the population and the cultural differences in consumption of soil would mean that there could be large differences in exposure. Furthermore, exposure would be difficult to determine, as the background levels of heavy metals in UK soils would not be appropriate to estimate exposure, as the soils consumed as part of geophagia are often imported from other parts of the world.

1.113 The Committee concluded that the risks of pica behaviour could not be quantified, however, Members considered whether or not pica behaviour should be discouraged on health grounds. Although anecdotally, anaemia had been associated with pica, the relevance of this was difficult to interpret as anaemia was almost ubiquitous in pregnancy. It may be necessary to stratify by socioeconomic status before being able to understand the nature and the direction of the relationship between pica and anaemia.

1.114 The Committee agreed that the chemicals of concern from pica were predominantly heavy metals as these had largely been covered elsewhere in the review of the maternal diet. Therefore, it was concluded that, given the limited data set, it would be more appropriate to include a general consideration of pica in the overarching statement for the maternal diet, which would be published at the completion of this work.

Lead in the maternal diet

1.115 The Scientific Advisory Committee on Nutrition (SACN) is reviewing the scientific evidence that bears on the Government's dietary recommendations for women of childbearing age. The SACN have requested that the COT review the risks of toxicity from chemicals in the maternal diet, including lead.

1.116 Lead is a heavy metal which is ubiquitous in the environment and is thus present in the diet of the general population, including women of childbearing age. However, dietary lead levels have fallen since the phasing out of lead in petrol, plumbing and paints.

1.117 Chronic lead poisoning from low level, repeated exposure gives clinical signs of persistent vomiting, encephalopathy, lethargy, delirium, convulsions, and coma. The central nervous system, erythropoietic system and the kidneys are most affected by lead exposure, but all bodily systems can be adversely affected. In pregnant women, lead can cause increased blood pressure and may be associated with preeclampsia and premature birth.

1.118 Potential risks from maternal exposures to lead were characterised by margins of exposure (MOEs), calculated as the ratio of the lower confidence limit of the benchmark dose (BMDL) to estimated exposures from diet, soil and air. A BMDL01 has been determined for the reduced development of intellectual function in offspring. Specifically, a dietary exposure of 0.5 µg/kg bw/day was associated with a 1% change in full scale IQ score (EFSA 2010). As the BMDL was for a small effect, derived from pooled analysis of multiple cohort studies of exposures in infants and children, it is likely to be conservative and protective for all other adverse effects of lead in all populations. EFSA therefore concluded that a margin of exposure of 10 or greater should be sufficient to ensure that there was no appreciable risk of a clinically significant effect on IQ. At lower MOEs, but greater than 1.0, the risk is likely to be low, but not such that it could be dismissed as of no potential concern (EFSA, 2010).

1.119 In 2013, the COT added that an MOE of >1 can be taken to imply that at most, any risk is likely to be small. MOEs <1 do not necessarily indicate a concern, but scientific uncertainties mean that a material risk cannot be ruled out. This applies particularly when MOEs are substantially <1. The COT further concluded, in agreement with EFSA, that neurodevelopmental effects represent the most sensitive endpoint for effects in the developing fetus whilst also being protective of the other toxicological end points in the mother (COT, 2013).

1.120 The Committee assessed exposure to lead from various sources (food, drink, air, soil, and dust). Overall, the committee noted that lead toxicity will depend on total exposure from all sources, it therefore considered an aggregate exposure to determine an overall likely level of risk.

1.121 A combined exposure assessment, considering exposure to lead from all sources, relative to the BMDL01 of 0.5 µg/kg bw/day, gives an MOE range of 1-2 depending on the individual contribution to the total of each source (food, drinking water, soil/dust). A scenario in which there are high levels of exposure to lead from food, drinking water and soil/ dust would result in an MOE of 1, however, this assumes a worst-case for all sources for a prolonged period of time. In a scenario where there are average levels of exposure to each source, the MOE is 2. These MOE values indicate that an aggregate risk of toxicity from lead in relation to the maternal diet and other potential sources of maternal exposure is likely to be small.

1.122 A statement setting out the Committee’s assessment of lead will be published in 2024.

Arsenic in the maternal diet

1.123 As part of the work on the maternal diet, the COT was asked to consider the potential effects of excess arsenic (As) intake. The COT most recently reviewed arsenic in 2016 as part of the programme of work with SACN on the diets of infants and young children and provided comments on the most recent Draft EFSA opinion (2023) for public consultation.

1.124 Arsenic is a metalloid that occurs in the environment in a variety of forms as a result of both natural and anthropogenic activity. Acute exposure to inorganic arsenic (iAs) results in clinical symptoms such as nausea, vomiting, colicky abdominal pain, and diarrhoea. Chronic iAs exposure results in non-specific symptoms including abdominal pain, diarrhoea, and sore throat and can result in multisystem disease and malignancy, including cancer, skin lesions,

developmental effects, cardiovascular disease, neurotoxicity and diabetes. Health outcomes resulting from iAs toxicity vary between individuals and different geographical areas.

1.125 It is generally accepted that iAs compounds are more toxic than the organic As compounds that are commonly found in fish, seafood, and other marine organisms (arsenobetaine, arsenosugars, and arsenolipids).

1.126 The potential risks from maternal exposures to inorganic arsenic were characterised by margins of exposure (MOEs), calculated as the ratio of the the lower confidence limit of the benchmark dose (BMDL) to estimated exposures from diet, soil and air (individually and aggregated). Previously in 2016, the COT concluded that the JECFA (2011) BMDL0.5 of 3.0 µg/kg bw/day for lung cancer should be used in the characterisation of the potential risks from exposure to inorganic arsenic. The JECFA BMDL was based on exposure to iAs via drinking water from shallow wells. The majority of the epidemiological studies have focused on exposures to iAs via drinking water and have not measured or reported total dietary exposure to iAs. The COT also previously concluded that an MOE of 10 or above would be considered of a low concern.

1.127 The main contribution to As exposure in the UK is from dietary sources; non-dietary sources such as water, air, soil, and dust contributed negligible quantities.

1.128 The aggregate exposure for iAs from all sources for average consumers resulted in an MOE of 11, while the MOE for high consumers was 6. A risk to the health of women of childbearing age, specifically for high consumers, could not be excluded.

1.129 During the COT’s evaluation of arsenic in the maternal diet EFSA published their draft opinion on arsenic in food. The Committee agreed that they would wait until EFSA formally publish their opinion, expected in early 2024, before finalising their discussions and subsequent statement, later in 2024.

Ginger in the maternal diet

1.130 As part of the current programme of work on the maternal diet, the Committee considered the use of herbal dietary supplements during pregnancy. These were supplements that were not officially recommended by the relevant authorities, but which were promoted by anecdotal evidence and unofficial sources as having various purported benefits. Ginger was identified as one of the

supplements that should be considered in more detail.

1.131 Ginger (*Zingiber officinale*) is a flowering tropical plant originating in Southeast Asia and grown in warm climates including China, India, Africa and the Caribbean. The rhizome (underground stem) of the ginger plant is commonly used as a spice and flavouring in many countries around the world and is increasingly growing in popularity as a natural remedy due to its purported immune system-boosting properties and also for motion sickness and post-operative nausea and vomiting.

1.132 The COT have previously reviewed the potential effects of ginger and in particular, the use of ginger supplements during pregnancy and lactation, reviewing the available data on toxicity to the mother, effects on the development of the fetus or embryo, and possible interactions with medicines. A revised statement was reviewed by the Committee in 2023 and included additional studies which had previously been identified by the COT to further inform the database on the possible influence of ginger components on cyclooxygenase (COX) and prostaglandin activity.

1.133 A further draft of the statement will be brought back to the Committee in 2024 with a clearer distinction between the forms of ginger; in particular, those used as traditional culinary spice compared to the more concentrated forms of ginger such as ‘shots’. Further clarification on several points highlighted by the COT would also be provided.

1.134 The statement will be finalised by the COT in 2024.

The potential risks from ergot alkaloids in the maternal diet

1.135 As part of the ongoing programme of work on the maternal diet, the Committee were asked to asses the risk from exposure to ergot alkaloids (EAs) in the diet to maternal health.

1.136 Ergot alkaloids (EA) are secondary metabolites produced by the fungi families *Clavicipitaceae* and *Trichocomaceae*, with *Claviceps purpurea* being the most widespread *Claviceps* species in Europe. Based on their occurrence and the available toxicological data, the EFSA considered six EAs in their risk assessment in 2005, namely: ergotamine, ergocornine, α- ergocryptine, ergosine, ergocristine (peptide ergot alkaloids) and ergometrine (a lysergic acid amide). EFSA further

included both forms (-ine and -inine) in their assessment; while the -inine forms are considered biologically inactive, interconversion occurs under various conditions (EFSA, 2005, Tasker and Wipf, 2021). Bromocriptine is synthetic ergoline derivate and it is used in the treatment of Parkinson's disease and pituitary tumours (Herdman et all., 2001).

1.137 Due to their structural similarities to neurotransmitters, EAs can act as agonists or antagonists of noradrenaline, dopamine and serotonin neurotransmitters (Arroyo-Manzanares et al., 2017, Fitzgerald and Dinan, 2008) and have been reported to produce direct peripheral effects such as uterotonic action or vasoconstriction, and central nervous system (CNS) effects such as induction of hypothermia and emesis (EFSA, 2012).

1.138 The potential risk from EAs in the maternal diet was discussed by the Committee in 2022. It was concluded that there was no concern that EAs would have adverse effects on maternal health at likely levels of exposure. A statement on ergot alkaloids will be published in 2024.

Statement on the risk assessment of cow's milk in children aged 1 to 5 years, in the context of evaluations of plant-based drinks

1.139 The Department for Health and Social Care (DHSC) is conducting an Equalities Analysis covering both the Nursery Milk Scheme and the Healthy Start Scheme, which considers equalities issues posed by the current legislation as it pertains both to plant-based drinks, and also to animal milks other than cow's milk. DHSC is keen to ensure that this Equalities Analysis reflects the most up-to-date advice on safety and toxicity issues from COT, and on nutritional issues from the Scientific Advisory Committee on Nutrition (SACN). Hence, this process is currently on hold until the SACN/COT Joint Working Group on Plant Based Drinks completes its benefit-risk assessment of plant-based drinks.

1.140 The COT agreed in July 2021 that cow's milk should serve as the main comparator for plant-based drinks and therefore a statement on potential chemical risks from cow's milk was developed.

1.141 Within this statement, the COT reviewed an extensive range of chemical compounds that could be present incidentally or as contaminants in cow's milk to allow comparison with plant-based dairy alternatives. The COT concluded that the vast majority of potential contaminants assessed presented no

risk of adverse health effects in children aged 6 months to 5 years of age at the levels observed within cow's milk. The exceptions are iodine, BaP and PAH4, AFM1 specifically and total aflatoxins due to the contribution of AFM1, for which any risk to health in children aged 6 months to 5 years of age is unlikely but cannot be completely excluded. The possible risks to health in these age groups from exposure to isoflavones in cow's milk is unknown, as no HBGVs have been established for these compounds in young children and hence there is a lack of knowledge on the toxicological significance of the levels that might be found in cow's milk.

1.142 The full statement can be found on the committees website: Statement on the risk assessment of cow's milk in children aged 1 to 5 years, in the context of plant-based drinks evaluations | Committee on Toxicity.

1.143 A lay summary will be published in 2024.

Review of dioxins – draft systematic review

1.144 Following the Committee's assessment of the scientific basis and implications for risk management of the 2021 EFSA tolerable weekly intake (TWI) for dioxins and dioxin-like polychlorinated biphenyls (PCBs), the COT decided to undertake their own review of the relevant endpoints.

1.145 The Committee acknowledged that the review of dioxins would be an extensive and lengthy undertaking. To assist with the work, a systematic literature review on dioxins was commissioned, focusing on the relevant endpoints; male reproductive toxicity, immunotoxicity, the mechanism of action of dioxins via the aryl hydrocarbon receptor (AhR). The review would be covering a predefined time frame from 2017 to 2021, identifying any new evidence since the extensive literature review undertaken by EFSA. The review also included a non-systematic consideration of the data on the potential carcinogenicity of dioxins and dioxin-like PCBs and whether this involved a genotoxic mechanism.

1.146 The Committee considered that the commissioned report was detailed and provided a large amount of data for review. However, information from lower scoring studies was excluded from the report. As these studies could potentially hold relevant information to the overall assessments, the Committee agreed that currently it was not possible to identify a key study or studies on which to establish a health-based guidance value (HBGV) and further consideration would be required.

1.147 Additional work in this area will commence in 2024.

Advice on the risk to human health from consumption of bivalve molluscs (shellfish) harvested from UK waters associated with marine biotoxins

1.148 The Food Standards Agency (FSA) is considering the current advice and monitoring programme for marine biotoxins and whether there is a need to update or change existing legislation in the UK. The main purpose of this work is to identify any emerging marine biotoxin threats in UK waters, including considerations on increasing occurrence with increasing temperatures due to climate change. The views of the COT were sought on whether any of these marine biotoxins would pose a risk to human health.

1.149 The FSA programme of work included a scoping paper on emerging marine biotoxins to be discussed by the Committee. The marine biotoxins reviewed were selected based on published assessments and reports on emerging marine biotoxins by other authorities, as well as a brief literature search. There was also specific consideration of pinnatoxins (PnTXs) and pectenotoxins (PTXs), due to the recent availability of additional analytical standards and recent removal from the EU monitoring programme, respectively.

Scoping paper on the advice on the risk to human health from consumption of bivalve molluscs (shellfish) harvested from UK waters associated with marine biotoxins

1.150 The Committee considered the emerging marine biotoxins of potential concern to human health, i.e., brevetoxins, cyclic imines, palytoxins, saxitoxins, tetrodotoxins, novel azaspiracid analogues, novel paralytic shellfish poisoning (PSP) analogues and domoic acid analogues, and cyanobacteria toxins. There was a substantial amount of data available on the toxicology and occurrence on a number of the toxins, most of which are known and have the potential to be of concern to human health. However, the potential risk of these toxins depends on their occurrence, and this data, especially for UK waters and shellfish is lacking.

The lack of data on their occurrence however did not exclude the possibility that these toxins were present in UK waters.

1.151 The Committee considered that to reach a conclusion on which of the marine biotoxins discussed would be of potential risk to UK consumers, further work is required, identifying, and tabulating the toxicological endpoints, lethal doses and occurrence data. It would also be useful to include information on the marine biotoxins which are already monitored and regulated, to put the potential risk of these emerging toxins into perspective.

1.152 The Committee will continue its work on this in 2024, aiming to identify the criteria to be fulfilled for a marine toxin to raise concern and consider how the previously discussed emerging marine biotoxins align with these criteria.

Pinnatoxin group

1.153 Pinnatoxins (PnTXs) are a group of paralytic neurotoxins that can be found in filter-feeding bivalve shellfish such as scallops and mussels. Although no confirmed cases of PnTX intoxication have been reported in humans, ingestion of PnTXs compounds by rodents under laboratory conditions can cause paralysis, respiratory depression, and death. PnTXs are not currently regulated in England or Wales, but with the availability of new analytical standards, future monitoring programs of PnTX could aim to include PnTX-G, -E and -F.

1.154 The COT was asked by the FSA to evaluate and consider the current toxicological evidence and the potential public health risk related to PnTXs. Consideration was also given to the likelihood of PnTXs becoming more prevalent due to climate change and rising sea water temperatures around the UK.

1.155 The Committee agreed that the toxicological data base for PnTx was limited. Although some acute toxicity studies existed in mice, there were substantial evidence gaps for both the toxicity of PnTXs and the exposure in humans. Overall, the Committee concluded that due to the lack of toxicological and occurrence data on PnTX it was not possible to determine the extent of any public health risk relating to PnTXs. Although no human intoxications have been reported to date and there is no strong evidence to suggest PnTXs are a risk to humans, based on the limited data, the Committee was unable to fully exclude a risk.

1.156 Members concluded that if the technology, i.e., chemical analysis, was already in place in the UK it would be reasonable to include PnTXs in any

monitoring programme.

Pectenotoxin group

1.157 PTXs are a group of toxins associated with diarrhetic shellfish poisoning (DSP), which are produced by dinoflagellate algae. They are accumulated by filter-feeding shellfish such as scallops and mussels. Although no confirmed cases of PTX intoxication have been reported in humans, ingestion of certain PTX compounds by rodents under laboratory conditions can cause gastrointestinal effects and liver toxicity. PTXs are a regulated biotoxin group in the UK and are included in the group of toxins which are monitored routinely in UK shellfish.

1.158 The COT was asked by the FSA to consider the evidence in the 2009 EFSA opinion on pectenotoxin, which was the basis for recent amendments to the European Union (EU) legislation removing PTXs from the list of monitored biotoxins in EU shellfish. In their 2009 opinion, EFSA concluded that PTXs were less toxic than okadaic acid (OA) - the toxin they are currently jointly regulated with – but when administered via the oral route, they have a different toxicological mode of action (MoA) and that they do not induce diarrhoea.

1.159 The COT found there was limited scientific data regarding the toxicity of PTXs, and the data that exist were for acute/short term exposure, rather than exposure over a prolonged period. Most of the available data were from rodent studies where PTXs were administered via injection, which was not directly relevant to assessing the risk of intoxication by shellfish consumption in humans. Considering only the studies where PTXs were orally administered to rodents, the Committee found the evidence was sufficient to conclude that PTXs have a lower oral toxicity than OA. They also agreed with EFSA that PTXs have a different MoA to OA and that PTXs should therefore not be expressed in OA equivalents. However, the Committee considered the evidence that PTX-group toxins do not cause diarrhoea inconclusive, with some studies in rodents reporting diarrhoea after PTXs administration.

1.160 Overall, the Committee concluded that based on effects seen in animals, a toxicological risk from exposure to PTXs was plausible, albeit probably low. However, due to the lack of toxicological and occurrence data on PTXs it was currently not possible to determine the extent of any public health risk of PTXs.

Assessment and draft interim position statement on bisphenol A (BPA)

1.161 Following public consultation in 2022, the EFSA Panel on Food Contact Materials, Enzymes and Processing Aids (CEP) established a new tolerable daily intake (TDI) of 0.2 ng Bisphenol A (BPA)/kg bw per day in April 2023.

1.162 The Committee discussed the final opinion published by EFSA and confirmed that they did not support EFSA's conclusion that the observed change in the number Th17 white blood cells would continuously result in an adverse immune effect/inflammatory response. An effect observed after forty hours represented an intermediate endpoint and was not appropriate for identification of a critical point of departure (POD) and subsequently a TDI. Given the uncertainties over the endpoint a more robust and transparent weight of evidence (WoE) approach and evidence integration should have been applied to a wider dataset to derive a more reliable and relevant endpoint on which to base a health-based guidance value (HBGV).

1.163 Following their diverging view from EFSA, the German Bundesinstitut fuer Risikobewertung (BfR) published a full assessment of BPA in 2023, establishing a TDI of 0.2 µg/kg bw per day (equivalent to 200 ng/kg bw per day) based on (male) reproductive effects.

1.164 While assessments of BPA by other authorities pre-dated the EFSA 2023 assessment, and were therefore not considered applicable, the Committee considered the BfR approach in more detail and concluded that the endpoint applied and approach taken were reasonable, albeit with a significant level of conservatism, and were in line with previous approaches taken by the Committee themselves.

1.165 Overall, the Committee considered it possible that the current UK TDI for BPA would need to be revised to account for new evidence and ensure it was sufficiently protective. However, on balance the weight of evidence did not support the conclusions drawn by EFSA, or a TDI set as low as that established by EFSA. The Committee instead agreed that the BfR approach was reasonable and to apply the TDI of 0.2 µg/kg bw per day as an interim measure.

1.166 The Committee will undertake their own weight of evidence approach and assessment of BPA in due course.

1.167 The work on BPA is ongoing but an interim position statement highlighting the discussions and considerations of the Committee will be published in spring 2024.

Aircraft cabin air

1.168 In 2007, the COT published a statement on aircraft cabin air, having been asked by the Department for Transport (DfT) to undertake an independent scientific review of data submitted by the British Airline Pilots Association (BALPA) relating to organophosphate (OP) compounds, the cabin air environment, ill-health in aircraft crews and the possible relationship to smoke/fume events in aircraft, due to concerns about the possible effects on aircrew health of oil/hydraulic fluid smoke/fume contamination incidents in commercial aircraft (COT, 2007).

1.169 In 2013, DfT asked the COT to undertake an independent scientific review of the results of DfT-funded aircraft cabin environment research commissioned in response to recommendations made by COT in 2007, after which the COT issued a position statement on cabin air (COT, 2013).

1.170 The COT was recently asked by DfT to investigate whether any new data have been published and to re-evaluate their previous views, and in particular consider the question “Is there evidence of exposure to chemical contaminants in cabin air that could have long-term health impacts, either from acute exposures or due to long-term low level exposures including mixtures, e.g., of volatile organic compounds (VOCs)?”.

1.171 In 2023, the Committee continued this consideration and reviewed discussion papers on concentrations of VOCs in European aircraft and comparison with regulatory standards and health-based guidance values and a paper on the basis of the regulatory values for carbon dioxide. The COT also considered drafts of the statement on this topic, and it is anticipated that the statement will be finalised in 2024.

Sub-statement on the potential risk(s) from exposure to microplastics: Inhalation route

1.172 In 2019, as part of horizon scanning, the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT) identified the potential risks from microplastics as a topic it should consider to inform Food

Standards Agency (FSA) discussions on this (TOX/2019/08). Since then, several discussion papers have been presented to the COT and in 2021, the COT published an overarching statement on the potential risks from exposure to microplastics (COT Statement 2021/02). This document provided a high-level overview of the current state of knowledge, data gaps and research requirements with regards to this topic.

1.173 There is evidence for the presence of plastic particles in the air (indoor and outdoor) and thus inhalation is a possible route of exposure.

1.174 The purpose of the sub-statement was to provide supplementary material to the overarching statement on microplastics (COT Statement 2021/02) and to consider in detail the potential toxicological risks of exposure from microplastics via the inhalation route (i.e., exposure resulting from the presence of microplastics in the air (indoor, outdoor and occupational settings)). It is based on currently available literature and data from internal tools at the UK FSA (these internal tools include: a literature search application and signal prioritising dashboards).

1.175 The final draft of this paper was presented at the end of 2023 and will be published in 2024, completing the current work on microplastics.

Novel formulations of supplement compounds designed to increase oral bioavailability

1.176 In their discussions on the safety of turmeric in 2022, the COT identified novel formulations, particularly those with the potential to increase oral bioavailability, as a key area of uncertainty in the risk assessment of dietary supplements. Such formulations include micellar, nano- and micro-formulations, including colloidal dispersions and liposomal systems. Therefore, the Committee proposed that novel formulations designed to increase the oral bioavailability of supplements should form the basis of a general discussion paper.

1.177 The Committee considered an overview of the structure and physicochemical properties of several novel supplement formulation types, including colloidal, liposomal, and micellar systems. The biological mechanisms through which such formulations may alter bioavailability were also reviewed. Pharmacokinetic studies in human subjects with novel formulations of three different supplements were reviewed as exemplars: vitamin C, curcumin, and cannabidiol (CBD).

1.178 In terms of establishing health-based guidance values (HBGVs) for novel supplement formulations, it was noted that this was important for consumer safety, as maximum dosage levels for certain compounds may not be applicable to novel formulations of the same compounds. The Committee concluded that the critical factor was understanding how external dose related to internal exposure for standard and novel formulations, and when/if these diverged. In the absence of specific kinetic data, it was stated that a worst-case approach would be to assume 100% bioavailability of the active compound. The Committee noted that these data are often unavailable, and that the pharmaceutical industry is likely to have more extensive datasets that might aid in these kinds of assessments.

1.179 The Committee agreed that they had reviewed sufficient information to reach general conclusions regarding novel formulations, and that no further and/or specific information was required. The Committee also agreed, given that supplements would vary on a case-by-case basis, it was not necessary to provide further case studies and/or exposure assessments to reach general conclusions

1.180 As a next step, a position paper will be drafted in 2024 that summarises the Committee's comments, which could potentially be included in future guidance documents.

UK COT FSA New Approach Methodologies Roadmap (2023) Draft Version 3

1.181 The UK FSA and the COT have been considering New Approach Methodologies (NAMs) to understand the best scientific methodologies available for use in the risk assessment of chemicals and to consider how these can be incorporated and accepted in a regulatory context.

1.182 In order to achieve this, the FSA and COT are developing a UK NAMs roadmap towards acceptance and integration of NAMs, including predictive toxicology methods using computer modelling, into safety and risk assessments for regulatory decision making. This will require not only the historic 3Rs approach (replacement, reduction and refinement of animal experiments) but the expansion to the 6R principle, which also includes reproducibility, relevance, and regulatory acceptance.

1.183 Following presentation of the roadmap at various international conferences, meetings and workshops, Members were asked to note and comment on the recent updated draft version of UK NAMs roadmap, which

incorporates the feedback received. This includes data integrity and capability, training, and the integrated transition into acceptance.

1.184 Work on the roadmap will continue, including incorporating any additional information gathered from conferences, meetings, and workshops as well as the outputs from the FSA literature review on NAMs to Support Regulatory Decisions for Chemical Safety.

Draft joint statement on the request for an assessment of tetra-methyl bisphenol F diglycidyl ether (TMBPF-DGE) in canned food packaging material

1.185 The Committee discussed the draft assessment on tetra-methyl bisphenol F diglycidyl ether (TMBPF-DGE), following previous discussions by the COT, the Joint Expert Group on Food Contact Materials (FCMJEG) and sister COM. The work is ongoing, but publication of the final assessment is expected in spring 2024. This item is reserved as the data are commercially confidential.

Assessment of ocean bound plastic (OBP)

1.186 The Food Standards Agency (FSA) and Food Standards Scotland (FSS) are currently undertaking work on the potential use of recycled plastic materials from the open environment in food packaging applications, specifically plastic materials intercepted before entering the marine environment.

1.187 Following initial discussions by the Joint Expert Group on Food Contact Materials (FCMJEG) and COT, the FSA and FSS undertook a call for evidence between March and October 2022. This was followed by additional data collection from the companies that engaged with the call, upon enquiry by the FCMJEG. Additional companies were also identified as suppliers of these materials between November 2022 and January 2024, and were contacted for any information they may hold.

1.188 The FCMJEG has assessed all information provided to the FSA and FSS to date and is currently in the process of drafting the final assessment, publication of which is expected in spring 2024.

Other Committee Activities: Joint Expert Groups, Presentations and Workshop -2023

In this guide

In this guide

1. About the Committees - 2023
2. COT Preface - 2023
3. COT evaluations - 2023
4. COT Assurance - 2023
5. Committee Procedures - 2023
6. Ongoing Work - COT 2023
7. Other Committee Activities: Joint Expert Groups, Presentations and Workshop -2023
8. 2023 Membership of the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment
9. Declaration of COT members' interests during the period of this report -2023
10. Sub-groups active in 2023
11. Committee on Mutagenicity of chemicals in Food, Consumer Products and the Environment Annual Report 2023
12. Ongoing work - COM 2023
13. Discussion Items -2023
14. 2023 Membership of the Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment
15. Declaration of COM members' interests during the period of this report -2023
16. Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment Annual Report 2023
17. COC Ongoing Topics - 2023
18. COC Workshop - 2023
19. Joint session Horizon scanning
20. COC input to COT work
21. 2023 Membership of the Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment
22. Declaration of COC members' interests during the period of this report -2023

23. Annex 1 - 2023 - Terms of Reference
24. Annex 2 - 2023 - Code of Conduct for members of the COC/COM/COT
25. Annex 3 – 2023 - Openness
26. Annex 4 – 2023 - Good Practice Agreement for Scientific Advisory Committees
27. Annex 5 – 2023 - Glossary of Terms
28. Annex 6 – 2023 - Previous Publications

Presentations

Presentation from the LIDo-TOX AI PhD Student

1.189 The FSA and COT have been considering New Approach Methodologies (NAMs) in order to understand the best scientific methodologies available for use in the risk assessment of chemicals, and to consider how these can be incorporated and accepted in a regulatory context.

1.190 In 2021, the FSA started funding a PhD Student at King's College London as part of their Interdisciplinary Doctoral Program (LIDo-TOX AI).

1.191 The PhD student has been working to understand how NAMs will improve indicative levels of safety in chemical risk assessment.

1.192 In addition, these new partnerships have helped with networking, research collaboration, training opportunities and other activities. The studentship also complements the work set out in the UK COT FSA NAMs Roadmap towards using new approach methodologies in chemical risk assessment.

1.193 The PhD student presented a yearly review to the Committee, updating them on his progress to date using Artificial Intelligence and in silico tools for the assessment of food safety.

1.194 The main work so far comprised three parts: (1) Exploration of dimensionality reduction algorithms, for powering Quantitative Structure Activity Relationship (QSAR) models of mutagenicity, constructed of simple feed-forward Deep Neural Networks (DNNs); (2) Development of Graph Convolutional Networks (GCNs) to improve mutagenicity predictions, via graph classification of molecules, while also allowing for mining of structural alerts (SAs); (3) Development of Graph Neural Networks (GNNs) for node classification of molecules, in order to predict toxicological properties of brominated flame retardants (BFRs), starting with

acute toxicity and comparing to predictions from the Toxicity Estimation Software Tool (TEST) of the United States (US) Environmental Protection Agency (EPA).

1.195 The COT Members were impressed with the progress to date and provided feedback to the PhD student.

Opportunities and outlook for United Kingdom Food and Chemicals regulation post European Union Exit-COT Workshop Report

1.196 The COT, UKHSA and FSA had organised a workshop in July 2022 on "Opportunities and outlook for UK food and Chemicals regulation post EU exit".

1.197 A report of the workshop was considered by the Committee in 2023.

1.198 The participants were from industry, academia and regulatory agencies and the day was divided into three sessions:

- The landscape of regulation post EU exit: UK stakeholder perspectives, international perspectives, opportunities and challenges for UK divergence;
- Major drivers for change and potential impact on chemical regulation; and
- Indirect Effects: food prices, food security, supply chain, fraud (Food regulation/human health).

1.199 Each of the sessions consisted of presentations followed by a roundtable discussion and included interactive sessions.

1.200 The workshop report is now available online and as a PDF. (DOI: https://doi.org/10.46756/sci.fsa.ebr546).

Evolving Our Assessment & Future Guiding Principles Workshop

1.201 The COT held a workshop in May 2023 to start work on updating their guidance on toxicity testing and its supporting principles. The starting point for the process is to use existing frameworks and guidance but with the aim of introducing innovative improvements where appropriate.

1.202 The workshop aimed to identify areas where guidance needed to evolve and included reviewing fundamental risk assessment principles, current guidance on risk assessment and what can be learned from it, integration of new approach

methodologies, exploring hazard vs risk and weight of evidence. The overall objective of the workshop was to discuss how the Committee moves forward in a new era of risk assessment.

1.203 Members discussed the output of the workshop, considering “must, could and should” priorities to be taken forward. It was emphasised that the most important aim was to have applicable guidance to ensure public safety.

1.204 The assessment of benefits was not within the terms of reference of the COT, but thought should be given as to how COT advice can be best aligned for this to be undertaken when needed or appropriate.

1.205 Members noted that to take the guidance forward, establishing an initial framework would be important; this could then be expanded and linked to other guidance as necessary. There were two parts to the work, to codify what the Committee currently do and then to provide guidance on areas where the approach was not yet codified such as benchmark dose modelling.

1.206 A sub-group would be formed in 2024 to take forward the next steps in updating the guidance. It was agreed that it would be important to work with policy colleagues from the relevant Government Departments and not to re-invent the risk analysis process. In particular, the required levels of protection needed for consumers should be considered.

1.207 The finalised report will be published in due course.

Horizon Scanning

1.208 The COT regularly organise a specific session on horizon scanning at their February meeting, where they review the work anticipated for the coming year; this includes ongoing topics, the annual workshop, current or planned working groups and the skills balance of the Committee, together with any emerging areas relevant to the work of the COT. However, Members are also encouraged to suggest topics for discussion throughout the year.

1.209 In 2023, In addition to the items outlined above, Members considered the following:

General horizon scanning

1.210 The COT terms of reference include advising, at the request of many different government departments, on a wide variety of chemicals and routes of

exposure, making them very broad, and potentially overlapping with those of a number of other Scientific Advisory Committees. While the Committee's work is mostly reactive, the terms of reference also include advising on important general principles and scientific discoveries in relation to toxic risks, which was more proactive. The Committee is constrained by a heavy workload, but it is important that it is proactive where it can be, taking a lead on advances in the application of novel science in the risk assessment of chemicals. The work on new approach methodologies and evidence integration are examples of this.

1.211 It is important that the Committee is aware of emerging topics and a databank of potential areas of interest could be created as it would be useful to know whether there were topics being discussed elsewhere, such as by EFSA and JECFA, that may be relevant to topics that should be addressed by the Committee.

Phosphate based flame retardants

1.212 In 2019, the COT published a statement on phosphate-based flame retardants (PFRs) and the potential for neurodevelopmental toxicity. The Committee concluded that PFRs were very unlikely to share the neurodevelopmental effects of other organophosphate compounds, but they could not exclude the possibility that PFRs could produce neurodevelopmental toxicity by some other mechanism.

1.213 In 2021, the COT became aware of new data relating to PFRs and developmental neurotoxicity and a literature search was carried out to capture any additional data published between 2019 and 2021. The Committee also requested such searches be carried out in subsequent years to capture any new published data.

1.214 The Committee reviewed the most recent update and considered that unless the Department of Health and Social Care (DHSC) requested another review, there was insufficient new information to justify taking this topic further at this time. However, the literature should continue to be monitored, though there was no need for an update every year, unless significant (in terms of toxicology or amount) new information became available.

The microbiome

1.215 It was agreed that the microbiome should remain under consideration by the Committee, with a view to re-examining the topic when new data become

available.

Joint Expert Groups

Assurance of Joint Expert Group opinions

1.216 The Joint Expert Groups (JEGs) were established by the FSA to assess applications for the authorisations of regulated products that were previously authorised by the European Food Safety Authority (EFSA). The two JEGs are the FCMJEG, which covers food contact materials and the AEJEG, which has responsibility for food additives, enzymes and other regulated products. In 2023, the COT provided support, challenge and assurance to the work of the two JEGs for assessments as set out below.

AEJEG assessments

1.217 The COT considered Risk Assessments prepared by the Joint Expert Group on Additives, Enzymes and other Regulated Products (AEJEG) regarding the following regulated product applications:

- For the modification of specifications to include fermentation by *Yarrowia lipolytica* as a production method for steviol glycosides.
- For the modification of specifications to include fermentation by *Saccharomyces cerevisiae* as a production method for steviol glycosides.
- For the modification of specifications to include production from stevia leaf extract by enzymatic conversion as a production method for steviol glycosides.
- The authorisation of a new flavouring 2-hydroxy-4-methoxybenzaldehyde.

1.218 All items are currently reserved as they cover draft AEJEG Committee Advice Papers not currently published.

1.219 AEJEG Committee Advice Papers will be published in 2024.

FCMJEG assessments

1.220 The COT considered Risk Assessments prepared by the Joint Expert Group on Food Contact Materials (FCMJEG) regarding the following regulated product application:

- On the safety of the use of 2-hydroxyethyl methacrylate (HEMAP) as a component in the manufacture of kitchen countertops and sinks. This assessment is for HEMAP only, and not the final reaction mixture used in the manufacture. This item is currently reserved as the Committee Advice Paper is not currently published. Publication of the final assessment is expected in 2024.
- On the safety assessment on the evaluation of the recycled poly(ethylene terephthalate) decontamination process operated by PETUK Ltd. for use in manufacture of articles in contact with food. The COT endorsed the assessment made by the FCMJEG. This item is currently reserved as the Committee Advice Paper is not currently published. Publication of the final assessment is expected in 2024.

Working Groups

Joint ACNFP/COT Working Group on Cannabidiol (CBD)

1.221 A joint Subgroup of the Advisory Committee on Novel Foods and Processes (ACNFP) and COT was formed to address a series of questions in relation to the safety of CBD-containing and hemp-derived ingredients. The overarching aim of the Subgroup is to enable the FSA to perform risk assessments for CBD in food. The group established an ADI for pure form CBD (>98% purity) of 0.15 mg/k bw/day (10 mg/day for a 70 kg adult) as set out in a joint statement. Work continues on the assessment of novel products containing a lower proportion of CBD.

1.222 The joint position paper from the ACNFP & COT on establishing a provisional acceptable daily intake (ADI) for pure form (≥98%) cannabidiol (CBD) in foods, based on new evidence can be found on the committees website: Joint position paper from ACNFP & COT on establishing provisional ADI for pure form CBD in foods | Advisory Committee on Novel Foods and Processes.

Joint SACN/COT Working Group in Plant-based drinks

1.223 Plant-based drinks have become increasingly popular in the United Kingdom (UK) both for individuals with an allergy to cow’s milk or lactose intolerance and those who wish to avoid dairy products for ethical or cultural reasons. Three such drinks were reviewed by the Committee, based on their market share, with a statement being published in 2022.

1.224 The Scientific Advisory Committee on Nutrition (SACN) have also considered these drinks from a nutritional perspective. To bring these two strands together, a joint Working Group was established to undertake a benefit risk-assessment of soya, oat and almond drinks as replacements for cow's milk. To support this work, a risk assessment of the components and contaminants, potentially present in cows' milk was conducted. The Working Group started work in December 2021 and it is hoped that a draft report will be published for consultation in 2024.

COT Working Group on PFAS

1.225 Following publication of the COT Interim position on per- and polyfluoroalkyl substances, a COT subgroup on PFAS has been formed.

1.226 The terms of reference for this subgroup are:

1.227 To provide guidance to UK Government Departments and Agencies to support human health risk assessments of per- and poly-fluoroalkyl substances (PFAS) where exposures to existing and legacy PFAS is occurring through food, drinking water and other environmental media. This will include:

- Undertaking an independent review of toxicological and epidemiological data, focusing on a number of critical endpoints, and considering the biological relevance of the endpoints assessed.
- Considering the toxicokinetics of PFAS.
- Determining whether different PFAS can be grouped for assessment and how this can be done.
- Establishing a HBGV or a number of HBGVs as the data allow.

1.228 The subgroup will endeavour to follow the guidance from the Joint COT and COC Synthesis and Integration of Epidemiological and Toxicological Evidence (SETE) subgroup in undertaking this assessment.

1.229 The subgroup held two meetings in 2023, which considered papers on animal and *in vitro* data on thyroid effects of PFAS and animal data on liver effects of PFAS. Further papers on these endpoints as well as papers on other endpoints will be considered in the future.

COT Working Group on the Codex report on food allergen thresholds

1.230 The COT were asked to carry out an assessment of the report of the joint FAO/WHO Expert Committee on the Risk Assessment of Food Allergens to Codex on establishing threshold levels for allergens of global importance (Part 2: review and establish threshold levels in foods for the priority allergens) to inform decisions by the FSA on whether it would be appropriate for the Eliciting Dose (ED) recommended in the report for establishing reference doses to be applied to regulated allergens in the UK.

1.231 The assessment was carried out by a subgroup comprising several COT members along with other. external experts, under the chairmanship of Prof Ian Kimber. The COT subgroup met virtually on four separate occasions. The Chair of the Expert Committee on allergen thresholds (2nd Joint FAO/WHO Expert Consultation meeting) was invited to attend one of these meetings to clarify and answer some questions about the Expert Committee's report.

1.232 In addressing questions posed in the Terms of Reference, the COT subgroup reached the following conclusions:

- There is no reason to suggest that the data are not sufficiently representative of the UK population.
- There are uncertainties regarding the way in which ED values have been derived – and, as a consequence, the accuracy of these values. Given the available data upon which derived ED values are based this is a limitation that must – at present – be acknowledged. However, there are no key gaps that can be filled using the published literature.

- There is insufficient evidence to demonstrate that using reference doses based on ED05, as opposed to ED01 values would not significantly impact on public health.

1.233 The report of the subgroup was then presented to the COT. The following comments were made:

1.234 It was noted that the underpinning data used to derive the EDs (both ED01 and ED05 values) in the Expert Committee report were not made available with the report and were not otherwise available. This made it difficult to confirm the conclusions and access to the raw data would have been beneficial.

1.235 The report contained few graphs showing the modelling used and those that were included did not give confidence that the proposed eliciting doses were appropriate values. The benchmark approach used was not the same as that normally used in toxicology. It was further noted that no safety factors were

included.

1.236 However, the COT acknowledged that while the dataset for some of the allergens was based upon very small numbers, there probably were no other data available in the literature to refine the dataset.

1.237 It was also noted that the reference to “mild anaphylaxis” in the report did not seem appropriate as NICE have a very clear definition that anaphylaxis is always a severe reaction.

1.238 The COT agreed with the way the assessment of the report had been undertaken by the COT subgroup and with the contents and key conclusions reached by them.

1.239 The COT also emphasised that since both ED01 and ED05 values represented effect levels, it was axiomatic that more people would be affected if the ED05 were used rather than the ED01 but the decision on which value to use will need to take into account additional considerations and was for risk managers to make rather than the COT.

1.240 The COT subgroup’s report can be viewed at: COT Codex Subgroup Report on Codex Allergen Thresholds Report.

2023 Membership of the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment

In this guide

In this guide

1. About the Committees - 2023
2. COT Preface - 2023
3. COT evaluations - 2023
4. COT Assurance - 2023

5. Committee Procedures - 2023
6. Ongoing Work - COT 2023
7. Other Committee Activities: Joint Expert Groups, Presentations and Workshop -2023
8. 2023 Membership of the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment
9. Declaration of COT members' interests during the period of this report -2023
10. Sub-groups active in 2023
11. Committee on Mutagenicity of chemicals in Food, Consumer Products and the Environment Annual Report 2023
12. Ongoing work - COM 2023
13. Discussion Items -2023
14. 2023 Membership of the Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment
15. Declaration of COM members' interests during the period of this report -2023
16. Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment Annual Report 2023
17. COC Ongoing Topics - 2023
18. COC Workshop - 2023
19. Joint session Horizon scanning
20. COC input to COT work
21. 2023 Membership of the Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment
22. Declaration of COC members' interests during the period of this report -2023
23. Annex 1 - 2023 - Terms of Reference
24. Annex 2 - 2023 - Code of Conduct for members of the COC/COM/COT
25. Annex 3 – 2023 - Openness
26. Annex 4 – 2023 - Good Practice Agreement for Scientific Advisory Committees
27. Annex 5 – 2023 - Glossary of Terms
28. Annex 6 – 2023 - Previous Publications

Chair

Professor Alan Boobis OBE, PhD, FBTS, FBPhS

Emeritus Professor of Toxicology in the Faculty of Medicine at Imperial College London.

Members

Dr Phil Botham BSc, PhD

Principal Science Advisor at Syngenta (part time).

Ms Jane Case

Lay Member. Trowers & Hamlins LLP.

Dr Stella Cochrane BSc PhD

Science Leader for Allergy and Immunology in Unilever’s Safety and Environmental Assurance Centre.

Dr James Coulson BSc MBBCh Dip Med Tox Dip Therapeutics LLM MD FRCP FRCPE ERT

Clinical Reader at Cardiff University, Honorary Professor in Clinical Pharmacology and Toxicology, Cardiff Metropolitan University, Honorary Consultant Physician, Clinical Pharmacologist and Toxicologist, Cardiff & Vale University Health Board.

Dr Silvia Gratz

Senior Research Fellow at the Rowett Institute, University of Aberdeen.

Professor Thorhallur I. Halldorsson

Professor at the Faculty of Food Science and Nutrition at the University of Iceland.

Professor Gary Hutchison

Professor of Toxicology and Dean of Applied Sciences at Edinburgh Napier University.

Dr Sarah Judge BSc, PhD.

Lecturer in Pharmacology in the School of Biomedical, Nutritional and Sport Sciences at Newcastle University.

Professor Gunter Kuhnle

Professor of Nutrition and Food Science, University of Reading.

Dr David Lovell

Emeritus Reader in Medical Statistics at St George’s Medical School, University of London.

Professor Shirley Price

Emerita Professor of Toxicology at the University of Surrey.

Dr Mac Provan

Director of Regulatory Science Ltd.

Ms Juliet Rix

Lay Member.

Dr Michael Routledge

Associate Professor of Medical Education at University of Leicester.

Dr Cheryl Scudamore

RCVS Specialist in Veterinary Pathology (laboratory animals) working as independent consultant in experimental and toxicological pathology.

Dr Natalie Thatcher

Mondelēz International.

Professor Mireille Toledano

Chair in Perinatal and Paediatric Environmental Epidemiology, Faculty of Medicine, School of Public Health, Imperial College London.

Dr Simon Wilkinson

Senior Lecturer in Pharmacology in the School of Biomedical, Nutritional and Sports Sciences at Newcastle University.

Professor Philippe Wilson

Professor of Animal Science and Bioinformatics, Nottingham Trent University, and Head of Conservation at the Rare Breeds Survival Trust.

Professor Matthew Wright BSc, PhD

Professor of Toxicology, Institute of Cellular Medicine, Newcastle University.

Professor Maged Younes

Independent expert on toxicology and biochemical pharmacology.

Professor Peter Barlow

Chair of Immunology & Infection, and Head of the Centre for Biomedicine & Global Health within the School of Applied Sciences at Edinburgh Napier University.

Dr Steven Enoch

Reader in Computational Toxicology, Liverpool John Moores University.

Associate Members

An associate member of the Science Advisory Committees (SACs) is a membership designed to allow early or mid-career researchers to become involved in the work of the FSA SACs. Creating this role allows the FSA to engage with a more diverse range of individuals, as well as encouraging interest in future SAC and FSA work.

Professor Jeanette Rotchell
University of Lincoln.

Dr Samantha Donnellan
Lecturer of Biomedical Sciences at Edinburgh Napier University.

Ms Eimear O'Rourke
Queens University Belfast.

Dr Ben Amies-Cull
Public health researcher at the University of Oxford.

Dr Charlotte Mills
Hugh Sinclair Lecturer in Nutritional Sciences within the Department of Food and Nutritional Sciences at University of Reading.

Dr Tarek Abdelghany

Lecturer of Pharmacology and Physiology at the Institute of Education in Healthcare and Medical Sciences, School of Medicine, Medical Sciences and Nutrition, the University of Aberdeen.

Co-opted Members

Dr Caroline Harris

Corporate vice president, Principal scientist and the Co-Director of the Centre for Chemical Regulation and Food Safety at Exponent International Ltd. Dr Harris was co-opted after her term on the committee expired on the 1st of March 2022.

Professor Paul Haggarty

Deputy Director, Rowett Institute of Nutrition and Health, University of Aberdeen. Prof Haggarty is a Co-opted member from the Scientific Advisory Committee on Nutrition (SACN).

Secretariat

Ms Catherine Mulholland BSc (Hons), ERT Scientific Secretary

Ms Britta Gadeberg BSc (Hons) MSc ERT Scientific Secretary – UK HSA

Dr David Gott BSc (Hons) PhD

Dr Alexander Cooper BSc (Hons) MSc PhD

Dr Barbara Doerr BSc (Hons) MSc PhD

Ms Jocelyn Frimpong Manso BSc (Hons) MSc

Ms Cleanncy Hoppie BSc (Hons) MSc

Mr Barry Maycock BSc (Hons) MSc

Dr Olivia Osborne BSc (Hons) (Exon) PhD ERT MIFST

Ms Claire Potter BSc (Hons) MSc ERT

Dr Joseph Shavila BSc (Hons) MSc PhD

Ms Sabrina Thomas BSc (Hons) MSc

Ms Chara Tsoulli BSc (Hons) MSc Ms

Ms Frederique Uy BSc (Hons) MSc

Miss Sophy Wells

Dr Gaetana Spedalieri

Mr Thomas Hornsby BSc (Hons) MSc

Ms Gail Drummond BSc (Hons) MSc, LLB, PG Dip (law)

Dr Emily Hudson BSc (Hons) Mres

Dr David Kovacic

Declaration of COT members' interests during the period of this report -2023

In this guide

In this guide

1. About the Committees - 2023
2. COT Preface - 2023
3. COT evaluations - 2023
4. COT Assurance - 2023
5. Committee Procedures - 2023
6. Ongoing Work - COT 2023
7. Other Committee Activities: Joint Expert Groups, Presentations and Workshop -2023
8. 2023 Membership of the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment
9. Declaration of COT members' interests during the period of this report -2023
10. Sub-groups active in 2023
11. Committee on Mutagenicity of chemicals in Food, Consumer Products and the Environment Annual Report 2023
12. Ongoing work - COM 2023
13. Discussion Items -2023
14. 2023 Membership of the Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment

15. Declaration of COM members' interests during the period of this report -2023
16. Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment Annual Report 2023
17. COC Ongoing Topics - 2023
18. COC Workshop - 2023
19. Joint session Horizon scanning
20. COC input to COT work
21. 2023 Membership of the Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment
22. Declaration of COC members' interests during the period of this report -2023
23. Annex 1 - 2023 - Terms of Reference
24. Annex 2 - 2023 - Code of Conduct for members of the COC/COM/COT
25. Annex 3 – 2023 - Openness
26. Annex 4 – 2023 - Good Practice Agreement for Scientific Advisory Committees
27. Annex 5 – 2023 - Glossary of Terms
28. Annex 6 – 2023 - Previous Publications

Chair

Professor Alan Boobis OBE, PhD, FBTS, FBPhS

Personal Interest	**Employee:** Imperial College London, Department of Medicine (retired June 2017, part-time appointment from Aug 2017-May 2019). Full retiral June 2019. Emeritus Professor of Imperial College London, National Heart & Lung Institute.

	Membership: ILSI & ILSI HESI (until 2021) Boards of Trustees; ILSI Europe, Board of Directors. Dept. of Health Committee on the Medical Effects of Air Pollutants WHO/FAO JMPR. WHO/FAO JECFA (vet) and WHO/FAO JMPR. WHO TobReg. WG10 TC126 (Intense Machine- smoking Regime for Testing Cigarettes) (until 2022).
Personal Interest	EUROTOX. British Pharmacological Society, British Toxicology Society, Society of Toxicology (USA). Michigan State University MSU Center for Research on Ingredient Safety (CRIS) (External Advisory Committee); Personal Care Products Council (PCPC) Sunscreen Consortium, Washington, D.C - Cancer risk assessment of sunscreen products; Advisory Board, brigid: Bridging the Gap between Microplastics and Human Health, Plastics Europe; Danone SA expert mtg to discuss emerging issues in food safety. Agency for Innovations in Food and Chemical Safety Programme. Science, Technology and Research, Singapore (A*STAR) (Scientific Advisory Board) (until 2022).
Non-Personal Interest	None.

Members

Dr Phil Botham

Personal Interest	**Employee:** Syngenta - Principal Science Advisor (part time).
Personal Interest	**Shareholder:** AstraZeneca, Regulatory Science Associates (Part, Time Consultant).
Personal Interest	**Consultancy:** Regulatory Science Associates (part time).
Personal Interest	**Membership:** British Toxicology Society (Vice President) Society of Toxicology (USA), European Centre for Ecotoxicology and Toxicology of Chemicals Scientific Committee, Crop Life International Human Health Group.
Non-Personal Interest	None.

Ms Jane Case

Personal Interest	**Employee:** Trowers & Hamlins LLP, Company Secretary of Muse Interiors.
Personal Interest	**Membership:** None.

Personal Interest	**Shareholder:** Standard Life Santander.
Non-Personal Interest	None.

Dr Stella Cochrane

Personal Interest	**Employee:** Unilever.
Personal Interest	**Membership / Affiliation:** Unilever representative on the UK FDF Allergen Steering Group (Deputy Chair), FDE Allergen Group and University of Nebraska Food Allergy Research & Resources Board.
Personal Interest	**Shareholder:** Unilever.
Non-Personal Interest	None.

Dr James Coulson

Personal Interest	**Employee:** Cardiff University, Director of Medical, Scientific and Toxicology Consultancy Ltd.

	Membership: British Medical Association, British Pharmacology Society, British Toxicology Society National Trust, Royal College of Physicians of London.
Personal Interest	
Non-Personal Interest	None.

Professor Thorhallur Ingi Halldorsson

Personal Interest	**Employee:** Faculty of Food Science and Nutrition, University of Iceland.
Personal Interest	**Membership:** European Food Safety Authority - Scientific committee and various working groups. Nordic Council of Ministers - revision of the 2022 Nordic Nutrition Recommendation). Icelandic Risk Assessment Committee for Food, Feed, Fertilizers and Seeds (IRAC) – occasional expert work. The Nutricia Research Foundation – review of applications once a year. The Icelandic Research Found (RANNIS) – occasional member of different expert panels.
Non-Personal Interest	None.

Professor Gary Hutchison

Personal Interest	**Employee:** Dean of Applied Sciences at Edinburgh Napier University.
Personal Interest	**Membership:** British Toxicology Society, Fellow of the Royal Society of Biology, Member of Governing Council of Marine Alliance for Science and Technology for Scotland (MASTS), Member of the Scottish Government Chemicals Policy Network, Member of Office for Product Safety & Standards.
Non-Personal Interest	None.

Dr Sarah Judge

Personal Interest	**Employee:** Newcastle University, Lowcock Properties Ltd.
Personal Interest	**Membership:** British Pharmacology Society, British Toxicology Society International Association for Neurotoxicology.

Non-Personal Interest	Research Funding.

Professor Gunter Kuhnle

Personal Interest	**Employee:** Professor of Nutrition and Food Science, University of Reading.
Personal Interest	**Membership:** Nutrition Society, Registered Nutritionist, British Mass Spectrometry Society, Scientific Committee of the British Nutrition Foundation.
Non-Personal Interest	Research Funding BBSRC.

Dr David Lovell

Personal Interest	**Employee:** Reader in Medical Statistics, St Georges Medical School, University of London.

Personal Interest	**Membership:** HESI GTTC – Biometrics Society, British Toxicology Society Genetics Society, Royal Society of Biology Laboratory Animal Science Association, Royal Statistical Society Statisticians in the Pharmaceutical Industry, United Kingdom Environment Mutagen Society (UKEMS), UK National Centre of Replacement, Refinement and Reduction of Animals in Research (NC3Rs), MRC EMINENT Scientific Review Board. **Also, private member of:** British Trust of Ornithologists (BTO) , English Heritage, Liberty, Campaign of the Protection of Rural England (CPRE), Kew Gardens, Sandwich Bay Bird Observatory Trust (SBBOT), Chelsea Physic Garden, National Trust.

Personal Interest	**Shareholder:** National Grid, Pfizer, AstraZeneca (spouse shareholder), National Grid plc (spouse shareholder).
Non-Personal Interest	None.

Professor Shirley Price

Personal Interest	**Employee:** None.
Personal Interest	**Membership:** None.
Non-Personal Interest	**Trusteeships:** Gas Safety Trust.
Non-Personal Interest	**Other:** I can confirm that as the President of the British Toxicology Society (BTS) I hold a non-personal and non-specific interest in both GSK and AstraZeneca on the Society's behalf. These non-personal and non-specific interests relate to donations provided by both companies to the British Toxicology Society (BTS) to support their Annual Congress and Education and Training.

Dr Mac Provan

Personal	**Interest**	**Employee:** Director of Regulatory Science Ltd.
Personal	**Interest**	**Membership:** None.
Non-Personal Interest		None.

Ms Juliet Rix

Personal	**Interest**	**Employee:** None.
Personal	**Interest**	**Membership:** None.
Non-Personal Interest		None.

Dr Michael Routledge

Personal	**Interest**	**Employee:** Lecturer/Senior Lecturer/Associate Professor University of Leicester.
Personal	**Interest**	**Membership:** Member of working group, European Food Safety Authority, 2018-2019. Vice-President of UKEMS (UK Environmental Muta-Genesis Society).

Non-Personal Interest	None.

Dr Cheryl Scudamore

Personal	**Interest**	**Employee:** Independent consultant in experimental and toxicological pathology.
Personal	**Interest**	**Membership:** None.
Non-Personal Interest		None.

Dr Natalie Thatcher

Personal	**Interest**	**Employee:** Mondelēz International.
Personal	**Interest**	**Membership:** None.
Non-Personal Interest		None.

Professor Mireille Toledano

Personal	**Interest**	**Employee:** Marit Mohn Chair in Perinatal & Paediatric Environmental Epidemiology, Imperial College London.
Personal	**Interest**	**Membership:** None.
Non-Personal Interest		None.

Dr Simon Wilkinson

Personal	**Interest**	**Consultancies and other fee-paid work:** Consultancy for L’Oreal, Paris.
Personal	**Interest**	**Membership:** None.
Non-Personal Interest		None.

Professor Phillipe Wilson

Personal	**Interest**	**Employee:** Nottingham Trent University, Rare Breeds Survival Trust.

Personal Interest	**Membership:** None.
Non-Personal Interest	None.

Professor Matthew Wright

Personal Interest	**Consultancies and Direct Employment:** Newcastle University.
Personal Interest	**Membership:** British Toxicology Society, Society of Toxicology (US), EFSA FAF Panel.
Personal Interest	**Miscellaneous:** Toxicology – Associate Editor.
Non-Personal Interest	**Support by Industry:** GSK, Lubrizol.

Professor Maged Younes

Personal Interest	**Employee:** Independent expert in toxicology and biochemical pharmacology.

Personal Interest	**Membership:** Chair of EFSA ANS panel, Chair Commission on evidence-based methods in risk assessment, Federal Institute for Risk Assessment (BfR), Germany. Society of Toxicology, USA German Society of Experimental and Clinical Pharmacology and Toxicology. Society for Risk Analysis.
Non-Personal Interest	None.

Dr Silvia Gratz

Personal	**Interest**	**Employee:** Rowett Institute, University of Aberdeen
Personal	**Interest**	**Membership:** The Nutrition Society (UK), The British Toxicology Society, FSA Register of Specialists.
Non-Personal Interest		None.

Professor Peter Barlow

Personal Interest	**Employee:** Chair of Immunology & Infection, and Head of the Centre for Biomedicine & Global Health within the School of Applied Sciences at Edinburgh Napier University.

Personal Interest	**Membership:** Member of the British Society for Immunology.
Non-Personal Interest	None.

Dr Steven Enoch

	Employee: Reader in Computational Toxicology, Liverpool John Moores University.
Personal Interest	**Consultancies and other fee-paid work:** Crop Life Europe funded work into how grouping and read-across can be used to fill to predict the toxicity of metabolites and residues of plant protection products. All work is in the open scientific literature**.**
Personal Interest	**Membership:** None.
Non-Personal Interest	None.

Associate Members Interests

Professor Jeanette Rotchell

Personal	**Interest**	**Employee:** University of Lincoln.
Personal	**Interest**	**Membership:** None.
Non-Personal Interest		None.

Dr Samantha Donnellan

Personal	**Interest**	**Employee:** Edinburgh Napier University
Personal	**Interest**	**Membership:** None.
Non-Personal Interest		**Fellowships:** Previously a Churchill Trust Fellow.

Ms Eimear O'Rourke

Personal	**Interest**	**Employee:** None.
Personal	**Interest**	**Membership:** EAACI Junior Member, EFA Youth Parliament Member.

Non-Personal Interest	None.

Dr Ben Amies-Cull

Personal Interest	**Employee:** University of Oxford, Salaried GP, National Health Service (NHS).
Personal Interest	**Membership:** None.
Non-Personal Interest	**Other non-personal interests**: Research funding from NIHR, MRC, Wellcome Trust.

Dr Charlotte Mills

Personal Interest	**Employee:** University of Reading.
Personal Interest	**Membership:** Academic member of Nutrition Society and co-chair of associated Special Interest Group on Phytochemicals and Health. Academic member and committee member (new investigator sub-committee) of International Society of Hypertension.
Non-Personal Interest	None.

Dr Tarek Abdelghany

Personal	**Interest**	**Employee:** The University of Aberdeen.
Personal	**Interest**	**Membership:** British Toxicology Society, British Pharmacology Society, American Society for Pharmacology and Experimental Therapeutics, Egyptian Pharmacists Syndicate.
Personal	**Interest**	**Other:** Visiting lectureship positions at Newcastle University and Cairo University.
Non-Personal Interest		None.

Co-opted Members Interests

Dr Caroline Harris

Personal	**Interest**	**Employee:** Exponent International Ltd.

Personal Interest		**Membership:** International Union of Pure and Applied Chemistry, Expert Committee on Pesticides.
		Fellowship: Royal Society of Chemistry.
Personal Interest		**Shareholder:** Exponent Inc.
Non-Personal Interest		None.

Professor Paul Haggarty

Personal Interest	**Employee:** Head of Lifelong Health at the Rowett Institute of Nutrition and Health, University of Aberdeen.
Personal Interest	**Membership:** Chair of the Biotechnology and Biological Sciences Research Council **(**BBSRC) Strategy Advisory Panel on Bioscience for an Integrated Understanding of Health. Dates: 2017 to 2022.
Non-Personal Interest	**Research project funding:** UK Research and Innovation (UKRI) Global Challenges Research Fund (GCRF) Dates: 2019 to 2024.

Sub-groups active in 2023

In this guide

In this guide

1. About the Committees - 2023
2. COT Preface - 2023
3. COT evaluations - 2023
4. COT Assurance - 2023
5. Committee Procedures - 2023
6. Ongoing Work - COT 2023
7. Other Committee Activities: Joint Expert Groups, Presentations and Workshop -2023
8. 2023 Membership of the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment
9. Declaration of COT members' interests during the period of this report -2023
10. Sub-groups active in 2023
11. Committee on Mutagenicity of chemicals in Food, Consumer Products and the Environment Annual Report 2023
12. Ongoing work - COM 2023
13. Discussion Items -2023
14. 2023 Membership of the Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment
15. Declaration of COM members' interests during the period of this report -2023
16. Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment Annual Report 2023
17. COC Ongoing Topics - 2023
18. COC Workshop - 2023
19. Joint session Horizon scanning
20. COC input to COT work
21. 2023 Membership of the Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment
22. Declaration of COC members' interests during the period of this report -2023
23. Annex 1 - 2023 - Terms of Reference
24. Annex 2 - 2023 - Code of Conduct for members of the COC/COM/COT
25. Annex 3 – 2023 - Openness

26. Annex 4 – 2023 - Good Practice Agreement for Scientific Advisory Committees
27. Annex 5 – 2023 - Glossary of Terms
28. Annex 6 – 2023 - Previous Publications

Sub-groups active in 2023	Current COT Members serving
Joint SACN-COT Working Group on plant- based drinks.	Professor Alan Boobis, Professor Gunter Kuhnle Sr Caroline Harris
Joint COT- ACNFP Working Group on Cannabidiol (CBD).	Professor Alan Boobis Dr Stella Cochrane Dr James Coulson Professor Gary Hutchison Professor Gunter Kuhnle Professor Shirley Price Dr Mac Provan Dr Simon Wilkinson

PFAS Working Group.	Professor Shirley Price (Chair) Dr Phil Botham Dr James Coulson Dr Steve Enoch Professor Thorhallur Ingi Halldórsson Professor Gunter Kuhnle Professor Matthew Wright Dr Peter Barlow (ad hoc) Dr Stella Cochrane (ad hoc) Professor Gary Hutchison (ad hoc) Dr Sarah Judge (ad hoc)
Titanium Dioxide Working Group.	Dr Peter Barlow Dr Phil Botham Professor Gary Hutchison Dr David Lovell Dr Cheryl Scudamore

Ad hoc working group to review Codex Expert Committee's report on establishing thresholds for allergens of global importance.

Dr Phil Botham

Dr Stella Cochrane

Dr David Lovell

Professor Mireille Toledano

Committee on Mutagenicity of chemicals in Food, Consumer Products and the Environment Annual Report 2023

In this guide

In this guide

1. About the Committees - 2023
2. COT Preface - 2023
3. COT evaluations - 2023
4. COT Assurance - 2023
5. Committee Procedures - 2023
6. Ongoing Work - COT 2023
7. Other Committee Activities: Joint Expert Groups, Presentations and Workshop -2023
8. 2023 Membership of the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment
9. Declaration of COT members' interests during the period of this report -2023
10. Sub-groups active in 2023
11. Committee on Mutagenicity of chemicals in Food, Consumer Products and the Environment Annual Report 2023
12. Ongoing work - COM 2023
13. Discussion Items -2023

14. 2023 Membership of the Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment
15. Declaration of COM members' interests during the period of this report -2023
16. Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment Annual Report 2023
17. COC Ongoing Topics - 2023
18. COC Workshop - 2023
19. Joint session Horizon scanning
20. COC input to COT work
21. 2023 Membership of the Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment
22. Declaration of COC members' interests during the period of this report -2023
23. Annex 1 - 2023 - Terms of Reference
24. Annex 2 - 2023 - Code of Conduct for members of the COC/COM/COT
25. Annex 3 – 2023 - Openness
26. Annex 4 – 2023 - Good Practice Agreement for Scientific Advisory Committees
27. Annex 5 – 2023 - Glossary of Terms
28. Annex 6 – 2023 - Previous Publications

Preface

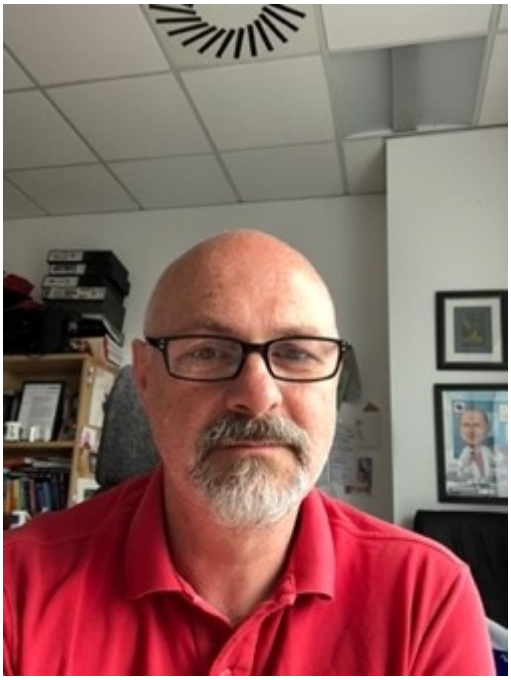

Photo of Professor Gareth Jenkins- Chair. The photo is a head and shoulders image. Gareth is wearing a red shirt, dark framed glasses and has facial hair. In

the background the image shows a ceiling covered in white square tiles, to the left a book shelf and to the right, framed pictures on the wall.

I am delighted to present this report on the work of the Committee on Mutagenicity (COM) during 2023.

The Committee on Mutagenicity (COM) provides advice on potential mutagenic activity of specific chemicals at the request of UK Government Departments and Agencies. Such requests generally relate to chemicals for which there are incomplete, non-standard or controversial data sets for which independent authoritative advice on potential mutagenic hazards and risks is required. Recommendations for further studies are, on occasions, made.

The Committee also advises on important general principles and on new scientific work related to the assessment of mutagenic risk and makes recommendations on wider aspects of mutagenicity testing. The membership of the Committee, declarations of their interests, agendas and minutes of meetings, and statements are all published on the internet (Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment - GOV.UK).

The membership of COM has undergone some changes in 2023 with members rotating off the committee and new vacancies being advertised.

In 2023, COM continued to develop its opinion paper on the genotoxicity of titanium dioxide (MUT/2022/05) following the updated opinion published by EFSA in 2021. This will be published in 2024.

In 2023, COM finalised the production of “lay summaries” to enhance public engagement. To begin with, this involved the description of the process of chemical risk assessment from a lay perspective (MUT/2022/03) and we have now begun the process of generating lay summaries of COM decision papers (MUT/2022/13).

In 2023, COM also commented on the genotoxicity of a novel can coating material (MUT/2023/02) and continued to draft an opinion on the use of *in silico* approaches for genotoxicity.

Professor Gareth Jenkins- Chair

Ongoing work - COM 2023

In this guide

In this guide

1. About the Committees - 2023
2. COT Preface - 2023
3. COT evaluations - 2023
4. COT Assurance - 2023
5. Committee Procedures - 2023
6. Ongoing Work - COT 2023
7. Other Committee Activities: Joint Expert Groups, Presentations and Workshop -2023
8. 2023 Membership of the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment
9. Declaration of COT members' interests during the period of this report -2023
10. Sub-groups active in 2023
11. Committee on Mutagenicity of chemicals in Food, Consumer Products and the Environment Annual Report 2023
12. Ongoing work - COM 2023
13. Discussion Items -2023
14. 2023 Membership of the Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment
15. Declaration of COM members' interests during the period of this report -2023
16. Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment Annual Report 2023
17. COC Ongoing Topics - 2023
18. COC Workshop - 2023
19. Joint session Horizon scanning
20. COC input to COT work
21. 2023 Membership of the Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment
22. Declaration of COC members' interests during the period of this report -2023
23. Annex 1 - 2023 - Terms of Reference
24. Annex 2 - 2023 - Code of Conduct for members of the COC/COM/COT
25. Annex 3 – 2023 - Openness

26. Annex 4 – 2023 - Good Practice Agreement for Scientific Advisory Committees
27. Annex 5 – 2023 - Glossary of Terms
28. Annex 6 – 2023 - Previous Publications

COM guidance series update

Guidance statement the use of biomarkers in genotoxicity in risk assessment

2.1 At the request of the COC, the COM considered a revised version of the COC Guidance Statement G04 ‘The use of biomarkers in carcinogenic risk assessment’ at the COM March 2022 meeting (MUT/2022/03). Particular focus was given to the ‘DNA damage’ and ‘genotoxicity biomarkers’ sections, both of which had had been shortened in the current version of G04 as part of a document revision process.

2.2 It was agreed that COM would produce a guidance statement that provided a more comprehensive overview of these areas, which could then be referred to by the other Committees. A draft scoping document outlining the proposed content of guidance statement was presented to the COM at its meeting in June 2022 (MUT/2022/06).

2.3 Several modifications to the scoping document were suggested by members and these were incorporated into a first draft document presented at the COM October 2022 meeting (MUT/2022/11). Members considered that the focus of the COM document should be *in vivo* biomarkers of DNA damage, with greater distinction from the COC Guidance Statement G04. Work is ongoing to progress a second draft document.

Non-expert summaries for COM website

2.4 At a previous COM meeting in June 2022, it was agreed that the general public could benefit from the addition of non-expert summaries to the start of each COM guideline document.

2.5 A draft non-expert summary for the overarching COM guideline, ‘Guidance on a strategy for genotoxicity testing of chemicals (MUT/2022/13) was presented at the COM October 2022 meeting. Members considered that some text could be removed, as this was available on the COM website, and a link provided to that

website. In addition, it was recommended that links to the glossary should be utilised fully as this provided an immediate and understandable definition for readers. Specific comments on the paper were discussed at the February and June COM meetings so that the paper could be finalised.

Discussion paper on tetra-methyl bisphenol f diglycidyl ether (tmbpf-dge) in canned food packaging materials

2.6 This item was presented as a reserved item as the data are commercially confidential.

2.7 Members discussed the toxicological information provided to the Committee on TMBPF-DGE, a can coating, as well as the previous discussions of the Joint Expert Group on Food Contact Materials (FCMJEG). Following the COMs assessment, a discussion paper was presented to the FCMJEG and to the Committee on Toxicity, including the discussions of the COM. The work is ongoing, a final assessment is expected in 2024.

In vitro data / *in vivo* data review of titanium dioxide genotoxicity

2.8 Following the publication of the EFSA opinion on titanium dioxide in 2021, which concluded that titanium dioxide could no longer be considered to be ‘safe’ for use in food, the Food Standards Agency (FSA) initiated a review of the EFSA opinion.

2.9 The EFSA opinion was presented to the COM in June 2021 (MUT/2021/03) and to the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT) in July 2021 (TOX/2021/36). The COM had a number of concerns over the EFSA opinion on the genotoxicity of titanium dioxide. Due to this and following the advice of the COT the FSA asked COM to initiate an independent evaluation of the safety of the use of titanium dioxide as a food additive.

2.10 In October 2021, paper MUT/2021/08 was presented to the COM, which summarised the available genotoxicity on titanium dioxide. Members considered that it was not possible to evaluate the genotoxicity of titanium dioxide at that stage. The COM suggested a sifting approach to the available genotoxicity should be adopted as a first step before evaluation. The Chair of the COM, a subgroup of the COM and the secretariat subsequently attended meetings to discuss and agree the criteria and methodology for sifting to identify suitable papers for the

evaluation of titanium dioxide.

2.11 At the COM June 2022 meeting, paper MUT/2022/05 provided information and papers on approaches relating to the sifting and evaluation of the quality genotoxicity studies and evaluating data on nanomaterials. As an update since that meeting, members were informed that a sub-group of the COM had met to discuss the process to select relevant and appropriate studies to be reviewed by the committee. A proforma had been produced, which would be shared with members. This considered two levels, namely, whether the characteristics of the test material had been sufficiently described (e.g., micro or nano sized particles) and the quality and reliability of how the genotoxicity studies had been conducted.

2.12 At the October 2023 meeting, the draft review on titanium dioxide was discussed in detail and members opinions were incorporated into the COM opinion and the subgroup aimed to get the final opinion ready for early 2024.

COM QSAR guidance – proposed workplan

2.13 The overarching COM guidance statement, “Guidance on a Strategy for Genotoxicity Testing of Chemical Substances” was revised in 2021. It recommends a tiered approach consisting of three stages: 0 (preliminary considerations including physico-chemical properties), 1 (*in vitro* genotoxicity tests), and 2 (*in vivo* genotoxicity tests), with the use of QSAR models being recommended for stage 0 only. During revision of the overarching guidance statement, COM agreed that a separate guidance statement on the development and use of QSARs was warranted as this was an impart field. Once developed, a more general narrative would be incorporated into the overarching guidance statement.

2.14 A sub-group of COM members are developing a guidance document for the use of QSARs both in the preliminary evaluation of a chemical (stage 0) and in the evaluation of impurities. This work is ongoing.

OECD Updates and COM input

2.15 COM members continue to input to OECD expert committees.

2.16 In 2022 there was an update to OECD Guidance on the *in vitro* micronucleus assay in terms of methodological adaptions that would allow appropriate genotoxicity testing of nanomaterials. It was expected that there

would be an interlaboratory trial with a view to updating the test guideline with a section on nanomaterials.

2.17 OECD project on the gamma H2AX *in vitro* assay this will progress with a Detailed Review Paper (DRP) moving toward a test guideline.

2.18 Update to OECD Test Guideline 489 on the *in vivo* comet assay to include germ cells. There had been a validation exercise in just one laboratory with five or six chemicals.

Discussion Items -2023

In this guide

In this guide

1. About the Committees - 2023
2. COT Preface - 2023
3. COT evaluations - 2023
4. COT Assurance - 2023
5. Committee Procedures - 2023
6. Ongoing Work - COT 2023
7. Other Committee Activities: Joint Expert Groups, Presentations and Workshop -2023
8. 2023 Membership of the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment
9. Declaration of COT members' interests during the period of this report -2023
10. Sub-groups active in 2023
11. Committee on Mutagenicity of chemicals in Food, Consumer Products and the Environment Annual Report 2023
12. Ongoing work - COM 2023
13. Discussion Items -2023
14. 2023 Membership of the Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment
15. Declaration of COM members' interests during the period of this report -2023
16. Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment Annual Report 2023
17. COC Ongoing Topics - 2023

18. COC Workshop - 2023
19. Joint session Horizon scanning
20. COC input to COT work
21. 2023 Membership of the Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment
22. Declaration of COC members' interests during the period of this report -2023
23. Annex 1 - 2023 - Terms of Reference
24. Annex 2 - 2023 - Code of Conduct for members of the COC/COM/COT
25. Annex 3 – 2023 - Openness
26. Annex 4 – 2023 - Good Practice Agreement for Scientific Advisory Committees
27. Annex 5 – 2023 - Glossary of Terms
28. Annex 6 – 2023 - Previous Publications

NC3Rs/Unilever Workshop "Opportunities for the UK to develop world-leading chemicals regulation" – Summary – Presentation by Natalie Burden (NC3Rs)

2.19 A summary of the recent workshop held jointly by the NC3Rs and Unilever was presented. The workshop discussed opportunities the UK may have, due to EU-exit, to develop world-leading chemicals regulation that could help reduce the reliance on animal testing. The aim of the workshop was to establish a consensus 5-year vision from the UK science base for a future UK chemicals policy, and attendees included representatives of industry, government, contract research organisations, trade associations and academia.

2.20 A draft 5-year vision had been prepared by the NC3Rs in conjunction with a steering group which formed the basis of the workshop discussions. This presented and discussed during the workshop. It was very useful for com to have an opportunity to have an early overview of the workshop discussions. It was suggested that the draft policy document should also be seen by COM at future meetings. This will allow UK to influence and bring onboard scientifically justified change sot regulation.

2023 Membership of the Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment

In this guide

In this guide

1. About the Committees - 2023
2. COT Preface - 2023
3. COT evaluations - 2023
4. COT Assurance - 2023
5. Committee Procedures - 2023
6. Ongoing Work - COT 2023
7. Other Committee Activities: Joint Expert Groups, Presentations and Workshop -2023
8. 2023 Membership of the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment
9. Declaration of COT members' interests during the period of this report -2023
10. Sub-groups active in 2023
11. Committee on Mutagenicity of chemicals in Food, Consumer Products and the Environment Annual Report 2023
12. Ongoing work - COM 2023
13. Discussion Items -2023
14. 2023 Membership of the Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment
15. Declaration of COM members' interests during the period of this report -2023
16. Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment Annual Report 2023
17. COC Ongoing Topics - 2023
18. COC Workshop - 2023
19. Joint session Horizon scanning
20. COC input to COT work

21. 2023 Membership of the Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment
22. Declaration of COC members' interests during the period of this report -2023
23. Annex 1 - 2023 - Terms of Reference
24. Annex 2 - 2023 - Code of Conduct for members of the COC/COM/COT
25. Annex 3 – 2023 - Openness
26. Annex 4 – 2023 - Good Practice Agreement for Scientific Advisory Committees
27. Annex 5 – 2023 - Glossary of Terms
28. Annex 6 – 2023 - Previous Publications

Chair

Professor Gareth Jenkins

Professor of Molecular Carcinogenesis, Faculty of Health, Medicine and Life Science, Swansea University.

Members

Dr Carol Beevers

Regulatory Toxicology, Corteva Agriscience.

Amit Bhagwat

Lay Member.

Professor Shareen Doak

Professor of Genotoxicology & Cancer, Faculty of Health, Medicine and Life Science, Swansea University.

Dr Ann Doherty

Head of Safety Innovation, Clinical Pharmacology and Safety Sciences, AstraZeneca.

Dr Paul Fowler

FSTox Consulting.

Dr Nathan Goldsmith

Associate Member, Exponent.

Professor David Harrison MD DSc FRCPath FRCPEd FRCSEd

Professor of Pathology, University of St Andrews.

Dr George Johnson

Associate Professor, Swansea University Medical School.

Ms Julia Kenny

Nonclinical Safety Project Toxicologist, GSK.

Dr Andrew Povey

Reader in Molecular Epidemiology, University of Manchester.

Mr Paul Rawlinson

Gentronix Ltd.

Mrs Madeleine Wang

Lay Member.

Secretariat

Dr Ovnair Sepai UKHSA Scientific Secretary.

Dr Cath Mulholland FSA Scientific Secretary.

Mr Tom Fraser Committee Administrator.

Declaration of COM members' interests during the period of this report -2023

In this guide

In this guide

1. About the Committees - 2023
2. COT Preface - 2023
3. COT evaluations - 2023
4. COT Assurance - 2023
5. Committee Procedures - 2023
6. Ongoing Work - COT 2023
7. Other Committee Activities: Joint Expert Groups, Presentations and Workshop -2023
8. 2023 Membership of the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment
9. Declaration of COT members' interests during the period of this report -2023
10. Sub-groups active in 2023
11. Committee on Mutagenicity of chemicals in Food, Consumer Products and the Environment Annual Report 2023
12. Ongoing work - COM 2023
13. Discussion Items -2023
14. 2023 Membership of the Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment
15. Declaration of COM members' interests during the period of this report -2023
16. Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment Annual Report 2023
17. COC Ongoing Topics - 2023
18. COC Workshop - 2023
19. Joint session Horizon scanning
20. COC input to COT work
21. 2023 Membership of the Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment
22. Declaration of COC members' interests during the period of this report -2023
23. Annex 1 - 2023 - Terms of Reference
24. Annex 2 - 2023 - Code of Conduct for members of the COC/COM/COT
25. Annex 3 – 2023 - Openness
26. Annex 4 – 2023 - Good Practice Agreement for Scientific Advisory Committees
27. Annex 5 – 2023 - Glossary of Terms
28. Annex 6 – 2023 - Previous Publications

Chair

Professor Gareth Jenkins

Personal Interest	**Employer:** Swansea University. **Honorary Contract:** Swansea Bay University Health Board. **Membership:** President of United Kingdom Environment Mutagen Society (UKEMS). Ex Officio Member, Committee on Carcinogenicity (Dept Health and Social Care) 2021-2027.
Personal Interest	**Member:** British Association for Cancer Research, Senior Editor Mutagenesis (OUP), Editorial Board (and former editor 2013-2015), Mutation Research (Elsevier), Health & Care Research Wales Grant panel (studentships) 2016-present.

Non-Personal Interest	**Grants:** Cancer Research Wales (2023-2026). **Former Grants:** Health & Care Research Wales (2016-2020), MRC/AstraZeneca PhD studentship (ITTP scheme) (2019-2023). Cancer Research Wales grant (2019-2023). External Examining roles (Bangor University DeMontfort University, University of Milan), National Centre of Replacement, Refinement and Reduction of Animals in Research (NC3Rs) (2018-2022), NC3Rs grants (2012-2016 & 2010-2014), Health & Care Research Wales (2016-2020, 2014-2017, Unilever studentship (2014-2017), MRC/AstraZeneca PhD studentship (ITTP scheme) (2019-2023), Cancer Research Wales (2019-2023), BBSRC/Algae UK grant (2020-2022).

Members

Dr Carol Beevers

Personal Interest	**Employee:** Corteva Agriscience (from 01 September 2022). **Pension:** Covance, Exponent International Ltd, Broughton Group, Corteva Agriscience (from September 2022).
Personal Interest	**Membership:** HESI GTTC (workgroup member), OECD (workgroup member), IWGT (work group chair), United Kingdom Environmental Mutagen Society (UKEMS).
Non-Personal Interest	None.

Mr Amit Bhagwat

Personal Interest	**Owner and Shareholder:** Research and Consulting Business.

	Bradford Teaching Hospitals NHS Foundation Trust - Public Governor (Rest of England & Wales). British Computer Society – the Chartered Institute for IT - Chair/Volunteer for Learned Events and Public Service Activities.
Non-Personal Interest	Member - Occupational Therapists Registration Board – Republic of Ireland. Member - Medical Scientists Registration Board – Republic of Ireland. Member of committees associated with impact evaluation and applications scrutiny for the Special EU Programmes body'.
	Membership: Public Ambassador – NHS England subsidiary board related to Digital Urgent & Emergency Care (DUEC), Prescribed Specialised Services Advisory Group, DHSC, Northern Ireland Practice and Education Council for Nursing and Midwifery (NIPEC).
Non-Personal Interest	**Contributor:** Learned and professional development activities within the British Computer Society (chairing, committee and speaking responsibilities).
	Trustee: Myrovlytis Trust (funds research into rare diseases) – Chairing responsibility, Regional inclusive volunteering charity – Chairing responsibility.

Professor Shareen Doak

Personal Interest	**Employee:** Swansea University. **Consultancy:** CEFIC/Titanium Dioxide Manufacturers Association (TDMA).
Personal Interest	**Memberships:** United Kingdom Environmental Mutagen Society (UKEMS), Fellow of the Learned Society of Wales Royal Society of Biology (FRSB), ILSI HESI (committee member), British Toxicology Society (BTS), Editor-In-Chief: Mutagenesis, Member of The Scientific Advisory Group on Chemical Safety of Non-Food and Non-Medicinal Consumer Products (SAG-CS), Commissioned By The Office For Product Safety and Standards (OPSS), Independent Member of The Health & Safety Executive (HSE), Science Quality Assurance Group (SQAG).
Non-personal Interest	**Trustee:** St David’s Medical Foundation (medical research & education charity). **PhD Studentship Grant:** Lhasa Ltd (2023 – 2027).

Dr Paul Fowler

Personal Interest	**Pension:** Unilever (UK), Private Pension (FSTox Consulting Ltd). **Misc:** Fstox Consulting – Director.
Personal Interest	**Membership:** IGG, UKEMS (Committee Member), Roundtable Of Toxicology, CONSULTANTS (RTC), British Toxicology Society (BTS), EEMGS (Committee Member).
Non-Personal Interest	None.

Dr Nathan Goldsmith

Personal Interest	**Employee:** Exponent International Ltd. **Grants:** UKHSA (Potential Exposure to Carcinogens Following E-Cigarette Use). **Pension:** GlaxoSmithKline/GSK.

Personal Interest	**Membership:** British Toxicology Society (BTS).
Non-Personal Interest	None.

Professor David Harrison

	Employee: University of St Andrews UK, NuCana plc UK. **Employee/Non-executive Director:** ILC Therapeutics Ltd, Benenox Ltd, UK – Non-executive Director (unpaid), PathAlba Ltd – Director (unpaid) – dormant. **Consultant:** NHS Lothian – Honorary Consultant.
Personal Interest	**Shareholder:** VBL Ltd, UK, Ryboquin Ltd, UK, ILC Therapeutics Ltd. **Misc:** Cunningham Trust – (Medical Research Charity) Trustee, University of Edinburgh, UK – Honorary Professor, University of Glasgow, UK – Honorary Professor, University of Florida, Adjunct Professor, Viewbank Leuchars Ltd – Director (no salary).
Personal Interest	**Membership:** Fellow Royal College of Pathologists, Fellow of Royal College of Physicians of Edinburgh, Fellow of Royal College of Surgeons of Edinburgh.

Non-Personal Interest	**Misc:** iCAIRD research consortium – Director (unpaid role), Pilgrim Care St Andrews (charity for the elderly) – Trustee (unpaid role), Visiopharm – Member, Scientific Advisory Board, EU Horizon 2020, Partner in KATY Award, grant support, Innovate UK/UKRI – Director of iCAIRD.

Dr George Johnson

Personal Interest	**Consultancy:** Fermenich, Cefic, American Chemistry Council, Teva, Greenberg Traurig Llp, Osler, Hoskin & Harcourt Llp, Janssen, Merck. **Pension:** Uss. University Superannuation Scheme. **Director:** Gtox Ltd.

	Membership:
	United Kingdom Environmental Mutagen Society (UKEMS),
	HESI (committee member),
Personal Interest	President of the European Environmental Mutagenesis and Genomics Society (EEMGS) 2019-2021,
	EMA Expert Member,
	IWGT, Expert Member,
	ICEM, Committee Member.
	Relevant Grant Funding:
	GSK, Post-Doctoral Research Funding – 2021-2022, Nitrosamine Research,
Non-Personal Interest	Sciensano,
	Mycx-It. 2020-Ongoing,
	Ema. Funding Through Fraunhofer Item. 2022-2023,
	HESI Fast Fund. Msc Tuition Fees. 2022.

Ms Julia Kenny

	Employee:
	GlaxoSmithKline/GSK.
	Pension:
Personal Interest	GlaxoSmithKline.
	Shareholder:
	GSK,
	HALEON.

Personal Interest	**Membership:** UK Environmental Mutagen Society (UKEMS).
Non-Personal Interest	None.

Dr Andrew Povey

Personal Interest	**Shareholder:** Lloyds, Standard Life, Halifax, Santander (Partner Shareholder), Norwich Union (Partner Shareholder), Roadchef Topco Ltd (Partner, Shareholder). **Misc:** European Crop Protection Agency – Part of consortium awarded grant on exposure assessment.
Personal Interest	**Membership:** UK Molecular Epidemiology Group (UK-MEG), UK Environmental Mutagen Society (UKEMS), American Association for Cancer Research (AACR), Molecular Epidemiology Group (MEG), British Association for Cancer Research (BACR).

Non-Personal Interest	**Departmental studentships:** Funded by industrial and other bodies.

Mr Paul Rawlinson

Personal Interest	**Employee:** Nufarm Limited. **Pension:** Nufarm pension scheme, St James Place, Formerly Syngenta.
Personal Interest	**Membership:** United Kingdom Environmental Mutagen Society (UKEMS).
Non-Personal Interest	None.

Ms Madeleine Wang

Personal Interest	None.
Non-Personal Interest	None.

Committee on Carcinogenicity of Chemicals in Food, Consumer

Products and the Environment Annual Report 2023

In this guide

In this guide

1. About the Committees - 2023
2. COT Preface - 2023
3. COT evaluations - 2023
4. COT Assurance - 2023
5. Committee Procedures - 2023
6. Ongoing Work - COT 2023
7. Other Committee Activities: Joint Expert Groups, Presentations and Workshop -2023
8. 2023 Membership of the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment
9. Declaration of COT members' interests during the period of this report -2023
10. Sub-groups active in 2023
11. Committee on Mutagenicity of chemicals in Food, Consumer Products and the Environment Annual Report 2023
12. Ongoing work - COM 2023
13. Discussion Items -2023
14. 2023 Membership of the Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment
15. Declaration of COM members' interests during the period of this report -2023
16. Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment Annual Report 2023
17. COC Ongoing Topics - 2023
18. COC Workshop - 2023
19. Joint session Horizon scanning
20. COC input to COT work
21. 2023 Membership of the Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment
22. Declaration of COC members' interests during the period of this report -2023
23. Annex 1 - 2023 - Terms of Reference
24. Annex 2 - 2023 - Code of Conduct for members of the COC/COM/COT

25. Annex 3 – 2023 - Openness
26. Annex 4 – 2023 - Good Practice Agreement for Scientific Advisory Committees
27. Annex 5 – 2023 - Glossary of Terms
28. Annex 6 – 2023 - Previous Publications

Preface

Head and shoulders image of Professor David Harrison in front of a grey background wearing a white shirt with a blue and yellow striped tie.

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 (Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment - GOV.UK).

The primary objective of COC is to provide guidance and advice to help protect the public from chemicals that increase the risk of cancer. In order to do this, Members of the Committee work with the Secretariat and others to sift data, review literature, weigh evidence and thus provide advice to many different bodies. An important outcome is to maintain up to date guidance statements which help regulators, policy makers, industry and other stakeholders decide how to manage risk. For some time, COC has wrestled with the concept that whether a chemical can cause cancer is not a simple binary decision, but rather risk is best understood as a sliding scale and is influenced by many other factors including age, sex, other exposures, intercurrent disease and so on. There are many new technologies which may help determine risk for individuals or different groups, and COC is keen to ensure that these new technologies are considered and

adopted where appropriate in order to improve our accuracy of prediction. The Committee has consulted widely and hosted workshops, the endpoint of which will be a new guideline document, to be developed in 2024, that encourages evidence based on new technologies to be presented to the Committee along with more traditionally required data. All of this has required much reading, debate and reflection and I am grateful to Members, other experts and the Secretariat for their unstinting efforts. The report that follows is brief but captures the flavour of the work of COC over the past year.

Professor David Harrison

MD DSc FRCPath FRCPEd FRCSEd

COT/COM/COC Annual Report 2023

COC Ongoing Topics - 2023

In this guide

In this guide

1. About the Committees - 2023
2. COT Preface - 2023
3. COT evaluations - 2023
4. COT Assurance - 2023
5. Committee Procedures - 2023
6. Ongoing Work - COT 2023
7. Other Committee Activities: Joint Expert Groups, Presentations and Workshop -2023
8. 2023 Membership of the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment
9. Declaration of COT members' interests during the period of this report -2023
10. Sub-groups active in 2023
11. Committee on Mutagenicity of chemicals in Food, Consumer Products and the Environment Annual Report 2023
12. Ongoing work - COM 2023
13. Discussion Items -2023

14. 2023 Membership of the Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment
15. Declaration of COM members' interests during the period of this report -2023
16. Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment Annual Report 2023
17. COC Ongoing Topics - 2023
18. COC Workshop - 2023
19. Joint session Horizon scanning
20. COC input to COT work
21. 2023 Membership of the Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment
22. Declaration of COC members' interests during the period of this report -2023
23. Annex 1 - 2023 - Terms of Reference
24. Annex 2 - 2023 - Code of Conduct for members of the COC/COM/COT
25. Annex 3 – 2023 - Openness
26. Annex 4 – 2023 - Good Practice Agreement for Scientific Advisory Committees
27. Annex 5 – 2023 - Glossary of Terms
28. Annex 6 – 2023 - Previous Publications

Hydroxyanthracene derivatives

3.1 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 derivates (HADs) based on consideration of the EFSA 2018 opinion on HADs and any additional new data that have become available.

3.2 Overall, the COM agreed that the available evidence indicates that emodin, aloe-emodin, and dantron are genotoxic *in vitro*, but concluded that there is reasonable evidence that there is no genotoxic effect or mechanism *in vivo*. The COM considered that the reported carcinogenic effects of HADs are caused by the high levels of irritation, inflammation, and diarrhoea.

3.3 The topic was then referred to COC in 2022, and in 2023, the Committee discussed a first draft interim position paper, which also included a dietary and dermal exposure assessment. COC considered that there were insufficient data to conclude on an appropriate health-based guidance value for HADs and noted that

HADs were a diverse group of compounds that should be assessed on an individual basis. The interim position paper is expected to be published in 2024.

Lung adenocarcinoma promotion by air pollutants

3.4 In July 2023, the COC considered a paper for information on lung cancer promotion by air pollutants (Hill et al (2023). Lung adenocarcinoma promotion by air pollutants. Nature 616 (7955): 159-167).

3.5 The paper had also been discussed by the Committee on the Medical Effects of Air Pollutants (COMEAP) at its meeting on 10th July 2023, subsequent to a presentation from Professor Swanton at the November 2022 COMEAP meeting. COMEAP had noted a number of aspects where input from COC would be helpful, namely: COMEAP had queried whether mechanisms by which air pollution promoted cancers characterised by the EGFR mutation would also lead to promotion of other cancers initiated by mutations in other genes; the study did not rule out the possibility that air pollutants, e.g. PAHs, might also have an initiating role in addition to the mechanisms demonstrated in the paper; and in view of a continuing possibility of a cancer initiation role, COMEAP was unlikely to revise recommendations with respect to cessation lag used in mortality impact assessments, which assume that some of the benefits of air pollution reductions might not be realised until up to 20 years later.

3.6 The Committee noted that the study was a thorough piece of work covering many different aspects associated with carcinogenicity, in particular the cancer promotion and non-genotoxic mechanisms associated with cancer. It was noted that a number of papers are available from the 1970’s and 1980’s indicating cancer promotion as a mechanism, i.e. it is not just direct genotoxicity that causes cancer. COC appreciated the thoroughness of this highly detailed exploration of cancer in the context of air pollution.

3.7 It was noted that there was unlikely to be a complete absence of mutation occurring as a result of exposure to air pollution, and there are a number of papers on mutations associated with particulate matter. Additionally, the particulate matter used in the study was low in PAHs content. It was noted that this might reduce the potential for genotoxicity. The COC agreed it would be useful to have a COM consideration of the topic. This is expected to be taken forward in 2024.

COC Workshop - 2023

In this guide

In this guide

1. About the Committees - 2023
2. COT Preface - 2023
3. COT evaluations - 2023
4. COT Assurance - 2023
5. Committee Procedures - 2023
6. Ongoing Work - COT 2023
7. Other Committee Activities: Joint Expert Groups, Presentations and Workshop -2023
8. 2023 Membership of the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment
9. Declaration of COT members' interests during the period of this report -2023
10. Sub-groups active in 2023
11. Committee on Mutagenicity of chemicals in Food, Consumer Products and the Environment Annual Report 2023
12. Ongoing work - COM 2023
13. Discussion Items -2023
14. 2023 Membership of the Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment
15. Declaration of COM members' interests during the period of this report -2023
16. Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment Annual Report 2023
17. COC Ongoing Topics - 2023
18. COC Workshop - 2023
19. Joint session Horizon scanning
20. COC input to COT work
21. 2023 Membership of the Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment
22. Declaration of COC members' interests during the period of this report -2023
23. Annex 1 - 2023 - Terms of Reference
24. Annex 2 - 2023 - Code of Conduct for members of the COC/COM/COT
25. Annex 3 – 2023 - Openness

26. Annex 4 – 2023 - Good Practice Agreement for Scientific Advisory Committees
27. Annex 5 – 2023 - Glossary of Terms
28. Annex 6 – 2023 - Previous Publications

3.8 The COC held a workshop in November 2023 as a follow up to the one in 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 consumer products, building on the considerations from the workshop on pesticides in 2022. The COC was joined at the meeting by representatives of the OPSS Scientific Advisory Group on Chemical Safety of Non-Food and Non-Medicinal Consumer Products (SAG-CS).

3.9 Dr Ruth Dempsey (COC Member and Science Speaks) presented a summary of the key points from the November 2022 workshop. This was followed by a presentation by Ms Frances Hill (OPSS) summarised the current regulatory approach for cosmetics and the responsibilities of industry in conducting cosmetic safety assessment. Ms Emma Meredith (Cosmetic, Toiletry and Perfumery Association (CTPA)) then provided a summary of actions taken by industry as animal testing for cosmetic products has been banned in the UK and EU. A presentation was then given by Dr Carl Westmoreland (Unilever) providing illustrative examples of using next generation risk assessment and the aim of health protection rather than prediction of adverse effects. A final presentation from Dr Gina Hilton (PETA Science Consortium International) provided a summary of work undertaken in the Rethinking Carcinogenicity Assessment for Agrochemicals Project (ReCAAP), the development of an integrated approach to testing and assessment (IATA) submitted to the OECD and flagged the need to normalise new approaches to assessing carcinogenicity.

3.10 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?

3.11 The COC will consider the discussions at the two workshops further in 2024.

Joint session Horizon scanning

In this guide

In this guide

1. About the Committees - 2023
2. COT Preface - 2023
3. COT evaluations - 2023
4. COT Assurance - 2023
5. Committee Procedures - 2023
6. Ongoing Work - COT 2023
7. Other Committee Activities: Joint Expert Groups, Presentations and Workshop -2023
8. 2023 Membership of the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment
9. Declaration of COT members' interests during the period of this report -2023
10. Sub-groups active in 2023
11. Committee on Mutagenicity of chemicals in Food, Consumer Products and the Environment Annual Report 2023
12. Ongoing work - COM 2023
13. Discussion Items -2023
14. 2023 Membership of the Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment
15. Declaration of COM members' interests during the period of this report -2023
16. Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment Annual Report 2023
17. COC Ongoing Topics - 2023
18. COC Workshop - 2023
19. Joint session Horizon scanning
20. COC input to COT work
21. 2023 Membership of the Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment
22. Declaration of COC members' interests during the period of this report -2023
23. Annex 1 - 2023 - Terms of Reference
24. Annex 2 - 2023 - Code of Conduct for members of the COC/COM/COT

25. Annex 3 – 2023 - Openness
26. Annex 4 – 2023 - Good Practice Agreement for Scientific Advisory Committees
27. Annex 5 – 2023 - Glossary of Terms
28. Annex 6 – 2023 - Previous Publications

3.12 COC and COM held a joint discussion session in October 2023 to discuss a new approach to undertaking horizon scanning for the Committees. Professor Jason Weeks (IEH Consulting) provided a facilitated discussion to consider emerging evidence, conducting a Strengths, Weaknesses, Opportunities and Threats (SWOT) analysis, and then considered the external drivers for the aspects identified using a Social, Technological, Environmental, Economic, Political, Legal and Ethical (STEEPLE) analysis. As assessment was then made of the time point at which the main impacts of the issues identified (short-term: 1-3 years, medium-term: 4-10 years, long-term: 10+ years)

3.13 A series of potential work-streams were identified:

a. It was agreed to develop a continuous programme of regular horizon scanning to identify and disseminate emerging issues (both positive and negative) on the short-, medium- and long-term horizons, with reporting at intervals to be agreed with the Secretariat.

b. A method was agreed to assess and prioritise the importance/likelihood and impact of the emerging issues identified in [a] above.

c. In the future a programme of deep dive studies will be developed to investigate the current state of science/evidence and possible future developments and determine the implications of issues identified as high priority (by respective committees).

COC input to COT work

In this guide

In this guide

1. About the Committees - 2023

2. COT Preface - 2023
3. COT evaluations - 2023
4. COT Assurance - 2023
5. Committee Procedures - 2023
6. Ongoing Work - COT 2023
7. Other Committee Activities: Joint Expert Groups, Presentations and Workshop -2023
8. 2023 Membership of the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment
9. Declaration of COT members' interests during the period of this report -2023
10. Sub-groups active in 2023
11. Committee on Mutagenicity of chemicals in Food, Consumer Products and the Environment Annual Report 2023
12. Ongoing work - COM 2023
13. Discussion Items -2023
14. 2023 Membership of the Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment
15. Declaration of COM members' interests during the period of this report -2023
16. Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment Annual Report 2023
17. COC Ongoing Topics - 2023
18. COC Workshop - 2023
19. Joint session Horizon scanning
20. COC input to COT work
21. 2023 Membership of the Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment
22. Declaration of COC members' interests during the period of this report -2023
23. Annex 1 - 2023 - Terms of Reference
24. Annex 2 - 2023 - Code of Conduct for members of the COC/COM/COT
25. Annex 3 – 2023 - Openness
26. Annex 4 – 2023 - Good Practice Agreement for Scientific Advisory Committees
27. Annex 5 – 2023 - Glossary of Terms
28. Annex 6 – 2023 - Previous Publications

Participation at COT workshop "Evolving Our Assessment & Future Guiding Principles

Workshop”

3.14 Some COC members were invited to participate in the COT workshop described in section 1.194, and a presentation was given jointly by the COC and COM Secretariat on the guidance statements from these Committees.

3.15 A report of this workshop is anticipated to be published in 2024.

Public consultation on EFSA’S 2023 re-evaluation of the risk to public health from inorganic arsenic in food

3.16 COC members provided input by correspondence to the COT response to the public consultation described in section 1.73 above.

3.17 COC members commented on EFSA’s approach with respect to extrapolation of country-specific data to an international perspective, the response rate chosen for the benchmark dose modelling, and the justification for not providing a steer on a margin of exposure of low concern due to lack of precedent with use of human data.

2023 Membership of the Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment

In this guide

In this guide

1. About the Committees - 2023
2. COT Preface - 2023

3. COT evaluations - 2023
4. COT Assurance - 2023
5. Committee Procedures - 2023
6. Ongoing Work - COT 2023
7. Other Committee Activities: Joint Expert Groups, Presentations and Workshop -2023
8. 2023 Membership of the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment
9. Declaration of COT members' interests during the period of this report -2023
10. Sub-groups active in 2023
11. Committee on Mutagenicity of chemicals in Food, Consumer Products and the Environment Annual Report 2023
12. Ongoing work - COM 2023
13. Discussion Items -2023
14. 2023 Membership of the Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment
15. Declaration of COM members' interests during the period of this report -2023
16. Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment Annual Report 2023
17. COC Ongoing Topics - 2023
18. COC Workshop - 2023
19. Joint session Horizon scanning
20. COC input to COT work
21. 2023 Membership of the Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment
22. Declaration of COC members' interests during the period of this report -2023
23. Annex 1 - 2023 - Terms of Reference
24. Annex 2 - 2023 - Code of Conduct for members of the COC/COM/COT
25. Annex 3 – 2023 - Openness
26. Annex 4 – 2023 - Good Practice Agreement for Scientific Advisory Committees
27. Annex 5 – 2023 - Glossary of Terms
28. Annex 6 – 2023 - Previous Publications

Chair

Professor David Harrison MD DSc FRCPath FRCPEd FRCSEd

Professor of Pathology, University of St Andrews.

Members

Mr Amit Bhagwat – From 01 April 2023

Public Interest Representative.

Mr Derek Bodey MA – To 31 May 2023

Public Interest Representative.

Dr Gill Clare BSc PhD – To 31 May 2023

Independent Consultant in Genetic Toxicology.

Dr Meera Cush

Senior Managing Consultant (Regulatory Toxicologist), Ramboll.

Dr Ruth Dempsey

Consultant, RD Science Speaks Consultancy.

Dr John Doe PhD – To 31 May 2023

Research Fellow, Liverpool John Moore’s University.

Dr Richard Haworth MA VetMB DPhil FRCPath DipECVP DABT

Head of Pathology, Clinical Pharmacology & Safety Sciences, AstraZeneca.

Professor Gareth Jenkins

Professor of Molecular Carcinogenesis, Faculty of Health, Medicine and Life Science, Swansea University.

Professor Neil Pearce BSc DipSci DipORS PhD DSc FRSNZ FMedSci FFPH

Professor of Epidemiology and Biostatistics, London School of Hygiene and Tropical Medicine.

Ms Juliet Rix – From 01 April 2023

Public Interest Representative.

Dr Lesley Stanley MA PhD ERT FBTS

Consultant in Investigative Toxicology.

Secretariat

Ms B Gadeberg BSc (Hons) MSc ERT UKHSA Scientific Secretary.

Dr D Gott BSc (Hons) PhD FSA Scientific Secretary.

Ms C Mulholland BSc (Hons) ERT FSA Scientific Secretary.

Mrs N Blowfield Administrative Secretary.

Declaration of COC members' interests during the period of this report -2023

In this guide

In this guide

1. About the Committees - 2023
2. COT Preface - 2023
3. COT evaluations - 2023
4. COT Assurance - 2023
5. Committee Procedures - 2023

6. Ongoing Work - COT 2023
7. Other Committee Activities: Joint Expert Groups, Presentations and Workshop -2023
8. 2023 Membership of the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment
9. Declaration of COT members' interests during the period of this report -2023
10. Sub-groups active in 2023
11. Committee on Mutagenicity of chemicals in Food, Consumer Products and the Environment Annual Report 2023
12. Ongoing work - COM 2023
13. Discussion Items -2023
14. 2023 Membership of the Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment
15. Declaration of COM members' interests during the period of this report -2023
16. Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment Annual Report 2023
17. COC Ongoing Topics - 2023
18. COC Workshop - 2023
19. Joint session Horizon scanning
20. COC input to COT work
21. 2023 Membership of the Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment
22. Declaration of COC members' interests during the period of this report -2023
23. Annex 1 - 2023 - Terms of Reference
24. Annex 2 - 2023 - Code of Conduct for members of the COC/COM/COT
25. Annex 3 – 2023 - Openness
26. Annex 4 – 2023 - Good Practice Agreement for Scientific Advisory Committees
27. Annex 5 – 2023 - Glossary of Terms
28. Annex 6 – 2023 - Previous Publications

Chair

Professor David Harrison

	Employee: University of St Andrews UK, NuCana plc UK. **Employee/Non-executive Director:** ILC Therapeutics Ltd, Benenox Ltd, UK – Non-executive Director (unpaid), PathAlba Ltd – Director (unpaid) – dormant. **Consultant:** NHS Lothian – Honorary Consultant.
Personal Interest	**Shareholder:** VBL Ltd UK, Ryboquin Ltd UK, ILC Therapeutics Ltd. **Misc:** Cunningham Trust – (Medical Research Charity) Trustee, University of Edinburgh, UK – Honorary Professor, University of Glasgow, UK – Honorary Professor, University of Florida, Adjunct Professor, Viewbank Leuchars Ltd – Director (no salary).
Personal Interest	**Membership:** Fellow Royal College of Pathologists, Fellow of Royal College of Physicians of Edinburgh, Fellow of Royal College of Surgeons of Edinburgh.

Non-Personal Interest	**Misc:** iCAIRD research consortium – Director (unpaid role), Pilgrim Care St Andrews (charity for the elderly) – Trustee (unpaid role), Visiopharm – Member, Scientific Advisory Board. EU Horizon 2020, Partner in KATY Award, grant support, Innovate UK/UKRI – Director of iCAIRD.

Members

Dr Meera Cush

Personal Interest	**Employee:** Ramboll UK Limited, University of Surrey (Visiting Lecturer).
Personal Interest	**Membership:** Royal Society of Biology.
Non-Personal Interest	None.

Dr Ruth Dempsey

Personal Interest	**Shareholder:** Rd Science Speaks Consultancy, Sarl (Shareholder and Director). **Pension:** Philip Morris International. **Consultant:** Philip Morris International, Doterra Europe.
Personal Interest	**Membership:** British Toxicology Society, Swiss society of Toxicology, Royal society of Biology.
Non-Personal Interest	None.

Dr Richard Haworth

Personal Interest	**Director:** RosettaPath Ltd. **Chief Scientific officer:** CureCollect Ltd. **Scientific advisory committee:** Aiforia. **Shareholder:** AstraZeneca, GlaxoSmithKline, Haleon, Shell (Spouse Shareholder).
Personal Interest	**Membership:** British Society of Toxicological Pathology, European Society of Toxicological Pathology, Society Of Toxicological Pathology.
Non-Personal Interest	None.

Professor Gareth Jenkins

Personal Interest	**Employer:** Swansea University. **Honorary Contract:** Swansea Bay University Health Board.

Personal Interest	**Membership:** President Of United Kingdom Environment Mutagen Society (Ukems) 2020 - 2023. **Member:** British Association for Cancer Research, Senior Editor Mutagenesis (Oup), Editorial Board (And Former Editor 2013-2015) Mutation Research (Elsevier), President of the International Association of Environmental Mutagenesis and Genomics Societies (IAEMGS).
Non-Personal Interest	**Grants:** National Centre of Replacement, Refinement and Reduction of Animals in Research (NC3Rs) (2018-2022), Former grants Health & Care Research Wales (2016-2020, 2014-2017), MRC/AstraZeneca PhD studentship (ITTP scheme) (2019-2023), Cancer Research Wales grants (2023-2026 and 2019-2023), External Examining roles (Bangor University DeMontfort University, University of Milan).

Professor Neil Pearce

Personal Interest	None.
Non-Personal Interest	None.

Dr Lesley Stanley

Self-employed:

Dr. Lesley Stanley, Consultant in Investigative Toxicology.

Direct Employment:

Deltohn Ltd, Builth Wells, LD2 3RX; six months' part-time employment, 01-Jun-23 to 30-Nov-23.

Consultancy

School of Medicine,

University of Dundee (2020 to date),

Details of previous consultancy contracts available upon request.

Expert Appointments:

REACH Independent Scientific Expert Pool,

Personal Interest

OPSS Register of Experts.

Honorary Appointment:

Associate, School of Life Sciences, Edinburgh Napier University (Non-Stipendiary).

Investments:

Investment Portfolio managed by Quilter Cheviot (joint with spouse),

FundsNetwork Stocks and Shares ISA,

Aviva Personal Pension Plan.

Ministry and Charities

Ordained Local Minister, Church of Scotland (non-stipendiary)

Honorary Chaplain, University of Stirling (non-stipendiary)

Supporter, Christian Aid *In Their Lifetime* programme and International Justice Mission.

	Membership:
Personal Interest	European Registered Toxicologist (ERT), Fellow of the British Toxicology Society (FBTS), Advisory Committee on Novel Foods and Processes (ACNFP).
Non-Personal Interest	None.

Mr Amit Bhagwat

Personal Interest	**Owner and Shareholder:** Research and Consulting Business. Bradford Teaching Hospitals NHS Foundation Trust - Public Governor (Rest of England & Wales). British Computer Society – the Chartered Institute for IT - Chair/Volunteer for Learned Events and Public Service Activities.
Non-Personal Interest	Member - Occupational Therapists Registration Board – Republic of Ireland. Member - Medical Scientists Registration Board – Republic of Ireland. Member of committees associated with impact evaluation and applications scrutiny for the Special EU Programmes body’.

	Membership Public Ambassador – NHS England Subsidiary Board Related To Digital Urgent & Emergency Care (DUEC). **Member:** Committee On Mutagenicity (Com), Prescribed Specialised Services Advisory Group, (DHSC), Northern Ireland Practice And Education Council For Nursing And Midwifery (NIPEC).
Non-Personal Interest	**Contributor:** Learned and Professional Development Activities Within The British Computer Society (Chairing, Committee And Speaking Responsibilities). **Trustee:** Myrovlytis Trust (Funds Research into Rare Diseases) – Chairing Responsibility. **Chair:** Regional Inclusive Volunteering Charity – Chairing Responsibility.

Ms Juliet Rix

Personal Interest	None.
Non-Personal Interest	None.

Annex 1 - 2023 - Terms of Reference

In this guide

In this guide

1. About the Committees - 2023
2. COT Preface - 2023
3. COT evaluations - 2023
4. COT Assurance - 2023
5. Committee Procedures - 2023
6. Ongoing Work - COT 2023
7. Other Committee Activities: Joint Expert Groups, Presentations and Workshop -2023
8. 2023 Membership of the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment
9. Declaration of COT members' interests during the period of this report -2023
10. Sub-groups active in 2023
11. Committee on Mutagenicity of chemicals in Food, Consumer Products and the Environment Annual Report 2023
12. Ongoing work - COM 2023
13. Discussion Items -2023
14. 2023 Membership of the Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment
15. Declaration of COM members' interests during the period of this report -2023
16. Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment Annual Report 2023
17. COC Ongoing Topics - 2023
18. COC Workshop - 2023
19. Joint session Horizon scanning
20. COC input to COT work
21. 2023 Membership of the Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment
22. Declaration of COC members' interests during the period of this report -2023
23. Annex 1 - 2023 - Terms of Reference
24. Annex 2 - 2023 - Code of Conduct for members of the COC/COM/COT
25. Annex 3 – 2023 - Openness
26. Annex 4 – 2023 - Good Practice Agreement for Scientific Advisory Committees
27. Annex 5 – 2023 - Glossary of Terms
28. Annex 6 – 2023 - Previous Publications

To advise at the request of:

Food Standards Agency,

Food Standards Scotland,

Public Health England,

Department of Health and Social Care,

Other Government Departments and Agencies and those of the UK devolved Administrations.

1. To assess and advise on the toxic risk to man of substances which are:

a) used or proposed to be used as food additives or used in such a way that they might contaminate food through their use or natural occurrence in agriculture, including horticulture and veterinary practice or in the distribution, storage, preparation, processing or packaging of food.

b) used or proposed to be used or manufactured or produced in industry, agriculture, food storage or any other workplace.

c) used or proposed to be used as household goods or toilet goods and preparations.

d) used or proposed to be used as drugs, when advice is requested by the Medicines and Healthcare products Regulatory Agency.

e) used or proposed to be used or disposed of in such a way as to result in pollution of the environment.

2. To advise on important general principles or new scientific discoveries in connection with toxic risks, to co-ordinate with other bodies concerned with the assessment of toxic risks and to present recommendations for toxicity testing.

Annex 2 - 2023 - Code of Conduct for members of the COC/COM/COT

In this guide

In this guide

1. About the Committees - 2023
2. COT Preface - 2023
3. COT evaluations - 2023
4. COT Assurance - 2023
5. Committee Procedures - 2023
6. Ongoing Work - COT 2023
7. Other Committee Activities: Joint Expert Groups, Presentations and Workshop -2023
8. 2023 Membership of the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment
9. Declaration of COT members' interests during the period of this report -2023
10. Sub-groups active in 2023
11. Committee on Mutagenicity of chemicals in Food, Consumer Products and the Environment Annual Report 2023
12. Ongoing work - COM 2023
13. Discussion Items -2023
14. 2023 Membership of the Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment
15. Declaration of COM members' interests during the period of this report -2023
16. Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment Annual Report 2023
17. COC Ongoing Topics - 2023
18. COC Workshop - 2023
19. Joint session Horizon scanning
20. COC input to COT work
21. 2023 Membership of the Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment
22. Declaration of COC members' interests during the period of this report -2023
23. Annex 1 - 2023 - Terms of Reference
24. Annex 2 - 2023 - Code of Conduct for members of the COC/COM/COT
25. Annex 3 – 2023 - Openness
26. Annex 4 – 2023 - Good Practice Agreement for Scientific Advisory Committees
27. Annex 5 – 2023 - Glossary of Terms
28. Annex 6 – 2023 - Previous Publications

Public service values

Members of the COC/COM/COT (hereafter referred to as “the Committee”) must at all times:

- Observe the highest standards of impartiality, integrity and objectivity in relation to the advice they provide and to the management of their Committee.

- Be accountable, through the Chair of the Food Standards Agency and the Chief Medical Officers, to Ministers, Parliament and the public for its activities and for the standard of advice it provides.

- In accordance with Government policy on openness, fully comply with the Freedom of Information Act 2000.

The Ministers of the sponsoring departments are answerable to Parliament for the policies and performance of the Committee, including the policy framework within which it operates.

Standards in Public Life

Members are expected to:

- Comply with this Code, and ensure they understand their duties, rights and responsibilities, and that they are familiar with the function and role of their Committee and any relevant statements of Government policy. If necessary members should consider undertaking relevant training to assist them in carrying out their role.

- Not misuse information gained in the course of their public service for personal gain or for political purpose, nor seek to use the opportunity of public service to promote their private interests or those of connected persons, firms, businesses or other organisations.

- Not hold any paid or high profile unpaid posts in a political party, and not engage in specific political activities on matters directly affecting the work of the Committee. When engaging in other political activities, Committee

members should be conscious of their public role and exercise proper discretion. These restrictions do not apply to MPs (in those cases where MPs are eligible to be appointed), to local councillors, or to Peers in relation to their conduct in the House of Lords.

- Follow the Seven Principles of Public Life set out by the Committee on Standards in Public Life [Committee on Standards in Public Life - GOV.UK (www.gov.uk)]

Selflessness

Holders of public office should take decisions solely in terms of the public interest. They should not do so in order to gain financial or other material benefits for themselves, their family, or their friends.

Integrity

Holders of public office should not place themselves under any financial or other obligation to outside individuals or organisations that might influence them in the performance of their official duties.

Objectivity

In carrying out public business, including making public appointments, awarding contracts, or recommending individuals for rewards and benefits, holders of public office should make choices on merit.

Accountability

Holders of public office are accountable for their decisions and actions to the public and must submit themselves to whatever scrutiny is appropriate to their office.

Openness

Holders of public office should be as open as possible about all the decisions and actions that they take. They should give reasons for their decisions and restrict information only when the wider public interest clearly demands.

Honesty

Holders of public office have a duty to declare any private interests relating to their public duties and to take steps to resolve any conflicts arising in a way that protects the public interests.

Leadership

Holders of public office should promote and support these principles by leadership and example.

These principles apply to all aspects of public life. The Committee has set them out here for the benefit of all who serve the public in any way.

Role of Members

Members have collective responsibility for the operation of their Committee. Members are appointed as individuals to fulfil the role of their respective Committees, not as representatives of their particular profession, employer or interest group and have a duty to act in the public interest. Members are appointed on a personal basis, even when they are members of stakeholder groups and organisations. If a member declares an organisation’s view rather than a personal view they should make it clear at the time of declaring that view.

Members must:

- Engage fully in collective consideration of the issues, taking account of the full range of relevant factors, including any guidance issued by the Food Standards Agency, Health Protection Agency and the Department of Health.
- Undertake on appointment to comply with the Code of Practice for Scientific Advisory Committees.
- Not divulge any commercially sensitive information, pre-publication or unpublished research data provided to the Committee.
- Agree an annual report.

- Ensure that an appropriate response is provided to complaints and other correspondence, if necessary with reference to the sponsor department.

- Ensure that the Committee(s) does not exceed its powers or functions.

A member's role on the Committee should not be limited by the expertise or viewpoint she or he was asked to bring to it. Any statement/report belongs to the whole Committee. Members should regard themselves free to question and comment on the information provided or the views expressed by any of the other members, even though the views or information provided do not relate to their own area of expertise.

If members believe the committee's method of working is not rigorous or thorough enough, they have the right to ask that any remaining concerns they have be put on the record. Individual members should inform the Chair (or the Secretariat on his or her behalf) if they are invited to speak in public in their capacity as a Committee member. Communications between members and the Food Standards Agency (FSA) Board, CMOs and/or Ministers will generally be through the Chair except where the Chair has agreed that an individual member should act on its behalf. Nevertheless, any member has the right of access to the FSA Board and/or the CMO on any matter that he or she believes raises important issues relating to his or her duties as a Committee member. In such cases the agreement of the rest of the Committee should normally be sought.

Committee appointments can be terminated early by either party, by giving 3 months' notice, in writing. Should the Committee be disbanded before the end of the period of appointment, appointments will terminate on dissolution.

In the event that a member is found guilty of grave misconduct their appointment will be terminated immediately, in the case of the COT by the Chair of the FSA. The Department of Health has delegated the powers for appointments to the COC and COM to the NHS Appointments Commission and it will terminate appointments in consultation with the PHE/DH.

Role of the Chair

The Chair has particular responsibility for providing effective leadership on the issues above. In addition, the Chair is responsible for:

- Ensuring that the Committee meets at appropriate intervals.

- Ensuring that the minutes of meetings accurately reflect proceedings and any reports to the FSA Board and/or Ministers accurately record the decisions taken.

- Ensuring that where appropriate, the views of individual members have been recorded.

- Representing the views of the Committee to the general public.

- Ensuring that new members are briefed on appointment (and their training needs considered), and providing an assessment of their performance, on an annual basis or when members are considered for re-appointment to the Committee or for appointment to the board of some other public body.

- Providing urgent advice to the FSA and HPA on issues within the remit of the Committee, in liaison with the Secretariat.

Role of the Deputy Chair

The Deputy Chair will assume the role of the Chair as described above if the Chair is not available.

Role of the Secretariat

The primary function of the Secretariat is to facilitate the business of the Committee. This includes supporting the Committee by arranging its meetings, assembling and analysing information, and recording conclusions. An important task is ensuring that proceedings of the Committee are properly documented and recorded. Minutes of all Committee meetings will be taken. These will accurately reflect the proceedings and discussions that take place and will be recorded on a non-attributable basis except where the views of one or more individual members need recording (for example, when declaring an interest).

The Secretariat is also a source of advice and guidance to members on procedures and processes. The Secretariat is drawn from staff of the Food Standards Agency and Public Health England. However, it is the responsibility of the Secretariat to be an impartial and disinterested reporter and at all times to respect the Committee's independent role. The Secretariat is required to guard against introducing bias during the preparation of papers, during meetings, or in the reporting of the Committee's deliberations. Current contact details for each of the Secretariats are shown on the back page of this report.

Role of the Assessor

Meetings of the Committee (and working groups) may be attended by Assessors. The Assessors are nominated by, and drawn from, the Agencies and Departments that sponsor the Committee, receive its advice, or have other relevant policy interests. Assessors are not members of the Committee and do not participate in Committee business in the manner of members.

The role of an Assessor is to keep their parent Department or Agency informed about the Committee's work and act as a conduit for the exchange of information. They do this by:

- Advising the Committee on relevant policy developments and the implications of Committee proposals.
- Informing the Committee work through the provision of information.
- Being informed by the Committee on matters of mutual interest.
- Sharing with the Secretariat the responsibility of ensuring that information is not needlessly withheld from the Committee. Assessors should make the Committee aware of the existence of any information that has been withheld from the Committee on the basis that it is exempt from disclosure under Freedom of Information legislation unless that legislation provides a basis for not doing so.
- Ensuring that their parent Department or Agency is promptly informed of any matters which may require a response from Government.

Role of other Officials, Invited Experts and Contractors

Officials from Government Departments (not departmental assessors), Regulatory Agencies and Devolved Administrations may be called upon to advise the Committee on relevant developments in order to help the Committee formulate its advice. Invited experts and contractors may also bring particular technical expertise, which may be requested by the Committee on some occasions. In the event of an official, invited expert or contractor not being able to attend written submissions may be sent via the Secretariat.

Role of Observers

Members of the public and other interested parties may attend meetings as observers. However, they should not attempt to participate in Committee discussions. If an interested party wishes to provide information relevant to a topic for consideration by the Committee, they should be submitted in writing to the Secretariat at least seven (7) working days before the meeting. The Secretariat will discuss with the Chair the most appropriate way to present the information to the committee and the Chair's decision will be final.

Observers who have submitted information in advance of the meeting may be invited to provide further explanation or to make brief comments at the discretion of the Chair. Observers and/or organisations must not interfere in the work of the Secretariat or input from invited experts, contractors, officials from Government Departments and Agencies in any way which, in the view of the Chair, constitutes harassment and/or might hinder the work of the Committee. Observers and/or organisations must allow other observers and other interested parties to attend items free from interference before, during and after a meeting.

Observers and/or organisations are required to respect the work of the Committee. The Committee's discussions represent the development of its view and any comments made in developing the agreed Committee view should not be attributed to individuals. Where a subject will be considered over several meetings, observers are asked to maintain the confidentiality of the discussion until an agreed Committee opinion is finalised. The Committee's conclusions are not finalised until completion of any necessary consultation and publication of a statement or report.

Under no circumstances will Observers be permitted to record Committee proceedings, on the basis that this might inhibit free discussion. The published minutes of the meeting would provide a record of the proceedings.

Failure to observe this code of conduct may lead to exclusion of individual observers and/or organisations from meetings of the Committee.

All observers and/or organisations are requested to read follow the Committees Openness policy (Annex 3).

Declaration of Members' Interests

Definitions

In this Code, 'the industry' means:

- Companies, partnerships or individuals who are involved with the production, manufacture, sale or supply of products subject to the following legislation.

General Food Regulations 2004,

The Food Safety Act 1990 (Amendment) Regulations 2004,

The Medicines Acts 1968 and 1971, 1981, 1986 & 2003,

The Food and Environmental Protection Act 1985,

The Consumer Protection Act 1987,

The Cosmetic (Safety) (Amendment) Regulations 2008,

Registration, Evaluation, Authorisation and Restriction of Chemicals (EC1970/2006),

- Trade associations representing companies involved with such products.

- Companies, partnerships or individuals who are directly concerned with research, development or marketing of a product which is being considered by the Committees on Toxicity, Mutagenicity, or Carcinogenicity of Chemicals in Food, Consumer Products and the Environment.

- ‘The Secretariat’ means the Secretariat of the COC, COM and COT.

- ‘The Agency’ means either the Food Standards Agency or the Health Protection Agency.

- References to “member(s)” includes the Chair.

Different types of Interest

The following is intended as a guide to the kinds of interests which should be declared. Where members are uncertain as to whether an interest should be declared, they should seek guidance from the Secretariat or, where it may concern a particular product which is to be considered at a meeting, from the Chair at that meeting.

If members have interests not specified in these notes but which they believe could be regarded as influencing their advice they should declare them.

However, neither the members nor the Secretariat are under any obligation to search out links of which they might reasonably not be aware. This Code suggests that interests of close family members are declared, members have in the past limited such declarations to personal partners, parents, children (minor and adult), brothers, sisters and the personal partners of any of these with the emphasis on disclosure only where the interest may or may be perceived (by a reasonable member of the public) to influence a members’ judgement.

The Secretariat is required to publish an up-to-date register of members’ interests, and these can be found on the relevant Committees website.

Personal Interests

A personal interest involves the member personally. The main examples are:

- Consultancies and/or direct employment: any consultancy, directorship, position in or work for industry which attracts regular or occasional payments in cash or kind.

- Fee-Paid Work: any work commissioned by industry for which the member is paid in cash or kind.

- Shareholdings: any shareholding in or other beneficial interest in shares of industry. This does not include shareholdings through unit trusts or similar arrangements where the member has no influence on financial management.

- Membership or Affiliation: any membership role or affiliation that you or a close family member has to clubs or organisations with an interest or involvement in the work of the Agency.

Non-Personal Interests

A non-personal interest involves payment which benefits the organisation in which the member works but is not received by the member personally. The main examples are:

- Fellowships: the holding of a fellowship endowed by industry.

- Support by Industry: any payment, other support or sponsorship which does not convey any pecuniary or material benefit to a member personally, but which does benefit their position or organisation, e.g.

- A grant for the running of a unit or department for which the member is responsible.

- A grant or fellowship or other payment to sponsor a post or a member of staff or a post graduate research programme for which the member is responsible. This does not include financial assistance for students.

- The commissioning of research or other work by, or advice from, staff who work in a unit for which the member is responsible.

Members are under no obligation to seek out knowledge of work done for, or on behalf of, the industry or other relevant bodies by departments in which they work, if they would not normally expect to be informed.

- Trusteeships: where a member is a trustee of a charity with investments in industry, the Secretariat can agree with the member a general declaration to cover this interest rather than draw up a detailed portfolio.

At meetings members are required to declare relevant interests and to state whether they are personal or non-personal interests and whether they are specific or nonspecific to the matter, product or substance under consideration.

Specific Interests

A member must declare a personal specific interest if they have at any time worked on a matter, product or substance under consideration and have personally received payment for that work, in any form.

A member must declare a non-personal specific interest if they are aware that the organisation in which they work has at any time worked on the matter, product or substance under consideration, but they have not personally received payment for that work, in any form.

Non-specific Interests

A member must declare a personal non-specific interest if they have a current personal interest in a company concerned with a matter, product or substance under consideration, which does not relate specifically to the matter, product or substance under discussion.

A member must declare a non-personal non-specific interest if they are aware that the organisation in which they work is currently receiving payment from the company concerned which does not relate specifically to the matter, product or substance under discussion.

If a member is aware that a substance, product or matter under consideration is or may become a competitor of a substance, product or matter manufactured, sold or supplied by a company in which the member has a current personal interest, they should declare their interest in the company marketing the rival product, substance or matter.

Handling conflicts of interests

The purpose of these provisions is to avoid any danger of Committee members being influenced, or appearing to be influenced, by their private interests in the exercise of their public duties. All members should declare any personal or business interest which may or may be perceived (by a reasonable member of the public) to, influence their judgement. A guide to the types of interest that should be declared is mentioned above.

Declaration of Interests to the Secretariat

Members are required to inform the Agency in writing prior to appoint of their current personal and non-personal interests, including the principal position(s) held. Members are not required to disclose the amount of any salary, fee, shareholding, grant etc. An interest is current if the member has an on-going financial involvement e.g., if he or she holds shares in industry, has a consultancy contract, or if they or the organisation for which they are responsible is in the process of carrying out work for the industry.

Following appointment members are asked to inform the Secretariat at the time of any change in their personal interests. However, the Secretariat will contact each member on an annual basis to update their declaration of interests. Changes in non-personal interests can be reported annually, and those involving less than £1000 from a particular company in the previous year need not be declared. The register of interests is kept up-to-date and open to the public via the website.

Declaration of Interest at Meetings

Members of the Committee are required to verbally declare any direct interests relating to salaried employment or consultancies, or those of close family 8 members in matters under discussion at each meeting, and if items are taken by correspondence between meetings. The declaration should note whether the interest is personal or nonpersonal, whether it is specific to the item under discussion, or non-specific and whether it is current or lapsed. Having fully explained the nature of their interest the Chair will, decide whether and to what extent the member should participate in the discussion and determination of the issue, and it should be recorded in the minutes of the meeting.

Withdrawal from meetings

If a declaration of interest has been made and the Committee decides that the member should not participate in the discussion and should withdraw from the meeting (even if held in public) and it should be recorded in the minutes of the meeting. The Chair may first allow them to make a statement on the item under discussion.

Personal liability of Committee members

The Department of Health has a formal statement of indemnity for its advisory committee members, which includes the COC and COM, its guidance is taken from the Cabinet Office “Model Code of Practice for Board Members of Advisory Non-Departmental Public Bodies” and states that “Legal proceedings by a third party against individual board members of advisory bodies are very exceptional. A board member may be personally liable if he or she makes a fraudulent or negligent statement which result in a loss to a third party; or may commit a breach of confidence under common law or criminal offence under insider dealing legislation, if he or she misuses information gained through their position. However, the Government has indicated that individual board members who have acted honestly, reasonably, in good faith and without negligence will not have to meet out of their own personal resources any personal civil liability which is incurred in execution or purported execution of their board functions. Board members who need further advice should consult the sponsor department.”9 except where the person has acted recklessly.

The FSA has also drawn up a formal statement of indemnity for its advisory committee members.

Indemnity by the Food Standards Agency to Members of the

Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment

The Food Standards Agency hereby undertakes with the members (including the Chair) of the Committee on Toxicity of Chemicals in food, Consumer products and the environment (COT) to indemnify them against all liability in respect of any action or claim which may be brought, or threatened to be brought, against them either individually or collectively by reason of or in connection with the performance of their duties as members, including all costs, charges and expenses which the Members may properly and reasonably suffer or incur in disputing any such action or claim.

The Members shall as soon as practicable notify the Food Standards Agency if any action or claim is brought or threatened to be brought against them in respect of which indemnity may be sought and if an action or claim is brought, the Food Standards Agency shall be entitled to take conduct of the defence, dispute, compromise or appeal of the action or claim and of any incidental negotiations relating to the action or claim.

The Food Standards Agency shall notify the Members as soon as practicable if it intends to so take conduct and the Members shall then provide to the Food Standards Agency such information and assistance as it shall reasonably request, subject to all out of pocket expenses properly and reasonably incurred by them being reasonably reimbursed. The Food Standards Agency shall, to the extent reasonable and practicable, consult with and keep the Members informed as and when reasonably requested by the Members in respect of any action or claim. If the Food Standards Agency does not so take conduct the Members shall keep the Food Standards Agency fully informed of the progress of the action or claim and any consequent legal proceedings and consult with the Food Standards Agency as and when required by the Food Standards Agency concerning the action or claim.

The indemnity shall not extend to any losses, claims, damages, costs, charges, expenses and any other liabilities:

- In respect of which the Members are indemnified by or through any defence organisation or insurers or,
- which may result from bad faith (including dishonesty), wilful default or recklessness on the part of the Members,
- which may result from any of the following circumstances:

1. any settlement made or compromise effected without the knowledge or consent of the Food Standards Agency on behalf of the Members of any action or claim brought, or threatened to be brought, against the Members.
2. Any admission by the Members of any liability or responsibility in respect of any action or claim brought, or threatened to be brought, against them.
3. Members taking action that they were aware, or ought reasonably to have been aware, might prejudice the successful defence of any action or claim, once the Members had become aware that such an action or claim had been brought or was likely to be brought.

Remuneration and Committee finance

In the financial year 2023/2024 the budget for the COT, excluding Secretariat resources was £125,857.00. Costs were met by the Food Standards Agency (FSA).

Committee members may claim a fee for Committee meetings:

COT Committee Chair £400 per day

COT Committee Member £300 per day

COT Members are able to claim for work undertaken between meetings at the above rates.

Different provisions apply to COC and COM Members. Details can be obtained from their respective Secretariats.

Review of fee rates

Fees in respect of the COT are set by the FSA and for COC and COM by the Department of Health and Social Care. The FSA will review and revise COT rates every 2 years with the intention that rates should rise in line with the recommendations of the Senior Salaries Review Board with regard to pay in the Senior Civil Service. The FSA will also take into account comparisons with rates paid in similar advisory bodies in the UK.

Travel and other expenses

Committee members are entitled to reimbursement of reasonable travel and subsistence expenses necessarily incurred on official committee business. Members must seek value for money and are encouraged to use the most cost effective and environmentally sustainable options for travel and accommodation.

Working Groups

The Committee may establish Working Groups to consider particular topics in depth or to make brief assessments of particular issues and advise the main Committee on the possible need for further action. Such Groups contain a number of Committee members (supplemented, as necessary, by external expertise in the particular subject being considered). A Committee Chair will play a leading role in deciding which Committee members should be invited to join such groups,

which may meet on a number of occasions in a particular year. Committee members may claim an allowance for participating on a Working Group.

Terms and conditions of appointment

Appointments of members may be staggered so that only a proportion retire or are re-appointed each year, to help ensure continuity. COC and COM Chairs are ex officio members of each other's Committees.)

COC and COM members are usually expected to attend 3 meetings in a year. COT members are expected to attend 7 meetings in a year. Members should allow appropriate preparation time. Meetings will usually be in London.

The COC/COM/COT Chair must also be available for a number of other activities including: attending, with the FSA Chief Scientist, the FSA Board's annual discussion of the Agency's science; engaging with the media on any high-profile relating to the Committee's work, and discussion with the Agency Chief Scientist and GACS Secretariat in planning and developing the Committee's work (including discussing and agreeing with the Agency's Chief Scientist a framework for providing assurance on the work of the Scientific Advisory Committees in providing advice to the Agency). It is expected that these additional activities might require 5-10 days input per year.

Feedback on performance

The COT Chair and members are asked to provide brief feedback on their experience on the committee each year to help the Agency ensure that the Committee operates effectively and identify any areas for improvement.

Committee members are normally appointed for a term of 3 years (a maximum 10 years/3 terms per member). The COT uses the feedback self-assessment form as one of the tools used to determine whether or not a committee member should be reappointed at the end of their (3 year) term.

COT/COM/COC Annual Report 2023

Annex 3 – 2023 - Openness

In this guide

In this guide

1. About the Committees - 2023
2. COT Preface - 2023
3. COT evaluations - 2023
4. COT Assurance - 2023
5. Committee Procedures - 2023
6. Ongoing Work - COT 2023
7. Other Committee Activities: Joint Expert Groups, Presentations and Workshop -2023
8. 2023 Membership of the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment
9. Declaration of COT members' interests during the period of this report -2023
10. Sub-groups active in 2023
11. Committee on Mutagenicity of chemicals in Food, Consumer Products and the Environment Annual Report 2023
12. Ongoing work - COM 2023
13. Discussion Items -2023
14. 2023 Membership of the Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment
15. Declaration of COM members' interests during the period of this report -2023
16. Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment Annual Report 2023
17. COC Ongoing Topics - 2023
18. COC Workshop - 2023
19. Joint session Horizon scanning
20. COC input to COT work
21. 2023 Membership of the Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment
22. Declaration of COC members' interests during the period of this report -2023
23. Annex 1 - 2023 - Terms of Reference
24. Annex 2 - 2023 - Code of Conduct for members of the COC/COM/COT
25. Annex 3 – 2023 - Openness
26. Annex 4 – 2023 - Good Practice Agreement for Scientific Advisory Committees
27. Annex 5 – 2023 - Glossary of Terms
28. Annex 6 – 2023 - Previous Publications

Introduction

1. The Committee on Toxicity (COT) and its sister committees the Committee on Mutagenicity (COM) and Committee on Carcinogenicity (COC) are non-statutory independent scientific advisory committees which advise the Chair of the Food Standards Agency and the Chief Medical Officers (for England, Scotland, Wales and Northern Ireland) and, through them, the Government on a wide range of matters concerning chemicals in food, consumer products and the environment.

2. The Government is committed to make the operation of scientific advisory committees such as the COT/COM/COC hereafter referred to as “the Committee” more open and to increase accountability. The Committee is aware that the disclosure of information that is of a confidential nature and is communicated in circumstances importing an obligation of confidence is subject to the common law of confidentiality. There are some circumstances making disclosure of confidential information lawful for example, where the individual to whom the information relates has consented; where disclosure is in the public interest; and where there is a legal duty to do so. However, guidance is set out in the Freedom of Information Act 2000 which gives any person legal rights of access to information which is held by a public authority.

3. The Committee has agreed to hold open meetings as standard practice. Interest groups, consumer organisations etc can attend (subject to the appropriate procedures for handling commercially sensitive information and research not in the public domain, paragraphs 9-15 refer).

4. The Committee appoints lay/public interest member(s) to help to increase public scrutiny of Committee business.

5. The Committee has agreed to the publication of agendas, draft and finalised minutes, discussion papers and statements on the internet.

6. Statements will summarise all the relevant data, such as information regarding potential hazards/risks for human health in respect of the use of products and chemicals, and any recommendations for further research.

7. The Committee will be asked for an opinion based on the data available at the time of consideration. It is recognised that, for many chemicals, the toxicological information is incomplete and that recommendations for further research to address these gaps may form part of the Committee's advice.

8. The release of documents (papers, minutes and statements) where the Committee has agreed an opinion on the available unpublished data but where

further additional information is required in order to finalise the Committee's conclusions, needs to be considered on a case-by case basis.

The relevant considerations include the likelihood that such additional data would alter the Committee's conclusion, any representations made by a company about, for example, commercial harm that early disclosure could cause and also the public interest in disclosure.

Procedures for handling commercially sensitive information and research data not in the public domain

Background

9. The Committee operates on a presumption of openness. However, it is recognised that the nature of the work will at times provide the Committee access to information that is not in the public domain. Decisions on confidentiality will be exercised consistently with consideration to the Freedom of Information Act 2000 and Environmental Information Regulations 2004.

10. Where there is a need to discuss matters that cannot be put in the public domain the Committee may hold a discussion in “Reserved Business”. These items will be generally discussed either at the beginning or the end of an open meeting. It is expected that such cases will be infrequent and only in clearly justified circumstances. For the most part this comprises information which is commercially sensitive such as product formulations/specifications, methods of manufacture, and reports of toxicological investigations and company evaluations and safety assessment. It would also include pre-publication or unpublished research data.

11. “Reserved Business” items will be clearly indicated as such. The Committee will advise its reasons for withholding any information, and, if possible, an indication of when and where the information withheld may be published. Information subject to such restriction, including reserved sections of the minutes will be placed in the public domain as soon as practicable should the restrictions cease to apply at a later date.

12. Normal procedure is to publish a summary of the Committee's advice on their respective websites, in the Annual Report and where necessary to ask companies to release full copies of submitted reports for retention by the British

Library at the completion of a review. Given the clear Ministerial commitment to the publication of detailed information regarding the activities of advisory committees, and in particular following the assessment of products which are already available to the general public, the Committee will publish statements via the Internet soon after they have been finalised.

13. Except in cases where there is legislation under which information has been submitted and which deals with disclosure and non-disclosure, the general principle of the common law duty of confidentiality will apply. This means that any information which is commercially sensitive, pre-publication or unpublished research data and has been obtained in circumstances importing a duty of confidence may not be disclosed unless consent has been given or there is an overriding public interest in disclosure (such as the prevention of harm to others).

14. The following procedure will be adopted which allows commercially sensitive information to be identified, assessed and appropriate statements to be drafted and published on the basis of a prior mutual understanding with the companies. There is scope for companies to make representations also after submission of the information and prior to publication regarding the commercial sensitivity of data supplied and to comment on the text of statements which are to be published. However, companies would not have a right of veto in respect of such statements.

Procedures prior to committee consideration

Initial discussions

15. Upon referral to Committee the Secretariat will liaise with the relevant company supplying the product in the UK to:

- Clearly state the policy of Committee openness (summarised above).
- Identify and request the information needed by the Committee (e.g., test reports, publications etc).

Commercially sensitive information

- The company will be asked to clearly identify any commercially sensitive information and the reason for confidentiality.

Pre-publication and unpublished research data

17. The Committee and Secretariat will respect the confidentiality of authors of (unpublished or pre-publication) research data.

Handling confidential data

- The procedures by which the Committee will handle commercially sensitive information, pre-publication or unpublished research data and the public availability of papers, minutes, conclusions and statements where reference is made to such data will be discussed with the company or author prior to submission of papers to the Committee and is outlined in paragraphs 9-15 above. Companies will be informed that confidential annexes to Committee papers (e.g. where detailed information supplied in confidence such as individual patient information and full study reports of toxicological studies) will not be disclosed but that other information will be disclosed unless agreed otherwise with an individual company.
- The following is a suggested list of information which may be disclosed in Committee documents (papers, minutes and statements). The list is not exhaustive and is presented as a guide:

a) name of product (or substance/chemical under consideration),

b) information on physico-chemical properties,

c) methods of rendering harmless,

d) a summary of the results and evaluation of the results of tests to establish harmlessness to humans,

e) methods of analysis,

f) first aid and medical treatment to be given in the case of injury to persons,

g) surveillance data (e.g. monitoring for levels in food, air, or water).

Procedures during and after Committee consideration

- The timing of release of Committee documents (papers, minutes and statements) where the item of business involved the consideration of

confidential data would be subject to the general provisions outlined in paragraphs 9-15 above. Documents would not be released until the Committee statement is available.

- The most important outcome of the Committee consideration is likely to be the agreed statement. Companies will be given an opportunity to comment on the statement prior to publication and to make representations (for example, as to commercial sensitivities in the statement). The Chair would be asked to consider any comments provided, but companies would not be able to veto the publication of a statement or any part of it. Companies will continue to be asked to release full copies of submitted reports for retention by the British Library at the completion of a review.

Dissenting views

16. The Committee should not seek consensus at the risk of failing to recognise different views on a subject. Any significant diversity of opinion among the members of the Committee that cannot be resolved should be accurately reflected in the minutes or report. Committee decisions should always include an explanation of where differences of opinion have arisen during discussions, specifically where there are unresolved issues and why conclusions have been reached. If however member(s) feel they cannot support the Committee conclusions they may declare a ‘minority report’ identifying which member(s) are making the minority report and setting out their position.

COC/COM/COT papers

17. Committee papers are available on the respective website. Papers will not include commercially sensitive documents, pre-publication, unpublished or material in the public domain. Where possible a cover page with weblinks (current at the time) will be provided.

Remuneration and Committee finance

18. In the financial year 2023/24 the budget for the COT, excluding Secretariat resources was £125,857.00. Costs were met by the Food Standards Agency (FSA).

Review of fee rates

19. Fees in respect of the COT are set by the FSA and for COC and COM by the Department of Health. The FSA will review and revise COT rates every 2 years with the intention that rates should rise in line with the recommendations of the Senior Salaries Review Board with regard to pay in the Senior Civil Service. The FSA will also take into account comparisons with rates paid in similar advisory bodies in the UK.

Travel and other expenses

20. Committee members are entitled to reimbursement of reasonable travel and subsistence expenses necessarily incurred on official committee business. Members must seek value for money and are encouraged to use the most cost effective and environmentally sustainable options for travel and accommodation.

Working Groups

21. The Committee may establish Working Groups to consider particular topics in depth or to make brief assessments of particular issues and advise the main Committee on the possible need for further action. Such Groups contain a number of Committee members (supplemented, as necessary, by external expertise in the particular subject being considered). A Committee Chair will play a leading role in deciding which Committee members should be invited to join such groups, which may meet on a number of occasions in a particular year. Committee members may claim an allowance for participating on a Working Group.

Terms and conditions of appointment

22. Appointments of members may be staggered so that only a proportion retire or are re-appointed each year, to help ensure continuity. (Note: The COC/COM/ COT Chairs are ex officio members of General Advisory Committee on Science (GACS) for the term of their appointment as the COC/COM/COT Chair. COC and COM Chairs are ex officio members of each other’s Committees.)

23. COC and COM members are usually expected to attend 3 meetings in a year. COT members are expected to attend 7 meetings in a year. Members should allow appropriate preparation time. Meetings will usually be in London.

24. The COC/COM/COT Chair must also be available for a number of other activities including: attending, with the FSA Chief Scientist, the FSA Board’s annual discussion of the Agency’s science; engaging with the media on any high-

profile relating to the Committee's work, and discussion with the Agency Chief Scientist and GACS Secretariat in planning and developing the Committee's work (including discussing and agreeing with the Agency's Chief Scientist a framework for providing assurance on the work of the Scientific Advisory Committees in providing advice to the Agency). It is expected that these additional activities might require 5-10 days input per year.

Feedback on performance

25. The COT Chair and members are asked to provide brief feedback on their experience on the committee each year to help the Agency ensure that the Committee operates effectively and identify any areas for improvement.

26. Committee members are normally appointed for a term of 3 years (a maximum 10 years/3 terms per member). The COT uses the feedback self-assessment form as one of the tools used to determine whether or not a committee member should be reappointed at the end of their (3 year) term.

Annex 4 – 2023 - Good Practice Agreement for Scientific Advisory Committees

In this guide

In this guide

1. About the Committees - 2023
2. COT Preface - 2023
3. COT evaluations - 2023
4. COT Assurance - 2023
5. Committee Procedures - 2023
6. Ongoing Work - COT 2023
7. Other Committee Activities: Joint Expert Groups, Presentations and Workshop -2023

8. 2023 Membership of the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment
9. Declaration of COT members' interests during the period of this report -2023
10. Sub-groups active in 2023
11. Committee on Mutagenicity of chemicals in Food, Consumer Products and the Environment Annual Report 2023
12. Ongoing work - COM 2023
13. Discussion Items -2023
14. 2023 Membership of the Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment
15. Declaration of COM members' interests during the period of this report -2023
16. Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment Annual Report 2023
17. COC Ongoing Topics - 2023
18. COC Workshop - 2023
19. Joint session Horizon scanning
20. COC input to COT work
21. 2023 Membership of the Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment
22. Declaration of COC members' interests during the period of this report -2023
23. Annex 1 - 2023 - Terms of Reference
24. Annex 2 - 2023 - Code of Conduct for members of the COC/COM/COT
25. Annex 3 – 2023 - Openness
26. Annex 4 – 2023 - Good Practice Agreement for Scientific Advisory Committees
27. Annex 5 – 2023 - Glossary of Terms
28. Annex 6 – 2023 - Previous Publications

Introduction

The Government Chief Scientific Adviser's Guidelines on the Use of Scientific and Engineering Advice in Policy Making set out the basic principles which government departments should follow in assembling and using scientific advice. The key elements are to:

- **Identify early** the issues which need scientific and engineering advice and where **public engagement** is appropriate.
- Draw on a **wide range of expert advice** sources, particularly when there is uncertainty.

- Adopt an **open and transparent approach** to the scientific advisory process and publish the evidence and analysis as soon as possible.
- **Explain publicly the reasons for policy decisions**, particularly when the decision appears to be inconsistent with scientific advice.
- **Work collectively** to ensure a joined-up approach throughout government to integrating scientific and engineering evidence and advice into policy making.

The Code of Practice for Scientific Advisory Committees and the Principles of Scientific Advice to Government provide more detailed guidance on the operation of Scientific Advisory Committees (SACs) and their relationship with their sponsor Departments.

The Food Standards Agency's Board adopted a **Science Checklist** in 2006 (updated in 2012) that makes explicit the points to be considered in the preparation of policy papers and proposals dealing with science-based issues, including those which draw on advice from the SACs.

These **Good Practice Guidelines** were drawn up in 2006 by the Chairs of the independent SACs that advise the FSA based on, and complementing, the Science Checklist. They were updated in 2012 in consultation with the General Advisory Committee on Science (GACS). (Note GACS has now been replaced by the FSA Science Council).

The Guidelines apply to the SACs that advise the FSA and for which the FSA is sole sponsor Department:

- Advisory Committee on Animal Feedingstuffs,
- Advisory Committee on Microbiological Safety of Food,
- Advisory Committee on Novel Foods and Processe,
- Science Council,
- Advisory Committee for Social Science (ACSS).

As well as those Committees, the FSA co-sponsors with the Department of Health and Social Care:

- Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment,
- Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment,
- Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment.

For the SACs with a shared sponsorship the Guidelines apply formally to their advice to the FSA; they may opt to follow them also in advising other sponsor Departments.

All these committees share important characteristics. They are:

- Independent,
- work in an open and transparent way,
- are concerned with risk assessment and/or science governance, not with decisions about risk management.

The Guidelines relate primarily to the risk assessment process since this is the main purpose of most of the SACs. However, the SACs may, where appropriate, comment on risks associated with different risk management options, highlight any wider issues raised by their assessment that they feel should be considered (distinguishing clearly between issues on which the SAC has an expert capability and remit, and any other issues), or any evidence gaps and/or needs for research or analysis.

In addition, the Science Council and ACSS may advise the FSA on aspects of the governance of risk management, or on research that relates to risk management.

Twenty-nine principles of good practice have been developed. However, the different committees have different duties and discharge those duties in different ways. Therefore, not all the principles set out below will be applicable to all of the committees, all of the time.

The SACs have agreed to review their application of the principles annually and report this in their Annual Reports. Compliance with the Guidelines will also be covered in the annual self-assessments by Members and annual feedback meetings between each SAC Chair and the FSA Chief Scientist.

Principles

Defining the problem and the approach

The FSA will ensure that issues it asks an SAC to address are clearly defined and take account of stakeholder expectations in discussion with the SAC Secretariat and where necessary the SAC Chair. The SAC Chair will refer back to the FSA if discussion suggests that further iteration and discussion of the task is necessary.

Where an SAC proposes to initiate a piece of work the SAC Chair and Secretariat will discuss this with FSA to ensure the definition and rationale for the work and its expected use by the FSA are clear.

Seeking input

The Secretariat will ensure that stakeholders are consulted at appropriate points in the SAC's considerations. It will consider with the FSA whether and how stakeholder views need to be taken into account in helping to identify the issue and frame the question for the committee.

Wherever possible, SAC discussions should be held in public.

The scope of literature searches made on behalf of the SAC will be clearly set out.

Steps will be taken to ensure that all available and relevant scientific evidence is rigorously considered by the committee, including consulting external/additional scientific experts who may know of relevant unpublished or pre-publication data.

Data from stakeholders will be considered and weighted according to quality by the SAC.

Consideration by the Secretariat and the Chair (and where appropriate the whole SAC) will be given to whether expertise in other disciplines will be needed.

Consideration will be given by the Secretariat or by the SAC, in discussion with the FSA, as to whether other SACs need to be consulted.

Validation

Study design, methods of measurement and the way that analysis of data has been carried out will be assessed by the SAC.

Data will be assessed by the committee in accordance with the relevant principles of good practice, e.g. qualitative social science data will be assessed with reference to guidance from the Government's Chief Social Researcher as set out in Quality in qualitative Evaluation: A Framework for Assessing Research Evidence or the Magenta Book

Formal statistical analyses will be included wherever appropriate. To support this, each SAC will have access to advice on quantitative analysis and modelling as needed.

When considering what evidence needs to be collected for assessment, the following points will be considered:

- the potential for the need for different data for different parts of the UK or the relevance to the UK situation for any data originating outside the UK.
- whether stakeholders can provide unpublished data.

The list of references will make it clear which references have been subject to external peer review, and which have been peer reviewed through evaluation by the Committee, and if relevant, any that have not been peer reviewed.

Uncertainty

When reporting outcomes, SACs will make explicit the level and type of uncertainty (both limitations on the quality of the available data and lack of knowledge) associated with their advice.

Any assumptions made by the SAC will be clearly spelled out, and, in reviews, previous assumptions will be challenged.

Data gaps will be identified and their impact on uncertainty assessed by the SAC.

An indication will be given by the SAC about whether the evidence base is changing or static, and if appropriate, how developments in the evidence base might affect key assumptions and conclusions.

Drawing conclusions

The SAC will be broad-minded, acknowledging where conflicting views exist and considering whether alternative interpretations fit the same evidence.

Where both risks and benefits have been considered, the committee will address each with the same rigour, as far as possible; it will make clear the degree of rigour and uncertainty, and any important constraints, in reporting its conclusions.

SAC decisions will include an explanation of where differences of opinion have arisen during discussions, specifically where there are unresolved issues, and why conclusions have been reached. If it is not possible to reach a consensus, a minority report may be appended to the main report, setting out the differences in interpretation and conclusions, and the reasons for these, and the names of those supporting the minority report.

The SAC's interpretation of results, recommended actions or advice will be consistent with the quantitative and/or qualitative evidence and the degree of uncertainty associated with it.

SACs will make recommendations about general issues that may have relevance for other committees.

Communicating the SACs' conclusions

Conclusions will be expressed by the SAC in clear, simple terms and use the minimum caveats consistent with accuracy.

It will be made clear by the SAC where assessments have been based on the work of other bodies and where the SAC has started afresh and there will be a clear statement of how the current conclusions compare with previous assessments.

The conclusions will be supported by a statement about their robustness and the extent to which judgement has had to be used.

As standard practice, the SAC secretariat will publish a full set of references (including the data used as the basis for risk assessment and other SAC opinions) at as early a stage as possible to support openness and transparency of decision-making. Where this is not possible, reasons will be clearly set out, explained and a commitment made to future publication wherever possible.

The amount of material withheld by the SAC or FSA as being confidential will be kept to a minimum. Where it is not possible to release material, the reasons will be clearly set out, explained and a commitment made to future publication wherever possible.

Where proposals or papers being considered by the FSA Board rest on scientific evidence produced by a SAC, the Chair of the SAC (or a nominated expert member) will be invited to the table at the Open Board meetings at which the paper is discussed. To maintain appropriate separation of risk assessment and risk management processes, the role of the Chairs will be limited to providing an independent view and assurance on how their committee's advice has been reflected in the relevant policy proposals, and to answer Board Members' questions on the science. The Chairs may also, where appropriate, be invited to provide factual briefing to Board members about particular issues within their committees' remits, in advance of discussion at open Board meetings.

The SAC will seek (and FSA will provide) timely feedback on actions taken (or not taken) in response to the SAC's advice, and the rationale for these.

Annex 5 – 2023 - Glossary of Terms

In this guide

In this guide

1. About the Committees - 2023
2. COT Preface - 2023
3. COT evaluations - 2023
4. COT Assurance - 2023
5. Committee Procedures - 2023
6. Ongoing Work - COT 2023
7. Other Committee Activities: Joint Expert Groups, Presentations and Workshop -2023
8. 2023 Membership of the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment
9. Declaration of COT members' interests during the period of this report -2023
10. Sub-groups active in 2023
11. Committee on Mutagenicity of chemicals in Food, Consumer Products and the Environment Annual Report 2023
12. Ongoing work - COM 2023
13. Discussion Items -2023
14. 2023 Membership of the Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment
15. Declaration of COM members' interests during the period of this report -2023
16. Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment Annual Report 2023
17. COC Ongoing Topics - 2023
18. COC Workshop - 2023
19. Joint session Horizon scanning
20. COC input to COT work
21. 2023 Membership of the Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment
22. Declaration of COC members' interests during the period of this report -2023
23. Annex 1 - 2023 - Terms of Reference
24. Annex 2 - 2023 - Code of Conduct for members of the COC/COM/COT

25. Annex 3 – 2023 - Openness
26. Annex 4 – 2023 - Good Practice Agreement for Scientific Advisory Committees
27. Annex 5 – 2023 - Glossary of Terms
28. Annex 6 – 2023 - Previous Publications

Numerical

3R’s principle: The 3Rs stand for Replacement, Reduction, Refinement. This is a strategy that is intended to reduce the number of animals used in experiments and to reduce animal experimentation overall; it also aims to mitigate the suffering and distress caused to the animals.

A

a priori: The formulation of an hypothesis based on theoretical considerations before undertaking an investigation or experiment.

Absolute risk (AR): is the probability or chance of an event. It is usually used for the number of events (such as a disease) that occurred in a group, divided by the number of people in that group.

Absorption (biological): Process of active or passive transport of a substance into an organism, in humans this is usually through the lungs, gastrointestinal tract or skin.

Acceptable daily intake (ADI): Estimate of the amount of a substance in food or drink, expressed on a bodyweight basis (e.g. mg/kg bodyweight), that can be ingested daily over a lifetime by humans without appreciable health risk.

Acceptable risk: Probability of suffering disease or injury which is considered to be sufficiently small to be societally acceptable.

Acute: Short term, in relation to exposure or effect.

Acute reference dose (ARfD): Estimate of the amount of a substance in food or drink, expressed on a body weight basis that can be ingested in a period of 24 hours or less without appreciable health risk.

Acute toxicity: Adverse effects that occur over a short period of time (up to 14 days) immediately following a single exposure.

Adaptive response: The process whereby a cell or organism responds to a xenobiotic so that the cell or organism will survive in the new environment that contains the xenobiotic without impairment of function.

Adduct: A chemical grouping which is covalently bound (see covalent binding) to a large molecule such as DNA (qv) or protein.

Adductome: The totality of the adduct profile, usually to DNA, in an individual.

Adenoma: A benign neoplasm arising from a gland forming epithelial tissue such as colon, stomach or respiratory tract.

Adverse Outcome Pathway (AOP): A sequence of key events linking a molecular initiating event (MIE) to an adverse outcome through different levels of biological organisation. AOPs span multiple layers of biological organisation.

Adverse response: Change in morphology, physiology, biochemistry, growth, development or lifespan of an organism or its progeny which results in impairment of functional capacity or impairment of capacity to compensate for additional stress or increase in susceptibility to the harmful effects of other environmental influences.

Aetiology: study of causation or origination.

Aggregate exposure: exposure to one chemical by all routes from all sources.

Ah receptor: The Ah (Aromatic hydrocarbon) receptor protein is a member of a group of regulatory sensor molecules. The identity of the natural endogenous chemicals which regulate the Ah receptor is unknown. Binding to the Ah receptor is an integral part of the toxicological mechanism of a range of chemicals, such as chlorinated dibenzodioxins and polychlorinated biphenyls.

Alkylating agents: Chemicals which leave an alkyl group covalently bound to biologically important molecules such as proteins and nucleic acids (see adduct). Many alkylating agents are mutagenic, carcinogenic and immunosuppressive.

Allele: Alternative form of a gene within the population.

Allergen: Substance capable of stimulating an allergic reaction.

Allergy: The adverse health effects that may result from the stimulation of a specific immune response.

Allergic reaction: an adverse reaction elicited by exposure to a previously sensitised individual to the relevant antigen.

Ames test: Also known as the bacterial reverse mutation assay. In vitro assay for bacterial gene mutations using strains of Salmonella typhimurium and Escherichia coli.

Androgen: The generic term for any natural or synthetic compound that can interact with and activate the androgen receptor. In mammals, androgens (for example, androstenedione and testosterone) are synthesised by the adrenal glands and the testes and promote development and maintenance of male secondary sexual characteristics.

Aneugen/aneugenic: (An agent) Inducing aneuploidy.

Aneuploidy: The circumstances in which the total number of chromosomes within a cell is not an exact multiple of the normal haploid (see 'polyploidy') number. Chromosomes may be lost or gained during cell division.

Apoptosis: A form of programmed, active cell death resulting in fragmentation of the cell into membrane-bound fragments (apoptotic bodies). These are usually rapidly removed in vivo by engulfment by phagocytic cells. Apoptosis occurs normally during development but can be triggered abnormally by toxic stimuli.

As low as is reasonably achievable/ As low as is reasonably practicable (ALARA/ALARP): A risk management approach under which exposure to a substance or mixture is reduced to the lowest level that it is deemed to be reasonably achievable or practicable in particular circumstances or by available technological solutions.

B

Base pair (bp): Two complementary nucleotide bases in DNA joined together by hydrogen bonds.

Benchmark dose (BMD) modelling: An alternative quantitative approach to dose-response assessment using more of the data than the NOAEL process. This approach utilises mathematical models to fit all available data points and uses the best fitting model to interpolate an estimate of the dose (benchmark dose) that corresponds to a particular level of response (a benchmark response). A measure of uncertainty is also calculated, and the lower confidence limit on the benchmark dose is called the BMDL. The BMDL accounts for the uncertainty in the

estimate of the dose-response that is due to characteristics of the experimental design such as sample size and biological variability. The BMDL can be used as the point of departure (see POD) for derivation of a health-based guidance value or a margin of exposure.

Benign tumour: Tumours showing a close morphological resemblance to their tissue of origin, growing in a slow expansile fashion and with a circumscribed form, usually encapsulated masses. They may stop growing and they may regress. Benign tumours do not infiltrate through local tissues, and they do not metastasise. They are rarely fatal.

Bias: An interference which at any stage of an investigation tends to produce results that depart systematically from the true values (to be distinguished from random error). The term does not necessarily carry an imputation of prejudice or any other subjective factor such as the experimenter's desire for a particular outcome.

Bioavailability: A term referring to the proportion of a substance which reaches the systemic circulation unchanged after a particular route of administration.

Bioinformatics: The science of informatics as applied to biological research. Informatics is the management and analysis of data using advanced computing techniques. Bioinformatics is particularly important as an adjunct to -omics research, because of the large amount of complex data this research generates.

Biological relevance: an effect considered by expert judgement as important and meaningful for human, animal, plant or environmental health. It therefore implies a change that may alter how decisions for a specific problem are taken.

Biomarker: Observable change (not necessarily pathological) in an organism, related to a specific exposure, effect or susceptibility.

Biomarker of effect: A measurable biochemical, physiologic, behavioural, or other alteration in an organism that, depending on the magnitude, can be recognised as associated with an established or possible health impairment or disease.

Biomarker of exposure: a chemical, its metabolite, or the product of an interaction between a chemical and some target molecule or cell that is measured in the human body indicative of exposure.

Biomarker of susceptibility: An indicator of an inherent or acquired ability of an organism to respond to the challenge of exposure to a specific chemical substance.

Biomonitoring (human): the direct measurement of people's integrated exposure to toxic substances by measuring the substances, their metabolites or a biochemical change in human specimens, such as blood or urine.

Biomonitoring equivalent: an estimated concentration or range of concentrations of an environmental chemical in humans which is consistent with existing health-based guidance values such as the TDI or RfD/RfC. BEs provide a way of interpreting biomonitoring data in the context of these values.

Body burden: Total amount of a chemical present in an organism at a given time.

Bradford Hill considerations: Sir Austin Bradford Hill established a set of ‘principles’ (not be taken as ‘criteria’) that may be used to assist in the interpretation of associations reported from epidemiological studies:

Strength – The stronger the association the more likely it is causal. The COC has previously noted that the relative risks of <3 need careful assessment for effects of bias or confounding.

Consistency – The association has been consistently identified by studies using different approaches and is also seen in different populations with exposure to the chemical under consideration.

Specificity – Limitation of the association to specific exposure groups or to specific types of disease increases likelihood that the association is causal.

Temporality – The association must demonstrate that exposure leads to disease. The relationship of time since first exposure, duration of exposure and time since last exposure are all important in assessing causality.

Biological gradient – If an association reveals a biological gradient or dose response curve, then this evidence is of particular importance in assessing causality.

Plausibility – Is there appropriate data to suggest a mechanism by which exposure could lead to concern? However, even if an observed association may be new to science or medicine it should not be dismissed.

Coherence – Cause and effect interpretation of data should not seriously conflict with generally known facts.

Experiment – Can the association be demonstrated experimentally? Evidence from experimental animals may assist in some cases. Evidence that removal of the exposure leads to a decrease in risk may be relevant.

Analogy – Have other closely related chemicals been associated with the disease?

Bronchial: Relating to the air passages conducting air from the trachea (windpipe) to the lungs.

C

Cancer: Synonym for a malignant neoplasm – that is, a tumour that grows progressively, invades local tissues and spreads to distant sites (see also tumour and metastasis).

Candidate gene: A gene that has been implicated in causing or contributing to the development of a particular disease.

Carcinogen: A causal agent that induces tumours. Carcinogens include external factors (chemicals, physical agents, viruses) and internal factors such as hormones. An important distinction can be drawn between **genotoxic** carcinogens which have been shown to damage DNA, and **nongenotoxic** carcinogens which act through other mechanisms. The activity of genotoxic carcinogens can often be predicted from their chemical structure - either of the parent compound or of active metabolites. Most chemical carcinogens exert their effects after prolonged exposure, show a dose-response relationship and tend to act on a limited range of susceptible target tissues. Carcinogens are sometimes species or sex-specific and the term should be qualified by the appropriate descriptive adjectives to aid clarity. Several different chemical and other carcinogens may interact, and constitutional factors (genetic susceptibility, hormonal status) may also contribute, emphasising the multifactorial nature of the carcinogenic process.

Carcinoma: Malignant tumour arising from epithelial cells lining, for example, the alimentary, respiratory and urogenital tracts and from epidermis, also from solid viscera such as the liver, pancreas, kidneys and some endocrine glands. (See also 'tumour').

Case-control study: (Synonyms - case comparison study, case referent study) A comparison is made of the proportion of cases who have been exposed to a particular hazard (e.g., a carcinogen) with the proportion of controls who have been exposed to the hazard.

Cell cycle (cell cycle arrest): The cell cycle is a series of events involving the growth, replication, and division of a eukaryotic cell. Cell cycle arrest: A regulatory process that halts progression through the cell cycle during one of the normal phases (G1, S, G2, M).

Cell transformation: The process by which a normal cell acquires the capacity for neoplastic growth. Complete transformation occurs in several stages both in vitro and in vivo. One step which has been identified in vitro is 'immortalisation' by which a cell acquires the ability to divide indefinitely in culture. Such cells do not have the capacity to form tumours in animals but can be induced to do so by extended passage in vitro, by treatment with chemicals, or by transfection with oncogene DNA. The transformed phenotype so generated is usually, but not always, associated with the ability of the cells to grow in soft agar and to form tumours when transplanted into animals. It should be noted that each of these stages of transformation can involve multiple events which may or may not be genetic. The order in which these events take place, if they occur at all, in vivo is not known.

Cholinergic: A substance which is capable of producing, altering or releasing the neurotransmitter acetylcholine.

Chromosomal aberrations: Collective term of particular types of chromosome damage induced after exposure to exogenous chemical or physical agents which damage the DNA (see also aneugen, clastogen). Such numerical or structural chromosome changes tend to be those which are evident using light microscopy.

Chromosome: In simple prokaryotic organisms, such as bacteria and most viruses, the chromosome consists of a single circular molecule of DNA containing the entire genetic material of the cell. In eukaryotic cells, the chromosomes are thread-like structures, composed mainly of DNA and protein, which are present within the nuclei of every cell. They occur in pairs, the numbers varying from one to more than 100 per nucleus in different species. Normal somatic cells in humans have 23 pairs of chromosomes, each consisting of linear sequences of DNA which are known as genes.

Chronic effect: Consequence which develops slowly and has a long-lasting course (often but not always irreversible).

Chronic exposure: Continued exposures occurring over an extended period of time, or a significant fraction of the life-time of a human or test animal.

Clastogen: An agent that produces chromosome breaks and other structural aberrations such as translocations. Clastogens may be viruses or physical agents as well as chemicals. Clastogenic events play an important part in the development of some tumours (clastogenicity).

Clearance: Volume of blood or plasma, or mass of an organ, effectively cleared of a substance by elimination (metabolism and excretion) in a given time interval. Total clearance is the sum of the clearances for each eliminating organ or tissue.

Clone: A term which is applied to genes, cells, or entire organisms which are derived from - and are genetically identical to - a single common ancestor gene, cell, or organism, respectively. Cloning of genes and cells to create many copies in the laboratory is a common procedure essential for biomedical research.

Coding regions: those parts of the DNA that contain the information needed to form proteins. Other parts of the DNA may have non-coding functions (e.g., start-stop, pointing or timer functions) or as yet unresolved functions or maybe even ‘noise’.

Codon: a set of three nucleotide bases in a DNA or RNA sequence, which together code for a specific amino acid.

Cohort: A defined population that continues to exist through a period of time, e.g., a group of individuals who had a specific occupation.

Cohort study: (Synonyms - follow-up, longitudinal study) The study of a group of people defined at a particular point in time (the cohort), who have particular characteristics in common, such as a particular exposure. They are then observed over a period of time for the occurrence of disease. The rate at which the disease develops in the cohort is compared with the rate in a comparison population, in which the characteristics (e.g., exposure) are absent.

Combined exposure: exposure to multiple chemicals by a single or multiple routes at the same or different times.

Comet assay: A genotoxicity assay in which DNA strand breaks in an individual cell are measured using single-cell gel electrophoresis. Cell DNA fragments

assume a "comet with tail" formation on electrophoresis and are detected with an image analysis system. Alkaline assay conditions facilitate sensitive detection of double-strand and single-strand damage, as well as alkali-labile sites. Modifications to standard methodology enable detection of types of DNA damage, e.g., DNA-DNA or DNA-protein cross-links and base-oxidation.

Complementary DNA (cDNA): cDNA is DNA that is synthesised in the laboratory from mRNA by reverse transcription. A cDNA is so-called because its sequence is the complement of the original mRNA sequence.

Confounding variable: (synonym - confounder) A confounding variable is a factor that is independently associated with both an intervention or exposure and the outcome of interest. Failure to account for this will distort the observed measure of association in the statistical analysis. For example, in observational studies, cigarette smoking is a confounding variable with respect to an association between alcohol consumption and heart disease because it is a risk factor for heart disease and is associated with alcohol consumption but is not a consequence of alcohol consumption. Similarly, if people in the experimental group of a controlled trial are younger than those in the control group, age could act as a potential confounder and make it difficult to ascertain whether a lower risk of death in one group is due to the intervention or the difference in ages.

Confounding may also occur in experimental studies, where in a feed trial, unpalatability might result in reduced food consumption and weight loss, rather than weight loss occurring through toxicity.

Congeners: Related compounds varying in chemical structure that often, but not always, share biological properties.

Continuous Data: Quantitative data that can be measured and has an infinite number of possible values within a selected range.

Copy number variants (CNVs): Alterations in the DNA of a genome that results in the cell having an abnormal number of copies of one or more sections of the DNA. CNVs correspond to relatively large regions of the genome that have been deleted (fewer than the normal number) or duplicated (more than the normal number) on certain chromosomes.

Covalent binding: Chemical bonding formed by the sharing of an electron pair between two atoms. Molecules are combinations of atoms bound together by covalent bonds (see adduct).

Critical effect size (CES): The magnitude of the adverse effect selected at which to determine the dose to serve as a point of departure in assessing the risk from exposure to a chemical. This term is often used synonymously with Benchmark Response (BMR). Choice of CES includes both statistical and toxicological considerations.

Cumulative exposure: exposure to multiple chemicals on the basis of grouping them on some common characteristic, such as mode of action, adverse effect, or inclusion in a product formulation.

P450 (CYP): An extensive family of haem-containing proteins involved in enzymic oxidation of a wide range of endogenous and xenobiotic substances and their conversion to forms that may be more easily excreted. In some cases, the metabolites produced may be chemically reactive and have increased toxicity. In other cases, the substances may be natural precursors of hormones (e.g., steroids).

Cytogenetic: Concerning chromosomes, their origin, structure and function.

D

(DNA) Deletion: A type of mutation where there is a loss of DNA (nucleotide base pairs) from the genome. Deletions may range in size from a single nucleotide to an entire chromosome. Such deletions may be harmless, may result in disease, or may in rare cases be beneficial.

Deoxyribonucleic acid (DNA): The carrier of genetic information for all living organisms except the group of RNA viruses. Each of the 46 chromosomes in normal human somatic cells consists of 2 strands of DNA containing an estimated 50 - 250 million nucleotides, specific sequences of which make up genes. DNA itself is composed of two interwound chains of linked nucleotides.

DNA damage: Injuries to DNA that introduce deviations from its normal, chemical structure and which may, if left unrepaired, result in a mutation or a block of DNA replication. These deviations can occur naturally or may be caused by environmental physical or chemical agents.

DNA methylation: A reversible biochemical modification of DNA more or less universally present in organisms from bacteria to humans. Methyl groups can be enzymatically added to or removed from cytosine (C). It is associated with silencing of DNA sequences.

DNA probe: A piece of single-stranded DNA, typically labelled so that it can be detected (for example, a radioactive or fluorescent label can be used), which can single out and bind with another specific piece of DNA. DNA probes can be used to determine which sequences are present in a given length of DNA or which genes are present in a sample of DNA.

DNA repair: Processes that repair potentially damaging changes in DNA, including those induced by chemical mutagens (see mutagen.) Through the action of enzymes, individual DNA bases may be replaced, or part of a strand of DNA may be replaced, using its opposite, paired strand as a template. These processes may themselves be prone to error and result in potentially deleterious changes.

DNA repair genes: Genes which code for proteins that repair damage in DNA sequences.

DNA damage response (DDR): Cells respond to the perception of DNA damage by arresting cell-cycle progression and attempting repair: collectively these actions are known as the DNA-damage response (DDR).

DNA sequencing: process by which the sequence of nucleotides along a strand of DNA is determined. Where either the whole genome or the exome (the region which encodes proteins) is sequenced this is referred to as whole genome/exome sequencing (WGS/WES).

Dominant lethal mutation: A dominant mutation (i.e., where mutation of a single allele is sufficient to cause a change in phenotype) that causes death of an early embryo.

Dopaminergic: Releasing or involving dopamine as a neurotransmitter.

Dose: Total amount of a substance administered to, taken or absorbed by an organism. May be qualified such as external dose, absorbed dose.

Dose-response relationship: how an effect caused by a chemical changes as the dose of the chemical changes, after a certain exposure time.

E

Endocrine active substance (EAS): A substance that can interact or interfere with the endocrine system.

Endocrine disrupter (ED): An exogenous substance or mixture that alters function(s) of the endocrine system and consequently causes adverse health effects in an intact organism or its progeny or (sub)populations.

Endonuclease: An enzyme that cleaves its nucleic acid substrate at internal sites in the nucleotide sequence.

Enterohepatic circulation: Cyclical process involving intestinal re-absorption of a substance that has been excreted through bile followed by transfer back to the liver, making it available for biliary excretion again.

Epidemiology: Study of factors determining the causes, frequency, distribution, and control of diseases in a human population.

Epigenetics: The study of heritable changes in gene function that occur without a change in the sequence of nuclear DNA and the processes involved in the unfolding development of an organism.

Epigenetic age: An estimate of biological age based on changes in epigenetic marks at particular locations along the genome.

Epigenetic drift: Divergence of the epigenome as a function of age due to stochastic changes in epigenetic marks.

Epigenetic marks: Features not directly governed by the genetic code, which include methylation of DNA and covalent modification of histone proteins. The latter may be tagged with methyl, acetyl, ubiquitin, phosphate, poly(ADP)ribose and other biochemical groups. These groups and their particular pattern of protein modification (e.g., mono-, bi-, tri-methylated at different amino acids and combinations of amino acids) modify the function of the tagged proteins and influence the way genes are expressed.

Epigenome: The comprehensive collection of genome-wide epigenetic phenomena, including DNA-methylation patterns, chromatin modifications, and non-coding RNA.

Epigenomic reprogramming: Resetting epigenetic marks so they resemble those of other cells from earlier developmental stages. This is of particular relevance for germline cells after the fusion of gametes when the genome is brought back into a "zero-state" of gene expression.

Epithelium: The tissue covering the outer surface of the body, the mucous membranes and cavities of the body.

Erythema: Reddening of the skin due to congestion of blood or increased blood flow in the skin.

Estrogen: Sex hormone or other substance capable of developing and maintaining female characteristics of the body (note UK spelling is oestrogen).

Exogenous: Arising outside the body.

Exposure Assessment: Process of measuring or estimating concentration or intensity, duration and frequency of exposure to an agent. The exposure could be via the environment, consumer products or the diet, or due to occupation.

F

Fetotoxic: Causing toxic, potentially lethal effects to the developing fetus.

Fibrosarcoma: A malignant tumour arising from connective tissue (see 'tumour').

First Pass Metabolism: rapid uptake and metabolism of an agent by the intestine or the liver, immediately after enteric absorption and before it reaches the systemic circulation.

Fluorescence In-Situ Hybridisation (FISH): A technique that allows individual chromosomes and their centromeres to be visualised in cells.

Forestomach: (See glandular stomach).

Free Radicals: any molecular species capable of independent existence that contains an unpaired electron in an atomic orbital. Many radicals are unstable and highly reactive.

Full gene sequence: the complete order of bases in a gene. This order determines which protein a gene will produce.

G

Gavage: Administration of a liquid via a stomach tube, commonly used as a dosing method in toxicity studies.

Gene: The functional unit of inheritance: a specific sequence of nucleotides along the DNA molecule, forming part of a chromosome.

Gene expression: The process by which the information in a gene is used to create proteins or polypeptides.

Gene families: Groups of closely related genes that make similar products.

Gene mutation: A permanent alteration in the DNA sequence that makes up a gene, such that the sequence differs from what is found in most people. Mutations range in size; they can affect anywhere from a single DNA building block (base pair) to a large segment of a chromosome that includes multiple genes.

Gene product: The protein or polypeptide coded for by a gene.

Genetic engineering: Altering the genetic material of cells or organisms in order to make them capable of making new substances or performing new functions.

Genetic polymorphism: a variation in germ-line DNA sequence among individuals, groups, or populations (e.g., a genetic polymorphism might give rise to blue eyes versus brown eyes, or population level differences in metabolic capacity). Genetic polymorphisms may be the result of chance processes or may have been induced by external agents (such as viruses or radiation). Generally, changes in DNA sequence which have been confirmed to be caused by external agents are called “mutations” rather than “polymorphisms”.

Genetic predisposition: susceptibility to a disease which is related to a polymorphism, which may or may not result in actual development of the disease.

Genetically modified organism (GMO): An organism which has had genetic material inserted into or removed from its cells.

Genome: All the genetic material in the chromosomes of a particular organism; its size is generally given as its total number of base pairs.

Genomic DNA: The basic chromosome set consisting of a species-specific number of linkage groups and the genes contained therein.

Genomic imprinting: The phenomenon whereby a small subset of all the genes in our genome are expressed according to their parent of origin.

Genomics: The study of genes and their function.

Genotoxic: A chemical or physical agent which has the ability to induce mutations or so-called indicator effects which are mechanistically associated with

the formation of mutations (e.g., induction of DNA modifications, DNA repair, or recombination). All mutagenic substances are genotoxic but not vice versa.

Genotype: The particular genetic pattern seen in the DNA of an individual. “Genotype” is generally used to refer to the particular pair of alleles that an individual possesses at a certain location in the genome. Compare this with phenotype.

Germ cells: Cells that give rise to the gametes of an organism that reproduces sexually. The cells undergo mitotic and meiotic cell division in the gonads followed by cellular differentiation into mature gametes, either oocytes or sperm.

Glandular stomach: The stomach in rodents consists of two separate regions – the forestomach and the glandular stomach. Only the glandular stomach is directly comparable to the human stomach.

H

Half-life: In the context of toxicokinetics, this is the time in which the concentration of a substance in vivo will be reduced by 50%, assuming a first order elimination process.

Hazard: Set of inherent properties of a substance, mixture of substances or a process involving substances that make it capable of causing adverse effects to organisms or the environment.

Health based guidance value (HBGV): A value indicating the amount of chemical in food that a person can consume on a regular basis usually over a lifetime without any significant risk to health.

Hepatic: Pertaining to the liver.

Hepatocyte: The principal cell type in the liver, possessing many metabolising enzymes (see 'metabolic activation').

Heterozygous: having two different forms (alleles) of a gene that controls a particular characteristic, one inherited from each parent, and therefore able to pass on either form.

Histone methylation: The modification of certain amino acids in a histone protein by the addition of methyl groups.

Histone modification: Covalent post-translational modifications to histone proteins including methylation, phosphorylation, acetylation, ubiquitylation, and sumoylation, which regulate gene expression. The modifications made to histones can impact gene expression by altering chromatin structure.

Histone tails: A structural aspect of histones that are major targets for post-translational modifications of histones (see Histone modifications).

Hodgkin's lymphoma: Cancer of the lymphatic system.

Homeostatic: Any self-regulation process by which biological systems tend to maintain stability while adjusting to conditions that are optimal for survival.

Horizon scanning: The systematic examination of potential threats, opportunities and likely future developments, which are at the margins of current thinking and planning. Horizon scanning may explore novel and unexpected issues, as well as persistent problems and trends. Overall, horizon scanning is intended to improve the robustness of policies and the evidence base.

Hypoxanthine-guanine Phosphoribosyltransferase **(HPRT) assay:**

This assay uses cultured mammalian somatic cells to detect mutagenic agents. The principle of the method relies on the fact that mutations (caused by mutagens) destroy the functionality or the HPRT gene or protein, which is detected by using a toxic analogue. The HPRT-mutants are viable colonies that can be scored.

Hypoxanthine-guanine Phosphoribosyltransferase **(HPRT) gene:**

A protein coding gene. This transferase allows cells to recycle purines, a building block of DNA and RNA.

Hypermethylation: Increase in the methylation of cytosine-guanosine base pairs in regulatory regions of DNA.

Hyperplasia: An increase in the size of an organ or tissue due to an increase in the number of cells through cell division.

Hypertrophy: An increase in the size of an organ or tissue due to an increase in the volume of individual cells within it.

Hypomethylation: The loss of the methyl group in 5-methylcytosine nucleotides in DNA. Hypomethylation can be used to describe the unmethylated state of

specific nucleotides or as a general phenomenon affecting large parts of the genome.

I

Idiosyncrasy: Specific (and usually unexplained) reaction of an individual to e.g., a chemical exposure to which most other individuals do not react at all. General allergic reactions do not fall into this category.

In silico: a term used to describe a computerised analysis of the structure of a chemical to assess its potential hazard.

In situ hybridisation (ISH): Use of a DNA or RNA probe to detect the presence of the complementary DNA sequence in cloned bacterial or cultured eukaryotic cells.

In vitro: A Latin term used to describe studies of biological material outside the living animal or plant (literally “in glass”).

In vivo: A Latin term used to describe studies in living animals or plants (literally “in life”).

Incidence: Number of discrete events, for example new cases of illness occurring during a given period in a specific population.

(Enzyme) Inducing agent: A chemical which, when administered to an animal, causes an increase in the expression of a particular enzyme. For example, chlorinated dibenzodioxins are inducing agents which act via the Ah-receptor (qv) to induce P450 (qv) CYP1A1.

Intraperitoneal: Within the abdominal cavity.

Isomer: Isomers are two or more chemical compounds with the same molecular formula but having different properties owing to a different arrangement of atoms within the molecule.

K

Key event: An empirically observable precursor step that is itself a necessary element of an AOP or MOA. A key event is a necessary, though usually not a sufficient, step in a process that results in an adverse outcome.

kilobase (kb): A length of DNA equal to 1000 nucleotides.

Knockout animals: Genetically engineered animals in which one or more genes, usually present and active in the normal animal, have been eliminated or inactivated.

L

LC50/LD50: The concentration or dose that causes death in 50% of a group of experimental animals to which it is administered. It can be used to assess the acute toxicity of a compound but is being superseded by more refined methods.

Less than lifetime (LTL) exposure: any exposure that is not continuous daily exposure, for example, short-term, intermediate or intermittent, or a combination of these.

Leukaemia: A group of neoplastic disorders (see tumour) affecting blood-forming elements in the bone marrow, characterised by uncontrolled proliferation and disordered differentiation or maturation. Examples include the lymphocytic leukaemia’s which develop from lymphoid cells and the myeloid leukaemia’s which are derived from myeloid cells (producing red blood cells, mainly in bone marrow).

Ligand: A molecule which binds to an allosteric binding site in a protein, such as a receptor.

Lipids: Fats, substances containing a fatty acid and soluble in alcohols or ether, but insoluble in water.

Lipophilic: 'Lipid liking' - a substance which has a tendency to partition into fatty materials.

Lowest observed adverse effect level (LOAEL): The lowest administered dose at which a statistically significant adverse effect, relative to that of the control, has been observed. Also given as LOEL when no ‘adverse’ effects are seen.

Lymphocyte: A type of white blood cell that plays central roles in adaptive immune responses.

Lymphoma: Malignant tumours arising from lymphoid tissues. They are usually

multifocal, involving lymph nodes, spleen, thymus and sometimes bone marrow, and other sites outside the anatomically defined lymphoid system. (See also 'tumour').

M

Malformations: The inheritance of an abnormal or anomalous formation of tissues and organs often referred to as a deformity.

Malignant tumour (synonym: cancer): A tumour (qv) composed of increasingly abnormal cells in term of their form and function. Some well differentiated examples still retain characteristics of their tissues of origin but these are progressively lost in moderately and poorly differentiated malignancies. Most malignant tumours grow rapidly, spread progressively through adjacent tissues and metastasise to distant sites.

Margin of exposure (MOE) approach: A methodology that allows the comparison of the risks posed by substances when it is not possible or not appropriate to establish a HBGV. This would include substances that are genotoxic and carcinogenic, and contaminants for which there is insufficient information to establish a Tolerable Daily Intake The MOE approach uses a reference point (or POD), often taken from an animal study, corresponding to a dose that causes no or a low response (for example the NAOEL, LOAEL, BMDL10). This reference point is then compared with various exposure estimates in humans. The lower the MOE, the greater the concern. The MOE considered to be of low or negligible concern is context specific. In general, for substances that are genotoxic and carcinogenic, and MOE of >10,000, when based on a reference point from an animal study, would be considered of low concern. For a non-genotoxic, non-carcinogenic contaminant, an MOE of > 100 would be considered of negligible concern.

Margin of safety (MOS) approach: A methodology used to assess relative risk when there is exceedance of a HBGV. The MOS is expressed as the ratio of the HBGV to measured or estimated exposure. The lower the MOS is below 1, the greater the concern.

Maximum tolerated dose: The MTD for a long-term study of carcinogenicity is a dose that produces minimal signs of toxicity on repeated administration, meaning no more than a 10% weight decrement, as compared to the appropriate control groups; and does not produce mortality, clinical signs of toxicity, or pathologic lesions (other than those that may be related to a neoplastic response)

that would be predicted to shorten the animal's natural life span.

Mechanism of action: an understanding of the molecular basis for an effect and its detailed description, so causation can be established in molecular terms.

Meiosis: The process of cell division in sexually reproducing organisms that reduces the number of chromosomes in reproductive cells from diploid to haploid leading to the production of gametes in animals and spores in plants. During the first meiotic division there is homologue pairing, efficient intergenic recombination between homologues during pairing, and the suppression of sister chromatid separation. S phase is absent at the start of the second meiotic division. Thus, the outcome of meiosis should be four genetically unique haploid cells.

Messenger RNA (mRNA): The DNA of a gene is transcribed (see transcription) into mRNA molecules, which then serve as a template for the synthesis of proteins.

Meta-analysis: In the context of epidemiology, a statistical analysis of the results from independent studies, which aims to produce a single estimate of an effect.

Metabolic activation: Metabolism of a compound leading to an increase in its activity, whether beneficial (e.g., activation of a pro-drug) or deleterious (e.g., activation to a toxic metabolite).

Metabolic activation system: A cell-free preparation (e.g., from the livers of rats pre-treated with an inducing agent (qv)) added to in vitro tests to mimic the metabolic activation typical of mammals.

Metabolism: Chemical modification of a compound by enzymes within the body, for example by reactions such as hydroxylation (see P450), epoxidation or conjugation. Metabolism may result in activation, inactivation, change in activity, accumulation or excretion of the compound.

Metabolite: Product formed by metabolism of a compound.

Metabolomics: The measurement of the amounts (concentrations) and locations of all metabolites in a cell.

Metabonomics: Metabonomics is a subset of metabolomics and is defined as the quantitative measurement of the multiparametric metabolic responses of living systems to pathophysiological stimuli or genetic modification.

Metaphase: Stage of cell division (mitosis and meiosis) during which the chromosomes are arranged on the equator of the nuclear spindle (the collection of microtubule filaments which are responsible for the movement of chromosomes during cell division). As the chromosomes are most easily examined in metaphase, cells are arrested at this stage for microscopical examination for chromosomal aberrations (qv) - known as metaphase analysis.

Metastasis: The process whereby malignant cells become detached from the primary tumour mass, disseminate (mainly in the blood stream or in lymph vessels) and seed out in distant sites where they form secondary or metastatic tumours. Such tumours tend to develop at specific sites and their anatomical distribution is often characteristic, i.e., it is non-random.

Microbiome (Human): Human microbiome is the full array of microorganisms (the microbiota) that live on and in humans and, more specifically, the collection of microbial genomes that contribute to the broader genetic portrait, or metagenome, of a human. Often a subset of the microbiome is the subject of interest, for example the intestinal or dermal microbiome.

Micronuclei: Whole or fragmented chromosomes that fail to segregate normally during cell division and may be lost from the main nuclei but remain in the body of the cell forming micronuclei. Centromere positive micronuclei contain DNA and/or protein material derived from the centromere. The presence of centromere positive micronuclei following exposure to chemicals in vitro or in vivo can be used to evaluate the aneugenic potential of chemicals.

Minimal risk level: defined in this document as an estimate of daily human exposure to a chemical, identified by expert judgement, that is likely to be associated with a negligible risk of carcinogenic effect over a specified duration of exposure (usually a lifetime).

Mitogen: A stimulus which provokes cell division in somatic cells.

Mitosis: The process in cell division in somatic cells by which the nucleus divides, typically consisting of four stages, prophase, metaphase, anaphase, and telophase, and normally resulting in two new nuclei, each of which contains a complete copy of the parental chromosomes. The outcome of mitosis should be two genetically identical diploid cells.

Mode of Action: a biologically plausible sequence of key events leading to an observed effect supported by robust experimental observations and mechanistic data. It describes key cytological and biochemical events, i.e., those that are

both measurable and necessary to the observed outcome, in a logical framework. It contrasts with mechanism of action.

Mode of genotoxic a**ction (MoGA):** The mode of action of a genotoxicant refers to the underlying events involved in the process whereby the chemical induces genotoxic effects. In order for a specific mode of action to be supported there needs to be evidence from robust mechanistic data to establish a biologically plausible explanation. Mode of genotoxic action should be distinguished from the term mechanism of action. The latter relates to having sufficient understanding of the molecular basis of the chemical genotoxicity to establish causality. Thus, mechanism of action is at the other end of a continuum from little or no evidence of mode of genotoxic action to scientific proof of mechanism of action.

Molecular initiating event (MIE): the initial point of chemical/stressor interaction at the molecular level within the organism that results in a perturbation that starts the AOP.

Mouse lymphoma assay: An in vitro assay for gene mutation in mammalian cells using a mouse lymphoma cell line L5178Y, which is heterozygous for the gene (carries only one functional allele rather than a pair) for the enzyme thymidine kinase (TK+/-). Mutation of that single gene is measured by resistance to toxic trifluorothymidine. Mutant cells produce two forms of colony - large, which represent mutations within the gene and small, which represent large genetic changes in the chromosome such as chromosome aberrations. Thus, this assay can provide additional information about the type of mutation which has occurred if colony size is scored.

Mucosal: Regarding the mucosa or mucous membranes, consisting of epithelium containing glands secreting mucus, with underlying layers of connective tissue and muscle.

Multigenerational effects: Effect seen in exposed generations, including those that may have been exposed in utero, as offspring or gametes. For effects in unexposed generations see ‘Transgenerational effects’.

Murine: Often taken to mean “of the mouse”, but strictly speaking means of the Family Muridae which includes rats and squirrels.

Mutagen: is a physical or chemical agent that changes the genetic information (usually DNA) of an organism that can be inherited by daughter cells.

Mutation: A permanent change in the amount or structure of the genetic material in an organism or cell, which can result in a change in phenotypic characteristics. The alteration may involve a single gene, a block of genes, or a whole chromosome. Mutations involving single genes may be a consequence of effects on single DNA bases (point mutations) or of large changes, including deletions, within the gene. Changes involving whole chromosomes may be numerical or structural. A mutation in the germ cells of sexually reproducing organisms may be transmitted to the offspring, whereas a mutation that occurs in somatic cells may be transferred only to descendent daughter cells.

Mutational signatures: Mutational signatures are characteristic profiles of mutation types arising from specific mutagenesis processes such as DNA replication infidelity, exogenous and endogenous genotoxins exposures, defective DNA repair pathways and DNA enzymatic editing.

Mycotoxin: Toxic compound produced by a fungus.

Nanomaterial: A natural, incidental or manufactured material containing particles, in an unbound state or as an aggregate or as an agglomerate and where, for 50% or more of the particles in the number size distribution, one or more external dimensions is in the size range 1 nm - 100 nm.

N

Neoplasia: the abnormal proliferation of benign or malignant cells.

Neoplasm: See 'tumour'.

Neoplastic: Abnormal cells, the growth of which is more rapid that that of other cells of the same tissue type.

Neural tube defect (NTD): Is a birth defect in which an opening in the spine or cranium remains from early in human development.

Neurobehavioural: Of behaviour determined by the nervous system.

Neurotransmitter: A chemical that is released from a nerve cell which thereby transmits an impulse from a nerve cell to another nerve, muscle, organ, or other tissue. A neurotransmitter is a messenger of neurologic information from one cell to another.

No observed adverse effect level (NOAEL): The highest administered dose at which no statistically significant adverse effect has been observed in comparison to the control. Also given as NOEL when no ‘adverse’ effects are seen.

Non-Hodgkin lymphomas: (NHLs) are a diverse group of hematologic cancers which encompass any lymphoma other than Hodgkin’s Lymphoma.

No observed genotoxic effect level (NOGEL): This is the highest experimental dose level where no statistically significant increase in the genotoxic effect measured in the study is identified.

Nucleic acid: One of the family of molecules which includes the DNA and RNA molecules. Nucleic acids were so named because they were originally discovered within the nucleus of cells, but they have since been found to exist outside the nucleus as well.

Nucleosome: A repeating subunit of DNA packaging consisting of DNA wound in sequence around histone proteins.

Nucleotide: the "building block" of nucleic acids, such as the DNA molecule. A nucleotide consists of a nucleoside attached a phosphate group. A nucleoside comprises one of four bases - adenine, guanine, cytosine, or thymine - attached to a sugar group. In DNA the sugar group is deoxyribose, while in RNA (a DNA-related molecule which helps to translate genetic information into proteins), the sugar group is ribose, and the base uracil substitutes for thymine. Each group of three nucleotides in a gene is known as a codon. A nucleic acid is a long chain of nucleotides joined together, and therefore is sometimes referred to as a "polynucleotide."

Null allele: Mutations that result in absence of gene product or a non-functional product.

Null hypothesis: type of conjecture used in statistical tests, which are formal methods of reaching conclusions or making decisions on the basis of data. In toxicology, a common null hypothesis is that there is no effect of treatment with a substance. Statistical testing may enable a conclusion that this is most likely incorrect, i.e., the null hypothesis is rejected with a stated probability of error, or it is not possible to reach a conclusion. It is not possible by conventional statistical testing to prove the null hypothesis is most likely correct, i.e., that there is no effect. This is the axiomatic difficulty of “proving a negative”.

O

Odds ratio (OR): The odds of disease in an exposed group divided by the odds of disease in an unexposed group.

Oedema: Excessive accumulation of fluid in body tissues.

Oligonucleotide: A molecule made up of a small number of nucleotides, typically fewer than 25.

‘Omics’ technologies: A scientific subdiscipline that combines the technologies of genomics and bioinformatics to identify and characterise mechanisms of action of known and suspected toxicants. The collective term ‘omics’ refers to the genomic (DNA sequence analysis) and post-genomic (e.g., transcriptomics, proteomics, metabolomics, epigenomics) technologies that are used for the characterisation and quantitation of pools of biological molecules (e.g. DNA, mRNAs, proteins, metabolites), and the exploration of their roles, relationships and actions within an organism.

Oncogene: A gene which is associated with the development of cancer (see proto-oncogene).

P

Pharmacodynamics: The process of interaction of drugs with target sites and the subsequent reactions leading to the desired biological effects (see toxicodynamics).

Pharmacokinetics: Description of the fate of drugs in the body, including a mathematical account of their absorption, distribution, metabolism and excretion (see toxicokinetics).

Pharmacogenomics: The science of understanding the correlation between an individual patient's genetic make-up (genotype) and their response to drug treatment. Some drugs work well in some patient populations and not as well in others. Studying the genetic basis of patient response to therapeutics allows drug developers and medical practitioners to design and use therapeutic treatments more effectively.

Phenotype: The observable physical, biochemical and physiological characteristics of a cell, tissue, organ or individual, as determined by its genotype

and the environment in which it develops.

Phenotypic change: A change in the observable physical or biochemical characteristics of an organism, as determined by both genetic makeup and environmental influences.

Physiologically based pharmacokinetic (PBPK) model: A mathematical model which is used to predict the absorption, distribution, metabolism and excretion of a chemical substance in humans.

Phytoestrogen: Any plant substance or metabolite that can mimic or modulate the actions of endogenous oestrogens, usually by binding to oestrogen receptors, and which can therefore induce biological responses.

Pig-A gene mutation assay: An assay which utilises the Pig-A gene which codes for one subunit of a glycosylphosphatidyl inositol anchor protein. Loss of function arising from Pig-A mutations can readily be assessed using straightforward immunochemistry and flow cytometric methods, thus making it useful to measure gene mutations induced by chemicals or radiation.

Plasmid: A structure composed of DNA that is separate from the cell's genome (qv). In bacteria, plasmids confer a variety of traits and can be exchanged between individuals, even those of different species. Plasmids can be constructed and manipulated in the laboratory to deliver specific genetic sequences into a cell.

Point of departure: a dose associated with a defined level of effect, which can be determined empirically or by modelling dose-response data from experimental studies, from which a health-based guidance value can be established, or which can be used for a margin of exposure assessment. Examples include a BMDL, NOAEL or LOAEL.

Polymer: A very large molecule comprising a chain of many similar or identical molecular sub units (monomers) joined together (polymerised). An example is the polymer glycogen, formed from linked molecules of the monomer glucose.

Polymerase chain reaction (PCR): A method for creating millions of copies of a particular segment of DNA. PCR can be used to amplify the amount of a particular DNA sequence until there are enough copies available to be detected.

Polymorphism: (see genetic polymorphism)

^{32}P postlabelling assay: An experimental method designed to measure low levels of DNA adducts induced by chemical treatment. It involves labelling of adducted nucelosides from digested DNA with ^{32}P and their quantification following chromatographic separation.

Prevalence: The number of discrete cases, for example of a disease, that are present in a population at a given time.

Primer: Short pre-existing polynucleotide chain to which new deoxyribonucleotides can be added by DNA polymerase.

Primordial germ cells: Highly specialised cells that are precursors of gametes, which, following meiosis, develop as haploid sperm and eggs that generate a new organism upon fertilisation.

Proteomics: The analysis of the entire protein complement of a cell, tissue, or organism under a specific, defined set of conditions.

Proto-oncogene: One of a group of normal genes that are concerned with the control of cellular proliferation and differentiation. They can be activated in various ways to forms (oncogenes) which are closely associated with one or more steps in carcinogenesis. Activating agents include chemicals and viruses. The process of proto-oncogene activation is thought to play an important part at several stages in the development of tumours.

Q

Quantal Data: When the response for an individual unit (well, animal etc) is a binary value, such as alive / dead, or response / no response, the data are treated as quantal. The responses are assumed to follow a binomial distribution within each dose group. This assumption is required for the calculations of confidence intervals and the p values resulting from statistical tests.

R

ras oncogene: The Ras protein family are a class of protein called small GTPase and have important roles in cell signalling. The ras gene is the most common oncogene involved in human cancer - mutations that permanently activate ras are found in 20-25% of all human tumours and up to 90% in certain types of cancer (e.g., pancreatic cancer).

Receptor: A small, discrete protein in the cell membrane or within the cell with which specific molecules interact to initiate a change in the working of a cell.

Recombinant DNA: DNA molecules that have been created by combining DNA from more than one source.

Reference nutrient intake (RNI): An amount of the nutrient that is sufficient, or more than sufficient, to ensure adequate nutrient function for most (usually at least 97%) people in a group. If the average intake of a group is at the RNI, then the risk of deficiency in the group is very small.

Regulatory gene: A gene which controls the protein-synthesising activity of other genes.

Relative potency factor (RPF): The toxic potency of a substance expressed relative to that of an index chemical to enable cumulative risk assessment (*qv)*. The RPF is similar to the TEF (*qv*) but is used when the information on common MIEs, toxicokinetics and outcomes of the members of an assessment group is less reliable than that required for application of the TEF approach.

Relative risk: A measure of the association between exposure and outcome. The rate of disease in the exposed population divided by the rate of disease among the unexposed population in a cohort study or a population-based case control study. A relative risk of 2 means that the exposed group has twice the disease risk compared to the unexposed group.

Reporter gene: A gene that encodes an easily assayed product that is coupled to the upstream sequence of another gene and transfected (qv) into cells. The reporter gene can then be used to see which factors activate response elements in the upstream region of the gene of interest.

Risk: Probability that a harmful event (death, injury or loss) arising from exposure to a chemical or physical agent may occur under specific conditions.

Risk assessment: process of evaluating a potential hazard, likelihood of suffering, or any adverse effects from certain human activities. Comprised of the four aspects, hazard identification, hazard characterisation, exposure assessment and risk characterisation. Can be carried out retrospectively or prospectively.

Risk management: process designed to identify, contain, reduce, or eliminate the potential for harm to the human population; usually concerned with the delivery system and site rather than performance.

Ribonucleic acid (RNA): a molecule similar to DNA, in that it is a nucleic acid comprised of a chain of nucleotides. However, unlike DNA, RNA exists as a single-stranded chain. RNA has various biological roles in coding, decoding, regulation and expression of genes.

S

Sarcoma: cancer that arises from transformed cells of mesenchymal (connective tissue) origin.

Serotonergic: Denoting a nerve ending that releases and or stimulated by serotonin.

Signal induction pathway: The molecular pathways that signal (i.e., turn on or off) biochemical pathways or biological functions (e.g., biochemical pathways leading to nerve conduction).

Single nucleotide polymorphism (SNP): DNA sequence variations that occur when a single nucleotide in the genome sequence is altered. For example, a SNP might change the DNA sequence A***A***GGCTAA to A***T***GGCTAA.

Strand breaks: Relating to DNA, a single strand break occurs when there is a break in double-stranded DNA in which only one of the two strands has been cleaved; the two strands have not separated from each other. Double strand breaks occur when both strands in the double helix are severed and are particularly hazardous to the cell because they can lead to genome rearrangements.

Sister chromatid exchange (SCE): Exchange of genetic material between two subunits of a replicated chromosome.

Somatic cells: Any biological cell that forms part of the body of an organism, excluding reproductive cells and undifferentiated stem cells.

Stakeholder: A person or organisation representing the interests and opinions of a group with an interest in the outcome of (for example) a review or policy decision.

Statistical significance: a conclusion drawn when, after carrying out a statistical test of the null hypothesis of no effect, the hypothesis is considered unlikely to be true. The criterion for the decision is often a probability (p) value, chosen to be, but not necessarily, $p<0.05$.

Stem cell: an unspecialized cell capable of perpetuating itself through cell division and having the potential to give rise to differentiated cells with specialized functions.

Suppressor gene: A gene which helps to reverse the effects of damage to an individual's genetic material, typically these are effects which might lead to uncontrolled cell growth (as would occur in cancer). A suppressor gene may, for example, code for a protein which checks genes for misspellings, and/or which triggers a cell's self-destruction if too much DNA damage has occurred.

Systematic review: A formalised review that has been prepared using a documented systematic approach to minimising biases and random errors.

Systems biology: The computational and mathematical analysis and modelling of complex biological systems.

Systems toxicology: The integration of classical toxicology with quantitative analysis of large networks of molecular and functional changes occurring across multiple levels of biological organisation.

T

T25: the dose eliciting a 25% increase in the incidence of a specific tumour above the background level.

TD50: For any particular sex, strain, species and set of experimental conditions, the TD50 is the dose rate (in mg/kg body weight/day) that, if administered chronically for a standard period - the "standard lifespan" of the species-will halve the mortality-corrected estimate of the probability of remaining tumourless throughout that period.

Teratogen: A substance that can cause congenital malformations (structural defects) in a developing fetus following maternal exposure.

Testicular dysgenesis syndrome (TDS): The hypothesis that maldevelopment (dysgenesis) of the fetal testis results from hormonal or other malfunctions of the testicular somatic cells which in turn predispose a male to the disorders that comprise the TDS, i.e., congenital malformations (cryptorchidism and hypospadias) in babies and testis cancer and low sperm counts in young men.

Threshold: the level of dose or exposure below which there is no effect above that in the control group or population. There are several different uses of the

term threshold, for example observable threshold, biological threshold, population threshold.

Threshold of toxicological concern (TTC): a pragmatic, scientifically valid methodology to prioritise substances of unknown toxicity found in food for further evaluation. It is used when there are limited chemical-specific toxicity data and can be used for substances with or without structural alerts for genotoxicity and for cancer and non-cancer endpoints.

Tolerable daily intake (TDI): An estimate of the amount of contaminant, expressed on a body weight basis (e.g., mg/kg bodyweight), that can be ingested daily over a lifetime without appreciable health risk. The term is preferred for substances that are unintentionally present.

Tolerable upper level (TUL): The highest level of nutrient that is likely to pose no risk of adverse health effects for almost all individuals in the general population. As intake increases above the TUL, the risk of adverse effects increases.

Toxic equivalency factor (TEF): A measure of relative toxicological potency of a chemical compared to a well characterised reference compound. TEFs can be used to sum the toxicological potency of a mixture of chemicals which are all members of the same chemical class, having common structural, toxicological and biochemical properties. TEF systems have been published for the chlorinated dibenzodioxins, dibenzofurans and dioxin-like polychlorinated biphenyls, and for polycyclic aromatic hydrocarbons.

Total toxic equivalent (TEQ): Is a method of comparing the total relative toxicological potency within a sample. It is calculated as the sum of the products of the concentration of each congener multiplied by the toxic equivalency factor (TEF).

Toxicodynamics: The process of interaction of chemical substances with target sites and the subsequent reactions leading to adverse effects.

Toxicogenic: producing or capable of producing toxins, e.g., a fungal strain.

Toxicokinetics: The description of the fate of potentially toxic chemicals in the body, including a mathematical account of their absorption, distribution, metabolism and excretion, particularly at doses that are toxic. (see pharmacokinetics)

Transcription: the process during which the information in a piece of DNA (qv) is used to construct an mRNA (qv) molecule.

Transcriptomics: Techniques used to identify mRNA from actively transcribed genes.

Transgenerational effects: Effects seen in generations that have not been exposed, either directly to the substance under consideration or indirectly as offspring or gametes via parental exposure. For effects in exposed populations, see ‘multigenerational effects’.

Transfer RNA (tRNA): RNA molecules which bond with amino acids and transfer them to ribosomes, where protein synthesis is completed.

Transfection: A process by which exogenous genetic material (DNA or RNA) is introduced into a cell with the object of altering the phenotype or genotype of the cell.

Transgenic: Genetically modified to contain genetic material from another species (see also genetically modified organism).

Transgenic animal models: Animals which have extra (exogenous) fragments of DNA incorporated into their genomes. This may include reporter genes to assess in-vivo effects such as mutagenicity in transgenic mice containing a recoverable bacterial gene (lacZ or lac I). Other transgenic animals may have alterations of specific genes believed to be involved in disease processes (e.g., cancer). For example, strains of mice have been bred which carry an inactivated copy of the p53 tumour suppressor gene, or an activated form of the ras oncogene which may enhance their susceptibility of the mice to certain types of carcinogenic chemicals.

Translation: In molecular biology, the process during which the information in mRNA molecules is used to construct proteins.

Tumour (Synonym - neoplasm): A mass of abnormal, disorganised cells, arising from pre-existing tissue, which are characterised by excessive and uncoordinated proliferation and by abnormal differentiation. Benign tumours show a close morphological resemblance to their tissue of origin; grow in a slow expansile fashion; and form circumscribed and (usually) encapsulated masses. They may stop growing and they may regress. Benign tumours do not infiltrate through local tissues, and they do not metastasise (qv). They are rarely fatal. Malignant tumours (synonym - cancer) resemble their parent tissues less closely

and are composed of increasingly abnormal cells in terms of their form and function. Well differentiated examples still retain recognisable features of their tissue of origin, but these characteristics are progressively lost in moderately and poorly differentiated malignancies: undifferentiated or anaplastic tumours are composed of cells which resemble no known normal tissue. Most malignant tumours grow rapidly, spread progressively through adjacent tissues and metastasise to distant sites. Tumours are conventionally classified according to the anatomical site of the primary tumour and its microscopical appearance, rather than by cause. Benign tumours may evolve to the corresponding malignant tumours; examples involve the adenoma → carcinoma sequence in the large bowel in humans, and the papilloma → carcinoma sequence in mouse skin.

Tumour initiation: A term originally used to describe and explain observations made in laboratory models of multistage carcinogenesis, principally involving repeated applications of chemicals to the skin of mice. Initiation, in such contexts, was the first step whereby small numbers of cells were irreversibly changed or initiated. Subsequent, separate events (see tumour promotion) resulted in the development of tumours. It is now recognised that these early, irreversible heritable changes in initiated cells were due to genotoxic damage, usually in the form of somatic mutations and the initiators used in these experimental models can be regarded as genotoxic carcinogens.

Tumour microenvironment: This is a complex system of many cell types, including cancer cells, fibroblasts, endothelial cells, leukocytes and antigen-presenting cells, together with connective tissue. The microenvironment is integral in determining the functionality, physiology and spread (metastasis) of cancer.

Tumour promotion: Originally used, like ‘tumour initiation’ to describe events in multistage carcinogenesis in experimental animals. In that context, promotion is regarded as the protracted process whereby initiated cells undergo clonal expansion to form overt tumours. The mechanisms of clonal expansion are diverse, but include direct stimulation of cell proliferation, repeated cycles of cell damage and cell regeneration and release of cells from normal growth-controlling mechanisms. Initiating and promoting agents were originally regarded as separate categories, but the distinction between them is becoming increasingly hard to sustain. The various modes of promotion are non-genotoxic, but it is incorrect to conclude that ‘non-genotoxic carcinogen’ and ‘promoter’ are synonymous.

U

Uncertainty factor: Value used in extrapolation from a reference point (or POD), determined in experimental animals, to humans (assuming that humans may be more sensitive) or from a sub-population of individuals to the general population: for example, a value applied to the NOAEL to establish an ADI or TDI. The value depends on the size and type of population to be protected and the quality of the toxicological information available.

Unscheduled DNA synthesis (UDS): DNA synthesis that occurs at some stage in the cell cycle other than the S period (the normal or 'scheduled' DNA synthesis period), in response to DNA damage. It is usually associated with DNA repair.

V

Volume of distribution: Apparent volume of fluid required to contain the total amount of a substance in the body at the same concentration as that present in the plasma, assuming equilibrium has been attained.

W

Weight of evidence: This approach uses a combination of several independent sources of evidence (e.g., toxicological or genotoxicity data) to arrive at a conclusion regarding potential hazard (such as mutagenicity).

WHO-TEQs: The system of Toxic Equivalency Factors (TEFs) used in the UK and a number of other countries to express the concentrations of the less toxic dioxin-like compounds (16 PCDDs/PCDFs and 12 PCBs) as a concentration equivalent to the most toxic dioxin 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) is that set by the World Health Organisation (WHO), and the resulting overall concentrations are referred to as WHO-TEQs (Total toxic equivalents) (see also Toxic Equivalency Factor).

X

Xenobiotic: A chemical foreign to the biologic system.

Xenoandrogen: A ‘foreign’ compound with androgenic activity (see androgen).

Xenoestrogen: A 'foreign' compound with oestrogenic activity (see oestrogen).

Organisational abbreviations

COC: Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment: is an independent scientific committee that provides advice the government and government agencies on whether substances are likely to cause cancer.

COM: Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment: is an independent scientific committee that assesses and advises the government and government agencies on mutagenic risks to humans.

COT Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment: is an independent scientific committee that provides advice to the government and government agencies on matters concerning the toxicity of chemicals.

EFSA European Food Safety Authority:

Expert Group on Vitamins and Minerals (EVM): An independent UK expert advisory committee which was asked to advise on safe levels of intakes of vitamins and minerals in food supplements and fortified foods.

Annex 6 – 2023 - Previous Publications

In this guide

In this guide

1. About the Committees - 2023
2. COT Preface - 2023
3. COT evaluations - 2023

4. COT Assurance - 2023
5. Committee Procedures - 2023
6. Ongoing Work - COT 2023
7. Other Committee Activities: Joint Expert Groups, Presentations and Workshop -2023
8. 2023 Membership of the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment
9. Declaration of COT members' interests during the period of this report -2023
10. Sub-groups active in 2023
11. Committee on Mutagenicity of chemicals in Food, Consumer Products and the Environment Annual Report 2023
12. Ongoing work - COM 2023
13. Discussion Items -2023
14. 2023 Membership of the Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment
15. Declaration of COM members' interests during the period of this report -2023
16. Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment Annual Report 2023
17. COC Ongoing Topics - 2023
18. COC Workshop - 2023
19. Joint session Horizon scanning
20. COC input to COT work
21. 2023 Membership of the Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment
22. Declaration of COC members' interests during the period of this report -2023
23. Annex 1 - 2023 - Terms of Reference
24. Annex 2 - 2023 - Code of Conduct for members of the COC/COM/COT
25. Annex 3 – 2023 - Openness
26. Annex 4 – 2023 - Good Practice Agreement for Scientific Advisory Committees
27. Annex 5 – 2023 - Glossary of Terms
28. Annex 6 – 2023 - Previous Publications

Publications produced by the Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment

1991 Annual Report of Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. HMSO ISBN 0 11 321529 0 Price £9.50.

1992 Annual Report of Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. HMSO ISBN 0 11 321604-1 Price £11.70.

1993 Annual Report of Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. HMSO ISBN 0 11 321808-7 Price £11.95.

1994 Annual Report of Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. HMSO ISBN 0 11 321912-1 Price £12.50.

1995 Annual Report of Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. HMSO ISBN 0 11 321988-1 Price £18.50.

1996 Annual Report of Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. The Stationery Office ISBN 0 11 322115-0 Price £19.50.

1997 Annual Report of Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. Department of Health.*

1998 Annual Report of Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. Department of Health.*

1999 Annual Report of Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. Department of Health.*

2000 Annual Report of Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. Department of Health.*

2001 Annual Report of Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. Food Standards Agency/Department of Health, FSA/0681/0802.$^{++}$

2002 Annual Report of Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. Food Standards Agency/Department of Health, FSA/0838/0803.++

2003 Annual Report of Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. Food Standards Agency/Department of Health, FSA/0900/0504.++

2004 Annual Report of Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. Food Standards Agency/Department of Health, FSA/0992/0804.++

2005 Annual Report of Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. Food Standards Agency/Department of Health, FSA/1098/0906.++

2006 Annual Report of Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. Food Standards Agency/Department of Health, FSA/1184/0707.++

2007 Annual Report of Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. Food Standards Agency/Department of Health, FSA/1260/0608.++

2008 Annual Report of Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. Food Standards Agency/Department of Health, FSA/1410/0709.++

2009 Annual Report of Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. Food Standards Agency/Department of Health, July 2010.++

2010 Annual Report of Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. Food Standards Agency/Department of Health, June 2011.++

2011 Annual Report of Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. Food Standards Agency/Department of Health, July 2012.

2012 Annual Report of Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. Food Standards Agency/Department of Health, April 2014.

2013 Annual Report of Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. Food Standards Agency/Department of Health, March 2015.

2014 Annual Report of Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. Food Standards Agency/Department of Health, November 2015.

2015 Annual Report of Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. Food Standards Agency/Department of Health, July 2016.

2016 Annual Report of Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. Food Standards Agency/Department of Health, August 2017.

2017 Annual Report of Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. Food Standards Agency/Department of Health, October 2017.

2018 Annual Report of Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. Food Standards Agency/Department of Health and Social Care, November 2018.

2019 Annual Report of Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. Food Standards Agency/Department of Health and Social Care, December 2019.

Guidelines for the Testing of Chemicals for Toxicity DHSS Report on Health and Social Subjects 27 HMSO ISBN 0 11 320815 4 Price £4.30.

Guidelines for the Evaluation of Chemicals for Carcinogenicity DH Report on Health and Social Subjects 42 HMSO ISBN 0 11 321453 7 Price £7.30.

Guidelines for the Testing of Chemicals for Mutagenicity DH Report on Health and Social Subjects 35 HMSO ISBN 0 11 321222 4 Price £6.80.

Guidelines for the Preparation of Summaries of Data on Chemicals in Food, Consumer Products and the Environment submitted to DHSS Report on Health and Social Subjects 30 HMSO ISBN 0 11 321063 9 Price £2.70.

Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment: Peanut Allergy, Department of Health (1998).**

Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment: Organophosphates, Department of Health (1998).**

Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment: Adverse Reactions to Food and Food Ingredients, Food Standards Agency (2000).++

Guidance on a Strategy for testing of chemicals for Mutagenicity. Department of Health (2000).*

Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment: Risk Assessment of Mixtures of Pesticides and Similar Substances, Food Standards Agency, FSA/0691/0902 (2002).++

Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment: Phytoestrogens and Health, Food Standards Agency, FSA/0826/0503 (2002).++

Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment: Variability and Uncertainty in Toxicology of Chemicals in Food, Consumer Products and the Environment, FSA/1150/0307 (2007).++

Guidance on a Strategy for the Risk Assessment of Chemical Carcinogens. Department of Health (2004).+

*Available at: Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment - GOV.UK (www.gov.uk).

** Available at: Le blog de l'actu européenne - EuropArchive.org.

+ Available at: Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment - GOV.UK.

++ Available at: All COT Reports.

Report of the Synthesising Epidemiological Evidence Subgroup (SEES) of the Committee on Toxicity and Committee on Carcinogenicity, Food Standards Agency/Department of Health and Social Care, September 2018. COT joint reports | Committee on Toxicity.

Available at: [ARCHIVED CONTENT] Synthesising Epidemiology Evidence Subgroup (SEES) Report | Food Standards Agency (nationalarchives.gov.uk).

Joint COT and COC Synthesis and Integration of Epidemiological and Toxicological Evidence subgroup (SETE). Food Standards Agency/Department of Health and

Social Care, November 2021. SETE | Committee on Toxicity (food.gov.uk).