Contents

ANNEX 1 - Terms of Reference

To advise at the request of:
Food Standards Agency
Food Standards Scotland
Public Health England
Department of Health
Department for Business, Innovation & Skills
Department of Transport, Local Government and the Regions
Health and Safety Executive
Veterinary Medicines Directorate
Medicines and Healthcare Products Regulatory Agency
Home Office

Scottish Executive
National Assembly for Wales
Northern Ireland Assembly
Other Government Departments and Agencies

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

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

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

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

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

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

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

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

Public service values

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

· observe the highest standards of **impartiality**, **integrity** and **objectivity** in relation to the advice they provide and to the management of their Committee;

· be **accountable**, through the Chair of the Food Standards Agency and the Chief Medical Officers, to Ministers, Parliament and the public for its activities and for the standard of advice it provides;

· in accordance with Government policy on **openness**, fully comply with the Freedom of Information Act 2000

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

Standards in Public Life

Members are expected to:

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

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

· not hold any paid or high profile unpaid posts in a political party, and not engage in specific political activities on matters directly affecting the work of the Committee. When engaging in other political activities, Committee members should be conscious of their public role and exercise proper discretion. These restrictions do not apply to MPs (in those cases where MPs are eligible to be appointed), to local councillors, or to Peers in relation to their conduct in the House of Lords.

· follow the Seven Principles of Public Life set out by the Committee on Standards in Public Life (http://www.public-standards.gov.uk/).

Selflessness

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

Integrity

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

Objectivity

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

Accountability

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

Openness

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

Honesty

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

Leadership

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

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

Role of Members

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

Members must:

· engage fully in collective consideration of the issues, taking account of the full range of relevant factors, including any guidance issued by the Food Standards Agency, Health Protection Agency and the Department of Health

· undertake on appointment to comply with the Code of Practice for Scientific Advisory Committees

· not divulge any commercially sensitive information, pre-publication or unpublished research data provided to the Committee
· agree an annual report
· ensure that an appropriate response is provided to complaints and other correspondence, if necessary with reference to the sponsor department; and;
· ensure that the Committee(s) does not exceed its powers or functions.

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

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

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

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

Role of the Chair

The Chair has particular responsibility for providing effective leadership on the issues above. In addition, the Chair is responsible for:
· ensuring that the Committee meets at appropriate intervals,
· ensuring that the minutes of meetings accurately reflect proceedings and any reports to the FSA Board and/or Ministers accurately record the decisions taken
· ensuring that where appropriate, the views of individual members have been recorded;
· representing the views of the Committee to the general public;
· ensuring that new members are briefed on appointment (and their training needs considered), and providing an assessment of their performance, on an annual basis or when members are considered for re-appointment to the Committee or for appointment to the board of some other public body.

· providing urgent advice to the FSA and HPA on issues within the remit of the Committee, in liaison with the Secretariat,

Role of the Deputy Chair

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

Role of the Secretariat

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

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

Role of the Assessor

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

The role of an Assessor is to keep their parent Department or Agency informed about the Committee's work and act as a conduit for the exchange of information. They do this by: · advising the Committee on relevant policy developments and the implications of Committee proposals;

· informing the Committee work through the provision of information

· being informed by the Committee on matters of mutual interest.

· sharing with the Secretariat the responsibility of ensuring that information is not needlessly withheld from the Committee. Assessors should make the Committee aware of the existence of any information that has been withheld from the Committee on the basis that it is exempt from disclosure under Freedom of Information legislation unless that legislation provides a basis for not doing so.

· ensuring that their parent Department or Agency is promptly informed of any matters which may require a response from Government.

Role of other Officials, Invited Experts and Contractors

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

Role of Observers

Members of the public and other interested parties may attend meetings as observers. However, they should not attempt to participate in Committee discussions. If an interested party wishes to provide information relevant to a topic for consideration by the Committee, they should be submitted in writing to the Secretariat at **least** seven (7) working days before the meeting. The Secretariat will discuss with the Chair the most appropriate way to present the information to the committee and the Chair's decision will be final. Observers who have submitted information in advance of the meeting **may** be invited to provide further explanation or to make brief comments at the discretion of the Chair. Observers and/or organisations must not interfere in the work of the Secretariat or input from invited experts, contractors, officials from Government Departments and Agencies in any way which, in the view of the Chair, constitutes harassment and/or might hinder the work of the Committee. Observers and/or organisations must allow other observers and other interested parties to attend items free from interference before, during and after a meeting.

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

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

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

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

Declaration of Members' Interests

Definitions

In this Code, 'the industry' means:

· Companies, partnerships or individuals who are involved with the production, manufacture, sale or supply of products subject to the following legislation;
General Food Regulations 2004
The Food Safety Act 1990 (Amendment) Regulations 2004
The Medicines Acts 1968 and 1971, 1981, 1986 & 2003
The Food and Environmental Protection Act 1985
The Consumer Protection Act 1987
The Cosmetic (Safety) (Amendment) Regulations 2008
Registration, Evaluation, Authorisation and Restriction of Chemicals (EC1970/2006)
· Trade associations representing companies involved with such products;
· Companies, partnerships or individuals who are directly concerned with research, development or marketing of a product which is being considered by the Committees on Toxicity, Mutagenicity, or Carcinogenicity of Chemicals in Food, Consumer Products and the Environment.
· 'the Secretariat' means the Secretariat of the COC, COM and COT;
· 'the Agency' means either the Food Standards Agency or the Health Protection Agency; and
· references to "member(s)" includes the Chair.

Different types of Interest

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

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

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

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

Personal Interests

A personal interest involves the member personally. The main examples are:
· **Consultancies and/or direct employment:** any consultancy, directorship, position in or work for industry which attracts regular or occasional payments in cash or kind;
· **Fee-Paid Work:** any work commissioned by industry for which the member is paid in cash or kind;

· **Shareholdings:** any shareholding in or other beneficial interest in shares of industry. This does not include shareholdings through unit trusts or similar arrangements where the member has no influence on financial management;
· **Membership or Affiliation:** any membership role or affiliation that you or a close family member has to clubs or organisations with an interest or involvement in the work of the Agency.

Non-Personal Interests

A non-personal interest involves payment which benefits the organisation in which the member works, but is not received by the member personally. The main examples are:
· **Fellowships:** the holding of a fellowship endowed by industry;
· **Support by Industry:** any payment, other support or sponsorship which
does not convey any pecuniary or material benefit to a member personally, but which does benefit their position or organisation, e.g.
i) a grant for the running of a unit or department for which the member is responsible;
ii) a grant or fellowship or other payment to sponsor a post or a member of staff or a post graduate research programme for which the member is responsible. This does not include financial assistance for students;
iii) the commissioning of research or other work by, or advice from, staff who work in a unit for which the member is responsible.
Members are under no obligation to seek out knowledge of work done for, or on behalf of, the industry or other relevant bodies by departments in which they work, if they would not normally expect to be informed.
· **Trusteeships**: where a member is a trustee of a charity with investments in industry, the Secretariat can agree with the member a general declaration to cover this interest rather than draw up a detailed portfolio.
At meetings members are required to declare relevant interests and to state whether they are personal or non-personal interests and whether they are specific or nonspecific to the matter, product or substance under consideration.

Specific Interests

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

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

Non-specific Interests

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

concerned which does not relate specifically to the matter, product or substance under discussion.

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

Handling conflicts of interests

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

(i) Declaration of Interests to the Secretariat

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

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

(ii) Declaration of Interest at Meetings

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

Withdrawal from meetings

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

Personal liability of Committee members

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

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

INDEMNITY BY THE FOOD STANDARDS AGENCY TO MEMBERS OF THE COMMITTEE ON TOXICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT

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

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

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

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

(a) in respect of which the Members are indemnified by or through any defence organisation or insurers or;
(b) which may result from bad faith (including dishonesty), wilful default or recklessness on the part of the Members; or
(c) which may result from any of the following circumstances:
(i) any settlement made or compromise effected without the knowledge or consent of the Food Standards Agency on behalf of the Members of any action or claim brought, or threatened to be brought, against the Members; or
(ii) any admission by the Members of any liability or responsibility in respect of any action or claim brought, or threatened to be brought, against them; or
(iii) Members taking action that they were aware, or ought reasonably to have been aware, might prejudice the successful defence of any action or claim, once the Members had become aware that such an action or claim had been brought or was likely to be brought.

ANNEX 3 – Openness

Introduction

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

2. The Government is committed to make the operation of scientific advisory committees such as the COT/COM/COC hereafter referred to as “the Committee” more open and to increase accountability. The Committee is aware that the disclosure of information that is of a confidential nature and is communicated in circumstances importing an obligation of confidence is subject to the common law of confidentiality. There are some circumstances making disclosure of confidential information lawful for example, where the individual to whom the information relates has consented; where disclosure is in the public interest; and where there is a legal duty to do so. However, guidance is set out in the Freedom of Information Act 2000[11] which gives any person legal rights of access to information which is held by a public authority.

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

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

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

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

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

8. The release of documents (papers, minutes and statements) where the Committee has agreed an opinion on the available unpublished data but where further additional information is required in order to finalise the Committee's conclusions, needs to be considered on a case-by case basis. The relevant considerations include the likelihood that such additional data would alter the Committee's conclusion, any representations made by a company about, for example, commercial harm that early disclosure could cause and also the public interest in disclosure.

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

Background

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

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

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

12. Normal procedure is to publish a summary of the Committee's advice on their respective websites, in the Annual Report and where necessary to ask companies to release full copies of submitted reports for retention by the British Library at the completion of a review. Given the clear Ministerial commitment to the publication of detailed information regarding the activities of advisory committees, and in particular following the assessment of products which are already available to the general public, the Committee will publish statements via the Internet soon after they have been finalised.

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

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

Procedures prior to committee consideration

Initial discussions

15. Upon referral to Committee the Secretariat will liaise with the relevant company supplying the product in the UK to:
i) clearly state the policy of Committee openness (summarised above)
ii) identify and request the information needed by the Committee (e.g. test reports, publications etc).

Commercially sensitive information

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

Pre-publication and unpublished research data

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

Handling confidential data

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

vi) The following is a suggested list of information which **may** be disclosed in Committee documents (papers, minutes and statements). The list is not exhaustive and is presented as a guide:
a) name of product (or substance/chemical under consideration),
b) information on physico-chemical properties,
c) methods of rendering harmless,
d) a summary of the results and evaluation of the results of tests to establish harmlessness to humans,
e) methods of analysis,
f) first aid and medical treatment to be given in the case of injury to persons,
g) surveillance data (e.g. monitoring for levels in food, air, or water).

Procedures during and after Committee consideration

vii) The timing of release of Committee documents (papers, minutes and statements) where the item of business involved the consideration of confidential data would be subject to the general provisions outlined in paragraphs 9-15 above. Documents would not be released until the Committee statement is available.

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

Dissenting views

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

COC/COM/COT papers

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

Remuneration and Committee finance

18. In the financial year 2018/19 the budget for the COT, excluding Secretariat resources was £68,000. Costs were met by the Food Standards Agency (FSA).

19. Committee members may claim a fee for Committee meetings:

COT Committee Chair £400 per day
COT Committee Member £300 per day

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

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

Review of fee rates

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

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

Working Groups

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

Terms and conditions of appointment

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

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

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

Feedback on performance

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

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

ANNEX 4 – Good Practice Agreement for Scientific Advisory Committees

INTRODUCTION

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

- **identify early** the issues which need scientific and engineering advice and where **public engagement** is appropriate;
- draw on a **wide range of expert advice** sources, particularly when there is uncertainty;
- adopt an **open and transparent approach** to the scientific advisory process and publish the evidence and analysis as soon as possible;
- **explain publicly the reasons for policy decisions**, particularly when the decision appears to be inconsistent with scientific advice; and
- **work collectively** to ensure a joined-up approach throughout government to integrating scientific and engineering evidence and advice into policy making.

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

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

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

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

- Advisory Committee on Animal Feedingstuffs
- Advisory Committee on Microbiological Safety of Foods
- Advisory Committee on Novel Foods and Processes
- Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment
- Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment
- Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment
- Science Council
- Social Science Research Committee

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

All these committees share important characteristics. They:

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

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

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

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

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

PRINCIPLES

Defining the problem and the approach

1. The FSA will ensure that issues it asks an SAC to address are clearly defined and take account of stakeholder expectations in discussion with the SAC Secretariat and where necessary the SAC Chair. The SAC Chair will refer back to the FSA if discussion suggests that further iteration and discussion of the task is necessary. Where an SAC proposes to initiate a piece of work the SAC Chair and Secretariat will discuss this with FSA to ensure the definition and rationale for the work and its expected use by the FSA are clear.

Seeking input

2. The Secretariat will ensure that stakeholders are consulted at appropriate points in the SAC's considerations. It will consider with the FSA whether and how stakeholder views need to be taken into account in helping to identify the issue and frame the question for the committee.
3. Wherever possible, SAC discussions should be held in public.
4. The scope of literature searches made on behalf of the SAC will be clearly set out.

5. Steps will be taken to ensure that all available and relevant scientific evidence is rigorously considered by the committee, including consulting external/additional scientific experts who may know of relevant unpublished or pre-publication data.
6. Data from stakeholders will be considered and weighted according to quality by the SAC.
7. Consideration by the Secretariat and the Chair (and where appropriate the whole SAC) will be given to whether expertise in other disciplines will be needed.
8. Consideration will be given by the Secretariat or by the SAC, in discussion with the FSA, as to whether other SACs need to be consulted.

Validation

9. Study design, methods of measurement and the way that analysis of data has been carried out will be assessed by the SAC.
10. Data will be assessed by the committee in accordance with the relevant principles of good practice, e.g. qualitative social science data will be assessed with reference to guidance from the Government's Chief Social Researcher[1].
11. Formal statistical analyses will be included wherever appropriate. To support this, each SAC will have access to advice on quantitative analysis and modelling as needed.
12. When considering what evidence needs to be collected for assessment, the following points will be considered:
    - the potential for the need for different data for different parts of the UK or the relevance to the UK situation for any data originating outside the UK; and
    - whether stakeholders can provide unpublished data.
13. The list of references will make it clear which references have been subject to external peer review, and which have been peer reviewed through evaluation by the Committee, and if relevant, any that have not been peer reviewed.

Uncertainty

14. When reporting outcomes, SACs will make explicit the level and type of uncertainty (both limitations on the quality of the available data and lack of knowledge) associated with their advice.
15. Any assumptions made by the SAC will be clearly spelled out, and, in reviews, previous assumptions will be challenged.
16. Data gaps will be identified and their impact on uncertainty assessed by the SAC.
17. An indication will be given by the SAC about whether the evidence base is changing or static, and if appropriate, how developments in the evidence base might affect key assumptions and conclusions.

Drawing conclusions

[1] Quality in Qualitative Evaluation: A Framework for assessing research evidence http://www.civilservice.gov.uk/wp-content/uploads/2011/09/a_quality_framework_tcm6-7314.pdf; The Magenta book http://www.hm-treasury.gov.uk/d/magenta_book_combined.pdf

18. The SAC will be broad-minded, acknowledging where conflicting views exist and considering whether alternative interpretations fit the same evidence.
19. Where both risks and benefits have been considered, the committee will address each with the same rigour, as far as possible; it will make clear the degree of rigour and uncertainty, and any important constraints, in reporting its conclusions.
20. SAC decisions will include an explanation of where differences of opinion have arisen during discussions, specifically where there are unresolved issues, and why conclusions have been reached. If it is not possible to reach a consensus, a minority report may be appended to the main report, setting out the differences in interpretation and conclusions, and the reasons for these, and the names of those supporting the minority report.
21. The SAC's interpretation of results, recommended actions or advice will be consistent with the quantitative and/or qualitative evidence and the degree of uncertainty associated with it.
22. SACs will make recommendations about general issues that may have relevance for other committees.

Communicating SACs' conclusions

23. Conclusions will be expressed by the SAC in clear, simple terms and use the minimum caveats consistent with accuracy.
24. It will be made clear by the SAC where assessments have been based on the work of other bodies and where the SAC has started afresh and there will be a clear statement of how the current conclusions compare with previous assessments.
25. The conclusions will be supported by a statement about their robustness and the extent to which judgement has had to be used.
26. As standard practice, the SAC secretariat will publish a full set of references (including the data used as the basis for risk assessment and other SAC opinions) at as early a stage as possible to support openness and transparency of decision-making. Where this is not possible, reasons will be clearly set out, explained and a commitment made to future publication wherever possible.
27. The amount of material withheld by the SAC or FSA as being confidential will be kept to a minimum. Where it is not possible to release material, the reasons will be clearly set out, explained and a commitment made to future publication wherever possible.
28. Where proposals or papers being considered by the FSA Board rest on scientific evidence produced by a SAC, the Chair of the SAC (or a nominated expert member) will be invited to the table at the Open Board meetings at which the paper is discussed. To maintain appropriate separation of risk assessment and risk management processes, the role of the Chairs will be limited to providing an independent view and assurance on how their committee's advice has been reflected in the relevant policy proposals, and to answer Board Members' questions on the science. The Chairs may also, where appropriate, be invited to provide factual briefing to Board members about particular issues within their committees' remits, in advance of discussion at open Board meetings.
29. The SAC will seek (and FSA will provide) timely feedback on actions taken (or not taken) in response to the SAC's advice, and the rationale for these.

Annex 5 – Glossary of Terms

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Aetiology: study of causation or origination

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

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

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

Allele: Alternative form of a gene within the population.

Allergen: Substance capable of stimulating an allergic reaction.

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

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

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

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

Aneugen/aneugenic: (An agent) Inducing aneuploidy.

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

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

As low as is reasonably achievable/ As low as is reasonably practicable (ALARA/ALARP): A risk management approach under which exposure to a substance or

mixture is reduced to the lowest level that it is deemed to be reasonably achievable or practicable in particular circumstances or by available technological solutions.

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

Benchmark dose (BMD) modelling: An alternative quantitative approach to dose-response assessment using more of the data than the NOAEL process. This approach utilises mathematical models to fit all available data points and uses the best fitting model to interpolate an estimate of the dose (benchmark dose) that corresponds to a particular level of response (a benchmark response). A measure of uncertainty is also calculated, and the lower confidence limit on the benchmark dose is called the BMDL. The BMDL accounts for the uncertainty in the estimate of the dose-response that is due to characteristics of the experimental design such as sample size and biological variability. The BMDL can be used as the point of departure (see POD) for derivation of a health-based guidance value or a margin of exposure.

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

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

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

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

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

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

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

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

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

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

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

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

Bradford Hill considerations: Sir Austin Bradford Hill established a set of 'principles' (not be taken as 'criteria') that may be used to assist in the interpretation of associations reported from epidemiological studies:
- Strength – The stronger the association the more likely it is causal. The COC has previously noted that the relative risks of <3 need careful assessment for effects of bias or confounding.
- Consistency – The association has been consistently identified by studies using different approaches and is also seen in different populations with exposure to the chemical under consideration.
- Specificity – Limitation of the association to specific exposure groups or to specific types of disease increases likelihood that the association is causal.
- Temporality – The association must demonstrate that exposure leads to disease. The relationship of time since first exposure, duration of exposure and time since last exposure are all important in assessing causality.
- Biological gradient – If an association reveals a biological gradient or dose response curve, then this evidence is of particular importance in assessing causality.
- Plausibility – Is there appropriate data to suggest a mechanism by which exposure could lead to concern? However, even if an observed association may be new to science or medicine it should not be dismissed.
- Coherence – Cause and effect interpretation of data should not seriously conflict with generally known facts.
- Experiment – Can the association be demonstrated experimentally? Evidence from experimental animals may assist in some cases. Evidence that removal of the exposure leads to a decrease in risk may be relevant.
- Analogy – Have other closely related chemicals been associated with the disease?

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

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

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

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

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

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

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

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

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

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

Chromosome: In simple prokaryotic organisms, such as bacteria and most viruses, the chromosome consists of a single circular molecule of DNA containing the entire genetic material of the cell. In eukaryotic cells, the chromosomes are thread-like structures, composed mainly of DNA and protein, which are present within the nuclei of every cell.

They occur in pairs, the numbers varying from one to more than 100 per nucleus in different species. Normal somatic cells in humans have 23 pairs of chromosomes, each consisting of linear sequences of DNA which are known as genes.

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

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

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

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

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

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

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

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

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

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

Comet assay: A genotoxicity assay in which DNA strand breaks in an individual cell are measured using single-cell gel electrophoresis. Cell DNA fragments assume a "comet with tail" formation on electrophoresis and are detected with an image analysis system. Alkaline assay conditions facilitate sensitive detection of double-strand and single-strand damage, as well as alkali-labile sites. Modifications to standard methodology enable

detection of types of DNA damage, e.g. DNA-DNA or DNA-protein cross-links and base-oxidation.

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

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

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

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

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

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

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

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

Cumulative exposure: exposure to multiple chemicals on the basis of grouping them on some common characteristic, such as mode of action, adverse effect, or inclusion in a product formulation.

P450 (CYP): An extensive family of haem-containing proteins involved in enzymic oxidation of a wide range of endogenous and xenobiotic substances and their conversion to forms that may be more easily excreted. In some cases, the metabolites produced may

be chemically reactive and have increased toxicity. In other cases, the substances may be natural precursors of hormones (e.g. steroids).

Cytogenetic: Concerning chromosomes, their origin, structure and function.

(DNA) Deletion: A type of mutation where there is a loss of DNA (nucleotide base pairs) from the genome. Deletions may range in size from a single nucleotide to an entire chromosome. Such deletions may be harmless, may result in disease, or may in rare cases be beneficial.

Deoxyribonucleic acid (DNA): The carrier of genetic information for all living organisms except the group of RNA viruses. Each of the 46 chromosomes in normal human somatic cells consists of 2 strands of DNA containing an estimated 50 - 250 million nucleotides, specific sequences of which make up genes. DNA itself is composed of two interwound chains of linked nucleotides.

DNA damage: Injuries to DNA that introduce deviations from its normal, chemical structure and which may, if left unrepaired, result in a mutation or a block of DNA replication. These deviations can occur naturally or may be caused by environmental physical or chemical agents.

DNA methylation: A reversible biochemical modification of DNA more or less universally present in organisms from bacteria to humans. Methyl groups can be enzymatically added to or removed from cytosine (C). It is associated with silencing of DNA sequences.

DNA probe: A piece of single-stranded DNA, typically labelled so that it can be detected (for example, a radioactive or fluorescent label can be used), which can single out and bind with another specific piece of DNA. DNA probes can be used to determine which sequences are present in a given length of DNA or which genes are present in a sample of DNA.

DNA repair: Processes that repair potentially damaging changes in DNA, including those induced by chemical mutagens (see mutagen.) Through the action of enzymes, individual DNA bases may be replaced, or part of a strand of DNA may be replaced, using its opposite, paired strand as a template. These processes may themselves be prone to error and result in potentially deleterious changes.

DNA repair genes: Genes which code for proteins that repair damage in DNA sequences.

DNA damage response (DDR): Cells respond to the perception of DNA damage by arresting cell-cycle progression and attempting repair: collectively these actions are known as the DNA-damage response (DDR).

DNA sequencing: process by which the sequence of nucleotides along a strand of DNA is determined. Where either the whole genome or the exome (the region which encodes proteins) is sequenced this is referred to as whole genome/exome sequencing (WGS/WES).

Dominant lethal mutation: A dominant mutation (i.e. where mutation of a single allele is sufficient to cause a change in phenotype) that causes death of an early embryo.

Dopaminergic: Releasing or involving dopamine as a neurotransmitter.

Dose: Total amount of a substance administered to, taken or absorbed by an organism. May be qualified such as external dose, absorbed dose.

Dose-response relationship: how an effect caused by a chemical changes as the dose of the chemical changes, after a certain exposure time.

Endocrine active substance (EAS): A substance that can interact or interfere with the endocrine system.

Endocrine disrupter (ED): An exogenous substance or mixture that alters function(s) of the endocrine system and consequently causes adverse health effects in an intact organism or its progeny or (sub)populations.

Endonuclease: An enzyme that cleaves its nucleic acid substrate at internal sites in the nucleotide sequence.

Enterohepatic circulation: Cyclical process involving intestinal re-absorption of a substance that has been excreted through bile followed by transfer back to the liver, making it available for biliary excretion again.

Epidemiology: Study of factors determining the causes, frequency, distribution, and control of diseases in a human population.

Epigenetics: The study of heritable changes in gene function that occur without a change in the sequence of nuclear DNA and the processes involved in the unfolding development of an organism.

Epigenetic age: An estimate of biological age based on changes in epigenetic marks at particular locations along the genome.

Epigenetic drift: Divergence of the epigenome as a function of age due to stochastic changes in epigenetic marks.

Epigenetic marks: Features not directly governed by the genetic code, which include methylation of DNA and covalent modification of histone proteins. The latter may be tagged with methyl, acetyl, ubiquitin, phosphate, poly(ADP)ribose and other biochemical groups. These groups and their particular pattern of protein modification (e.g. mono-, bi-, tri-methylated at different amino acids and combinations of amino acids) modify the function of the tagged proteins and influence the way genes are expressed.

Epigenome: The comprehensive collection of genome-wide epigenetic phenomena, including DNA-methylation patterns, chromatin modifications, and non-coding RNA.

Epigenomic reprogramming: Resetting epigenetic marks so they resemble those of other cells from earlier developmental stages. This is of particular relevance for germline cells after the fusion of gametes when the genome is brought back into a "zero-state" of gene expression.

Epithelium: The tissue covering the outer surface of the body, the mucous membranes and cavities of the body.

Erythema: Reddening of the skin due to congestion of blood or increased blood flow in the skin.

Estrogen: Sex hormone or other substance capable of developing and maintaining female characteristics of the body (note UK spelling is oestrogen).

Exogenous: Arising outside the body.

Exposure Assessment: Process of measuring or estimating concentration or intensity, duration and frequency of exposure to an agent. The exposure could be via the environment, consumer products or the diet, or due to occupation.

Fetotoxic: Causing toxic, potentially lethal effects to the developing fetus.

Fibrosarcoma: A malignant tumour arising from connective tissue (see 'tumour').

First Pass Metabolism: rapid uptake and metabolism of an agent by the intestine or the liver, immediately after enteric absorption and before it reaches the systemic circulation.

Fluorescence In-Situ Hybridisation (FISH): A technique that allows individual chromosomes and their centromeres to be visualised in cells.

Forestomach: (See glandular stomach).

Free Radicals: any molecular species capable of independent existence that contains an unpaired electron in an atomic orbital. Many radicals are unstable and highly reactive.

Full gene sequence: the complete order of bases in a gene. This order determines which protein a gene will produce.

Gavage: Administration of a liquid via a stomach tube, commonly used as a dosing method in toxicity studies.

Gene: The functional unit of inheritance: a specific sequence of nucleotides along the DNA molecule, forming part of a chromosome.

Gene expression: The process by which the information in a gene is used to create proteins or polypeptides.

Gene families: Groups of closely related genes that make similar products.

Gene mutation: A permanent alteration in the DNA sequence that makes up a gene, such that the sequence differs from what is found in most people. Mutations range in size; they can affect anywhere from a single DNA building block (base pair) to a large segment of a chromosome that includes multiple genes.

Gene product: The protein or polypeptide coded for by a gene.

Genetic engineering: Altering the genetic material of cells or organisms in order to make them capable of making new substances or performing new functions.

Genetic polymorphism: a variation in germ-line DNA sequence among individuals, groups, or populations (e.g. a genetic polymorphism might give rise to blue eyes versus brown eyes, or population level differences in metabolic capacity). Genetic polymorphisms may be the result of chance processes or may have been induced by external agents (such as viruses or radiation). Generally, changes in DNA sequence which have been confirmed to be caused by external agents are called “mutations” rather than “polymorphisms”.

Genetic predisposition: susceptibility to a disease which is related to a polymorphism, which may or may not result in actual development of the disease.

Genetically modified organism (GMO): An organism which has had genetic material inserted into or removed from its cells.

Genome: All the genetic material in the chromosomes of a particular organism; its size is generally given as its total number of base pairs.

Genomic DNA: The basic chromosome set consisting of a species-specific number of linkage groups and the genes contained therein.

Genomic imprinting: The phenomenon whereby a small subset of all the genes in our genome are expressed according to their parent of origin.

Genomics: The study of genes and their function.

Genotoxic: A chemical or physical agent which has the ability to induce mutations or so-called indicator effects which are mechanistically associated with the formation of mutations (e.g. induction of DNA modifications, DNA repair, or recombination). All mutagenic substances are genotoxic but not vice versa.

Genotype: The particular genetic pattern seen in the DNA of an individual. “Genotype” is generally used to refer to the particular pair of alleles that an individual possesses at a certain location in the genome. Compare this with phenotype.

Germ cells: Cells that give rise to the gametes of an organism that reproduces sexually. The cells undergo mitotic and meiotic cell division in the gonads followed by cellular differentiation into mature gametes, either oocytes or sperm.

Glandular stomach: The stomach in rodents consists of two separate regions – the forestomach and the glandular stomach. Only the glandular stomach is directly comparable to the human stomach.

Half-life: In the context of toxicokinetics, this is the time in which the concentration of a substance in vivo will be reduced by 50%, assuming a first order elimination process.

Hazard: Set of inherent properties of a substance, mixture of substances or a process involving substances that make it capable of causing adverse effects to organisms or the environment.

Health based guidance value (HBGV): A value indicating the amount of chemical in food that a person can consume on a regular basis usually over a lifetime without any significant risk to health.

Hepatic: Pertaining to the liver.

Hepatocyte: The principal cell type in the liver, possessing many metabolising enzymes (see 'metabolic activation').

Heterozygous: having two different forms (alleles) of a gene that controls a particular characteristic, one inherited from each parent, and therefore able to pass on either form

Histone methylation: The modification of certain amino acids in a histone protein by the addition of methyl groups.

Histone modification: Covalent post-translational modifications to histone proteins including methylation, phosphorylation, acetylation, ubiquitylation, and sumoylation, which regulate gene expression. The modifications made to histones can impact gene expression by altering chromatin structure.

Histone tails: A structural aspect of histones that are major targets for post-translational modifications of histones (see Histone modifications).

Hodgkin's lymphoma: Cancer of the lymphatic system.

Homeostatic: Any self-regulation process by which biological systems tend to maintain stability while adjusting to conditions that are optimal for survival.

Horizon scanning: The systematic examination of potential threats, opportunities and likely future developments, which are at the margins of current thinking and planning. Horizon scanning may explore novel and unexpected issues, as well as persistent problems and trends. Overall, horizon scanning is intended to improve the robustness of policies and the evidence base.

Hypoxanthine-guanine phosphoribosyltransferase (HPRT) assay: This assay uses cultured mammalian somatic cells to detect mutagenic agents. The principle of the method relies on the fact that mutations (caused by mutagens) destroy the functionality or the HPRT gene or protein, which is detected by using a toxic analogue. The HPRT-mutants are viable colonies that can be scored.

Hypoxanthine-guanine phosphoribosyltransferase (HPRT) gene: A protein coding gene. This transferase allows cells to recycle purines, a building block of DNA and RNA.

Hypermethylation: Increase in the methylation of cytosine-guanosine base pairs in regulatory regions of DNA.

Hyperplasia: An increase in the size of an organ or tissue due to an increase in the number of cells through cell division.

Hypertrophy: An increase in the size of an organ or tissue due to an increase in the volume of individual cells within it.

Hypomethylation: The loss of the methyl group in 5-methylcytosine nucleotides in DNA. Hypomethylation can be used to describe the unmethylated state of specific nucleotides or as a general phenomenon affecting large parts of the genome.

Idiosyncrasy: Specific (and usually unexplained) reaction of an individual to e.g. a chemical exposure to which most other individuals do not react at all. General allergic reactions do not fall into this category.

In silico: a term used to describe a computerised analysis of the structure of a chemical to assess its potential hazard.

In situ hybridisation (ISH): Use of a DNA or RNA probe to detect the presence of the complementary DNA sequence in cloned bacterial or cultured eukaryotic cells.

In vitro: A Latin term used to describe studies of biological material outside the living animal or plant (literally “in glass”).

In vivo: A Latin term used to describe studies in living animals or plants (literally “in life”).

Incidence: Number of discrete events, for example new cases of illness occurring during a given period in a specific population.

(Enzyme) Inducing agent: A chemical which, when administered to an animal, causes an increase in the expression of a particular enzyme. For example, chlorinated dibenzodioxins are inducing agents which act via the Ah-receptor (qv) to induce P450 (qv) CYP1A1.

Intraperitoneal: Within the abdominal cavity.

Isomer: Isomers are two or more chemical compounds with the same molecular formula but having different properties owing to a different arrangement of atoms within the molecule.

Key event: An empirically observable precursor step that is itself a necessary element of an AOP or MOA. A key event is a necessary, though usually not a sufficient, step in a process that results in an adverse outcome.

kilobase (kb): A length of DNA equal to 1000 nucleotides.

Knockout animals: Genetically engineered animals in which one or more genes, usually present and active in the normal animal, have been eliminated or inactivated.

LC50/LD50: The concentration or dose that causes death in 50% of a group of experimental animals to which it is administered. It can be used to assess the acute toxicity of a compound but is being superseded by more refined methods.

Less than lifetime (LTL) exposure: any exposure that is not continuous daily exposure, for example, short-term, intermediate or intermittent, or a combination of these.

Leukaemia: A group of neoplastic disorders (see tumour) affecting blood-forming elements in the bone marrow, characterised by uncontrolled proliferation and disordered differentiation or maturation. Examples include the lymphocytic leukaemia's which develop from lymphoid cells and the myeloid leukaemia's which are derived from myeloid cells (producing red blood cells, mainly in bone marrow).

Ligand: A molecule which binds to an allosteric binding site in a protein, such as a receptor.

Lipids: Fats, substances containing a fatty acid and soluble in alcohols or ether, but insoluble in water.

Lipophilic: 'Lipid liking' - a substance which has a tendency to partition into fatty materials.

Lowest observed adverse effect level (LOAEL): The lowest administered dose at which a statistically significant adverse effect, relative to that of the control, has been observed. Also given as LOEL when no 'adverse' effects are seen.

Lymphocyte: A type of white blood cell that plays central roles in adaptive immune responses.

Lymphoma: Malignant tumours arising from lymphoid tissues. They are usually multifocal, involving lymph nodes, spleen, thymus and sometimes bone marrow, and other sites outside the anatomically defined lymphoid system. (See also 'tumour').

Malformations: The inheritance of an abnormal or anomalous formation of tissues and organs often referred to as a deformity.

Malignant tumour (synonym: cancer): A tumour (qv) composed of increasingly abnormal cells in term of their form and function. Some well differentiated examples still retain characteristics of their tissues of origin but these are progressively lost in moderately and poorly differentiated malignancies. Most malignant tumours grow rapidly, spread progressively through adjacent tissues and metastasise to distant sites.

Margin of exposure (MOE) approach: A methodology that allows the comparison of the risks posed by substances when it is not possible or not appropriate to establish a HBGV. This would include substances that are genotoxic and carcinogenic, and contaminants for which there is insufficient information to establish a Tolerable Daily Intake The MOE approach uses a reference point (or POD), often taken from an animal study, corresponding to a dose that causes no or a low response (for example the NAOEL, LOAEL, BMDL10). This reference point is then compared with various exposure estimates in humans. The lower the MOE, the greater the concern. The MOE considered to be of

low or negligible concern is context specific. In general, for substances that are genotoxic and carcinogenic, and MOE of >10,000, when based on a reference point from an animal study, would be considered of low concern. For a non-genotoxic, non-carcinogenic contaminant, an MOE of > 100 would be considered of negligible concern.

Margin of safety (MOS) approach: A methodology used to assess relative risk when there is exceedance of a HBGV. The MOS is expressed as the ratio of the HBGV to measured or estimated exposure. The lower the MOS is below 1, the greater the concern.

Maximum tolerated dose: The MTD for a long-term study of carcinogenicity is a dose that produces minimal signs of toxicity on repeated administration, meaning no more than a 10% weight decrement, as compared to the appropriate control groups; and does not produce mortality, clinical signs of toxicity, or pathologic lesions (other than those that may be related to a neoplastic response) that would be predicted to shorten the animal's natural life span.

Mechanism of action: an understanding of the molecular basis for an effect and its detailed description, so causation can be established in molecular terms.

Meiosis: The process of cell division in sexually reproducing organisms that reduces the number of chromosomes in reproductive cells from diploid to haploid leading to the production of gametes in animals and spores in plants. During the first meiotic division there is homologue pairing, efficient intergenic recombination between homologues during pairing, and the suppression of sister chromatid separation. S phase is absent at the start of the second meiotic division. Thus, the outcome of meiosis should be four genetically unique haploid cells.

Messenger RNA (mRNA): The DNA of a gene is transcribed (see transcription) into mRNA molecules, which then serve as a template for the synthesis of proteins.

Meta-analysis: In the context of epidemiology, a statistical analysis of the results from independent studies, which aims to produce a single estimate of an effect.

Metabolic activation: Metabolism of a compound leading to an increase in its activity, whether beneficial (e.g. activation of a pro-drug) or deleterious (e.g. activation to a toxic metabolite).

Metabolic activation system: A cell-free preparation (e.g. from the livers of rats pre-treated with an inducing agent (qv)) added to in vitro tests to mimic the metabolic activation typical of mammals.

Metabolism: Chemical modification of a compound by enzymes within the body, for example by reactions such as hydroxylation (see P450), epoxidation or conjugation. Metabolism may result in activation, inactivation, change in activity, accumulation or excretion of the compound.

Metabolite: Product formed by metabolism of a compound.

Metabolomics: The measurement of the amounts (concentrations) and locations of all metabolites in a cell.

Metabonomics: Metabonomics is a subset of metabolomics and is defined as the quantitative measurement of the multiparametric metabolic responses of living systems to pathophysiological stimuli or genetic modification.

Metaphase: Stage of cell division (mitosis and meiosis) during which the chromosomes are arranged on the equator of the nuclear spindle (the collection of microtubule filaments which are responsible for the movement of chromosomes during cell division). As the chromosomes are most easily examined in metaphase, cells are arrested at this stage for microscopical examination for chromosomal aberrations (qv) - known as metaphase analysis.

Metastasis: The process whereby malignant cells become detached from the primary tumour mass, disseminate (mainly in the blood stream or in lymph vessels) and seed out in distant sites where they form secondary or metastatic tumours. Such tumours tend to develop at specific sites and their anatomical distribution is often characteristic, i.e. it is non-random.

Microbiome (Human): Human microbiome is the full array of microorganisms (the microbiota) that live on and in humans and, more specifically, the collection of microbial genomes that contribute to the broader genetic portrait, or metagenome, of a human. Often a subset of the microbiome is the subject of interest, for example the intestinal or dermal microbiome.

Micronuclei: Whole or fragmented chromosomes that fail to segregate normally during cell division and may be lost from the main nuclei but remain in the body of the cell forming micronuclei. Centromere positive micronuclei contain DNA and/or protein material derived from the centromere. The presence of centromere positive micronuclei following exposure to chemicals in vitro or in vivo can be used to evaluate the aneugenic potential of chemicals.

Minimal risk level: defined in this document as an estimate of daily human exposure to a chemical, identified by expert judgement, that is likely to be associated with a negligible risk of carcinogenic effect over a specified duration of exposure (usually a lifetime).

Mitogen: A stimulus which provokes cell division in somatic cells.

Mitosis: The process in cell division in somatic cells by which the nucleus divides, typically consisting of four stages, prophase, metaphase, anaphase, and telophase, and normally resulting in two new nuclei, each of which contains a complete copy of the parental chromosomes. The outcome of mitosis should be two genetically identical diploid cells.

Mode of Action: a biologically plausible sequence of key events leading to an observed effect supported by robust experimental observations and mechanistic data. It describes key cytological and biochemical events, i.e. those that are both measurable and necessary to the observed outcome, in a logical framework. It contrasts with mechanism of action.

Mode of genotoxic a**ction (MoGA):** The mode of action of a genotoxicant refers to the underlying events involved in the process whereby the chemical induces genotoxic effects.

In order for a specific mode of action to be supported there needs to be evidence from robust mechanistic data to establish a biologically plausible explanation. Mode of genotoxic action should be distinguished from the term mechanism of action. The latter relates to having sufficient understanding of the molecular basis of the chemical genotoxicity to establish causality. Thus, mechanism of action is at the other end of a continuum from little or no evidence of mode of genotoxic action to scientific proof of mechanism of action.

Molecular initiating event (MIE): the initial point of chemical/stressor interaction at the molecular level within the organism that results in a perturbation that starts the AOP.

Mouse lymphoma assay: An in vitro assay for gene mutation in mammalian cells using a mouse lymphoma cell line L5178Y, which is heterozygous for the gene (carries only one functional allele rather than a pair) for the enzyme thymidine kinase (TK+/-). Mutation of that single gene is measured by resistance to toxic trifluorothymidine. Mutant cells produce two forms of colony - large, which represent mutations within the gene and small, which represent large genetic changes in the chromosome such as chromosome aberrations. Thus, this assay can provide additional information about the type of mutation which has occurred if colony size is scored.

Mucosal: Regarding the mucosa or mucous membranes, consisting of epithelium containing glands secreting mucus, with underlying layers of connective tissue and muscle.

Multigenerational effects: Effect seen in exposed generations, including those that may have been exposed in utero, as offspring or gametes. For effects in unexposed generations see ‘Transgenerational effects’.

Murine: Often taken to mean “of the mouse”, but strictly speaking means of the Family Muridae which includes rats and squirrels.

Mutagen: is a physical or chemical agent that changes the genetic information (usually DNA) of an organism that can be inherited by daughter cells.

Mutation: A permanent change in the amount or structure of the genetic material in an organism or cell, which can result in a change in phenotypic characteristics. The alteration may involve a single gene, a block of genes, or a whole chromosome. Mutations involving single genes may be a consequence of effects on single DNA bases (point mutations) or of large changes, including deletions, within the gene. Changes involving whole chromosomes may be numerical or structural. A mutation in the germ cells of sexually reproducing organisms may be transmitted to the offspring, whereas a mutation that occurs in somatic cells may be transferred only to descendent daughter cells.

Mutational signatures: Mutational signatures are characteristic profiles of mutation types arising from specific mutagenesis processes such as DNA replication infidelity, exogenous and endogenous genotoxins exposures, defective DNA repair pathways and DNA enzymatic editing.

Mycotoxin: Toxic compound produced by a fungus.

Nanomaterial: A natural, incidental or manufactured material containing particles, in an unbound state or as an aggregate or as an agglomerate and where, for 50% or more of the particles in the number size distribution, one or more external dimensions is in the size range 1 nm - 100 nm.

Neoplasia: the abnormal proliferation of benign or malignant cells.

Neoplasm: See 'tumour'.

Neoplastic: Abnormal cells, the growth of which is more rapid that that of other cells of the same tissue type.

Neural tube defect (NTD): Is a birth defect in which an opening in the spine or cranium remains from early in human development.

Neurobehavioural: Of behaviour determined by the nervous system.

Neurotransmitter: A chemical that is released from a nerve cell which thereby transmits an impulse from a nerve cell to another nerve, muscle, organ, or other tissue. A neurotransmitter is a messenger of neurologic information from one cell to another.

No observed adverse effect level (NOAEL): The highest administered dose at which no statistically significant adverse effect has been observed in comparison to the control. Also given as NOEL when no ‘adverse’ effects are seen.

Non-Hodgkin lymphomas: (NHLs) are a diverse group of hematologic cancers which encompass any lymphoma other than Hodgkin’s Lymphoma

No observed genotoxic effect level (NOGEL): This is the highest experimental dose level where no statistically significant increase in the genotoxic effect measured in the study is identified.

Nucleic acid: One of the family of molecules which includes the DNA and RNA molecules. Nucleic acids were so named because they were originally discovered within the nucleus of cells, but they have since been found to exist outside the nucleus as well.

Nucleosome: A repeating subunit of DNA packaging consisting of DNA wound in sequence around histone proteins.

Nucleotide: the "building block" of nucleic acids, such as the DNA molecule. A nucleotide consists of a nucleoside attached a phosphate group. A nucleoside comprises one of four bases - adenine, guanine, cytosine, or thymine - attached to a sugar group. In DNA the sugar group is deoxyribose, while in RNA (a DNA-related molecule which helps to translate genetic information into proteins), the sugar group is ribose, and the base uracil substitutes for thymine. Each group of three nucleotides in a gene is known as a codon. A nucleic acid is a long chain of nucleotides joined together, and therefore is sometimes referred to as a "polynucleotide."

Null allele: Mutations that result in absence of gene product or a non-functional product.

Null hypothesis: type of conjecture used in statistical tests, which are formal methods of reaching conclusions or making decisions on the basis of data. In toxicology, a common null hypothesis is that there is no effect of treatment with a substance. Statistical testing may enable a conclusion that this is most likely incorrect, i.e. the null hypothesis is rejected with a stated probability of error, or it is not possible to reach a conclusion. It is not possible by conventional statistical testing to prove the null hypothesis is most likely correct, i.e. that there is no effect. This is the axiomatic difficulty of "proving a negative".

Odds ratio (OR): The odds of disease in an exposed group divided by the odds of disease in an unexposed group.

Oedema: Excessive accumulation of fluid in body tissues.

Oligonucleotide: A molecule made up of a small number of nucleotides, typically fewer than 25.

'Omics' technologies: A scientific subdiscipline that combines the technologies of genomics and bioinformatics to identify and characterise mechanisms of action of known and suspected toxicants. The collective term 'omics' refers to the genomic (DNA sequence analysis) and post-genomic (e.g. transcriptomics, proteomics, metabolomics, epigenomics) technologies that are used for the characterisation and quantitation of pools of biological molecules (e.g. DNA, mRNAs, proteins, metabolites), and the exploration of their roles, relationships and actions within an organism.

Oncogene: A gene which is associated with the development of cancer (see proto-oncogene).

Pharmacodynamics: The process of interaction of drugs with target sites and the subsequent reactions leading to the desired biological effects (see toxicodynamics).

Pharmacokinetics: Description of the fate of drugs in the body, including a mathematical account of their absorption, distribution, metabolism and excretion (see toxicokinetics).

Pharmacogenomics: The science of understanding the correlation between an individual patient's genetic make-up (genotype) and their response to drug treatment. Some drugs work well in some patient populations and not as well in others. Studying the genetic basis of patient response to therapeutics allows drug developers and medical practitioners to design and use therapeutic treatments more effectively.

Phenotype: The observable physical, biochemical and physiological characteristics of a cell, tissue, organ or individual, as determined by its genotype and the environment in which it develops.

Phenotypic change: A change in the observable physical or biochemical characteristics of an organism, as determined by both genetic makeup and environmental influences.

Physiologically based pharmacokinetic (PBPK) model: A mathematical model which is used to predict the absorption, distribution, metabolism and excretion of a chemical substance in humans.

Phytoestrogen: Any plant substance or metabolite that can mimic or modulate the actions of endogenous oestrogens, usually by binding to oestrogen receptors, and which can therefore induce biological responses.

Pig-A gene mutation assay: An assay which utilises the Pig-A gene which codes for one subunit of a glycosylphosphatidyl inositol anchor protein. Loss of function arising from Pig-A mutations can readily be assessed using straightforward immunochemistry and flow cytometric methods, thus making it useful to measure gene mutations induced by chemicals or radiation.

Plasmid: A structure composed of DNA that is separate from the cell's genome (qv). In bacteria, plasmids confer a variety of traits and can be exchanged between individuals, even those of different species. Plasmids can be constructed and manipulated in the laboratory to deliver specific genetic sequences into a cell.

Point of departure: a dose associated with a defined level of effect, which can be determined empirically or by modelling dose-response data from experimental studies, from which a health-based guidance value can be established or which can be used for a margin of exposure assessment. Examples include a BMDL, NOAEL or LOAEL.

Polymer: A very large molecule comprising a chain of many similar or identical molecular sub units (monomers) joined together (polymerised). An example is the polymer glycogen, formed from linked molecules of the monomer glucose.

Polymerase chain reaction (PCR): A method for creating millions of copies of a particular segment of DNA. PCR can be used to amplify the amount of a particular DNA sequence until there are enough copies available to be detected.

Polymorphism: (see genetic polymorphism)

^{32}P postlabelling assay: An experimental method designed to measure low levels of DNA adducts induced by chemical treatment. It involves labelling of adducted nucelosides from digested DNA with ^{32}P and their quantification following chromatographic separation.

Prevalence: The number of discrete cases, for example of a disease, that are present in a population at a given time.

Primer: Short pre-existing polynucleotide chain to which new deoxyribonucleotides can be added by DNA polymerase.

Primordial germ cells: Highly specialised cells that are precursors of gametes, which, following meiosis, develop as haploid sperm and eggs that generate a new organism upon fertilisation.

Proteomics: The analysis of the entire protein complement of a cell, tissue, or organism under a specific, defined set of conditions.

Proto-oncogene: One of a group of normal genes that are concerned with the control of cellular proliferation and differentiation. They can be activated in various ways to forms (oncogenes) which are closely associated with one or more steps in carcinogenesis. Activating agents include chemicals and viruses. The process of proto-oncogene activation is thought to play an important part at several stages in the development of tumours.

Quantal Data: When the response for an individual unit (well, animal etc) is a binary value, such as alive / dead, or response / no response, the data are treated as quantal. The responses are assumed to follow a binomial distribution within each dose group. This assumption is required for the calculations of confidence intervals and the p values resulting from statistical tests.

ras oncogene: The Ras protein family are a class of protein called small GTPase, and have important roles in cell signalling. The ras gene is the most common oncogene involved in human cancer - mutations that permanently activate ras are found in 20-25% of all human tumours and up to 90% in certain types of cancer (e.g. pancreatic cancer).

Receptor: A small, discrete protein in the cell membrane or within the cell with which specific molecules interact to initiate a change in the working of a cell.

Recombinant DNA: DNA molecules that have been created by combining DNA from more than one source.

Reference nutrient intake (RNI): An amount of the nutrient that is sufficient, or more than sufficient, to ensure adequate nutrient function for most (usually at least 97%) people in a group. If the average intake of a group is at the RNI, then the risk of deficiency in the group is very small.

Regulatory gene: A gene which controls the protein-synthesising activity of other genes.

Relative potency factor (RPF): The toxic potency of a substance expressed relative to that of an index chemical to enable cumulative risk assessment (*qv)*. The RPF is similar to the TEF (*qv*) but is used when the information on common MIEs, toxicokinetics and outcomes of the members of an assessment group is less reliable than that required for application of the TEF approach.

Relative risk: A measure of the association between exposure and outcome. The rate of disease in the exposed population divided by the rate of disease among the unexposed population in a cohort study or a population-based case control study. A relative risk of 2 means that the exposed group has twice the disease risk compared to the unexposed group.

Reporter gene: A gene that encodes an easily assayed product that is coupled to the upstream sequence of another gene and transfected (qv) into cells. The reporter gene can then be used to see which factors activate response elements in the upstream region of the gene of interest.

Risk: Probability that a harmful event (death, injury or loss) arising from exposure to a chemical or physical agent may occur under specific conditions.

Risk assessment: process of evaluating a potential hazard, likelihood of suffering, or any adverse effects from certain human activities. Comprised of the four aspects, hazard identification, hazard characterisation, exposure assessment and risk characterisation. Can be carried out retrospectively or prospectively.

Risk management: process designed to identify, contain, reduce, or eliminate the potential for harm to the human population; usually concerned with the delivery system and site rather than performance.

Ribonucleic acid (RNA): a molecule similar to DNA, in that it is a nucleic acid comprised of a chain of nucleotides. However, unlike DNA, RNA exists as a single-stranded chain. RNA has various biological roles in coding, decoding, regulation and expression of genes.

Sarcoma: cancer that arises from transformed cells of mesenchymal (connective tissue) origin.

Serotonergic: Denoting a nerve ending that releases and or stimulated by serotonin.

Signal induction pathway: The molecular pathways that signal (i.e. turn on or off) biochemical pathways or biological functions (e.g. biochemical pathways leading to nerve conduction).

Single nucleotide polymorphism (SNP): DNA sequence variations that occur when a single nucleotide in the genome sequence is altered. For example, a SNP might change the DNA sequence A***A***GGCTAA to A***T***GGCTAA.

Strand breaks: Relating to DNA, a single strand break occurs when there is a break in double-stranded DNA in which only one of the two strands has been cleaved; the two strands have not separated from each other. Double strand breaks occur when both strands in the double helix are severed and are particularly hazardous to the cell because they can lead to genome rearrangements.

Sister chromatid exchange (SCE): Exchange of genetic material between two subunits of a replicated chromosome.

Somatic cells: Any biological cell that forms part of the body of an organism, excluding reproductive cells and undifferentiated stem cells.

Stakeholder: A person or organisation representing the interests and opinions of a group with an interest in the outcome of (for example) a review or policy decision.

Statistical significance: a conclusion drawn when, after carrying out a statistical test of the null hypothesis of no effect, the hypothesis is considered unlikely to be true. The criterion for the decision is often a probability (p) value, chosen to be, but not necessarily, $p<0.05$.

Stem cell: an unspecialized cell capable of perpetuating itself through cell division and having the potential to give rise to differentiated cells with specialized functions.

Suppressor gene: A gene which helps to reverse the effects of damage to an individual's genetic material, typically these are effects which might lead to uncontrolled cell growth (as would occur in cancer). A suppressor gene may, for example, code for a protein which checks genes for misspellings, and/or which triggers a cell's self-destruction if too much DNA damage has occurred.

Systematic review: A formalised review that has been prepared using a documented systematic approach to minimising biases and random errors.

Systems biology: The computational and mathematical analysis and modelling of complex biological systems.

Systems toxicology: The integration of classical toxicology with quantitative analysis of large networks of molecular and functional changes occurring across multiple levels of biological organisation.

T25: the dose eliciting a 25% increase in the incidence of a specific tumour above the background level.

TD_{50}: For any particular sex, strain, species and set of experimental conditions, the TD_{50} is the dose rate (in mg/kg body weight/day) that, if administered chronically for a standard period - the "standard lifespan" of the species-will halve the mortality-corrected estimate of the probability of remaining tumourless throughout that period.

Teratogen: A substance that can cause congenital malformations (structural defects) in a developing fetus following maternal exposure.

Testicular dysgenesis syndrome (TDS): The hypothesis that maldevelopment (dysgenesis) of the fetal testis results from hormonal or other malfunctions of the testicular somatic cells which in turn predispose a male to the disorders that comprise the TDS, i.e. congenital malformations (cryptorchidism and hypospadias) in babies and testis cancer and low sperm counts in young men.

Threshold: the level of dose or exposure below which there is no effect above that in the control group or population. There are several different uses of the term threshold, for example observable threshold, biological threshold, population threshold.

Threshold of toxicological concern (TTC): a pragmatic, scientifically valid methodology to prioritise substances of unknown toxicity found in food for further evaluation. It is used when there are limited chemical-specific toxicity data and can be used for substances with or without structural alerts for genotoxicity and for cancer and non-cancer endpoints.

Tolerable daily intake (TDI): An estimate of the amount of contaminant, expressed on a body weight basis (e.g. mg/kg bodyweight), that can be ingested daily over a lifetime without appreciable health risk. The term is preferred for substances that are unintentionally present.

Tolerable upper level (TUL): The highest level of nutrient that is likely to pose no risk of adverse health effects for almost all individuals in the general population. As intake increases above the TUL, the risk of adverse effects increases.

Toxic equivalency factor (TEF): A measure of relative toxicological potency of a chemical compared to a well characterised reference compound. TEFs can be used to sum the toxicological potency of a mixture of chemicals which are all members of the same chemical class, having common structural, toxicological and biochemical properties. TEF systems have been published for the chlorinated dibenzodioxins, dibenzofurans and dioxin-like polychlorinated biphenyls, and for polycyclic aromatic hydrocarbons.

Total toxic equivalent (TEQ): Is a method of comparing the total relative toxicological potency within a sample. It is calculated as the sum of the products of the concentration of each congener multiplied by the toxic equivalency factor (TEF).

Toxicodynamics: The process of interaction of chemical substances with target sites and the subsequent reactions leading to adverse effects.

Toxicogenic: producing or capable of producing toxins, e.g. a fungal strain.

Toxicokinetics: The description of the fate of potentially toxic chemicals in the body, including a mathematical account of their absorption, distribution, metabolism and excretion, particularly at doses that are toxic. (see pharmacokinetics)

Transcription: the process during which the information in a piece of DNA (qv) is used to construct an mRNA (qv) molecule.

Transcriptomics: Techniques used to identify mRNA from actively transcribed genes.

Transgenerational effects: Effects seen in generations that have not been exposed, either directly to the substance under consideration or indirectly as offspring or gametes via parental exposure. For effects in exposed populations, see ‘multigenerational effects’.

Transfer RNA (tRNA): RNA molecules which bond with amino acids and transfer them to ribosomes, where protein synthesis is completed.

Transfection: A process by which exogenous genetic material (DNA or RNA) is introduced into a cell with the object of altering the phenotype or genotype of the cell.

Transgenic: Genetically modified to contain genetic material from another species (see also genetically modified organism).

Transgenic animal models: Animals which have extra (exogenous) fragments of DNA incorporated into their genomes. This may include reporter genes to assess in-vivo effects such as mutagenicity in transgenic mice containing a recoverable bacterial gene (lacZ or lac I). Other transgenic animals may have alterations of specific genes believed to be involved in disease processes (e.g. cancer). For example, strains of mice have been bred which carry an inactivated copy of the p53 tumour suppressor gene, or an activated form of the ras oncogene which may enhance their susceptibility of the mice to certain types of carcinogenic chemicals.

Translation: In molecular biology, the process during which the information in mRNA molecules is used to construct proteins.

Tumour (Synonym - neoplasm): A mass of abnormal, disorganised cells, arising from pre-existing tissue, which are characterised by excessive and uncoordinated proliferation and by abnormal differentiation. Benign tumours show a close morphological resemblance to their tissue of origin; grow in a slow expansile fashion; and form circumscribed and (usually) encapsulated masses. They may stop growing and they may regress. Benign tumours do not infiltrate through local tissues and they do not metastasise (qv). They are rarely fatal. Malignant tumours (synonym - cancer) resemble their parent tissues less closely and are composed of increasingly abnormal cells in terms of their form and function. Well differentiated examples still retain recognisable features of their tissue of origin but these characteristics are progressively lost in moderately and poorly differentiated malignancies: undifferentiated or anaplastic tumours are composed of cells which resemble no known normal tissue. Most malignant tumours grow rapidly, spread progressively through adjacent tissues and metastasise to distant sites. Tumours are conventionally classified according to the anatomical site of the primary tumour and its microscopical appearance, rather than by cause. Benign tumours may evolve to the corresponding malignant tumours; examples involve the adenoma → carcinoma sequence in the large bowel in humans, and the papilloma → carcinoma sequence in mouse skin.

Tumour initiation: A term originally used to describe and explain observations made in laboratory models of multistage carcinogenesis, principally involving repeated applications of chemicals to the skin of mice. Initiation, in such contexts, was the first step whereby small numbers of cells were irreversibly changed or initiated. Subsequent, separate events (see tumour promotion) resulted in the development of tumours. It is now recognised that these early, irreversible heritable changes in initiated cells were due to genotoxic damage, usually in the form of somatic mutations and the initiators used in these experimental models can be regarded as genotoxic carcinogens.

Tumour microenvironment: This is a complex system of many cell types, including cancer cells, fibroblasts, endothelial cells, leukocytes and antigen-presenting cells, together with connective tissue. The microenvironment is integral in determining the functionality, physiology and spread (metastasis) of cancer.

Tumour promotion: Originally used, like ‘tumour initiation’ to describe events in multistage carcinogenesis in experimental animals. In that context, promotion is regarded as the protracted process whereby initiated cells undergo clonal expansion to form overt tumours. The mechanisms of clonal expansion are diverse, but include direct stimulation of cell proliferation, repeated cycles of cell damage and cell regeneration and release of cells from normal growth-controlling mechanisms. Initiating and promoting agents were originally regarded as separate categories, but the distinction between them is becoming increasingly hard to sustain. The various modes of promotion are non-genotoxic, but it is incorrect to conclude that ‘non-genotoxic carcinogen’ and ‘promoter’ are synonymous.

Uncertainty factor: Value used in extrapolation from a reference point (or POD), determined in experimental animals, to humans (assuming that humans may be more sensitive) or from a sub-population of individuals to the general population: for example, a value applied to the NOAEL to establish an ADI or TDI. The value depends on the size

and type of population to be protected and the quality of the toxicological information available.

Unscheduled DNA synthesis (UDS): DNA synthesis that occurs at some stage in the cell cycle other than the S period (the normal or 'scheduled' DNA synthesis period), in response to DNA damage. It is usually associated with DNA repair.

Volume of distribution: Apparent volume of fluid required to contain the total amount of a substance in the body at the same concentration as that present in the plasma, assuming equilibrium has been attained.

Weight of evidence: This approach uses a combination of several independent sources of evidence (e.g. toxicological or genotoxicity data) to arrive at a conclusion regarding potential hazard (such as mutagenicity).

WHO-TEQs: The system of Toxic Equivalency Factors (TEFs) used in the UK and a number of other countries to express the concentrations of the less toxic dioxin-like compounds (16 PCDDs/PCDFs and 12 PCBs) as a concentration equivalent to the most toxic dioxin 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) is that set by the World Health Organisation (WHO), and the resulting overall concentrations are referred to as WHO-TEQs (Total toxic equivalents) (see also Toxic Equivalency Factor).

Xenobiotic: A chemical foreign to the biologic system.

Xenoandrogen: A ‘foreign’ compound with androgenic activity (see androgen).

Xenoestrogen: A 'foreign' compound with oestrogenic activity (see oestrogen).

Organisational abbreviations

COC: Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment: is an independent scientific committee that provides advice the government and government agencies on whether substances are likely to cause cancer.

COM: Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment: is an independent scientific committee that assesses and advises the government and government agencies on mutagenic risks to humans.

COT Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment: is an independent scientific committee that provides advice to the government and government agencies on matters concerning the toxicity of chemicals.

EFSA European Food Safety Authority

Expert Group on Vitamins and Minerals (EVM): An independent UK expert advisory committee which was asked to advise on safe levels of intakes of vitamins and minerals in food supplements and fortified foods.

FSA: Food Standards Agency

International Council on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH): This initiative brings together the regulatory authorities and pharmaceutical industry to discuss scientific and technical aspects of pharmaceuticals and develop ICH guidelines. ICH aims to achieve greater harmonisation worldwide to ensure that safe, effective and high quality medicines are developed, and registered and maintained in the most resource efficient manner whilst meeting high standards.

JECFA: WHO Joint Expert Committee on Food Additives

Organisation for Economic Cooperation and Development (OECD) Guidelines for the testing of chemicals: Tools for assessing the potential effects of chemicals on human health and the environment. Accepted internationally as standard methods for safety testing and assessment of chemicals.

PHE: Public Health England

SACN: Scientific Advisory Committee on Nutrition.

SAHSU: Small Area Health Statistics Unit.

ANNEX 6 - Index to Subjects and Substances considered in previous annual reports of the Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment

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ANNEX 7 – Previous Publications

Publications produced by the Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment

1991 Annual Report of Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. HMSO ISBN 0 11 321529 0 Price £9.50.

1992 Annual Report of Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. HMSO ISBN 0 11 321604-1 Price £11.70.

1993 Annual Report of Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. HMSO ISBN 0 11 321808-7 Price £11.95.

1994 Annual Report of Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. HMSO ISBN 0 11 321912-1 Price £12.50.

1995 Annual Report of Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. HMSO ISBN 0 11 321988-1 Price £18.50.

1996 Annual Report of Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. The Stationery Office ISBN 0 11 322115-0 Price £19.50.

1997 Annual Report of Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. Department of Health.*

1998 Annual Report of Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. Department of Health*.

1999 Annual Report of Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. Department of Health*.

2000 Annual Report of Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. Department of Health.*

2001 Annual Report of Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. Food Standards Agency/Department of Health, FSA/0681/0802.++

2002 Annual Report of Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. Food Standards Agency/Department of Health, FSA/0838/0803.++

2003 Annual Report of Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. Food Standards Agency/Department of Health, FSA/0900/0504.++

2004 Annual Report of Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. Food Standards Agency/Department of Health, FSA/0992/0804.++

2005 Annual Report of Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. Food Standards Agency/Department of Health, FSA/1098/0906.++

2006 Annual Report of Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. Food Standards Agency/Department of Health, FSA/1184/0707++

2007 Annual Report of Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. Food Standards Agency/Department of Health, FSA/1260/0608++

2008 Annual Report of Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. Food Standards Agency/Department of Health, FSA/1410/0709++

2009 Annual Report of Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. Food Standards Agency/Department of Health, July 2010++

2010 Annual Report of Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. Food Standards Agency/Department of Health, June 2011++

2011 Annual Report of Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. Food Standards Agency/Department of Health, July 2012

2012 Annual Report of Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. Food Standards Agency/Department of Health, April 2014

2013 Annual Report of Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. Food Standards Agency/Department of Health, March 2015.

2014 Annual Report of Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. Food Standards Agency/Department of Health, November 2015.

2015 Annual Report of Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. Food Standards Agency/Department of Health, July 2016.

2016 Annual Report of Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. Food Standards Agency/Department of Health, August 2017.

Guidelines for the Testing of Chemicals for Toxicity DHSS Report on Health and Social Subjects 27 HMSO ISBN 0 11 320815 4 Price £4.30.

Guidelines for the Evaluation of Chemicals for Carcinogenicity DH Report on Health and Social Subjects 42 HMSO ISBN 0 11 321453 7 Price £7.30.

Guidelines for the Testing of Chemicals for Mutagenicity DH Report on Health and Social Subjects 35 HMSO ISBN 0 11 321222 4 Price £6.80.

Guidelines for the Preparation of Summaries of Data on Chemicals in Food, Consumer Products and the Environment submitted to DHSS Report on Health and Social Subjects 30 HMSO ISBN 0 11 321063 9 Price £2.70.

Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment: Peanut Allergy, Department of Health (1998)**

Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment: Organophosphates, Department of Health (1998)**

Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment: Adverse Reactions to Food and Food Ingredients, Food Standards Agency (2000)++

Guidance on a Strategy for testing of chemicals for Mutagenicity. Department of Health (2000)*

Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment: Risk Assessment of Mixtures of Pesticides and Similar Substances, Food Standards Agency, FSA/0691/0902 (2002).++

Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment: Phytoestrogens and Health, Food Standards Agency, FSA/0826/0503 (2002).++

Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment: Variability and Uncertainty in Toxicology of Chemicals in Food, Consumer Products and the Environment, FSA/1150/0307 (2007).++

Guidance on a Strategy for the Risk Assessment of Chemical Carcinogens. Department of Health (2004)+

*Available on the COM website at: https://www.gov.uk/government/organisations/committee-on-mutagenicity-of-chemicals-in-food-consumer-products-and-the-environment

** Available on the COT archive at:
http://tna.europarchive.org/20130802141804/http://cot.food.gov.uk/cotstatements/

+ Available on the COC website at
https://www.gov.uk/government/groups/committee-on-carcinogenicity-of-chemicals-in-food-consumer-products-and-the-environment-coc

++ http://cot.food.gov.uk/cotreports/