Committee on Toxicity

Committee on Carcinogenicity

Committee on Mutagenicity

Annual Report

2024

Committee on Toxicity of Chemicals in Food, Consumer, Products and the Environment Annual Report 2024

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About the Committees

This is the 34th 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.

Preface

Professor Alan Boobis (Chair)

OBE PhD FBTS FBPhS

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 2024.

Amongst the range of topics discussed by the Committee were bamboo biocomposites, marine biotoxins, the mycotoxins T2 and HT2, benchmark dose-modelling techniques, and New Approach Methodologies (NAMs). The long-standing assessment of titanium dioxide and bisphenol A were completed.

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 ergot alkaloids, ginger, echinacea, raspberry leaf tea and calcidiol.

In 2024, the Committee continued to oversee and assure the risk assessment of regulated products, which were previously assessed in Europe, considering a number of Joint Expert Groups (JEGs) opinions on food additives, food contact materials, and recycling processes.

The Committee are now also receiving requests for advice from the Nutrition Labelling Composition and Standards Policy Group, who co-ordinate the policy approach in this area across the UK, such as that on such as the authorisation of iron enriched yeast.

The joint COT and SACN Working Group continued their 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 peer review consultation. Committee Members have been involved in several other working groups and joint working groups, covering areas as diverse as cannabidiol (CBD) and PFAS. The Committee has also worked closely with their sister Committee on Mutagenicity on the review of titanium dioxide.

The Committee held a workshop "Gut reactions: Xenobiotics and the microbiome".

In 2024, the Committee welcomed new Members Dr Alison Yeates, Dr Meera Cush, Dr Chris Morris and Dr Andreas Kolb along with two new lay Members Mr Nick Richardson and Mr Gordon Burton. The Committee said goodbye to Deputy Chair Dr Sarah Judge, Dr Phil Botham, Professor Matthew Wright and lay Members Ms Juliet Rix and Ms Jane Case, whose terms on the Committee have expired. I would like to thank them all for their invaluable contributions and to wish them well for the future.

Professor Shirley Price has accepted the role of Deputy Chair to the Committee and following on from some discussions on the Committee's ways of working will be focusing particularly on the regulated products and strengthening links with the Joint Expert Groups.

This will be my final Annual Report as Chair of the COT, and I would like to acknowledge the contributions of Members and staff, not over just the past year but throughout the 10 years of my tenure as Chair.

It has been truly a privilege to chair the Committee and while there have been challenges, I have found the experience very rewarding. I owe a huge thank you to all Members of the Committee and its sub-groups, both past and present, for their commitment, hard work and expertise in ensuring the quality of the advice provided by the COT.

I owe an equal debt of gratitude to the joint Scientific Secretaries and their respective staffs, who have provided such tremendous support to both me personally as Chair and to the Committee as a whole. Their professionalism and expertise have been essential in ensuring the quality of the COT's work.

I will be sorry to leave the Committee, but I know that it is in good hands, and I am confident that it will continue to provide the highest level of scientific advice in the future.

COT evaluations

Safety of Titanium dioxide (E171) as a Food Additive

1.1 Food grade titanium dioxide (TiO_2) was an authorised Food Additive (E171) in the EU, but from the 7th of August 2022, its use in food has been banned in light of the European Food Safety Authority's (EFSA's) conclusion that such use could no longer be considered as safe. It currently remains authorised in Great Britain. Food grade TiO_2 comprises a mixture of micro- and nanosized (<100 nm) particles and is used in food as a colour (white pigment). Titanium dioxide is also widely used in cosmetics and medicines.

1.2 Titanium dioxide has been the subject of multiple safety evaluations including three recent evaluations by EFSA in 2016, 2019 and 2021.

1.3 In their most recent Opinion (2021), the EFSA Panel concluded that E171 could no longer be considered as safe for use as a food additive, due to uncertainties in some of the data, such as on genotoxicity (DNA damaging effects). Following this, in 2021 the COT published an interim position on titanium dioxide in which the Committee expressed its scientific concern about the basis of the EFSA conclusions. A detailed review has now been undertaken by the COT, which includes the conclusions on genotoxicity (DNA damaging effects) from the Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment (COM), to assess the safety of TiO_2 as a food additive.

1.4 The COT has reviewed toxicological studies that have been conducted using any form of TiO_2, including nanoparticles, but its conclusions are based primarily on those which used food grade TiO_2 (E171), which predominantly consists of aggregates, of smaller primary particles, with a median particle size of 200 – 300 nm. The following endpoints were reviewed by the COT: the development of aberrant crypt foci (ACF) in the intestine (as a potential indicator of carcinogenicity),

inflammation and immunotoxicity, reproductive and developmental toxicity and neurotoxicity. The COM reviewed the data on genotoxicity (damage to DNA which could ultimately lead to cancer) and reported their findings to the COT in May 2024.

1.5 The COT considered that the data from the relevant studies available indicated that TiO_2 did not induce ACF, nor were there significant effects in studies that assessed inflammation and immunotoxicity, reproductive and developmental toxicity, and neurotoxicity. On balance, the Committee considered that a no observed adverse effect level (NOAEL) of 1,000 mg/kg bw per day, was robust.

1.6 Overall, the COM concluded that there was little evidence in the literature to suggest that food grade TiO_2 (E171) caused induction of genotoxicity (DNA damaging effects), and that there was unlikely to be any health concern related to genotoxicity induction from use of TiO_2 (E171) as a food additive. Following discussions of the COM report at their meeting in March 2024, the COT included the COM conclusions in their overall review of the evidence.

1.7 The COT concluded that 1,000 mg/kg bw per day was a robust Point of Departure (POD) on which to base a health-based guidance value (HBGV). This was the highest dose tested, so it is not known how much more TiO_2 would have to be administered before effects were seen.

1.8 A standard uncertainty factor of 100 (10 for inter-species differences and 10 for inter-individual variability) was agreed by Members and applied to the POD which resulted in a HBGV (acceptable daily intake) of 10 mg/kg bw per day.

1.9 Titanium dioxide (E171) can be found in a number of food categories, and the exposures calculated and considered by the COT for infants, toddlers, children, adolescents, adults, and the elderly used food consumption data from UK surveys and maximum occurrence levels of titanium dioxide reported by EFSA (2021).

1.10 Estimated exposures for adults (18+) and the elderly are below the established HBGV. Although exposures for infants, toddlers, children and adolescents consuming a lot of TiO_2-containing food are estimated to be 1.3 - to 2.6-fold higher than the HBGV, actual exposures are likely to be lower and in addition,

the HBGV is likely to be conservative. Therefore, adverse health effects would not be expected.

1.11 The COT concludes that it is unlikely that there would be a risk to health from current UK dietary exposures of E171 TiO_2.

1.12 The full COT statement can be found at: Safety of Titanium dioxide (E171) as a Food Additive.

Statement on the potential health effects of raspberry leaf tea in the maternal diet

1.13 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. To help SACN in this, the COT was asked to review the risks of toxicity from certain chemicals and products in the maternal diet. This statement focuses on the possible risks from taking raspberry leaf tea, or extracts of raspberry leaf, in tablets or tinctures, during pregnancy.

1.14 Raspberry leaf, as tea, tablet or tincture, is most commonly taken during pregnancy as a dietary supplement in the belief that it stimulates and facilitates labour and shortens its duration. A recent study in Australia reported use by 38% of pregnant women, while a UK study in 2007-2008 reported use by approximately 24% of pregnant women. In addition to such preparations, several raspberry leaf products are registered as traditional herbal medicines in the UK. However, these are directed at non-pregnant women for the symptomatic relief of menstrual cramps. Some clinics offer enemas containing raspberry leaf, though it is not clear whether any are aimed at pregnant women.

1.15 A number of studies, starting in the 1940s, have investigated the effects of extracts of raspberry leaf on the uterus (womb) or other smooth muscle, either in intact animals or isolated from animals. The results of these studies were highly variable, with some showing smooth muscle contraction and others relaxation. This variability was likely due to factors such as differences in the components in the

extracts and doses of the extracts tested, the type of smooth muscle tissue tested, pregnancy status of the animal, and whether the study was in an intact animal or on isolated uterus or other smooth muscle. The mechanism by which raspberry leaf could have the claimed effects on labour is also poorly understood, and it is unclear what the active components might be. A number of mechanisms have been suggested, but the evidence for these is limited and contradictory.

1.16 Limited data were available on the reproductive toxicity of raspberry leaf in laboratory animals, and only one study was identified that had evaluated it for short-term repeat-dose toxicity, conducted in mice. Another source of uncertainty was a lack of specific information on the absorption, distribution, metabolism and excretion of the constituents of raspberry leaf by the body following their consumption. However, some evidence indicated that raspberry leaf extracts are less toxic when given to mice orally than when injected intravenously. This suggests that they have poor oral bioavailability; that is, that only small amounts of the toxic constituents reach the systemic circulation following ingestion.

1.17 Limited data were found on levels of contaminants, such as heavy metals, in raspberry leaf, and on levels of pesticide residues. However, the data available did not indicate any safety concerns.

1.18 The COT also took into account the available human data. These included two studies conducted in Australia. The first identified women who had given birth in hospital and who had taken raspberry leaf tea, tablets and/or tinctures during pregnancy, and compared them to matched women who had not taken raspberry leaf during pregnancy. No adverse effects were identified in the mothers or infants, or on the delivery, from consuming raspberry leaf. The second study, by the same group, was a double-blind, placebo-controlled trial, in which women were randomly assigned to receive raspberry leaf tablets or placebo tablets during pregnancy. No adverse effects were identified, with the possible exception of constipation, which was reported exclusively by 4 of the 96 women receiving raspberry leaf. However, the COT noted that estimates of UK consumption of raspberry leaf tea, or of raspberry leaf from tea, tinctures and capsules combined, which were based on data

collected from online sources, were up to four or more times higher than the raspberry leaf dose tested in this trial.

1.19 In addition, the COT took into account data collected by the UK Teratology Information Service (UKTIS), a national service that collects pregnancy outcome data from women exposed to medicines and chemicals in pregnancy. There have been very few reports of adverse effects in pregnant women taking raspberry leaf or their children received by the UKTIS since its inception in 1983 to the present date, despite the reported high prevalence of use of raspberry leaf.

1.20 Overall, the COT concluded that the risk associated with raspberry leaf use during pregnancy was low but with high uncertainty due to the data limitations. The COT considered that poor oral bioavailability of the toxic constituents of raspberry leaf (based on indirect information) might also contribute to why it appears to have little adverse effect on human health. However, if raspberry leaf products that are modified to increase their bioavailability become available in the future, these may require a separate safety evaluation.

1.21 The full COT Statement can be found at: Statement on raspberry leaf tea.

Hepatotoxicity of green tea catechins

1.22 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 European Food Safety Authority (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.

1.23 Following a request to the Food Standards Agency from DHSC under the Nutrition, Labelling, Composition and Standards (NLCS) Common Framework, 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. Conclusions made by the Committee will help inform the next steps for risk management. 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.

1.24 The COT concluded that EFSA's conclusions were still applicable and that 800 mg/day EGCG was probably safe. However, it is possible that some sensitive individuals will experience an idiosyncratic reaction below this dose.

1.25 The technical statement and lay summary have been published and are available on the COT website and through the following DOI link: https://doi.org/10.46756/sci.fsa.wii944.

Assessment of Bisphenol A (BPA)

1.26 Following extensive reviews and discussions of the scientific evidence of the new European Food Safety Authority (EFSA) tolerable daily intake (TDI) for bisphenol A (BPA), and the subsequent assessment by the German Federal Institute for Risk Assessment (BfR) in 2023, the COT adopted the tolerable daily intake (TDI) of 0.2 µg/kg bw per day established by the BfR.

1.27 The Committee noted that the scientific issues raised by the BfR aligned with the concerns and comments highlighted by the COT during their discussions and the public consultation held by EFSA.

1.28 The use of a male reproductive endpoint, i.e. sperm count and mobility, by the BfR was consistent with the critical endpoint used in previous COT assessments. While the COT agreed that the BfR had added a significant degree of conservatism in their establishment of the TDI, they could not identify any endpoint that would be

more suitable and concluded that the overall assessment by the BfR and endpoint applied, and approach taken was reasonable.

1.29 In line with EFSA and the BfR, the Committee highlighted that the most recent exposure data available predates the 2015 EFSA opinion. To be able to undertake a full risk assessment, the COT will require up to date exposure data, which will enable the Committee to fully assess realistic exposures in, and potential risks to, the UK population.

1.30 The position paper was published in May 2024 and can be viewed using this link: Position paper on bisphenol A | Committee on Toxicity.

1.31 The Committee will be publishing a supplementary statement in 2025, providing more detail on their discussions of the EFSA opinion and BfR assessment, their evaluation of the evidence base, and deliberations to adopt the TDI established by the BfR.

Updated position paper on Bamboo Bio-Composites in Food Contact Materials

1.32 Risk assessment advice on biobased food contact materials (BBFCMs) has been increasingly requested from the Food Standards Agency (FSA), hence it was considered timely for the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT) to review the available toxicological information on BBFCMs (COT, 2021) including bamboo bio-composites.

1.33 In 2019, the European Commission (EC) asked the European Food Safety Authority (EFSA) to assess whether the authorisation of untreated wood flour and fibres (FCM no. 96) as an additive in plastic food contact materials was still in accordance with EC Regulation 1935/2004, and also to consider whether bamboo could be considered under the scope of this authorisation. Following EFSA conclusion that wood and bamboo should be considered distinct, and each material regarded on a case-by case basis, the EC recommended that Member States should take stringent action on bamboo composite FCMs and set out a coordinated control plan. In addition, the food safety authorities of Belgium, Luxembourg and the

Netherlands (Benelux) published a joint letter calling for the market withdrawal of bamboo-melamine plastics. The FSA is aware of the stance by the EC and of the individual Member States and is considering an appropriate course of action based on scientific evidence.

1.34 In December 2020, reports to the FSA in relation to bamboo composite FCMs were predominantly related to misleading labelling on packaging and/or their advertisement, as well as incidences of formaldehyde/melamine migration levels exceeding legal limits. In 2021, and due to the EU's conclusion, that bamboo is an unauthorised additive within plastic FCMs, reports received by the FSA had predominantly been of non-compliance of plastic-bamboo FCMs in the European market. This included the advertisement of products from UK businesses on EU facing markets. Hence, the COT undertook a more detailed review of the potential health risks of bamboo composites in Food Contact Materials (FCMs).

1.35 The COT assessed the reports by the German Federal Institute for Risk Assessment (BfR) and the Netherlands Food and Consumer Product Safety Authority (NVWA) and noted that the BfR applied their own tolerable daily intake (TDI) of 0.6 mg/kg/day for formaldehyde whereas the NVWA and EFSA used a lower TDI of 0.15 mg/kg/day.

1.36 Overall, the COT concluded that the exposure assessments were conservative but not necessarily worst-case. It was agreed that although the NVWA and BfR opinions took slightly different approaches, in general the same conclusions were reached. Based on the assessment of the BfR and NVWA reports the Committee concluded that the migration of formaldehyde and melamine from bamboo composite cups was a potential concern to human health.

1.37 To assist the COT with their assessment the FSA launched a call for evidence in 2023 to obtain further information from industry, consumers, or interested parties on the safety and stability of plastic contact materials and articles containing bamboo and other plant-based material. In March 2024, the COT assessed the information submitted to the FSA in response to the call for evidence as well as an additional report (EU-ChinaSafe, 2022).

1.38 Based on the considerations of the new evidence submitted to the FSA and the currently available data, the COT agreed that there was still insufficient exposure data on which to perform a complete risk assessment. Concerns remained regarding the migration of formaldehyde and melamine from these FCMs, while the actual composition of these products remained uncertain.

1.39 The updated position paper can be viewed using this link: TOX-2021-59 Interim position paper on bamboo composites in food contact materials.

Joint statement on the safety assessment of Tetra-methyl bisphenol F diglycidyl ether (TMBPF-DGE)

1.40 Towards the end of 2021 the UK Food Standards Agency (FSA) policy team received a request by the food contact can coating sector to assess the suitability of tetra-methyl bisphenol F diglycidyl ether (TMBPF-DGE) for use in coatings in canned food packaging materials.

1.41 As the European Food Safety Authority (EFSA) had not carried out an assessment this necessitated national authorities to consider the safety and use of TMBPF-DGE as an epoxy in can coatings. In 2022, the Dutch Authorities included TMBPF-DGE in their revision of the Dutch Commodities Act (Warenwet), allowing it to be used as a coating in canned food packaging subject to specific restrictions. In accordance with mutual recognition principles, goods lawfully placed on the market within an EU member state can be freely placed on the market within Northern Ireland (NI). This does not apply to Great Britain (GB).

1.42 TMBPF-DGE is being suggested as a possible replacement for bisphenol A (BPA) in can coatings, with several global brands already marketing cans coated with TMBPF-DGE-based polymers in the European Union (EU). Manufacturers are now intending to apply the coating to cans destined for the GB market.

1.43 All information provided to the FSA on TMBPF-DGE has been considered by the Joint Expert Group on Food Contact Materials (FCMJEG), the Committee on

Toxicity of Chemicals, Consumer Products and the Environment (COT) and the Committee on Mutagenicity (COM), for their specific expertise.

1.44 TMBPF-DGE is a mixture derived from the reaction of tetramethyl bisphenol F (TMBPF) with epichlorohydrin. TMBPF-DGE is then further processed to form an epoxy resin and polymer dispersion, which is then used as a component in coatings in canned food packaging materials, in contact with all food types (including beverages). It should be noted, that while testing was performed on TMBPF-DGE, as well as the epoxy resin, the assessment is on the safety of TMBPF-DGE only and does not include evaluation of any of the other chemicals included in the manufacture of the epoxy resin or final product.

1.45 TMBPF-DGE contains epoxy (glycidyl) groups which are intended to be reactive. TMBPF-DGE derived epoxy groups may remain in the resin however after polymerisation they are incorporated into the finished (cured) polymer resin hence no availability for interaction with food substances is anticipated.

1.46 The migration of TMBPF-DGE and its derivatives was based on extraction in acetonitrile, which the Committees agreed was the worst-case extraction and hence would represent the worst-case migration of TMBPF-DGE. The anticipated migration was within the specific migration limit and also below the restriction to bisphenol A diglycidyl ether (BADGE) and Bisphenol F diglycidyl ether (BFDGE), its closest comparators.

1.47 The Committees considered TMBPF-DGE to be genotoxic *in vitro*. However, while some uncertainties remain, specifically around the potential of TMBPF-DGE to induce polyploidy, the *in vivo* genotoxicity data were negative and provided a sufficient margin of safety. Overall, the Committees agreed that it is unlikely that there would be a risk to human health from any mutagenic effect of TMBPF-DGE.

1.48 Members concluded that the available, albeit screening-level, data on non-genotoxic endpoints did not indicate any reproductive or developmental effects at a concentration of 300 mg/kg or raise any other toxicological concerns at exposures of ≤ 100 mg/kg.

1.49 While not a requirement for the assessment, the endocrine data available for TMBPF-DGE epoxy resin were of good quality with the Committees concluding that there was no concern over endocrine effects of TMBPF-DGE at the expected exposure levels.

1.50 Members did not consider it appropriate to establish a HBGV due to the lack of a long term/chronic toxicity study and other database deficiencies.

1.51 When considering all available information, including a comparison of TMBPF-DGE with BADGE, its closest comparator, the available data did not identify any safety concerns for the usage of TMBPF-DGE in can coatings. The MOE was at least 67,000, well above the value of 1000 considered to indicate a lack of any safety concern. In addition, the TTC approach provided re-assurance, given its in-built conservatism and supported the conclusion that the estimated exposure to TMBPF-DGE would be below any level of potential concern. Hence, the FCMJEG and COT did not see any scientific reason to apply restrictions to the proposed usage of TMBPF-DGE.

1.52 Given that there is no legislative framework in place for the assessment of substances in can coatings nor the ability to create or amend a positive list at present, the FSA policy team therefore does not anticipate formal authorisation of TMBPF-DGE but would take into account the finalised risk assessment in their risk management considerations. The objective will be to ensure that it appropriately sets out operator requirements and expectations.

1.53 The joint statement was published in 2024 and can be viewed using this link: Summary and Introduction | Committee on Toxicity.

Aircraft cabin air

1.54 The COT was asked to 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?”. This follows a COT statement in 2007 addressing aircraft cabin air, relating to organophosphate compounds, the

cabin air environment, ill-health in aircraft crews and the possible relationship to smoke or fume events (COT, 2007) and subsequently a position statement following research on aircraft cabin environment (COT, 2013).

1.55 The objective of the present review was to investigate whether specific chemicals commonly identified in aircraft cabin air could potentially cause ill-health in aircrew. This review did not look for other potential causes of aircrew ill-health (these were considered in the 2007 review).

1.56 For the present review the COT considered a number of papers on organophosphates, volatile organic compounds, carbon monoxide and carbon dioxide.

1.57 Most of the published information on these chemicals in aircraft cabin air related to background levels during normal flight operation. There continued to be only very limited information on levels following smoke or fume events, with little additional data since COT's previous work in 2007 and 2013. Smoke or fume events are when abnormal odours, smoke, haze or fumes occur in the aircraft cabin, which may come from various internal or external sources.

1.58 The COT considered the potential risk to health from organophosphate exposure in aircraft cabin air (TOX/2022/40). Two studies investigated health effects in aircrew. The COT considered there were shortcomings with both studies, in particular neither study reported the levels of organophosphate exposure the crew had experienced. However, the COT agreed with the authors' conclusions that the data did not indicate any association between impact on mental ability and organophosphate exposures.

1.59 One paper carried out a risk assessment for a specific organophosphate, tri-ortho-cresyl phosphate, commonly used in aviation lubricants. Levels of exposure to this organophosphate were substantially below those at which a risk of adverse effects on health might arise.

1.60 The Committee concluded that it was unlikely that exposure to organophosphates at the low levels identified in aircraft cabin air would have adverse effects on aircrew.

1.61 For volatile organic compounds, levels in aircraft were compared with levels in other modes of transport (TOX/2022/46) or other work environments (TOX/2022/55) in the UK and EU. If the highest average levels of an individual compound in aircraft were above all the highest average levels in other environments in which that individual compound was measured, the COT carried out a specific risk assessment for that chemical.

1.62 The reported levels of six volatile organic compounds in aircraft were above the levels in other UK and EU modes of transport or work environments (TOX/2023/15). However, the concentrations were all lower than relevant guidelines and standards, indicating that no risk to health is anticipated at these levels. Mixtures of volatile organic compounds were considered using a hazard index approach. This compares the level of each chemical with the level below which there would not be a risk to health and adds these ratios together. In considering the volatile organic compounds in aircraft cabin air, the result of this hazard index approach indicated that no effects, including mixture effects, are anticipated.

1.63 Levels of carbon monoxide and carbon dioxide in UK and EU-operated aircraft were collated and compared with various standards as well as levels that cause discernible symptoms (TOX/2022/65 and TOX/2023/14). The Committee considered these data and concluded that levels of carbon monoxide and carbon dioxide reported in aircraft are unlikely to be associated with any short- or long-term adverse health effects.

1.64 Overall, the COT concluded that the levels of the chemical contaminants reviewed (organophosphates, volatile organic compounds including as mixtures, carbon monoxide and carbon dioxide) in aircraft cabin air, at the concentrations reported, are unlikely to cause adverse health effects in aircrew after being exposed for long or short time periods. However, there is still limited information about the levels of chemicals in cabin air following smoke or fume events.

1.65 The full COT statement can be found at:

Statement on Aircraft Cabin Air Quality | Committee on Toxicity.

COT Procedures

Benchmark dose modelling in a UK chemical risk assessment framework

1.66 In 2021, as part of a horizon scanning exercise, the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT) identified the UK in future may need benchmark dose (BMD) modelling guidance. As part of its ongoing evaluation of New Approach Methodologies (NAMs) in chemical risk assessment, the Food Standards Agency (FSA) and the COT were considering the use and practice of BMD modelling within a UK food safety context.

1.67 The discussion paper set out the theory and practice of BMD modelling. The paper drew on previous evaluations by regulatory bodies and authorities. It also included a discussion of the areas of consensus and divergence between organisations and expert groups. The paper included a case study from the FSA Computational Fellow.

1.68 BMD modelling represents a useful tool in toxicology, but the No-observed-adverse-effect level (NOAEL) approach remains valid and, in many cases, is the only option (e.g. where effects are observed only at the highest dose). The requirement for deeper knowledge of the statistical and computational basis of the BMD approach may represent a barrier for further adoption in traditional toxicology. Applying the BMD approach to toxicology data is a more complex undertaking than the traditional NOAEL approach. Some areas where BMD modelling may provide advantages over the traditional NOAEL approach include potency comparison, establishing toxicological equivalency factors (TEFs) and for situations where a reference point needs to be identified in the absence of a NOAEL.

1.69 With respect to the development of new BMD software these have their own capabilities, which allow them to be tailored for specific scenarios and tasks.

However, there is concern that the use of different software might lead to further divergence rather than convergence of BMD approaches. For example, the recent development of Bayesian BMD software as part of European Food Safety Authority (EFSA's) modelling suite raised concerns around how the Bayesian BMD modelling is used in practice, specifically with the selection of priors and whether this would introduce subjectivity into the analysis. Uncertainties have been expressed in the literature with respect to the Environmental Protection Agency (EPA) Bayesian modelling software.

1.70 There is debate about the role of benchmark dose modelling in other areas, such as genotoxicity testing, and the COT is aware of the views on BMD modelling by other UK Scientific Advisory Committees notably the COC and COM. BMD modelling is already being used by some expert groups, such as the UK Expert Committee on Pesticides and it would be useful to capture their experience.

1.71 The Committee acknowledged the rapidly developing nature of the BMD guidance, the development of new approaches, such as Bayesian approaches; and the recent proliferation of new BMD software but noted that it was still uncertain if, or what, important divergences existed between these developments.

1.72 BMD modelling should be viewed as a step towards a larger goal of more realistic, toxicodynamic systems approaches to risk assessment. This may become more feasible with the further development of models based on *in silico* and *in vitro* approaches.

1.73 The Committee noted that BMD modelling should be taken into consideration when updating COT guidance.

COT ways of working

1.74 The workload of the Committee and in particular the Chair has increased over recent years, partly, though not solely, as a result of the UK's exit from the EU, including the additional activities associated with the authorisation of regulated products. It was therefore timely to review the current working practices of the

Committee to ensure that it remains sustainable. In addition, due to the increase in hybrid and virtual meetings, it was important to ensure the Committee can work in an effective manner, with Members being able to fully contribute and be engaged. Committee Chairs are appointed through an open recruitment process so it would not be appropriate to train current Members for the role or to have a formal succession planning process. However, it was agreed that, in addition to chairing the meeting when the Chair was unavailable or had a conflict of interest, it could be useful for the Deputy Chair to lead in a particular topic area to reduce the workload of the Chair. It was subsequently agreed that the COT Deputy Chair, Professor Shirley Price, would focus on regulated products to strengthen links between the COT and the Joint Expert Groups.

1.75 The process by which small groups of Members were allocated to particular papers to lead the Committee review was discussed. It was agreed that the small group work should start at an earlier stage for more complex topics and could also follow the process through to the preparation of first draft statements. Lay members and/or associate members could also be included in the small groups where appropriate.

1.76 Since final statements and position papers were the final output of the Committee, later drafts needed to be considered and agreed by the full Committee since they represented a collective view.

1.77 Since over half of the Committee's meeting are fully online, Members discussed some potential changes to the current procedures; No changes were agreed but the topic remans under review.

1.78 The role of the lay Members was considered; while they may sometimes find it difficult to participate at meetings due to the very technical content, their contribution was much valued. It was agreed that lay Members from different Committees should meet to share their perspectives and consider best practice.

Ongoing work

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

1.79 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 legislative standards. The main purpose of this work is to identify any emerging marine biotoxins 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 emerging marine biotoxins would pose a risk to human health.

1.80 In December 2023 a scoping paper was presented to the Committee on whether a number of emerging marine biotoxins would pose a risk to human health. Following the discussions, and to aid the Committee in ranking the risk of each emerging marine biotoxin, the Secretariat produced a discussion paper in July 2024 providing a table with the main toxicological information. In addition, a table of the main toxicological information of currently regulated marine biotoxins was included, for comparison.

1.81 Limited estimates of potential adult exposures to the unregulated marine biotoxins, based on the European Food Safety Authority's (EFSA) shellfish portion size of 400 g, and a fish portion size of 140 g, as suggested by the Ministry of Agriculture, Fisheries and Food portion size book and assuming a body weight of 78.6 kg were also provided. The aim of the estimated exposures was to help Members establish whether occurrence at the levels reported in the literature would be of potential risk. However, this was not a detailed exposure assessment, and consumption data was not based on UK consumers, and hence may have overestimated actual exposures in the UK. Going forward it may be more appropriate, if required, to use data from the National Diet and Nutrition Survey (NDNS) to enable a more accurate and refined exposure assessment, although data for consumption of shellfish from this survey may still be limited.

1.82 Data on adverse effects of marine biotoxins were commonly from animal studies, and not from human data. Nonetheless, specifically for cyclic imines (CIs)

monitoring was undertaken in some countries even though no human intoxications had been reported. The route of administration in animal studies differed widely, adding to the uncertainty in the available data, but intraperitoneal injection appeared to increase toxicity in a number of studies compared to oral administration.

1.83 The COT considered it useful for the UK to have a more formal strategy for the reporting of potential marine biotoxin intoxications; however, they acknowledged that this may prove difficult for some marine toxins as standard testing may not be available.

1.84 There would however be benefits from enhanced UK surveillance programmes and looking at monitoring programmes in other countries, specifically e.g. in Scotland and Northern Ireland, and whether they could be adapted for England or rolled out UK wide. The Committee acknowledged the potential cost of such monitoring programmes but noted that this was outside the Committee's remit and would sit with the FSA.

1.85 Given the potential impact of climate change on the presence of marine biotoxins in UK waters, it could also prove useful to feed into the climate change impact strategy when considering the effects/impact of global warming on the ecosystem.

1.86 The Committee agreed that there were significant data gaps, especially the occurrence data for the UK therefore making it difficult to conclude on potential risk based on the currently available information.

1.87 However, the COT considered risk ranking the emerging marine biotoxins based on a scoring system, adapting a system that had previously been applied to mycotoxins. This would consist of assigning a numerical score to each emerging toxin for the following categories: toxicity, occurrence in UK waters, human health impact, and monitoring and/or regulation. Toxins exhibiting severe health effects and demonstratable occurrence in UK waters would score high and therefore should be prioritised for monitoring in UK fish and shellfish.

1.88 The Committee have asked the Secretariat to produce a discussion paper providing a risk ranking for each toxin, considering the different weighting of factors that would influence the final score.

1.89 The full 2024 discussion paper can be found at: Advice on the risk to human health from consumption of bivalve molluscs (shellfish) harvested from UK waters associated with marine biotoxins | Committee on Toxicity.

1.90 A final discussion paper/statement is expected for 2025.

Deriving a health-based guidance value for antimony to support development of UK Drinking Water Standards

1.91 The UK Health Security Agency (UKHSA) advises the Drinking Water Inspectorate (DWI) on potential health risks from chemicals in drinking water. Post EU exit, the DWI is reviewing the regulatory standards for some chemicals in drinking water, including antimony. UKHSA is seeking advice from the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT) with respect to an appropriate health-based guidance value (HBGV) for antimony.

1.92 In 2024, the COT considered an initial discussion paper on the study underpinning evaluations by the World Health Organization (WHO, 2003), the US Agency for Toxic Substances and Disease Registry (ATSDR, 2019) and Health Canada (Health Canada, 2024). The COT will consider further papers in 2025.

Citrinin in the maternal diet

1.93 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 Committee on Toxicity (COT) review the risks of toxicity from chemicals in the maternal diet, including citrinin.

1.94 Citrinin is a mycotoxin produced by several species of fungi of the genera *Aspergillus*, *Penicillium* and *Monascus* and is generally formed after harvest under storage conditions. It occurs mainly in grains but can also occur in other products of

plant origin e.g. beans, fruits, fruit and vegetable juices, herbs and spices as well as in spoiled dairy products.

1.95 Citrinin is acutely nephrotoxic in mice and rats, rabbits, pigs and poultry, causing swelling and eventual necrosis of the kidneys. Citrinin also affects liver function but to a lesser extent. Both *in vitro* and *in vivo* studies have provided evidence for reproductive and developmental toxicity of citrinin.

1.96 The potential risk from citrinin in the maternal diet was discussed by the Committee in October 2024. It was concluded that citrinin would not have adverse effects on maternal health at likely levels of exposure. A statement on citrinin will be presented to the COT in 2025.

The potential risks from ergot alkaloids in the maternal diet

1.97 As part of the ongoing programme of work on the maternal diet (see above), the Committee were asked whether exposure to ergot alkaloids (EAs) would pose a risk to maternal health.

1.98 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 European Food Safety Authority (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. Bromocriptine is a synthetic ergoline derivate used in the treatment of Parkinson’s disease, suppression of lactation and to treat pituitary tumours.

1.99 Due to their structural similarities to neurotransmitters, EAs have been suggested as agonists or antagonists of noradrenaline, dopamine and serotonin neurotransmitters. As a consequence, they can produce direct peripheral effects

such as uterotonic action or vasoconstriction, and central nervous system (CNS) effects such as induction of hypothermia and emesis.

1.100 In 2022 the Committee discussed the potential risk from EAs in the maternal diet and concluded that EAs would not have adverse effects on maternal health at the estimated levels of exposure in the UK.

1.101 A second draft statement was presented to the Committee in February 2024. Following the discussions, the Committee requested for additional paragraphs to be added regarding the effects of ergot alkaloids on the immune system and on the overall exposure.

1.102 The statement is expected to be published in 2025.

Ginger in the maternal diet

1.103 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.

1.104 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.

1.105 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 foetus or embryo, possible interactions with medicines and the possible influence on cyclooxygenase (COX) and prostaglandin activity.

1.106 The final statement on ginger in the maternal diet will be published in 2025.

Discussion paper on the effects of Calcidiol supplementation during pregnancy

1.107 As part of the current programme of work on the maternal diet, the Committee considered the exposure to excess calcidiol would pose a risk to maternal health, as part of this review. This follows the previous review of vitamin D published in 2023.

1.108 Calcidiol is a novel source of vitamin D3 which is formed via chemical synthesis from cholestatrienol. Calcidiol has many forms including calcidiol monohydrate, 25-hydroxycholecalciferol monohydrate (25(OH)D3 monohydrate), calcifediol or 25-hydroxyvitamin D (25(OH)D), with the latter two being the forms used in supplementation. Calcidiol is a synthetic form of 25(OH)D, which is an inactive precursor to the biologically active form of vitamin D known as 1,25-dihydroxyvitamin D (1,25 (OH)2D).

1.109 In 2024 the ACNFP established a Tolerable Upper Level (TUL) of 40 µg/day for an application submitted for calcidiol monohydrate. A conversion factor of 2.5 was applied to the EFSA TUL of 100 µg/day for vitamin D to calculate the TUL for calcidiol. However, EFSA determined a safe level of intake of 10 µg/day for the same calcidiol monohydrate product, which may have reflected the request from the applicant.

1.110 Exposures to calcidiol from food sources did not exceed the ANCFP TUL of 40 µg/day or the EFSA safe level of intake of 10 µg/day. Combined exposures from food and supplements showed intakes were below the ACNFP TUL but exceeded the EFSA safe level of intake up to 2.1-fold.

1.111 The COT were unable to conclude on an appropriate Health Based Guidance Value (HGBV) for risk characterisation and requested the paper return to the COT with more clarification on how EFSA derived a safe level of intake of 10 µg/day.

1.112 A final COT statement is due to be published in 2025.

Assessment of ocean bound plastic (OBP)

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

1.114 Following the FSA and FSS call for evidence between March and October 2022 and the identification of additional suppliers of these materials between November 2022 and January 2024, the Food Contact Materials Joint Expert Group (FCMJEG) have assessed all information provided to the FSA and FSS up until January 2024.

1.115 The final assessment by the FCMJEG on environmental plastic and ocean bound plastic, and confidential supplementary material from the call for evidence was discussed by the COT and overall, the COT was content with the position statement of the FCMJEG. Publication is expected in early 2025.

Risk assessment of T2 and HT2 mycotoxins in food

1.116 The assessment of T-2 and HT-2 mycotoxins in food was initiated following a proposal by the European Commission in 2020 to establish maximum levels for these mycotoxins, which are lower than the indicative levels set under EU Recommendation 2013/165/EU. The FSA requested the COT evaluate the potential risks these toxins pose to UK consumers. This review aimed to support the FSA's reassessment of mycotoxin limits and inform potential risk management strategies, particularly as T-2 and HT-2 are known to contaminate cereal grains and products, posing possible health risks through dietary exposure.

1.117 At the July 2024 committee meeting, the discussion centred on a scoping paper that presented an initial exposure assessment based on UK dietary habits and occurrence data from both industry submissions and national surveys. This assessment employed data spanning 2008 to 2023, reflecting the inherent variability

in mycotoxin levels due to weather conditions and agricultural practices. However, most data represented unprocessed food commodities, adding uncertainty to the exposure estimates. For example, the lack of consideration of the effect of processing such as dehulling or scouring, which would significantly reduce mycotoxin levels thus exposures are likely to be overestimated.

1.118 The approach also relied on consumption data from the National Diet and Nutrition Survey (NDNS), applying high-percentile consumption models across multiple food groups. This methodology assumes an unrealistically high exposure scenario, as it is improbable that a single individual would consistently consume foods at the 97.5th percentile across all categories. These factors, combined with variability in analytical methods over time, resulted in significant uncertainties in the risk assessment.

1.119 During the meeting, the Committee raised questions about the reliability of the data and analytical methods, highlighting the need for validation of industry-supplied occurrence data. The absence of robust data on processed food products and actual consumer consumption patterns further limited the assessment. More targeted surveys and studies, particularly focusing on processed foods, will be crucial for refining exposure estimates. The potential utility of biomonitoring data, such as urinary mycotoxin levels in specific populations, was also noted as a promising avenue for understanding actual exposures.

1.120 The review considered health-based guidance values (HBGVs) established by EFSA and JECFA for both acute and chronic exposures. Preliminary findings indicated that while mean exposures were generally below the acute reference dose (ARfD), high-percentile chronic exposures exceeded the tolerable daily intake (TDI) in some population groups. However, these exceedances were uncertain due to the limitations of the exposure model. Consequently, the Committee concluded that it could not definitively characterise the health risks associated with these mycotoxins at this stage.

1.121 The Committee acknowledged the importance of addressing these uncertainties and refining the risk assessment process. Suggestions included improved occurrence data collection, accounting for processing factors, and trend

analysis to better understand mycotoxin variability. A refined exposure assessment and risk characterisation, incorporating these elements, is planned for presentation in 2025. This will enable more informed advice and public health guidance concerning the safety of T-2 and HT-2 mycotoxins in the UK food supply.

Application to authorise iron enriched yeast as a permitted form of iron which can be voluntarily added to foods for specific groups, food supplements and general foods (Reserved)

1.122 Following a request from the DHSC under the Nutritional Labelling Standards and Composition Group (NLCS) framework, the COT reviewed an Application from Danstar Ferment AG a subsidiary company of Lallemand Inc. to include iron enriched yeast (*Saccharomyces cerevisiae*) as an optional permitted form of iron which can be added to fortify foods, food supplements and categories in scope of foods for specific groups (FSG) in the following Great Britain legislations: Annex II of assimilated Regulation (EC) No 1925/2006, assimilated Regulation (EU) No 609/2013 and Schedule 1 & 2 of The Nutrition (Amendment etc.) (EU Exit) Regulations 2019.

1.123 This item was reserved as the application contains confidential information and is still under review by the COT.

Other Committee Activities: Joint Expert Groups, Presentations and Workshop

Postdoctoral Fellow presentation

1.124 The FSA and COT have been reviewing New Approach Methodologies (NAMs) to scope the best scientific methodologies available to be used in the risk assessment of chemicals in foods and the environment, and to understand how these can be incorporated and accepted in a regulatory context. NAMs include but are not limited to, high throughput screening and other in vitro assays, omics and in

silico computer modelling strategies (e.g. Artificial Intelligence (AI) and machine learning) for the evaluation of hazard and exposure in risk assessment

1.125 In 2021, the FSA started funding a 4-year computational toxicology postdoctoral fellow at the University of Birmingham and a PhD Student (London Interdisciplinary Doctoral Program-LIDo) at King's College London on the use of artificial intelligence in chemical risk assessment.

1.126 The fellow and PhD student have been working alongside other government departments to understand how NAMs will improve indicative levels of safety in chemical risk assessment.

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

1.128 The Postdoctoral Fellow prepared a yearly review and gave a presentation to the Committee on progress of the two case studies that have been conducted, to date.

1.129 The first case study focused on the plasticiser di-2-ethylhexyl terephthalate (DEHTP) and the main objective was to derive a health-based guidance value HBGV. Concentration-response data obtained from ToxCast, via the Chemicals Dashboard (US EPA), was used.

1.130 The second case study was to establish HBGV for a perfluorinated substance, perfluorooctanoic acid (PFOA) using a workflow utilising multiple NAM approaches including *in vitro* hepatic microtissues and Physiologically Based Pharmacokinetic (PBPK) modelling as well as benchmark dose modelling.

1.131 The Fellow also presented some preliminary work on the third case study, which is on tropane alkaloids.

1.132 The COT Members were impressed with the progress to date and gave feedback to the Fellow.

Marine biotoxins – Presentation on occurrence and exposure to pinnatoxin (data reserved)

1.133 The FSA is considering the current advice and monitoring programme for marine biotoxins and whether there is a need to update or change existing legislative standards.

1.134 As pinnatoxins (PnTX) are not currently regulated in England or Wales, the views of the COT were sought on whether PnTX would pose a risk to UK consumers. Therefore, in July 2023, the information and data on the risks associated with PnTX in shellfish were discussed. At the meeting the Committee concluded that due to the lack of toxicological and occurrence data it was currently not possible to determine the extent of any public health risk. Occurrence data on PnTX would be useful to help fill some data gaps, including whether the UK population would be exposed to PnTX from shellfish consumption.

1.135 The recent availability of new analytical standards has allowed PnTX to be monitored in UK shellfish. Liquid chromatography–mass spectrometry (LCMS) monitoring data for PnTX-G were available to the FSA by the Agri-Food and Biosciences Institute (AFBI) in Northern Ireland and by Food Standards Scotland (FSS) and these data were discussed by the Committee in May 2024. The data are currently confidential as they are awaiting publication by the respective institutes.

1.136 The available occurrence data also allowed for some preliminary PnTX exposure estimates to be carried out for UK consumers, using EFSA's estimated shellfish portion size of 400 g (excluding shells). The Committee noted that the exposures estimated by EFSA using this portion size assumed that a consumer would eat 400 g of a single shellfish type and questioned how likely this would be for some shellfish species. It was noted that cultural differences could also lead to variation in the amounts and types of shellfish consumed. Data from the National Diet and Nutrition Survey (NDNS) showed that in the UK shellfish is consumed in

lower quantities than EFSA's estimated 400 g. Therefore, some of the exposure estimates presented may be overestimations of UK exposures.

1.137 The Committee questioned whether PnTX-G was known to co-occur with other marine biotoxins, however, there did not appear to be any reports of regular co-occurrence. It was noted that the different feeding habits of shellfish could potentially influence toxin levels.

1.138 With respect to reducing the levels of PnTXs in shellfish, there were no data available on the efficacy of depuration tanks and as PnTXs are lipophilic biotoxins this would make extraction into clean water less likely. The toxins are relatively heat stable but processes such as cooking or dehydration of the meat during steaming and canning could lead to different levels of PnTX in the final product compared to the raw shellfish.

1.139 Overall, the Committee thought the information presented was useful but reiterated that there were significant data gaps on PnTX, especially regarding its toxicity.

New Approach Methodologies (NAMs) in regulatory decisions for chemical safety presentation and review

1.140 Dr Letizia Carramusa from the Yordas Group presented the results of a FSA-funded literature review on New Approach Methodologies (NAMs) to Support Regulatory Decisions for Chemical Safety to the Committee.

1.141 It was explained that the objectives of the project were: to collate, review and categorise the most up-to-date scientific literature for the UK's own evaluation of NAMs in the field of chemical risk assessment; to assess the regulatory readiness of NAMs and the degree to which these technologies have been successfully integrated into regulatory frameworks; to gather and summarise expert opinions on the gaps that hinder the further adoption of New Approach Methodologies (NAMs) in the regulatory process.

1.142 The literature search and methodology were outlined. Publications were retrieved from 2014 onwards to prioritise the most recent literature and ensure the relevance of the studies. NAMs published more than a decade ago were excluded from the literature review as they were considered to be either well-established within the regulatory framework or have been superseded by improved methods, meaning that research into them had halted.

1.143 Global stakeholder interviews were then undertaken. Topics and key findings from the interviews included: views on the term “NAM”; research investment focus; how NAMs integrate with traditional hazard assessment and when they will become the primary approach, either to supplement existing approaches, or to completely replace animal testing; regulatory application, especially for food; how are NAMs best used for regulatory activities and how food regulations integrate NAMs; the barriers to integration of NAMs and how they can be overcome; and the types of substance or material where NAMs can play a role in the near future. It was concluded that no single NAM can replace animal studies entirely and the FSA should explore the adoption of concepts like "endorsement" or "qualification" used in the US for tier-one decisions.

1.144 Members complimented the Yordas Group for a comprehensive, interesting and thorough review.

1.145 The Committee noted that physiologically based pharmacokinetic (PBPK) modelling was more commonly used than described in the report. Specifically, JECFA reports on contaminants regularly utilized PBPK modelling, emphasizing its critical role in determining Tolerable Daily Intakes (TDIs).

1.146 The Committee discussed the report with respect to recommendations related to qualification and validation of NAMs. There is a need for mechanisms to qualify, validate, and generate confidence in the suitability of the novel approaches and there are challenges in securing funding for this purpose. This, and previous, reports have noted funding in the area of NAMs predominantly supports innovation rather than translation of research. The lack of funding avenues for translation through UK Research and Innovation (UKRI) was noted and the need for alternative funding solutions stressed. The distinction between scientific validation and qualification for

regulatory application was noted, with more focus on the latter being apparent. There is ongoing work in the USA and Asia on this area, and collaboration within the Organisation for Economic Co-operation and Development (OECD) framework is recommended.

1.147 Members noted unavoidable bias in retrospective evaluations of the adequacy of conventional animal toxicity studies, particularly in pharmaceuticals since the drugs evaluated in human studies were a selective subset as many did not make it through the pre-clinical development process, and NAMs were likely used as part of that process. As an example of this, pre-clinical testing was very effective in identifying direct hepatotoxins before market release, and those drugs that were withdrawn for liver toxicity post-marketing almost always involved idiosyncratic reactions, which were not detectable in animal studies or even clinical trials.

1.148 It was noted that genetic toxicology methods such as the Ames test had been deemed “Out of Scope” prior to the report being written, as they were already well established.

1.149 The importance of understanding adverse outcome pathways (AOPs) in making more informed safety assessments was noted, despite their inherent uncertainties. It was important to strengthen AOPs to allow meaningful risk assessment, and there should be focus on working within the OECD framework.

1.150 The Committee suggested that they along with other advisory groups should highlight gaps in evidence, particularly where additional data from the use of NAMs could improve confidence in decision-making. Furthermore, the Committee highlighted the need to champion the use of the best science in regulatory risk assessment, including the use of NAMs as appropriate, which would require stimulating engagement from developers, especially in the context of limited funding.

FSA Research Programme Presentation

1.151 A presentation was given to Members to update them on the updated structure of the FSA research programme and provide a brief overview on the roles

and responsibilities of individuals and groups involved in the commissioning and delivery of the research programme.

1.152 The Research Evidence Programme (REP) most closely aligned to the work of the COT is the Chemical, Radiological and Food Hypersensitivity REP. The external research projects currently being delivered within this programme and of interest to the Committee are:

- Advancing in silico Methods of Assessing Toxicological Risk (Fellowship).
- TOX-AI: Digitalising Toxicological Databases using artificial intelligence and in silico tools for food safety (Studentship).
- Multi-allergen analysis using multiplex PCR, include case study for mustard allergen detection (L&S).
- Projects due to be commissioned in early 2025 are: Determination of the bioavailability of cyanogenic glycosides on consumption.
- Literature review of nitrates and nitrites as food additives.

1.153 Updates on the status of the Chemical, Radiological and Hypersensitivity REP will be provided to the Committee periodically and the outputs from some projects may be brought to the Committee for peer review.

Evolving Our Assessment & Future Guiding Principles Workshop Report

1.154 The COT held a workshop in May 2023 to start work on updating their guidance on toxicity testing and its supporting principles. The overall objective of the workshop was to discuss how the Committee moves forward in a new era of risk assessment.

1.155 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 (NAMs), exploring hazard vs risk and weight of evidence. The four sessions were: Where are we at; What we need to improve; How to achieve; and Looking to the future - moving forward.

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

1.157 The workshop report is now available online and as a PDF.
(DOI: https://doi.org/10.46756/sci.fsa.qpo647)

Gut reactions: xenobiotics and the microbiome workshop

1.158 The COT held a workshop in October 2024 in London, United Kingdom on xenobiotics and the microbiome. The workshop included themed sessions consisting of short flash presentations followed by roundtable discussions. There was attendance from multiple stakeholders including academia, government and industry.

1.159 The workshop set out to explore the complex current state of the science of the microbiome pathophysiology and the possible impact of xenobiotics on host-microbiome interactions and vice versa, including possible mechanisms and health implications, with a particular emphasis on the gut microbiome and dietary exposure.

1.160 In addition, the aim was to enable new insights, review the science, initiate discussions to determine where the data gaps are in research, what effects are of concern, and how might xenobiotics be evaluated practically for such effects in the future.

1.161 The four sessions were: Interactions of the host microbiome system; Gut microbiome and xenobiotics; Assessing the impact on the microbiome; Possible ways to evaluate in the short to medium term and microbiome interventions for maintaining health and treating disease and Future Directions.

1.162 The finalised report will be published in due course.

Hazardous Substances Advisory Committee (HSAC) discussion on the effects of flame retardants on human health: developing a work programme

1.163 The COT was invited by Defra to comment, along with the Hazardous Substances Advisory Committee (HSAC), on developing a work programme on flame retardants and using information on human risk to aid prioritising the compounds or groups of compounds for review.

1.164 The COT provided a number of comments with respect to availability of evidence on effectiveness, toxicity and exposure data to allow comparisons across different flame retardants. Grouping and read-across were suggested as a means to aid prioritisation. A number of aspects related to sources and routes of chemical exposure were noted for consider.

1.165 Defra thanked the COT for its input which it would take forward with the Secretariat and other partners.

Horizon Scanning

1.166 The COT undertake 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. However, Members are also encouraged to suggest topics for discussion throughout the year.

1.167 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. Thus, 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 continuing work on new approach methodologies is an example of this.

1.168 A number of topics were suggested for potential consideration as either individual papers or as a future COT workshop; these included potential regulatory changes to chemicals in the environment, the microbiome (including the effects of chemicals other than antimicrobials), the presence of novel contaminants in the oceans that could enter the food chain, vegan/vegetarian foods and their ultra-processed replacements (where these were in the COT remit), non-EATS (estrogen, androgen, thyroid and steroidogenesis) mechanisms for endocrine disruption, and obesogens.

1.169 Horizon scanning techniques were discussed more generally, with a view to considering what would be the most useful approach for the Committee to take and it was agreed to review this at a future date.

Joint Expert Groups

FCMJEG

1.170 The COT considered risk assessments prepared by the Joint Expert Group on Food Contact Materials (FCMJEG) regarding the following regulated product applications:

- On the safety of the use of phosphoric acid, mixed esters with 2-hydroxyethyl methacrylate (HEMAP) as a component in the manufacture of kitchen countertops and sinks. This assessment was for HEMAP only, and not the final reaction mixture used in the manufacture. The final assessment was published in July 2024.

- On the safety of the use of calcium tert-butylphosphonate as an additive used in the manufacture of plastic materials and articles intended to come into contact with food. The final assessment is expected to be published early 2025.

On the safety of the recycling processes:

- Document on the evaluation of the recycled poly(ethylene terephthalate) decontamination process operated by LINPAC for use in the manufacture of articles in contact with food.

- On the recycled poly(ethylene terephthalate) decontamination process operated by Wellman Neufchâteau Recyclage (subsidiary of Indorama Ventures) for use in the manufacture of materials and articles in contact with food.

- On the evaluation of the safety of the process for the recycling of post-consumer poly(ethylene terephthalate) into food contact materials.

1.171 These items above are currently reserved as the Committee Advice Papers are not currently published.

Committee Advice Document on the safety of 2-hydroxyethyl methacrylate phosphate as a monomer for use in the manufacture of plastic food contact materials and articles

1.172 The COT considered a Committee Advice Document (CAD) prepared by the Joint Expert Group on Food Contact Materials (FCMJEG) regarding an application for 2-hydroxyethyl methacrylate phosphate (HEMAP) as a monomer in a commercial product for use in the manufacture of kitchen countertops and sinks that are intended for contact with all types of food (RP1190).

1.173 All components of the commercial product are listed in assimilated Regulation EU No. 10/2011 on plastic materials and articles intended to come into contact with food. The application and the following assessment are for HEMA only, not the commercial product.

1.174 Satisfactory information regarding the identity of substance, physical and chemical properties, intended application of substance, data on migration of substance and toxicological data were submitted.

1.175 The toxicological information that formed the basis of the risk assessment was a bacterial reverse mutation test (Ames test), and an *in vitro* mammalian micronucleus test, on the commercial product. Results of the Ames test and *in vitro* micronucleus (MN) test showed no mutagenic, clastogenic or aneugenic potential for the commercial product under the experimental conditions described.

1.176 The specific migration of the sum of HEMAP plus its phosphate and diphosphate esters under the worst-case conditions of use was 24.8 µg/6 dm2 (assumed that this is equivalent to contact with 1 kg food). Taking into account that the specific migration of the sum of HEMA plus its phosphate and diphosphate esters is not expected to exceed 50 µg/kg food and the negative results in the Ames and *in vitro* micronucleus tests, the FCMJEG proposed a specific migration limit (SML) of 0.05 mg/kg food for HEMA.

1.177 Overall, the COT considered the information and data provided in the FCMJEG CAD sufficient to conclude that there was no concern for a risk to human health from the use of HEMA in the specific final commercial mixture in the manufacture of kitchen countertops and sinks up to a maximum percentage in formulation of 0.35%.

1.178 The full FCM JEG CAD can be found at: FCMJEG Applications | Committee on Toxicity.

Committee Advice Document on calcium *tert*-butylphosphonate as an additive for use in the manufacture of plastic food contact materials and articles

1.179 The COT considered a Committee Advice Document (CAD) prepared by the FCMJEG regarding an application for calcium *tert*- butylphosphonate as an additive used in the manufacture of plastic materials and articles intended to come into contact with food (RP1702).

1.180 The information on the identity of calcium *tert*- butylphosphonate, the physical and chemical properties and intended application were considered satisfactory.

1.181 Results from the overall and specific migration tests from the plastic to the test food demonstrated the migration of calcium *tert*-butylphosphonate to be close to or below the limit of detection (up to 10 µg/kg).

1.182 Owing to the low migration of calcium *tert*-butylphosphonate as an additive under the conditions of use specified in the application, limited toxicology testing was required. Results of the Ames test and *in vitro* micronucleus (MN) as tests for possible carcinogenicity and genotoxicity, test showed no mutagenic, clastogenic or aneugenic potential for the commercial product under the experimental conditions described.

1.183 The FCM JEG concluded that calcium *tert*-butylphosphonate is unlikely to be of concern for potential genotoxicity, especially based on the likely low exposure to humans.

1.184 Overall, there is unlikely to be a risk to health from the use of calcium *tert*-butylphosphonate as an additive in the manufacture of plastic materials and articles intended to be in contact with food. However, the potential health risk to infants <younger than 16 weeks via feeding bottles could not be assessed because infants <younger than 16 weeks are expected to be exclusively fed on breast milk and/or infant formula. There is a lack of data including exposure data for this age group.

1.185 Calcium *tert*-butylphosphonate was therefore recommended for approval. Risks associated with calcium *tert*-butylphosphonate in infants was not assessed for use as an additive to plastics as outlined in the application and specified above other than for uses with contact with infant formula and human milk.

1.186 The full FCM JEG CAD is due to be published shortly and can be found at: FCMJEG Applications | Committee on Toxicity.

AEJEG assessments

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

- Committee Advice on the safety of the Application to modify the conditions of use of E 401 (sodium alginate) for use as a surface treatment in entire fruits and vegetables.
- Extension of use of nisin (E 234) to a new food category “egg analogues”.
- Application for a change in the steviol glycoside specification in the United Kingdom to include a new manufacturing method for Steviol Glycosides including Rebaudioside D.
- Authorisation of new food additive substance Glycolipids.

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

1.189 AEJEG Committee Advice Papers will be published in 2025.

Working Groups

Joint ACNFP/COT Working Group on Cannabidiol (CBD)

1.190 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 cannabidiol (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.

1.191 The Subgroup has now reviewed the group A ‘pure’ compounds and established an provisional ADI for pure form CBD (>98% purity) of 0.15 mg/kg bw/day (10 mg/day for a 70 kg adult) as set out in a joint statement.

1.192 The Subgroup is continuing to review the different purity groups of CBD products including considering the less pure Group of B compounds with a lower proportion of CBD and “Group C products” which are products that contain between 2.5 and 67% CBD.

Plant-based drinks

1.193 Plant-based drinks have become increasingly popular in the (UK) both for individuals with an allergy to cows’ milk or lactose intolerance and those who wish to avoid dairy products for ethical or cultural reasons. The three most commonly consumed drinks were reviewed by the Committee, with a statement being published in 2022.

1.194 The Scientific Advisory Committee on Nutrition (SACN) has 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 cows’ milk. The Working Group started work in December 2021 with a draft report being published for peer review in 2024. It is anticipated that the final report will be published in 2025.

PFAS Subgroup

1.195 The COT subgroup on per- and poly-fluoroalkyl substances (PFAS) was set up to help 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.

1.196 The subgroup held one meeting in 2024, which considered the evidence on thyroid effects and liver effects of PFAS. Further papers on other endpoints will be considered in 2025 and beyond.

Titanium dioxide (TiO2) Subgroup

1.197 The TiO2 Subgroup had been set up to develop the text of the statement. A TiO2 subgroup had been set up to develop the text of a statement outlining the assessment of COT on the potential hazards of TiO2 in food products. The Subgroup had three meetings at the start of 2024 and due to the work of the subgroup the statement was signed off by the COT at the May meeting. An executive summary and the full statement were published in 2024 along with a lay summary of the statement.

Smoke Flavourings Working Group

1.198 Smoke Flavourings Working Group (SFWG) of the AEJEG continued their assessment and started phase 3 assessment of these flavourings (conclusions on genotoxicity, assessment of general toxicity and Extended One Generation Reproductive Toxicity (EOGRT)).

1.199 The SFWG has also discussed a “weight of evidence” update paper on flavourings to be used in their assessments.

Other Regulators Opinions (ORO) and Abbreviated (ABB) decisions

1.200 To inform the FSA Scientific Advisory Committees (SACs) and Joint Expert Groups (JEGs) that support the regulated products service, a ways-of-working paper (as TOX-2024-10 for COT) was presented to Members. This explained two additional ways in which the FSA would be assessing regulated products. These updated ways of working were 1) the use of other regulator’s opinions (ORO) by the FSA and 2) the use of an ‘abbreviated process’ (ABB) for safety assessments. These processes involve internal assurance via an FSA decision panel that is chaired by a senior leader from the Risk Assessment Unit with regular oversight from the FSA Chief Scientific Advisor. Applications progressing through these assessment routes would not routinely be considered by SACs, but a summary of the applications would be periodically presented to the COT for information.

2024 Membership of the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment

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 (until March 2024)

Principal Science Advisor at Syngenta (part time).

Ms Jane Case (Up until March 2024)

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 (Up until March 2024)

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 (Up until March 2024)

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 (Up until March 2024)

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.

Dr Chris Morris (from April 2024 onwards)

Senior Lecturer at Newcastle University.

Dr Meera Cush (from April 2024 onwards)

Senior Managing Consultant in Regulatory Toxicology at Ramboll UK Limited.

Mr Gordon Burton (from April 2024 onwards)
Public Interest Representative (Lay Member).

Mr Nick Richardson (from April 2024 onwards)

Public Interest Representative (Lay Member),

Defence Science and Technology Laboratory (Dstl).

Dr Alison Yeates (from April 2024 onwards)

Lecturer in Biomedical Science within the School of Biomedical Sciences at Ulster University.

Dr Andreas Kolb (from April 2024 onwards)

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

Secretariat

Ms Catherine Mulholland BSc (Hons), ERT (Scientific Secretary)
Ms Britta Gadeberg BSc (Hons) MSc ERT (Scientific Secretary – UK HAS)
Dr David Gott BSc (Hons) PhD (until May 2024)
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 (until October 2024)
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 Orphanos
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 Rachel Kerr BSc PhD
Ms Polly Bevan BSc MSc
Mr James Metcalfe BSc
Ms Alba Ureña Rusillo BSc MSc

Sub-groups active in 2024

Sub-groups active in 2024	**Current COT Members serving**
Joint SACN-COT Working Group on plant-based drinks	Professor Alan Boobis Professor Gunter Kuhnle Dr Caroline Harris (ad hoc)
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

Declaration of members' interests during the period of this report - 2024

Chair Professor Alan Boobis OBE, PhD, FBTS, FBPhS

Current

Personal Interests

Employment.	Emeritus Professor of Imperial College London, National Heart & Lung Institute.
Consultancies and other fee-paid work.	None.
Shareholdings.	Bank Santander, Barclays Bank, BT Group, Centrica, Iberdrola SA, Lloyds, National Grid.

Clubs, other organisations and advocacy groups.	Fellow of British Toxicology Society, Fellow of British Pharmacological Society, Honorary member of EUROTOX, Member of the US Society of Toxicology, Member of Board of Directors of International Life Sciences Institute (ILSI) - Europe, Member of Committee on Medical Effects of Air Pollutants; chair/vice-chair of FAO/WHO JECFA (vet), Member of FAO/WHO JMPR, Member of WHO TobReg.
Other personal interests.	Member of External Advisory Committee, Michigan State University (MSU) Center for Research on Ingredient Safety (CRIS); Chair/Member of a number of ILSI Europe technical committees and working groups addressing generic risk assessment issues (microplastics, threshold of toxicological concern, packaging migrants, benefit-risk assessment), Member of Expert Advisory Group, The Personal Care Products Council, Washington, D.C: carcinogenic risk of sunscreen products, Member of Science Advisory Board, Plastics Europe bridging project: Bridging the Gap between Microplastics and Human Health, Member of the Science Management Team of the National Alternative Protein Innovation Centre (NAPIC).

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Historic interests

Personal Interests

Direct employment.	Imperial College London, Department of Medicine (retired June 2017, part-time appointment from Aug 2017-May 2019), Full retiral June 2019.
Consultancies and other fee-paid work.	None.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	Fellow of Royal Society of Biology (until 2019), Member of Board of Trustees, Health and Environmental Sciences Institute (until 2021), Member of Board of Trustees, ILSI (until 2023), Convenor (chair) of ISO TC126 Working Group 10 (Intense Smoking Regime), nominated by UK Department of Health (until 2022).
Other personal interests.	Member of Science Advisory Board, Swiss Centre for Applied Human Toxicology, Basel, Switzerland (until 2020), Member of Scientific Advisory Board, Long Range Research Strategy (LRSS), Cosmetics Europe (dormant), Member of Scientific Advisory Board of the Agency for Innovations in Food and Chemical Safety Programme, Science, Technology and Research, Singapore (A*STAR) (until 2022), Member of Scientific Advisory Board of Owlstone Medical (until 2021).

Non-Personal

Fellowships.	None.
Indirect support.	European Commission Horizon 2020: EUROMIX: Assessing the health risks of combined human exposure to multiple food-related toxic substances (until 2019).
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Full Members

Professor Peter Barlow

Current

Personal Interests

Direct employment.	Edinburgh Napier University (2011-Current).
Consultancies and other fee-paid work.	Expert Advisor, Dunedin Solutions Ltd (Nov 2023-Present) Unremunerated role.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	Chair – Chief Scientist Office Clinical Academic Fellowship Committee (non-remunerated role), Chair – NHS Assure Grant Funding Panel (non-remunerated role), Member of British Society of Immunology.
Other personal interests.	Co-Founder of an emerging Edinburgh Napier spinout entity (PlusPEP). Future commercial focus around the application of Sodium Butyrate and/or vitamin D for the treatment of rhinovirus infection in humans (International patent WO2021198691A1). Grant holder and Principal Investigator, Interface Innovation Voucher, held with Mercel Ltd. “Algumer Enzyme Protection”.

Non-Personal

Fellowships.	Fellow of the Royal Society of Biology (current).
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Historic interests

Personal Interests

Direct employment.	United States Centers for Disease Control and Prevention (US Government Agency) (2009-2011), University of Edinburgh (2005-2009), Policy officer at the Health Department, Scottish Government (2004-2005).

Consultancies and other fee-paid work.	None.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	None.
Other personal interests.	None.

Non-Personal

Fellowships.	British Science Association Media Fellowship (2018), hosted by BBC Scotland.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Dr Phil Botham

Membership ended 31/03/2024. Retained as a Co-Opted Member for the PFAS, BPA and Titanium Dioxide Subgroups.

Current

Personal Interests

Direct employment.	Syngenta - Principal Science Advisor, Product Safety.
Consultancies and other fee-paid work.	Regulatory Science Associates – Leadership Consultant.
Shareholdings.	AstraZeneca.
Clubs, other organisations and advocacy groups.	Crop Life International, Crop Life Europe – Chair or Member of Expert Groups, European Centre for Ecotoxicology and Toxicology (ECETOC) – Member of Scientific Committee and Task Forces, British Toxicology Society (Fellow and Member of Executive Committee; President since 2024), Society of Toxicology - Member, Royal College of Pathologists - Fellow.
Other personal interests.	My wife also works for Syngenta.

Non-Personal

Fellowships.	None.

Indirect support.	The British Toxicology Society receives donations from a number of companies (e.g. AstraZeneca, Corteva, GSK, Syngenta, Unilever, Apconix, Charles River, BIBRA) to support its activities, including an Annual Congress and Education and Training opportunities.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Historic interests

Personal Interests

Direct employment.	None.
Consultancies and other fee-paid work.	None.
Shareholdings.	Syngenta.
Clubs, other organisations and advocacy groups.	NC3Rs – Board Member, ECVAM Scientific Advisory Committee – Member, Advisory Committee on Pesticides Medical and Toxicological Panel - Member.
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Mr Gordon Burton

Membership commenced 01/03/2024.

Current

Personal Interests

Direct employment.	None.
Consultancies and other fee-paid work.	None.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	None.
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	Wife is a member of the Food Standards Agency Advisory Committee on Animal Feeding stuffs (ACAF).
Other non-personal interests.	None.

Historic interests

Personal Interests

Direct employment.	None.
Consultancies and other fee-paid work.	Consultancy Nottingham Trent University (Silicon Supplement development), Silicon Active, my Wife is a shareholder.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	None.
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Ms Jane Case

Membership ended 31/03/2024.

Current

Personal Interests

Direct employment.	Trowers & Hamlins LLP, Company Secretary of Muse Interiors.

Consultancies and other fee-paid work.	None.
Shareholdings.	Standard Life Santander.
Clubs, other organisations and advocacy groups.	None.
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Historic Interests

Personal Interests

Direct employment.	None.
Consultancies and other fee-paid work.	None.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	None.
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Dr Stella Cochrane

Current

Personal Interests

Direct employment.	Unilever employee.

Consultancies and other fee-paid work.	None.
Shareholdings.	Unilever shareholder.
Clubs, other organisations and advocacy groups.	Chair of the UK Food and Drink Federation Allergen Steering Group, Chair of Food Drink Europe Allergen Steering Group. University of Nebraska Food Allergy Research & Resources Board (FARRP).
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Historic Interests

Personal Interests

Direct employment.	None.
Consultancies and other fee-paid work.	None.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	None.
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Dr James Coulson

Current

Personal Interests

Direct employment.	Cardiff University.
Consultancies and other fee-paid work.	Director of Medical, Scientific & Toxicological Consultancy Ltd.
Shareholdings.	50% shareholder of Medical, Scientific & Toxicological Consultancy Ltd.
Clubs, other organisations and advocacy groups.	National Trust Member.
Other personal interests.	None.

Non-Personal

Fellowships.	Royal College of Physicians of London, Royal College of Physicians of Edinburgh, British Pharmacology Society, Royal Society of Biology.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	Herbal Medicines Advisory Committee (MHRA) , Expert Committee on Pesticides (HSE).
Other non-personal interests.	None.

Historic interests

Personal Interests

Direct employment.	None.
Consultancies and other fee-paid work.	None.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	None.
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.

Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Dr Meera Cush

Current

Personal Interests

Direct employment.	Ramboll UK Limited.
Consultancies and other fee-paid work.	Membership: UKHSA Committee on Carcinogenicity, HSE UK REACH Independent Scientific Expert Pool (RISEP) RISEP.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	Ramboll is a member of Food and Drink Federation (FDF) and I am the lead contact.
Other personal interests.	I work for clients who are food and food contact material manufacturers.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	Member of the UKHSA Committee on Carcinogenicity (COC).
Other non-personal interests.	None.

Historic interests

Personal Interests

Direct employment.	None.
Consultancies and other fee-paid work.	None.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	None.

Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Dr Steven Enoch

Current

Personal Interests

Direct employment.	Liverpool John Moores University Reader in Computational Toxicology.
Consultancies and other fee-paid work.	Consultancy (on-going projects): Crop Life Europe (2020 – present; total value: €200,000), BASF (2025 – present; total value €25,000), P&G (2025 – present; total value €25,000).
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	None.
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Historic interests

Personal Interests

Direct employment.	None.
Consultancies and other fee-paid work.	Regulatory Science Associates: 2024 for 6 months: £8,000, BASF: 2020 for 12 months: €35,000.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	None.
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Professor Gary Hutchison

Current

Personal Interests

Direct employment.	Professor of Toxicology and Dean of Applied Sciences at Edinburgh Napier University.
Consultancies and other fee-paid work.	None.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	Member of British Toxicology Society.
Other personal interests.	None.

Non-Personal

Fellowships.	Fellow of Royal Society of Biology, Senior Fellow Higher Education Academy.

Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	Office for Product Safety & Standards Register of Specialists 2020 – present.
Other non-personal interests.	Chair of Board of Governance, Scottish Institute of Policing Research, Member of Governing Council of Marine Alliance for Science and Technology for Scotland (MASTS), Member of the Scottish Government Chemicals Policy Network.

Historic interests

Personal Interests

Direct employment.	Medical Research Council (2004-2007).
Consultancies and other fee-paid work.	None.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	None.
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	Member of Hazardous Substances Advisory Committee (2012-2021), Member of Defra's College of Scientific Experts 2017 - 2021.
Other non-personal interests.	None.

Dr Silvia Gratz

Current

Personal Interests

Direct employment.	Rowett Institute, University of Aberdeen.

Consultancies and other fee-paid work.	None.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	None.
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Historic interests

Personal Interests

Direct employment.	None.
Consultancies and other fee-paid work.	None.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	Lapsed member of the British Toxicology Society, The Nutrition Society (UK).
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Professor Thorhallur Ingi Halldorsson

Current

Personal Interests

Direct employment.	Faculty of Food Science and Nutrition, University of Iceland (2009 – ongoing).
Consultancies and other fee-paid work.	European Food Safety Authority - Scientific committee and various working groups (2015 – ongoing). Icelandic Risk Assessment Committee for Food, Feed, Fertilizers and Seeds (IRAC) – occasional expert work (2021 – ongoing), The Icelandic Research Found (RANNIS) – occasional member of different expert panels (2011 – ongoing), I am a member of an expert group established by the Danish Ministry of Environment tasked to assess nitrate in drinking water and the need to revising the current drinking water limit (2024 - ongoing). The final assessment is expected in 2025.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	None.
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Historic interests

Personal Interests

Direct employment.	None.

Consultancies and other fee-paid work.	Nordic Council of Ministers - revision of the 2022 Nordic Nutrition Recommendation). 2017 – 2023), The Nutricia Research Foundation – review of applications once a year. Involvement ended in (2017 2022).
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	None.
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Dr Sarah Judge

Membership ended 31/03/2024.

Current

Personal Interests

Direct employment.	Newcastle University, Lowcock Properties Ltd.
Consultancies and other fee-paid work.	None.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	British Pharmacology Society, British Toxicology Society International Association for Neurotoxicology.
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.

Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Historic interests

Personal Interests

Direct employment.	None.
Consultancies and other fee-paid work.	None.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	None.
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	Research Funding.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Dr Andreas Kolb

Membership commenced 01/03/2024.

Current

Personal Interests

Direct employment.	Senior Research Fellow at the Rowett Institute, University of Aberdeen.
Consultancies and other fee-paid work.	None.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	None.
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.

Other public appointments.	None.
Other non-personal interests.	None.

Historic interests

Personal Interests

Direct employment.	None.
Consultancies and other fee-paid work.	None.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	None.
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	Part-time PhD student funded by industry.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Professor Gunter Kuhnle

Current

Personal Interests

Direct employment.	University of Reading.
Consultancies and other fee-paid work.	None.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	None.
Other personal interests.	Longstanding research collaboration with Mars -arising from previous funded projects (funding now expired). Financial contribution now limited to acceptance of travel and hospitality.

Non-Personal

Fellowships.	None.
Indirect support.	None.

Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	Director of an analytical facility at the University of Reading, where users may be indirectly funded by commercial sources, or work has been directly commissioned by them (if this is accurate), Member of the Scientific Committee of the British Nutrition Foundation. Member of the British Mass Spectrometry Society.

Historic interests

Personal Interests

Direct employment.	None.
Consultancies and other fee-paid work.	EQT (Consultancy, payment to University).
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	None.
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Dr David Lovell

Current

Personal Interests

Direct employment.	Emeritus Reader in Medical Statistics at City St George's, University of London. Pension – Pfizer.
Consultancies and other fee-paid work.	None.
Shareholdings.	National Grid plc, AstraZeneca (Spouse Shareholder),

	National Grid plc (Spouse Shareholder).
Clubs, other organisations and advocacy groups.	Biometrics Society, British Toxicological Society (BTS), Genetics Society, Royal Society of Biology (RSB), Laboratory Animal Science Association (LASA), Royal Statistical Society (RSS), Statisticians in the pharmaceutical industry (PSI), United Kingdom Environment Mutagen Society (UKEMS), Member of the UK Committee on Toxicity in Chemicals in Food Consumer Products and the Environment (COT) and sub-groups, Member of BEIS SAG-CS, Member of the joint FAO/WHO Expert Committee on Food Additives (JECFA) 92, Member of HESI/GTCC (Genetic Toxicology Genetic Committee), MRC EMINENT Scientific Review Board, RISEP Challenge Panel Member, Member of OECD Expert Groups, ILSI Europe (Combined Toxicity Expert Group), 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.
Other personal interests.	None.

Non-Personal

Fellowships.	None.

Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Historic interests

Personal Interests

Direct employment.	None.
Consultancies and other fee-paid work.	None.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	EFSA Scientific Committee, COM, COC, Member of UK National Centre of Replacement, Refinement and Reduction of Animals in Research (NC3Rs) Board (until Dec 2022), MHRA ISAC, ILSI Europe (TTC Expert group}, OECD (Workgroup Member), IWGT (Workgroup Member).
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Dr Chris Morris

Membership commenced 01/03/2024.

Current

Personal Interests

Direct employment.	Newcastle University

Consultancies and other fee-paid work.	None.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	None.
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Historic interests

Personal Interests

Direct employment.	None.
Consultancies and other fee-paid work.	None.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	Member of the Committee on Pesticides, (2012 - January 2022).
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Professor Shirley Price

Current

Personal Interests

Direct employment.	None.
Consultancies and other fee-paid work.	UK Science Advisory Committees (Paid honoraria) including:

	Office for Product Safety and Standards (OPSS) Science Advisory Group on Consumer Safety (SAG-CS): Chair 2021-Current. Medicines and Healthcare Regulatory Agency: Paediatric Medicines Expert Advisory Group (PMEAG) Member since 2023. Medicines and Healthcare Regulatory Agency: Various Expert working Groups.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	British Toxicology Society; Honorary Fellow and General Secretary, CO Research Trust Board: Member since 2020.
Other personal interests.	None.

Non-Personal

Fellowships.	FRSB, HonFBTS, FRSC;FHEA.
Indirect support.	None.
Trusteeships.	CO Research Trust; BTS; Godalming 6th Form College.
Land and property.	None.
Other public appointments.	Associate Editor for Toxicology Research, Member of the FAO and WHO roster of experts, Royal Society of Chemistry (RSC) UN SPP Engagement Group, RSC Toxicology Group Member, Skills Gap Project-Chair of Steering Group and Advisory Board 2022-Present.
Other non-personal interests.	None.

Historic interests

Personal Interests

Direct employment.	None.
Consultancies and other fee-paid work.	Commissioner on the Commission of Human Medicines from 2010-2022.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	British Society of Toxicological Pathologists. Resigned as a member in 2020. Held position as President 2020-2022.

Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	Royal Grammar School.
Land and property.	None.
Other public appointments.	President of the British Toxicology Society.
Other non-personal interests.	None.

Dr Mac Provan

Current

Personal Interests

Direct employment.	Director, Regulatory Science Ltd.
Consultancies and other fee-paid work.	None.
Shareholdings.	I am the major shareholder in a consultancy that operates within the pharmaceutical, agrochemical and general chemicals sectors. I do not perform work within any of these sectors, having only a, non-technical, business monitoring/advisory role. I do not take a salary but take dividends annually.
Clubs, other organisations and advocacy groups.	None.
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Historic interests

Personal Interests

Direct employment.	None.

Consultancies and other fee-paid work.	None.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	None.
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Ms Juliet Rix

Membership ended 31/03/2024.

Current

Personal Interests

Direct employment.	None.
Consultancies and other fee-paid work.	None.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	None.
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Historic interests

Personal Interests

Direct employment.	None.
Consultancies and other fee-paid work.	None.

Shareholdings.	None.
Clubs, other organisations and advocacy groups.	None.
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Nick Richardson

Current

Personal Interests

Direct employment.	Defence Science and Technology Laboratory.
Consultancies and other fee-paid work.	None.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	None.
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Historic interests

Personal Interests

Direct employment.	None.
Consultancies and other fee-paid work.	None.
Shareholdings.	None.

Clubs, other organisations and advocacy groups.	None.
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Dr Michael Routledge

Current

Personal Interests

Direct employment.	Associate Professor of Environmental Toxicology in the School of Medicine at Leicester
Consultancies and other fee-paid work.	None.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	None.
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	President of UK Environmental Mutagen Society.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Historic interests

Personal Interests

Direct employment.	None.
Consultancies and other fee-paid work.	None.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	None.

Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Dr Cheryl Scudamore

Current

Personal Interests

Direct employment.	None.
Consultancies and other fee-paid work.	Regulatory Science Associates. This is an ongoing agreement since 2019. I am not an employee but do occasional paid consultancy work for their clients largely in the pesticide industry.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	None.
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	Member of the Expert Committee on Pesticides (ECP).
Other non-personal interests.	None.

Historic interests

Personal Interests

Direct employment.	Visiting Chair in Veterinary Pathology at Surrey University Veterinary School 2013-2021.
Consultancies and other fee-paid work.	Regulatory Science Associates. Ongoing ad hoc consultancy work since 2019 onwards.
Shareholdings.	None.

Clubs, other organisations and advocacy groups.	None.
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Dr Natalie Thatcher

Current

Personal Interests

Direct employment.	Mondelēz International
Consultancies and other fee-paid work.	None.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	None.
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Historic interests

Personal Interests

Direct employment.	None.
Consultancies and other fee-paid work.	None.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	None.

Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Professor Mireille Toledano

Current

Personal Interests

Direct employment.	Imperial College London.
Consultancies and other fee-paid work.	None.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	None.
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Historic interests

Personal Interests

Direct employment.	None.
Consultancies and other fee-paid work.	None.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	None.
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Dr Simon Wilkinson

Current

Personal Interests

Direct employment.	Senior Lecturer in Pharmacology in the School of Biomedical, Nutritional and Sports Sciences at Newcastle University since November 2018.
Consultancies and other fee-paid work.	None.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	None.
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Historic interests

Personal Interests

Direct employment.	None.
Consultancies and other fee-paid work.	L'Oreal Research and Development, Paris.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	None.
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Professor Phillipe Wilson

Current

Personal Interests

Direct employment.	York St John University.
Consultancies and other fee-paid work.	NHS
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	President-Elect of the Comparative Council of the Royal Society of Medicine.
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	UKGLE Committee at DEFRA.
Other non-personal interests.	None.

Historic interests

Personal Interests

Direct employment.	Nottingham Trent University, De Montfort University (ended 2024), Rare Breeds Survival Trust (March 2020-Jan 2021).
Consultancies and other fee-paid work.	None.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	Chair of Royal Society of Biology EMB.
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Professor Matthew Wright

Membership ended 31/03/2024.Retained as a Co-Opted Member for the PFAS. Subgroup.

Current

Personal Interests

Direct employment.	Retired.
Consultancies and other fee-paid work.	None.
Shareholdings.	HSE (Expert Committee on Pesticides), member, EFSA (FAF Panel WG member), Elsevier (Chief Editor, Food and Chemical Toxicology).
Clubs, other organisations and advocacy groups.	BTS (retired member).
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Historic interests

Personal Interests

Direct employment.	Newcastle University (until Aug 2024).
Consultancies and other fee-paid work.	EFSA (FAF Panel member),

	Elsevier (Associate Editor, Toxicology).
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	None.
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Dr Alison Yeates

Membership commenced 01/03/2024.

Current

Personal Interests

Direct employment.	Ulster University.
Consultancies and other fee-paid work.	None.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	None.
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Historic interests

Personal Interests

Direct employment.	None.
Consultancies and other fee-paid work.	None.

Shareholdings.	None.
Clubs, other organisations and advocacy groups.	Research advisor, School and Nursery Milk Alliance (SNMA).
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Professor Maged Younes

Current

Personal Interests

Direct employment.	None.
Consultancies and other fee-paid work.	None.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	None.
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	Two properties for personal use (Spain).
Other public appointments.	Chair, EBM in RA Committee, BfR.
Other non-personal interests.	None.

Historic interests

Personal Interests

Direct employment.	Retired.
Consultancies and other fee-paid work.	None.
Shareholdings.	None.

Clubs, other organisations and advocacy groups.	None.
Other personal interests.	FAF Panel Chair, EFSA and Member of the SC of EFSA, till 2024.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Co-Opted Members

Dr Caroline Harris

Current

Personal Interests

Direct employment.	Exponent International Ltd.
Consultancies and other fee-paid work.	Member of the Expert Committee on Pesticides, Member of the UKHSA Committee on Carcinogenicity (COC).
Shareholdings.	Exponent Inc.
Clubs, other organisations and advocacy groups.	Technical member, International Union of Pure and Applied Chemistry.
Other personal interests.	None.

Non-Personal

Fellowships.	Royal Society of Chemistry.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Historic interests

Personal Interests

Direct employment.	None.
Consultancies and other fee-paid work.	None.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	None.
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Professor Paul Haggarty

Current

Personal Interests

Direct employment.	Head of Lifelong Health at the Rowett Institute of Nutrition and Health, University of Aberdeen.
Consultancies and other fee-paid work.	None.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	None.
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	UK Research and Innovation (UKRI) Global Challenges Research Fund (GCRF) Dates: 2019 to 2024.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Historic interests

Personal Interests

Direct employment.	None.
Consultancies and other fee-paid work.	None.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	None.
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	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.
Other non-personal interests.	None.

Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment Annual Report 2024

Preface

I am proud to report on the work of the Committee on Mutagenicity (COM) during 2024. I was also delighted to be “renewed” as Chair of COM in 2024 for a further 3 years. 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 committees website: Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment - GOV.UK.

The membership of COM has undergone some changes in 2024 with members rotating off the committee and new members joining COM.

In 2024, COM published its long-awaited opinion on the genotoxicity of titanium dioxide, an opinion that was 3 years in the making. I’d like to thank the COM members and secretariat for their hard work on this aspect. Published document can be viewed using this link: Statement on the COM assessment of in vitro and in vivo

genotoxicity of titanium dioxide - GOV.UK. This COM opinion was published alongside wider toxicological opinion published by our sister committee, COT.

In 2024, COM was also involved in initiating a working group to look at quantitative structure activity relationship (QSAR) approaches, an *in silico* tool for predicting genotoxicity. Other aspects covered by COM in 2024 included further discussion on germ cell mutagens and a new approach for horizon scanning.

Professor Gareth Jenkins – Chair

Completed Work

Review of genotoxicity of titanium dioxide – summary of *in vitro* and *in vivo* data

2.1 In 2021, the European Food Safety Authority (EFSA) published an opinion concluding that food additive titanium dioxide (E171) could no longer be considered to be safe for use in food. The Food Standard Agency (FSA) initiated a review of the EFSA Opinion. Identifying a number of concerns, it was decided that the Opinion should be referred to the UK's Scientific Advisory Committees for independent expert review. The EFSA opinion was presented to the COM and COT (MUT/2021/03 and TOX/2021/36), and the committees considered that the conclusions were not robust, and it was decided that the UK should undertake an independent evaluation.

2.2 FSA asked COM to initiate an independent evaluation of the genotoxicity data of titanium dioxide specifically as a food additive.

2.3 In October 2021, paper MUT/2021/12 was presented to COM, summarizing the available studies on the genotoxicity of titanium dioxide. However, members concluded that it was not possible to evaluate its genotoxicity at that stage. As a preliminary step, the COM recommended a sifting approach to identify high-quality studies before conducting a full evaluation. A subgroup of COM was tasked with

evaluating the evidence. The subgroup established criteria and methodology for the selection of studies.

2.4 In June 2022 meeting, paper MUT/2022/05 introduced the agreed methodology for systematically sifting the papers and evaluation of the quality of the genotoxicity studies and evaluating data on nanomaterials. A subgroup of the COM later refined this approach, developing a proforma which 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.

2.5 By October 2023, a 3-tiered screening and selection approach was presented by the subgroup to evaluate the publicly available literatures and assigned a quality rating based on its robustness (MUT/2023/07 and MUT/2023/08). It was agreed that revised draft papers would be prepared by incorporating members opinions and the subgroup aimed to finalize the opinion by early 2024.

2.6 At the February 2024 meeting, the final assessment of *in vitro* and *in vivo* data was reviewed (MUT/2024/01 and MUT/2024/02).

2.7 Regarding the in vitro studies, the COM concluded that overall, there is little evidence that titanium dioxide nanoparticles are genotoxic in vitro, with the limited number of positive studies all reporting no dose-response effects. There was also a lack of replication of study outcomes using the same nanoparticle in different labs. With regards to the titanium dioxide food grade additive E171 specifically, COM commented that: ‘currently a definitive assessment of the safety of E171 is difficult when there are no high-quality OECD-compliant studies that adequately incorporate the study design considerations and characterisation of the nanoparticulate fraction present in E171. The studies identified in this report were not representative of E171, where the fraction of nanoparticulate is <50% and according to the recent "Guidance on the implementation of the Commission Recommendation 2022/C 229/01 on the definition of nanomaterial" (https://data.europa.eu/doi/10.2760/143118), E171 would

not fall under the definition of a NM, hence GLP studies with E171 would be required to definitively assess the hazard.

2.8 Regarding the in vivo studies, the COM concluded that overall, there is little evidence in the literature to suggest that there is a health concern related to genotoxicity induction by titanium dioxide, particularly via the oral route of exposure and especially the micro sized titanium dioxide fraction (most studies used the nano-sized material). With regards to E171 specifically, COM comments that: 'currently a definitive assessment of the safety of food grade E171 is difficult when there are no high-quality OECD-compliant studies that adequately incorporate the study design considerations and characterisation of the nanoparticulate fraction present in E171. COM also noted that there is a dearth of high-quality data sets that are OECD compliant, and this has led to a lot of conflicting data and uncertainty in the risk assessment for titanium dioxide.

2.9 In October 2024, the COT published a statement on the safety of titanium dioxide (E171) as a food additive, included the conclusions on genotoxicity from COM. The COM concluded that there was a little evidence in the literature to suggest that titanium dioxide posed a genotoxicity risk, especially via the oral route. Notably, most studies analysed focused on nano-sized titanium dioxide, whereas food-grade titanium dioxide (E171) is primarily micro-sized. Hence, any genotoxicity risk from dietary food grade titanium dioxide (E171) was considered to be low.

Ongoing work

Guidance on the use of QSARs - draft paper for discussion

2.10 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. In June 2024, paper MUT/2024/3 was presented by this subgroup, outlining best practices for using (Q)SAR in genotoxicity evaluation, including the prioritization of compounds, selection of the (Q)SAR model, reporting of

(Q)SAR predictions, considerations of expert knowledge, read-across approaches, and integration of findings into a weight-of-evidence evaluation.

2.11 The approach taken so far to produce this discussion paper had been to evaluate existing guidance on (Q)SARs (e.g., OECD, ECHA, ICH and SCCS). It was determined that current guidance is limited in its specificity for genotoxicity, especially clastogenicity. Therefore, to address this information gap, the primary literature was also reviewed.

2.12 During discussions, COM members considered that the current paper outlines the 'state of the science' and a more specific set of COM recommendations on how to use QSARs for evaluating genotoxicity should be established, based on the synthesis of information in the paper. The inclusion of case studies from Government departments and agencies in the final COM guidance was thought to be useful, but these may be hard to define. Members noted that the COM recommendations should have improved narration of data quality and a clear identification of the strengths and weaknesses of the different (Q)SAR models. In addition, incorporation of a summary of recommendations at the start of the document, possibly in the form of a flow-chart as per the overarching COM Guidance, was considered important for the accessibility of information to users.

2.13 A follow-up meeting with the subgroup was agreed upon to review feedback and finalize next steps. The target completion for the guidance document was set for the March 2025.

UN GHS germ cell mutagenicity – for information

2.14 In June 2024, members of the COM were informed (MUT/2024/04) that UK REACH Independent Scientific Expert Pool (RISEP) had comments regarding the classification of mutagens. In response to these comments, the Health and Safety Executive (HSE) drafted a document on the classification of germ cell mutagenicity and had requested this to be considered by the COM. The COM recommended preparing a background document on CLP and UK REACH to provide context before

detailed discussions. This document was circulated to members, and a more detailed discussion paper from HSE is scheduled for a future meetings.

Horizon scanning

Presentation from Alexander Kalian, King's College London, on work related to computational methods and mutagenicity

2.15 At the June 2024 meeting, Alexander Kalian from King's College London gave a presentation that reported findings from his PhD, supported by the UK Food Standards Agency, which aims to develop AI-driven models to improve the assessment of toxicity related to food. Of interest to COM is the use of such technology to predict mutagenicity. At present, food safety hazard assessments are carried out using experimental, analytical, and computational approaches but all of these have potential limitations including scientific validity, ethical considerations, and cost effectiveness. Of the currently available computational approaches, QSAR models are widely used to predict activities of molecules without data as they are very broad and versatile, however the models are very data intensive.

2.16 An AI-driven QSAR model utilising SMILES and deep learning (neural networks) was developed by the speaker which determined mutagenicity in a binary classification (YES/NO) with 78% accuracy (checked against Ames data). The model was further developed to use a convolutional neural network approach, which looks at aspects of images. As molecules are graph structured data, and may not fit into image analysis easily, graph convolutional neural networks (GCN) were developed to achieve this. In addition, the speaker evaluated the use of Explainable AI (XAI) with the model to determine the reasoning behind the mutagenic predictions made, and to mine structural alerts. The model (incorporating node enrichment) was used to predict the mutagenicity (YES/NO) of 5625 molecules, for which Ames data is available, and the output compared to that obtained using a language-based transformer model. An accuracy of between 74% and 78% was achieved (depending on node features used). This represents 85% AUC (area under the curve) which is comparable to other available models, with the transformer model also having 84% AUC (now retrained to give 90% AUC).

2.17 When XAI was used to mine structural alerts from the GCN model, an accuracy of 85% was achieved (using a threshold of 0.7). Very similar identification of fragments (mutagenic and non-mutagenic) was obtained using the language-based transformer model, but not using the QSARpy model and this requires further investigation. In addition, some identified structural alerts did not make complete sense and this also needs investigation. Prior to releasing the model for public use, the OECD guidelines require formalisation of the identity of its applicability domain, and it will also need to be applied to different toxicological endpoints.

2.18 During discussions, the model's ability to assess the possibility of positional (stearic) hinderance was queried, which may be the reason why some fragments that are initially identified as DNA reactive are not so. The speaker replied that many of the fragments identified are very similar and while it is theoretically possible to look at positional hinderance, the false positives may also be due to other fragments being present, so the reasons are likely to be multifaceted. A member also asked whether the 3D structure of the molecule was important in determining whether it is DNA reactive. The speaker replied that the model developed here utilised fragments rather than 3D structure, however, there are examples where stearic chemistry is important to DNA reactivity and that the influence of stearic chemistry is often neglected as it is difficult to study and would need a more advanced model. Suggestions were made to the speaker by a member of COM to address some of the potential issues with the model.

2.19 The Chair thanked the speaker on behalf of the Committee and concluded that these approaches are not used at a regulatory level at the moment. However, these tools show how current approaches may be replaced in the near future and it is important that COM is prepared and understands them.

Presentation from Paul Rees, Swansea University, on Artificial Intelligence and mutagenicity data

2.20 At the June 2024 meeting, Paul Rees from Swansea University provided a presentation on Artificial Intelligence and mutagenicity data. The speaker outlined a case study to show how traditional machine learning is used to evaluate the cell cycle using a set of label free flow cytometry images. CellProfiler is used to extract the cell features following training of the model (supervised machine learning) with features from annotated images obtained using biomarkers for different parts of the cell cycle. AI models can provide a classification for the cell without adding cell stains (label free) with an accuracy of around 90%; it is important for some applications that cell biomarkers are not used. In addition, regression analysis has been used to predict DNA content from label free cell images.

2.21 Paul Rees noted that deep learning (neural networks) is a key concept in AI, but this does not have the same knowledge base as traditional learning. AI and deep learning are built around an artificial neuron which forms a neural network, and artificial weightings are given to determine how well they are connected. Although these have been around for 60 years, it is only now that computers are fast enough to develop deep learning. A commonly used network is the convolution neural network and the speaker outlined how this is used to synthesise an array (matrix) of numbers from the input image to allow matching with matrices from training images. Deep neural networks have been used to score micronucleus images for nine different phenotypes (from mononucleate to tetranucleate) with an accuracy of 96% (compared to human scoring). Label free detection has also been applied to leukaemia cells which reduces analysis (diagnostic) time considerably, to look at the change in morphology of red cells on storage, and to classify pollen grain in Arctic ice.

2.22 Another type of neural network is object detection, and this has been used to identify binucleated cells with micronuclei with 100% accuracy, following minimal training (175 binucleated cells with micronuclei images). Without retraining, the system detected tetranucleated and trinucleated cells, with and without micronuclei, with an accuracy of 90%. Other developments include the evaluation of cell painting to detect genotoxic events in cells, which is an unbiased cell profiling method. The greatest use of the technique has been for drug discovery, but it has now been

applied to look for genotoxic changes. Detection of micronuclei, gH2AX foci, fragmented nuclei etc., was achieved using CellProfiler (previously trained) in the same CellPainting pipeline. This has important advantages as very large, freely available datasets for chemical structure, imaging and gene expression have been developed using cell painting and these will be able to now be an available resource to support future work.

2.23 During discussions, a COM member asked how independent the variables are in the model and can additional ones be added easily. The speaker replied that you do not have to start from scratch as the variables are independent and so you just introduce the new ones. A member also asked how to ensure that the available classifiers have been validated. The speaker replied that expert scientists need to produce annotated data sets, so we have known valid sets to use. It is also possible that, in the future, the datasets will need to be regulated to help regulatory submissions where this data is used. A comment was made that it is likely there will be an OECD guideline for using AI for genotoxicity assessment in the future. A point of clarification was also given that, at present, Cell Painting data is only being used at the early stage of drug discovery and is not being seen by regulators. A member also asked what level of accuracy has been obtained with the deep learning approach and the speaker replied that it has not been taken past the 90%, obtained with machine learning, as the availability of images to develop a classification set is limited at the moment.

OECD Test Guideline Programme

2.24 At the COM February 2024 meeting, members were informed that United Kingdom, along with several other countries, would submit a Standard Project Submission Form (SPSF) to the OECD to propose adaptations to the test guideline *in vitro* micronucleus assay (TG487). These adaptations would aim to include updates to the considerations necessary for evaluating nanomaterials. An independent interlaboratory trial is required to achieve this, which is the primary focus of the SPSF project. The trial would aim to provide the necessary data and evidence to facilitate the adaptation of TG487 for nanomaterials. The proposal is

scheduled to be presented at the April OECD meeting, primarily for sign-off. The project is anticipated to commence in early summer.

2.25 In June 2024, the members were informed that the process of generating data for this project is currently in progress and the committee is expected to hear more information about this in the upcoming meetings.

2024 Membership of the Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment

Chair

Professor Gareth Jenkins

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

Ex-Officio Chair of the Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment (COC).

Members

Professor David Harrison MD DSc FRCPath FRCPEd FRCSEd

Professor of Pathology, University of St Andrews.

Dr Carol Beevers (to 31 December 2024)

Regulatory Toxicology, Corteva Agriscience.

Dr Ann Doherty (from 1 May 2024)

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

Dr Paul Fowler

FSTox Consulting.

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.

Dr Robert Searle Foster (from 1 May 2024)

Lhasa Ltd.

Dr Robert Smith (from 1 May 2024)

Labcorp.

Mrs Madeleine Wang

Lay Member.

Mr Amit Bhagwat (to 31 August 2024)

Lay Member.

Dr Nathan Goldsmith

Associate Member, Exponent.

Secretariat

Dr Ovnair Sepai	UKHSA Scientific Secretary
Mr Stephen Robjohns	UKHSA Scientific Secretariat
Ms Cath Mulholland	FSA Scientific Secretary
Ms Claire Potter	FSA Scientific Secretariat

Mr Tom Fraser	Committee Administrator, UKHSA

Declaration of members interests during the period of this report

Professor Gareth Jenkins

Current

Personal Interests

Direct employment.	Swansea University
Consultancies and other fee-paid work.	None.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	President of United Kingdom Environment Mutagen Society (UKEMS), Ex Officio Member, Committee on Carcinogenicity (Dept Health and Social Care) 2021-2027 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.
Other personal interests.	Honorary Contract Swansea University

Non-Personal

Fellowships.	None.
Indirect support.	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). Two-month summer work placement (systematic review) by close family member at Swansea University on nanoparticle oxidative stress funded by Health and Environment Sciences Institute (HESI). Supervised by Dr Steve Evans (August-September 2024). National Centre of Replacement, Refinement and Reduction of Animals in Research (NC3Rs) (2018-2022). Former NC3Rs grants (2012-2016 & 2010-2014). Former grants 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).
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Members

Professor David Harrison

Current

Personal Interests

Direct employment.	University of St Andrews, UK, NuCana plc, UK. Employee/Non-executive Director: ILC Therapeutics Ltd (unpaid),

	PathAlba Ltd – Director (unpaid) – dormant.
Consultancies and other fee-paid work.	NHS Lothian – Honorary Consultant.
Shareholdings.	VBL Ltd, UK, Ryboquin Ltd, UK, ILC Therapeutics Ltd.
Clubs, other organisations and advocacy groups.	None.
Other personal interests.	None.

Non-Personal

Fellowships.	University of Edinburgh, UK – Honorary Professor, University of Florida, Adjunct Professor.
Indirect support.	None.
Trusteeships.	Cunningham Trust – (Medical Research Charity)
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	Viewbank Leuchars Ltd – Director (no salary).

Dr Carol Beevers (To 31 December 2024)

Current

Personal Interests

Direct employment.	Corteva Agriscience (from 01 September 2022)
Consultancies and other fee-paid work.	None.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	HESI GTTC (Committee co-chair and workgroup lead), OECD (workgroup member), IWGT (Steering committee member and work group chair),

	United Kingdom Environmental Mutagen Society (UKEMS), Member of the FSA Joint Expert Group on Additives, Enzymes and other Regulated Products (AEJEG).
Other personal interests.	Pension: Covance, Exponent International Ltd, Broughton Group, Corteva Agriscience (from September 2022).

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Dr Ann Doherty From 1 May 2024

Current

Personal Interests

Direct employment.	AstraZeneca
Consultancies and other fee-paid work.	None.
Shareholdings.	AstraZeneca
Clubs, other organisations and advocacy groups.	UK Environmental Mutagen Society (UKEMS) Committee member, ILSI HESI GTTC member, British Toxicology Society, MRC Toxicology Unit Review Board member.
Other personal interests.	**Pension:** AstraZeneca.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Dr Paul Fowler

Current

Personal Interests

Direct employment.	FSTox Consulting – Director.
Consultancies and other fee-paid work.	Regulatory Science Associates – Consultant.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	UKEMS EEMGS (treasurer) Roundtable of Toxicology Consultants (RTC) Royal Society of Biology (ERT) HESI GTTC member Genetic Toxicology Association (GTA)
Other personal interests.	Pension: Unilever (UK).

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Dr George Johnson

Current

Personal Interests

Direct employment.	Director: GTox ltd.
Consultancies and other fee-paid work.	Fermenich, Cefic, American Chemistry Council, Teva, Greenberg Traurig llp, Osler, Hoskin & Harcourt llp, Janssen, Merck.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	United Kingdom Environmental Mutagen Society (UKEMS), HESI (committee member), President of the European Environmental Mutagenesis and Genomics Society (EEMGS) 2019-2021, EMA expert member, IWGT, expert member, ICEM, committee member.
Other personal interests.	Pension: USS University Superannuation Scheme.

Non-Personal

Fellowships.	None.
Indirect support.	GSK, post-doctoral research funding – 2021-2022. nitrosamine research. SCIENSANO. MYCX-IT. 2020-ongoing. EMA. funding through Fraunhofer item. 2022-2023.

	HESI. fast fund. MSc tuition fees. 2022.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Ms Julia Kenny

Current

Personal Interests

Direct employment.	GlaxoSmithKline/GSK
Consultancies and other fee-paid work.	None.
Shareholdings.	GSK, Haleon.
Clubs, other organisations and advocacy groups.	UK Environmental Mutagen Society (UKEMS), Member of the European Federation of Pharmaceutical Industries and Associations (EFPIA) TiO2 Safety Working Group. GSK Representative on the European Federation of Pharmaceutical Industries and Associations (EFPIA) PreClinical Development Expert Group.
Other personal interests.	Pension: GlaxoSmithKline.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Dr Andrew Povey

Current

Personal Interests

Direct employment.	None.
Consultancies and other fee-paid work.	None.
Shareholdings.	Lloyds, Standard Life, Halifax, Santander (Partner Shareholder), Norwich Union (Partner Shareholder), Aviva (Partner Shareholder),
Clubs, other organisations and advocacy groups.	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).
Other personal interests.	European Crop Protection Agency – Part of consortium awarded grant on exposure assessment.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	Departmental studentships funded by industrial and other bodies.

Mr Paul Rawlinson

Current

Personal Interests

Direct employment.	Nufarm Limited
Consultancies and other fee-paid work.	None.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	United Kingdom Environmental Mutagen Society (UKEMS), ILSI HESI GTTC member, Society of Toxicology member, Croplife Europe Human Health Experts Group Committee member.
Other personal interests.	Pension: Nufarm pension scheme, St James Place, Formerly Syngenta.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Dr Robert Searle Foster from 1 May 2024

Current

Personal Interests

Direct employment.	Lhasa Limited, Consult Lhasa.

Consultancies and other fee-paid work.	None.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	Genetic Toxicology Association (GTA). Royal society of chemistry (RSC), Royal society of chemistry (RSC) toxicology group committee
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Dr Robert Smith from 1 May 2024

Current

Personal Interests

Direct employment.	Labcorp
Consultancies and other fee-paid work.	None.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	Secretary of the UK environmental mutagen society (UKEMS). Start date June 2017 – July 2024. HESI genetic toxicology committee (GTTC) workgroup member. OECD expert group on genotoxicity workgroup member. Secretary UKEMS next generation sequencing (NGS) special interest

	group (SIG). Start date 2023, end date July 2024.
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Ms Madeleine Wang

Current

Personal Interests

Direct employment.	None.
Consultancies and other fee-paid work.	None.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	None.
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Amit Bhagwat to 31 August 2024

Current

Personal Interests

Direct employment.	None.
Consultancies and other fee-paid work.	Owner and Shareholder: Research and Consulting Business.
Shareholdings.	Owner and Shareholder: Research and Consulting Business.
Clubs, other organisations and advocacy groups.	None.
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	Myrovlytis Trust (Funds Research into Rare Diseases) – Chairing responsibility. Regional Inclusive Volunteering Charity – Chairing responsibility.
Land and property.	None.
Other public appointments.	Occupational Therapists Registration Board – Republic of Ireland. Steering Structure of The Special Eu Programmes Body – Republic of Ireland/Eu. Medical Scientists Registration Board – Republic of Ireland. Northern Ireland Practice and Education Council for Nursing and Midwifery (NIPEC). Public Member – NHS ENGLAND subsidiary board related to digital urgent & emergency care (DUEC).
Other non-personal interests.	None.

Dr Nathan Goldsmith

Current

Personal Interests

Direct employment.	Exponent.
Consultancies and other fee-paid work.	None.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	UK Environmental Mutagen Society (UKEMS).
Other personal interests.	Pension: Exponent.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Committee on the Carcinogenicity of Chemicals in Food, Consumer Products and the Environment Annual Report 2024

Preface

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

The membership of the Committee, agendas and minutes of meetings, and statements are all published on the internet Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment - GOV.UK.

The Committee on Carcinogenicity exists to provide the best advice that will protect the public from an increased risk of cancer. This is based on careful scrutiny of available information and robust discussion, with complete transparency and full declaration of any possible conflicting interests by Members who are drawn from widely different backgrounds, appointed after a robust, open recruitment process. No one Member is more important than any other and each Member can be, and often is, challenged respectfully by colleagues. Each Member brings unique skills and experience: all of this variety contributes to discussions. Members routinely demit

office and I am grateful to all those who have given of their time to serve without remuneration.

Our aim is to distil all the evidence, using the skills Members bring from many different disciplines, to provide comprehensive advice that is useful, not just erudite. Sometimes, advice is targeted to a specific situation or request, but more often the Committee seeks to provide and review guidelines that are a framework for industry, regulators and researchers.

Members appreciate that our advice is only part of any assessment and that other factors are important before policy makers or regulators come to firm conclusions. To that end we have tried to “complete the loop” by identifying how Committee deliberations have helped make decisions. This is ongoing. Through a process of horizon scanning, the Committee spends time trying to discern situations, threats and concerns that may arise, whilst keeping up to date with new methods and technologies that may help (or possibly hinder) future assessments.

The Committee is supported by an excellent Secretariat, to whom I express gratitude, and also by contracted research consultants who ensure we delve deeply into published literature.

At Committee meetings, many assessors from different departments attend, and we do encourage all attendees to contribute to discussion where appropriate, though of course the Committee Members ultimately take responsibility for conclusions.

I finish where I started: COC’s purpose is to help provide advice regarding the increased risk of cancer associated with some chemicals and mixtures of chemicals in a way that supports clear, informed action where required, or reassurance that such action is not needed.

Professor David Harrison - Chair

MD DSc FRCPath FRCPEd FRCSEd

COC Evaluations

Hydroxyanthracene derivatives

3.1 Hydroxyanthracene derivatives (HADs) are a class of phenolic, anthranoid compounds found in various botanical families and genera. Most notably these are plants from the genera Rheum which includes rhubarb; Cassia which includes senna, Indian laburnum and cinnamon; Rhamnus which includes buckthorn; and Aloe which includes aloe vera and bitter aloe. Many of the active compounds under discussion will occur in plants from more than one genus.

3.2 In 2013, the EFSA Panel on Dietetic Products, Nutrition, and Allergies (NDA) published an assessment of the health claims related to the use of HADs in food for the improvement of bowel function (EFSA, 2013). The Panel established a cause-and-effect relationship for this effect (that is, stimulation of colonic motility, which reduces fluid absorption from faecal mass, leading to short-term alleviation of constipation). The Panel considered that in order to obtain the beneficial effect, a product should provide 10mg HADs/day in the adult population.

3.3 In 2018, at the request of the European Commission, EFSA published a scientific opinion on the safety of HADs for use in food, namely emodin, aloe-emodin, danthron, and their preparations. In this opinion, the EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS) concluded that HADs should be considered as genotoxic and carcinogenic unless there is specific data to the contrary, and that there is a safety concern for extracts containing HADs, although uncertainty persists. The ANS Panel was unable to provide advice on a daily intake of HADs that does not give rise to health concerns. Subsequently, the European Commission proposed restrictions on food supplements that are prepared from Aloe species as they contain HADs.

3.4 Representatives of the food supplements industry noted that the restrictions also apply to preparations of Aloe species where the level of HADs has been removed as far as is technically possible. An additional industry concern was that

some Aloe species products contain lower levels of HADs compared to those products that were assessed by EFSA. Overall, industry representatives consider that other risk mitigation measures (such as setting a maximum level for HADs, imposing labelling requirements, and collecting additional safety data) would allow EFSA to refine its assessment on the health risk posed by Aloe preparations.

3.5 The Nutrition Labelling Composition and Standards (NLCS) policy group has been set up under the NLCS provisional common framework, to maintain a consistent and co-ordinated policy approach across the UK (DHSC, 2020). The NLCS framework sets out arrangements for co-operation between officials in DHSC, Food Standards Scotland (FSS) (representing Scottish Government), Welsh Government (WG) and the Food Standards Agency Northern Ireland (FSANI) with regard to NLCS policy.

3.6 All future policy proposals relating to nutrition are considered on a 4-nation basis via the NLCS policy group, with the impact assessed on the UK as a whole not just each individual nation or Great Britain (GB). The risk assessment and risk management processes of amendments to legislation (including food supplements) in scope of the provisional NLCS framework includes seeking scientific evaluation from the relevant scientific advisory committee, where appropriate.

3.7 On the request of the NLCS policy group, the UK FSA commissioned an independent view from the Committee on Mutagenicity (COM) to advise on the genotoxicity of HADs based on the 2018 EFSA opinion and any new data that has become available since that was published.

3.8 Following the evaluation by the Committee on Mutagenicity (COM), it was taken for review to the Committee on Carcinogenicity (COC) for their opinion on the carcinogenic potential of HADs.

3.9 The FSA had requested that the COC review relevant carcinogenicity studies, evaluate the risk of the HADs and whether a health-based guidance can be derived from the available information.

3.10 The NLCS policy group will assess whether or not to restrict food products containing HADs in GB, considering the conclusions of the COM and COC.

Summary of the Genetic Toxicity Evaluation by COM

3.11 In September 2021, a summary of the EFSA ANS opinion (2018) and additional literature review of relevant publications since the 2018 EFSA opinion was presented to the COM for its consideration on the genotoxic potential of HADs (COM, 2021).

3.12 The COM agreed at the September 2021 meeting, that, overall, the available evidence, namely from Ames tests, indicates that emodin, aloe-emodin, and danthron are genotoxic in vitro. Where mixed results for in vitro genotoxicity have been reported in the literature, this is sometimes due to a lack of clarity on the preparation used for testing: decolourised extracts (which are generally negative as they contain a far lower concentration of HADs), and whole extract (which are positive as they contain greater concentrations of HADs). However, more information is needed to be confident that there was also genotoxicity in the mammalian cell assays, because the mouse lymphoma and micronucleus data that is summarised by the EFSA opinion were published in 1996 (since then, changes have been made to how genotoxicity is evaluated, for example to make sure excessive doses are not used), and also because Müller et al. (1996) did not perform statistical evaluation of the data. Therefore, overall, it was not clear to the COM if the positive results in the mammalian cell assays are indeed positive, or rather, reflective of excessively high concentrations. In terms of in vivo genotoxicity, there was a question as to how much weight should be placed on negative mouse data published after 2018, as EFSA agreed that mice appear to be less sensitive than rats to the gastrointestinal effects caused by HADs. The COM agreed that the studies published after 2018 are mostly negative in vivo data, which weaken the evidence that there is a genotoxic effect in vivo.

3.13 The COM considered that the genotoxic effects of HADs, including those seen in the comet assay of colon cells, are caused by the high levels of irritation, inflammation, and diarrhoea. The 2-fold increase in tail moment (present at all dose

levels) in colon cells under the comet assay was not caused by DNA reactivity, but rather an indirect mechanism involving ROS generation and/or topoisomerase II inhibition (mechanisms that were indicated from in vitro data).

Summary of the Carcinogenicity Evaluation by COC

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

3.15 The COC determined that there were currently insufficient data from the shorter-term studies available to inform an assessment and conclude whether or not there was a safety concern for plant extracts containing HADs. Additionally, the COC established that it would not be possible to set a HBGV for HADs as a single group as they are complex mixtures of different compounds with different mechanisms of action.

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

3.17 In July 2022 an additional article was presented to the Committee, the article suggested a potential HBGV for HADs. Members determined, as this HBGV was not based upon any new data, that the value presented was based upon many different variables including different strains of animals used, different dosing regimens and varied endpoints analysed. The Committee decided that, at present, there were insufficient data to conclude on an appropriate HBGV for HADs.

3.18 The Annex to the statement presents consumption levels of HADs for a variety of foodstuffs for which there is data and a subsequent exposure analysis.

Based on the single value presented for combined exposure for food, aloe drinks and cosmetics the exposure to humans is probably less than would be expected to cause adverse health effects in humans. However, there are large knowledge gaps that would need to be addressed in order to conclude on the safety in humans.

3.19 Future work would have to address that HADs are a diverse group of compounds. Therefore, each compound would need to be analysed and assessed in their own right according to their mechanisms of action and individual levels of exposure from the diet, and cosmetics. There is likely to be a great degree of variation between different HAD compounds. The data presented in Annexe A does not represent an exhaustive list of commodities that contain HADs and are therefore likely to be an underestimation of their consumption in the diet. More information on the level of individual HADs in a wider spectrum of foodstuffs would be required for a full exposure assessment. In addition to food, aloe drinks and cosmetics, exposure from supplements should also be included in a full exposure assessment. Currently, data for supplements is not available.

3.20 Due to insufficient UK data, the COC was unable to make recommendations on a HBGV for HADs, individually or together. Should sufficient data on the toxicity and UK exposure of individual HADs become available, it may then be possible to undertake full and specific risk assessments.

3.21 The interim position can be found here: Interim position on the safety of hydroxyanthracene derivatives for use in food - GOV.UK.

COC Ongoing topics

Development of new guidance statement "A case for change - the challenge to develop a better approach to assessing risk of cancer caused by chemicals"

3.22 Throughout 2024, COC discussed development of a new guidance statement building on the two COC workshops held in November 2022 and November 2023, to consider making progress in the way in which risk assessment for carcinogenicity of chemicals is undertaken.

3.23 A draft of the guidance statement has been prepared and was planned for publication in 2025.

Guidance statements

3.24 The COC discussed its guidance statement series, which has been subject to a rolling process of review and update since it was published in sections online from 2012.

3.25 The importance and utility of the guidance statements was noted by the Secretariat and Assessors, as it underpins the risk assessments and evaluations undertaken by Government Departments and Agencies. It was also recognised that COC guidance enables quality risk assessment which in turn supports better risk management approaches by the regulatory teams in Government.

3.26 It was noted that a challenge in updating the guidance is the need for an update of the underpinning evidence base, which can become an extensive review and critique, while providing clear guidance. Suggestions were made with respect to more efficiently undertaking such review and formulating guidance, for example having short, concise, standalone guidance with an underpinning evidence review document, use of working groups of members to recast some of the existing guidance documents and keeping in review areas where guidance might be required.

3.27 Further consideration of this would be made in 2025, and in particular utilising input from Lay members to support communication of COC guidance.

Horizon scanning

3.28 COC further explored horizon scanning through 2024, following the joint discussion with COM in October 2023, with a view to considering a sustainable approach to horizon scanning for the Committees. This was facilitated through

discussion with Professor Jason Weeks (IEH Consulting) in March 2024 and November 2024.

3.29 A demonstration of an approach using an information aggregator tool bringing together information from a range of sources was provided identifying themes of potential interest and relevance to the Committee. This allowed Members to consider such an approach and the potential utility of the types of insights identified.

3.30 At the November 2024 meeting, a number of insights were identified from the tool:

- The risk evaluation for tris(2-chloroethyl) phosphate (TCEP).
- A reconsideration of car flame retardants.
- Human risk exposure to microplastics and microfibres.
- The presence of toxic chemicals in air fresheners used in the home.
- The hazards of chemicals used in hair relaxers.
- The risk of cancer from the regular use of mouth wash.
- Broader issues raised included gender and race specific topics, managing misinformation and continued reemergence of topics previously considered to be resolved.

3.31 It was noted that some of these insights and issues were not necessarily within COC's remit and would also need to be considered by the Secretariat for relevance to FSA and DHSC/UKHSA priorities. However, it was considered to be a useful early assessment of trends and challenges, gaps in knowledge, and potentially emerging future risks.

3.32 Further discussion would take place in 2025 to determine how horizon scanning can be taken forward in the future.

COC input to other work

Presentation by Dr John Doe "Revised strategy for the assessment of Chemical Carcinogenicity"

3.33 In March 2024, Dr John Doe joined the COC meeting to present on a paper he was preparing on a revised strategy for assessment of chemical carcinogenicity.

3.34 The presentation outlined the caveats with the current approach with respect to the adequacy of the animal studies conducted and the need to move to a graded rather than a binary outcome to carcinogenicity assessment. A framework for evidence evaluation was presented, and a matrix of potential outcomes suggested. Examples were provided indicating that removing data from the two-year bioassay and also human epidemiological data on cancer still provided sufficient information to support decision making on the potential for cancer.

3.35 Members welcomed the presentation of this strategy alongside case examples of chemicals to demonstrate how a different approach could be utilised in practise. Suggestions were made with respect to possible further improvements which could include consideration of how a margin of exposure approach would look without two-year rodent bioassay data. It was noted that there was a benefit in the approach with respect to drawing in mechanistic, in vitro, in silico and toxicokinetic data into the assessment approach.

3.36 Dr Doe was thanked for his presentation.

EFSA Consultation on draft "Scoping paper on the revision of the opinion on the Margin of Exposure for chemicals which are both genotoxic and carcinogenic"

3.37 COC provided comments in response to the EFSA consultation on the draft "Scoping paper on the revision of the opinion on the Margin of Exposure for chemicals which are both genotoxic and carcinogenic".

3.38 The COC welcomed EFSA's proposed review of the opinion on the margin of exposure for chemicals which are genotoxic and carcinogenic. The COC agreed with the anticipation that there will be a decrease in carcinogenicity studies conducted in the future, and therefore it will be important to develop an approach that utilises data from other studies.

3.39 The COC recognised the intention in this scoping document to make useful steps in the move away from using animal test data for risk assessment and communication.

3.40 The COC was uncomfortable with the continued assumption that chemicals can be categorised as carcinogenic or not carcinogenic, suggesting instead that the outcome should be an expression of risk if increasing the possibility of cancer occurring modification of cancer risk by chemicals | Toxicology Research | Oxford Academic (Harrison, D.J. and Doe, J.E., 2021. The modification of cancer risk by chemicals. Toxicology Research, 10(4), pp.800-809).

3.41 The COC noted the use of BMDLs and T25 as the reference point as a basis for an MOE approach in the 2005 opinion, however often insufficient information was available to derive a BMDL so e.g. a NOAEL has to be used. COC welcomed development of advice on a range of options for reference points that can be used with an MOE approach.

3.42 The COC recognised EFSA's ambition to develop an approach which does not necessarily require animal carcinogenicity studies. COC noted that EFSA may wish to consider how much data would be adequate for an assessment and using an MOE approach, e.g. for some compounds a single dose 90-day study may be all that is available to form the basis of a risk assessment.

3.43 The COC agreed that it would be helpful for EFSA to consider any further guidance or clearer definitions on MOEs which are less than 10,000 as can be the case for natural contaminants. Similarly, it would be helpful to strengthen the scientific rationale and explanation for use of an MOE of 10,000 with a BMDL10 from an animal carcinogenicity study to support risk managers.

3.44 The COC noted that it would be helpful to supplement the planned considerations on the toxicology evidence, with further consideration of the

uncertainties in occurrence data to support the exposure assessment aspect of an MOE approach. This could also include guidance for less than lifetime exposures.

EFSA Consultation on draft "Request for scientific review of the methodologies available to assess the long-term toxicity and carcinogenicity of plant protection products and mixtures"

3.45 COC provided a number of comments to EFSA on the consultation on the draft "Request for scientific review of the methodologies available to assess the long-term toxicity and carcinogenicity of plant protection products and mixtures".

3.46 The COC suggested clarity on the focus of the document which was predominantly relating to mixture effects and recommended obtaining additional support from expert in metabolism and/or toxicokinetics. Some specific comments were also provided on the different sections of the document.

OECD submissions related to carcinogenicity

3.47 UKHSA leads for the UK on human health discussions at the OECD meetings of the Working Group of National Coordinators of the Test Guidelines Programme (WNT). A number of submissions were made in 2024 on assays of relevance to carcinogenicity and UKHSA requested COC comments on these submissions. COC provided a number of comments on the various assays which supported the UK response.

2024 Membership of the Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment

Chair

Professor David Harrison MD DSc FRCPath FRCPEd FRCSEd

Professor of Pathology, University of St Andrews.

Members

Dr Emma Barnes – from July 2024

Head of Product Safety Science Delivery, Syngenta.

Mr Amit Bhagwat

Public Interest Representative.

Dr Meera Cush

Senior Managing Consultant (Regulatory Toxicologist), Ramboll.

Dr Ruth Dempsey – to November 2024

Consultant, RD Science Speaks Consultancy.

Professor Shareen Doak – from July 2024

Professor of Genotoxicology & Cancer, Swansea University.

Dr John Doe – from July 2024

Independent Consultant and Visiting Lecturer, Liverpool John Moore's University.

Dr Caroline Harris – from July 2024

Exponent.

Dr Richard Haworth MA VetMB DPhil FRCPath DipECVP DABT – to November 2024

Director, RosettaPath Ltd.

Professor Gareth Jenkins

Professor of Molecular Carcinogenesis, 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

Public Interest Representative.

Dr Susanne Stalford – from July 2024

Lhasa Ltd.

Rev Prof Lesley Stanley ERT FBTS

Visiting Professor of Toxicology, Edinburgh Napier University and Consultant in Investigative Toxicology.

Secretariat

Ms B Gadeberg BSc (Hons) MSc ERT	UKHSA Scientific Secretary
Dr D Gott BSc (Hons) PhD	FSA Scientific Secretary to July 2024
Ms C Mulholland BSc (Hons) ERT	FSA Scientific Secretary
Mr T Fraser	Administrative Secretary

Declaration of members interests during the period of this report

Professor David Harrison

Current

Personal Interests

Direct employment.	University of St Andrews, UK, NuCana plc, UK. Employee/Non-executive Director: ILC Therapeutics Ltd (unpaid), PathAlba Ltd – Director (unpaid) – dormant.
Consultancies and other fee-paid work.	NHS Lothian – Honorary Consultant.
Shareholdings.	VBL Ltd, UK, Ryboquin Ltd, UK, ILC Therapeutics Ltd.
Clubs, other organisations and advocacy groups.	None.
Other personal interests.	Fellow Royal College of Pathologists, Fellow of Royal College of Physicians of Edinburgh, Fellow of Royal College of Surgeons of Edinburgh.

Non-Personal

Fellowships.	University of Edinburgh, UK – Honorary Professor, University of Florida, Adjunct Professor.
Indirect support.	None.
Trusteeships.	Cunningham Trust – (Medical Research Charity)

Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	Viewbank Leuchars Ltd – Director (no salary).

Dr Emma Barnes from June 2024

Current

Personal Interests

Direct employment.	Syngenta Ltd.
Consultancies and other fee-paid work.	None.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	British Toxicology Society (BTS), CropLife International Human Health Expert Group.
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Mr Amit Bhagwat

Current

Personal Interests

Direct employment.	None.
Consultancies and other fee-paid work.	Owner and Shareholder: Research and Consulting Business.

Shareholdings.	Owner and Shareholder: Research and Consulting Business.
Clubs, other organisations and advocacy groups.	None.
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	Myrovlytis Trust (Funds Research into Rare Diseases) – Chairing responsibility. Regional Inclusive Volunteering Charity – Chairing responsibility.
Land and property.	None.
Other public appointments.	Occupational Therapists Registration Board – Republic of Ireland. Steering Structure of The Special Eu Programmes Body – Republic of Ireland/Eu. Medical Scientists Registration Board – Republic of Ireland. Northern Ireland Practice and Education Council for Nursing and Midwifery (NIPEC). Public Member – NHS ENGLAND subsidiary board related to digital urgent & emergency care (DUEC).
Other non-personal interests.	None.

Dr Meera Cush

Current

Personal Interests

Direct employment.	Ramboll UK Limited, University of Surrey (Visiting Lecturer)
Consultancies and other fee-paid work.	None.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	Royal Society of Biology
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Dr Ruth Dempsey to November 2024

Current

Personal Interests

Direct employment.	None.
Consultancies and other fee-paid work.	Philip Morris International, doTERRA Europe.
Shareholdings.	RD Science Speaks Consultancy, Sarl (Shareholder and director).
Clubs, other organisations and advocacy groups.	None.

Other personal interests.	Pension - Philip Morris International.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	British Toxicology Society, Swiss society of Toxicology, Royal society of Biology.
Other non-personal interests.	None.

Prof. Shareen Doak

Current

Personal Interests

Direct employment.	Swansea University
Consultancies and other fee-paid work.	Consultancy work for CEFIC/Titanium Dioxide Manufacturers Association (TDMA).
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	United Kingdom Environmental Mutagen Society (UKEMS) 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).
Other personal interests.	None.

Non-Personal

Fellowships.	Fellow of the Learned Society of Wales
Indirect support.	PhD Studentship Grant: Lhasa Ltd (2023 – 2027)
Trusteeships.	Trustee: St David's Medical Foundation (medical research & education charity)
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Dr John Doe from June 2024

Current

Personal Interests

Direct employment.	None.
Consultancies and other fee-paid work.	ECETOC
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	British Toxicology Society (BTS)
Other personal interests.	Pension: Syngenta

Non-Personal

Fellowships.	Liverpool John Moores University (Honorary Research Fellow).
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.

Other public appointments.	None.
Other non-personal interests.	None.

Dr Caroline Harris from June 2024

Current

Personal Interests

Direct employment.	Exponent International Ltd.
Consultancies and other fee-paid work.	Co-opted member of the Committee on Toxicology (plant-based drinks working group).
Shareholdings.	Exponent Inc.
Clubs, other organisations and advocacy groups.	None.
Other personal interests.	None.

Non-Personal

Fellowships.	Fellow of the Royal Society of Chemistry.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	Member of the Expert Committee on Pesticides,
Other non-personal interests.	None.

Dr Richard Haworth to November 2024

Current

Personal Interests

Direct employment.	Director: RosettaPath Ltd, Chief Scientific officer: CureCollect Ltd.

Consultancies and other fee-paid work.	Scientific advisory committee Aiforia.
Shareholdings.	AstraZeneca, GlaxoSmithKline, Haleon, Shell (Spouse, Shareholder).
Clubs, other organisations and advocacy groups.	British Society of Toxicological Pathology, European Society of Toxicological Pathology, Society of Toxicological Pathology.
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Professor Gareth Jenkins

Current

Personal Interests

Direct employment.	Swansea University. Honorary Contract: Swansea Bay University Health board.
Consultancies and other fee-paid work.	None.
Shareholdings.	None.

Clubs, other organisations and advocacy groups.	President of United Kingdom Environment Mutagen Society (UKEMS) 2020 – 2023. 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).
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	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).
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Professor Neil Pearce

Current

Personal Interests

Direct employment.	None.
Consultancies and other fee-paid work.	None.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	None.
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Ms Juliet Rix

Current

Personal Interests

Direct employment.	None.
Consultancies and other fee-paid work.	None.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	None.
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Dr Susanne Stalford from June 2024

Current

Personal Interests

Direct employment.	Lhasa LTD.
Consultancies and other fee-paid work.	None.
Shareholdings.	None.
Clubs, other organisations and advocacy groups.	HESI GTTC Committee, HESI ESTAR Committee.
Other personal interests.	None.

Non-Personal

Fellowships.	None.
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	None.
Other non-personal interests.	None.

Dr Lesley Stanley

Current

Personal Interests

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

	Self Employed: Dr. Lesley Stanley, Consultant in Investigative Toxicology.
Consultancies and other fee-paid work.	School of Medicine, University of Dundee (2020 to date). Details of previous consultancy contracts available upon request.
Shareholdings.	Investment Portfolio managed by Quilter Cheviot (joint with spouse). FundsNetwork Stocks and Shares ISA, Aviva Personal Pension Plan.
Clubs, other organisations and advocacy groups.	European Registered Toxicologist (ERT), Fellow of the British Toxicology Society (FBTS), Advisory Committee on Novel Foods and Processes (ACNFP).
Other personal interests.	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.

Non-Personal

Fellowships.	Associate, School of Life Sciences, Edinburgh Napier University (Non-Stipendiary).
Indirect support.	None.
Trusteeships.	None.
Land and property.	None.
Other public appointments.	Expert Appointments: REACH Independent Scientific Expert Pool, OPSS Register of Experts.
Other non-personal interests.	None.

Committee on Toxicity

2024