ANNEX 1

TERMS OF REFERENCE

To advise at the request of:

Department of Health

Food Standards Agency

Department for the Environment, Food and Rural Affairs

Department of Transport, Local Government and the Regions

Department of Trade and Industry

Health and Safety Executive

Pesticide Safety Directorate

Veterinary Medicines Directorate

Medicines and Healthcare products Regulatory Agency

Home Office

Scottish Executive

National Assembly for Wales

Northern Ireland Executive

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 Control Agency, Section 4 Committee or the Licensing Authority;

   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 ADVISORY COMMITTEES

Public service values

Members must at all times:

- observe the highest standards of impartiality, integrity and objectivity in relation to the advice they provide and the management of this Committee;

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

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

Standards in Public Life

All Committee members must:

- follow the Seven Principles of Public Life set out by the Committee on Standards in Public Life (see page 148);

- comply with this Code, and ensure they understand their duties, rights and responsibilities, and that they are familiar with the function and role of this 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 this 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.

Role of Committee members

Members have collective responsibility for the operation of this Committee. They 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; the Department of Health and sponsor departments or the responsible Minister;
- in accordance with Government policy on openness, ensure that they adhere to the Code of Practice on Access to Government Information (including prompt responses to public requests for information); agree an Annual Report; and, where practicable and appropriate, provide suitable opportunities to open up the work of the Committee to public scrutiny
- not divulge any information which is provided to the Committee in confidence;
- 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 does not exceed its powers or functions.

Individual members should inform the Chairman (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 the Committee and the Food Standards Agency (FSA) Board and/or Ministers will generally be through the Chairman except where the Committee 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 Ministers 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.

Individual members can be removed from office by the FSA Board if they fail to perform the duties required of them in line with the standards expected in public office.

The role of the Chairman

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

- ensuring that the Committee meets at appropriate intervals, and that the minutes of meetings and any reports to the FSA Board accurately record the decisions taken and, where appropriate, the views of individual members;

- representing the views of the Committee to the general public; and

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

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 at pages 276 to 277.

(i) Declaration of Interests to the Secretariat

Members of the Committee should inform the Secretariat in writing of their current personal and non-personal interests, when they are appointed, including the principal position(s) held. Only the name of the company and the nature of the interest are required; the amount of any salary etc. need not be disclosed. An interest is current if the member has an on-going financial involvement with industry, eg if he or she holds shares in industry, has a consultancy contract, or if the member or the department for which he or she is responsible is in the process of carrying out work for industry. Members are asked to inform the Secretariat at any time of any change of their personal interests and will be invited to complete a declaration form once a year. It is sufficient if changes in non-personal interests are reported in the annual declaration form following the change. (Non-personal interests involving less than £1,000 from a particular company in the previous year need not be declared to the Secretariat).

The register of interests should be kept up-to-date and be open to the public.

(ii) Declaration of Interest and Participation at Meetings

Members of the Committee are required to declare any direct interests relating to salaried employment or consultancies, or those of close family members[1], in matters under discussion at each meeting. Having fully explained the nature of their interest the Chairman will, having consulted the other members present, decide whether and to what extent the member should participate in the discussion and determination of the issue. If it is decided that the member should leave the meeting, the Chairman may first allow them to make a statement on the item under discussion.

[1] Close family members include personal partners, parents, children, brothers, sisters and the personal partners of any of these.

Personal liability of Committee members

A Committee member may be personally liable if he or she makes a fraudulent or negligent statement which results in a loss to a third party; or may commit a breach of confidence under common law or a criminal offence under insider dealing legislation, if he or she misuses information gained through their position. However, the Government has indicated that individual 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 Committee functions save where the person has acted recklessly. To this effect a formal statement of indemnity has been drawn up.

THE SEVEN PRINCIPLES OF PUBLIC LIFE

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.

DIFFERENT TYPES OF INTEREST

The following is intended as a guide to the kinds of interests that 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 Chairman 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. For example, either through not being aware of all the interests of family members, or of not being aware of links between one company and another.

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 commissioned work by industry for which the member is paid in cash or kind;
- **Shareholdings**: any shareholding 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;

Non-Personal Interests

A non-personal interest involves payment which benefits a department for which a member is responsible, 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 department e.g.:

  i) a grant for the running of a unit or department for which a 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 in the unit for which a 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 for which they are responsible, 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.

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;

The Food Safety Act 1990

The Medicines Acts 1968 and 1971

The Food and Environmental Protection Act 1985

The Consumer Protection Act 1987

The Cosmetic (Safety) (Amendment) Regulations 1987

The Notification of New Substances Regulations 1982

- 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, Mutageneticity, or Carcinogenicity of Chemicals in Food, Consumer Products and the Environment.

In this Code 'the Secretariat' means the Secretariat of the COT.

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 advisory committees who advise the Chairman of the Food Standards Agency and the Chief Medical Officer 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 advisory committees such as the COT/COC/COM more open and to increase accountability. Proposals were published in "Quangos-Opening the Doors" (Cabinet Office, July 1998). As a result of these proposals, in 1999, the Committees adopted new principles of working in order to increase openness. relating to among other things, the handling of confidential data, the publication of meeting agendas, finalised minutes and agreed conclusions and statements. (These principles have been reproduced as an Annex to the Committees' Annual Reports since 1999).

3. In the following years, the Committees considered a number of options for greater openness of committee business. Relevant guidelines are contained in the Office of Science and Technology Code of Practice for Scientific Advisory Committees, the Government response to the report of the BSE enquiry (the Phillips Enquiry) and the Food Standards Agency Review of Scientific Committees which included a number of recommendation on openness.

4. As a result of these discussions the principles have been reviewed and revised to reflect the new procedures on openness as agreed by the Committees. The table below contains a summary of the agreed proposals for committee openness:

Issue	Comment
Meetings	All meetings held in open session subject to arrangements for handling confidential or sensitive information.
Agenda	Made publicly available via internet site prior to meeting.
Papers	Made publicly available via internet site prior to meeting. Papers may be edited to remove confidential information.
Minutes	Anonymised minutes to be made publicly available following the committee meeting. Subject to the temporary withholding of items subject to regulatory decisions or confidentiality. Minutes are available in draft prior to agreement by the Committee.
Conclusions/statements	Made publicly available as working papers prior to meetings and as finalised documents via internet site. Subject to temporary withholding of information that may be subject to regulatory decision or confidentiality.
Annual Report	The COT/COC/COM publish an Annual Report, which is available on request and can be viewed on the Committees' respective websites.
Reports on specific issues	Produced by the Committees and Working Groups. Available on request and can be viewed on the Committees' respective websites.

5. Corporate information on the work of the Committees, their members (and their declared interests) and information on the Committees activities can also be found on the relevant on website.

Procedures for handling confidential information

Background

6. COT/COM/COC quite often consider information that has been supplied in confidence. For the most part this comprises information that is commercially sensitive. For example, this could include product formulations/specifications, methods of manufacture, and reports of toxicological investigations and company evaluations and safety assessments.

7. Normal procedure in the past has been to publish a summary of the Committee's advice in the Annual Report and 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 COT/COM/COC have adopted where possible a more open style of business and detailed working papers are published on the Internet before they have been finalised as final statements.

8. 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 of a confidential character 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). The following procedure will be adopted which allows confidential information to be identified, assessed and appropriate conclusions/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

9. Upon referral to COT/COM/COC the Secretariat will liaise with the relevant company supplying the product in the UK to:

i) Clearly state the policy of Committee openness (as summarised above).

ii) To identify and request the information needed by the COT/COM/COC (eg test reports, publications etc).

Confidential data

iii) The company will be asked to clearly identify any confidential data and the reason for confidentiality.

Handling confidential data

iv) The procedures by which the COT/COM/COC will handle confidential data and the public availability of papers, minutes, conclusions and statements where reference is made to such data will be discussed with the company prior to submission of papers to the Committee(s). 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.

v) The following is a suggested list of information which might be disclosed in COT/COM/COC documents (papers, minutes, conclusions 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 for holding Committee meetings in open session

10. The COT has been holding its meetings in open session since April 2003. The COC and COM followed in 2004. It has been recognised that holding meetings in open session needs to be managed to ensure that there is no adverse impact on the ability of the Committee to function effectively and to provide adequate security for members and officials.

11. It was therefore agreed that a protocol should be prepared that would address the advertising of meetings, application process, any restrictions on attendees, limitations on attendance and specify how attendees would be selected. The protocol would also set out the circumstances where discussion would not be possible in public and arrangements for discussions to be held in closed session.

12. The procedures adopted by the Committees for holding meetings in open session are detailed on their respective websites. The respective information for COT/COC/COM can be viewed at:

    http://www.food.gov.uk/science/ouradvisors/toxicity/cotmeets/arrangementcotopenmeetings/

    and

    http://www.advisorybodies.doh.gov.uk/foi/open.htm

ANNEX 4

GLOSSARY OF TERMS

a priori: The formulation of a hypothesis before undertaking an investigation or experiment.

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

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

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

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

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

Adverse effect: Change in morphology, physiology, biochemistry, growth, development or lifespan of an organism 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.

Ah receptor: The Ah (Aromatic hydrocarbon) receptor protein regulates some specific gene expressions associated with toxicity. The identity of the natural endogenous chemicals which bind to 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.

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: *In vitro* (qv) assay for bacterial gene mutations (qv) using strains of *Salmonella typhimurium* developed by Ames and his colleagues.

Aneugenic: Inducing aneuploidy (qv).

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 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 can occur normally during development, but is often triggered by toxic stimuli.

Base pair (bp): Two complementary nucleotide (qv) bases joined together by chemical bonds.

Bias: In the context of epidemiological studies, 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 genomics research, because of the large amount of complex data this research generates.

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

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

Bradford Hill Criteria: Sir Austin Bradford-Hill established 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? Evidence from experimental animals may assist in some cases. Evidence that removal of the exposure leads to a decrease in risk may be relevant.

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

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

C. elegans: *Caenorhabditis elegans*, a nematode or roundworm, the first animal to have its genome completely sequenced and all the genes fully characterised.

Cancer: Synonym for a malignant neoplasm – that is, a tumour (qv) 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.

Carcinogenesis: The origin, causation and development of tumours (qv). The term applies to benign as well as malignant neoplasms and not just to carcinomas (qv).

Carcinogenicity bioassay: Tests carried out in laboratory animals, usually rats and mice, to determine whether a substance is carcinogenic. The test material is given throughout life to groups of animals at different dose levels.

Carcinogens: The causal agents which induce tumours. They include external factors (chemicals, physical agents, viruses) and internal factors such as hormones. Chemical carcinogens are structurally diverse and include naturally-occurring substances as well as synthetic compounds. An important distinction can be drawn between *genotoxic* (qv) carcinogens which have been shown to react with and mutate DNA, and *non-genotoxic* 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 (qv). 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, retrospective 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 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.

Chromosomal aberrations: Collective term of particular types of chromosome damage induced after exposure to exogenous chemical or physical agents which damage the DNA. (see clastogen).

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 (qv).

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.

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 or 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 unique amino acid.

Cohort: A defined population that continues to exist through time.

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.

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) An extraneous variable that satisfies BOTH of 2 conditions: (1) it is a risk factor for the disease under study (2) it is associated with the study exposure but is not a consequence of exposure. For example cigarette smoking is a confounding variable with respect to an association between alcohol consumption and heart disease. Failure to adjust for a confounding variable results in distortion of the apparent magnitude of the effect of the exposure under study. (In the example, smoking is a risk factor for heart disease and is associated with alcohol consumption but is not a consequence of alcohol consumption.)

Congeners: Related compounds varying in chemical structure but with similar biological properties.

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.

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

Deletion: A chromosomal aberration in which a proportion of the chromosome is lost. Deletions may range in size from a single nucleotide (qv) to an entire chromosome. Such deletions may be harmless, may result in disease, or may in rare cases be beneficial.

DNA (Deoxyribonucleic Acid): The carrier of genetic information for all living organisms except the group of RNA viruses. Each of the 46 chromosomes in normal human cells consists of 2 strands of DNA containing up to 100,000 nucleotides, specific sequences of which make up genes (qv). DNA itself is composed of two interwound chains of linked nucleotides (qv).

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 (and only 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 genes: Genes which code for proteins that correct damage in DNA sequences. When these genes are altered, mutations may be able to accumulate in the genome, ultimately resulting in disease.

Dominant lethal assay: See dominant lethal mutation.

Dominant lethal mutation: A dominant mutation that causes death of an early embryo.

Dose: Total amount of a substance administered to, taken or absorbed by an organism

Endocrine modulator (synonym – endocrine disruptor): A chemical, which can be naturally occurring or man-made, that causes adverse health effects in an organism, as a result of changes in hormonal function.

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

Epidemiology: Study of the distribution and the aetiology of disease in humans.

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.

Erythrocyte: Red blood cell.

Estrogen: Sex hormone or other substance capable of developing and maintaining female characteristics of the body.

Exogenous: Arising outside the body.

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

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

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

Forestomach: (See glandular stomach).

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 (qv).

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 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 difference in DNA sequence among individuals, groups, or populations (e.g. a genetic polymorphism might give rise to blue eyes versus brown eyes, or straight hair versus curly hair).

Genetic polymorphisms may be the result of chance processes, or may have been induced by external agents (such as viruses or radiation). Changes in DNA sequence which have been confirmed to be caused by external agents are generally 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.

Genomics: The study of genes and their function.

Genotoxic: The ability of a substance to cause DNA damage, either directly or after metabolic activation (see also carcinogens).

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

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: Time in which the concentration of a substance will be reduced by half, 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.

Hepatic: Pertaining to the liver

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

Hepatotoxic: Causing toxicity to the liver.

Human Genome Project: An international research effort aimed at discovering the full sequence of bases in the human genome, led in the UK by the Wellcome Trust and Medical Research Council.

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

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

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 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 effects in biological material outside the living animal (literally "in glass")

In-vivo: A Latin term used to describe effects in living animals (literally "in life").

Incidence: Number of new cases of illness occurring during a given period in a specific population.

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 cytochrome 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. The ß-isomer of alitame is formed when the compound degrades and the atoms within the molecule are rearranged.

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, are absent or inactive.

LD50: The dose of a toxic compound 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.

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 leukaemias which develop from lymphoid cells and the myeloid leukaemias which are derived from myeloid cells (producing red blood cells, mainly in bone marrow).

Ligand: A molecule which binds to 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.

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').

Malignancy: See 'tumour'.

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 cytochrome P450), epoxidation or conjugation. Metabolism may result in activation, inactivation, accumulation or excretion of the compound.

Metabolite: Product formed by metabolism of a compound.

Metabonomics: Techniques available to identify the presence and concentrations of metabolites in a biological sample.

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; it is non-random.

Micronuclei: Isolated or broken chromosome fragments which are not expelled when the nucleus is lost during cell division, 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 can be used to evaluate the aneugenic (qv) potential of chemicals.

Micronucleus test: See Micronuclei.

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

Mitosis: The type of cell division which occurs in somatic cells when they proliferate. Each daughter cell has the same complement of chromosomes as the parent cell.

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 gene 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.

Mouse spot test: An *in-vivo* test for mutation, in which pregnant mice are dosed with the test compound and mutations are detected by changes (spots) in coat colour of the offspring. Mutations in the melanocytes (skin pigment cells) of the developing fetus are measured.

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

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

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.

Mycotoxin: Toxic compound produced by a fungus.

Neoplasm: See 'tumour'.

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

Nephrotoxicity: Toxicity to the kidney.

Neurobehavioural: Of behaviour determined by the nervous system.

Neurotoxicity: Toxicity to the nervous system.

No observed adverse effect level (NOAEL): The highest administered dose at which no adverse (qv) effect has been observed.

Non-genotoxic: See 'carcinogens'.

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.

Nucleotide: the "building block" of nucleic acids, such as the DNA molecule. A nucleotide consists of one of four bases – adenine, guanine, cytosine, or thymine – attached to a phosphate-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: inactive form of a gene.

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.

Oestrogen: (See estrogen)

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

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

Organochlorine: A group of chemical compounds, containing multiple chlorine atoms, that are usually of concern as environmental pollutants. Some organochlorines have been manufactured as pesticides or coolants and others arise as contaminants of manufacturing processes or incineration.

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 to design 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.

Phytoestrogen: Any plant substance or metabolite that induces biological responses in vertebrates and can mimic or modulate the actions of endogenous estrogens usually by binding to estrogen receptors.

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 manipulated in the laboratory to deliver specific genetic sequences into a cell.

Plasticiser: A substance which increases the flexibility of certain plastics.

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: A sensitive experimental method designed to measure low levels of DNA adducts induced by chemical treatment.

Prevalence: The number of cases 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.

Proteomics: The determination of the function of all of the proteins encoded by the organism's entire genome.

Proto-oncogene: One of a group of normal genes which 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.

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 more than one source.

Reference nutrient intake (RNI): An amount of the nutrient that is enough, or more than enough, for most (usually at least 97%) of 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 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

Renal: Relating to the kidney.

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

RNA (ribonucleic acid): a molecule similar to DNA (qv), which helps in the process of decoding the genetic information carried by DNA.

Safety: Practical certainty that injury will not result from a hazard under defined conditions.

SCF: The European Commission's Scientific Committee on Food (formerly the Scientific Committee for Food).

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. By convention, SNPs occur in at least 1% of the population.

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

Suppressor gene: A gene which helps to reverse the effects of damage to an individual's genetic material, typically 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 review that has been prepared using a documented systematic approach to minimising biases and random errors.

TDI: See 'Tolerable Daily Intake'.

Teratogen: A substance which, when administered to a pregnant woman or animal, can cause congenital malformations (structural defects) in the baby or offspring.

Threshold: Dose or exposure concentration below which an effect is not expected.

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.

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.

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

Toxicogenomics: A new scientific subdiscipline that combines the emerging technologies of genomics and bioinformatics to identify and characterise mechanisms of action of known and suspected toxicants. Currently, the premier toxicogenomic tools are the DNA microarray and the DNA chip, which are used for the simultaneous monitoring of expression levels of hundreds to thousands of genes.

Toxicokinetics: The description of the fate of chemicals in the body, including a mathematical account of their absorption, distribution, metabolism and excretion. (see pharmacokinetics)

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

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

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 the genetic material carried by an individual cell is altered by incorporation of exogenous DNA into its genome.

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 (eg cancer). For example strains of mice have been bred which carry an inactivated copy of the p53 tumour suppressor gene (qv) -, 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. Some common examples of nomenclature are as follows:

- Tumours arising from epithelia (qv): benign – adenomas, papillomas; malignant – adenocarcinomas, papillary carcinomas.

- Tumours arising from connective tissues such as fat, cartilage or bone: benign – lipomas, chondromas, osteomas; malignant – fibrosarcomas, liposarcomas, chondrosarcomas, osteosarcomas.

- Tumours arising from lymphoid tissues are malignant and are called lymphomas (qv); they are often multifocal. Malignant proliferations of bone marrow cells are called leukaemias.

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 (qv).

Tumour promotion: An increasingly confusing term, 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' (qv) and 'promoter' are synonymous.

Uncertainty factor: Value used in extrapolation from experimental animals to man (assuming that man may be more sensitive) or from selected individuals to the general population: for example, a value applied to the NOAEL to derive 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.

Xenobiotic: A chemical foreign to the biologic system.

Xenoestrogen: A 'foreign' compound with estrogenic activity (see estrogen).

ANNEX 5

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

Subject	Year	Page
Accelerator Mass Spectrometry – An aid to carcinogen risk assessment	2000	103
Acceptable Daily Intakes	1992	15
Acetyl tributyl citrate (ATBC)	1994	24
	1997	63
Acrylamide	1992	54
in fried and baked food	2002	7
Ad hoc expert group on vitamins and minerals (EVM)	1997	6
Additives	1991	22
and behaviour	2002	11
Hyperactivity and,	2000	27
Adverse Reactions to Food and Food Ingredients	2000	10
Adverse trends in the development of the male reproductive system	2003	21
Advisory Committee on Novel Foods and Processes (ACNFP)	1991	21
Agaritine	1992	36, 54
	1996	34
Air quality guidelines: consideration of genotoxins	1992	58
Alcohol and alcoholic beverages		
Mutagenicity	1995	28
Carcinogenicity	1995	46
Evaluation of sensible drinking message	1995	58
and breast cancer	2002	133
	2003	196
Alitame	1992	36
	1999	7
	2000	10
	2001	7
Alternaria toxins	1991	50
Amalgam, Dental	1997	13
Amano 90	2000	15
	2001	12

Amnesic Shellfish Poisoning	2001	7
Aneuploidy inducing chemicals	1993	36
Thresholds for,	1995	37
	1996	42
Aneuploidy, ECETOC Monograph on	1997	78
Aniline	1992	40
Antimony trioxide	1997	62
Arsenic		
in drinking water	1994	32
Total and inorganic in food: results of the 1999 Total Diet Study	2002	20
	2003	7
Ascorbyl palmitate	1991	15
Aspartame	1992	12
	1996	12
	1996	56
Astaxanthin in farmed fish	1991	15
Avoparcin	1992	56
Azodicarbonamide	1994	6
Benz(a)pyrene in drinking water	1994	35
Benzene	1991	45
induced carcinogenicity	1997	114
Consideration of evidence for a threshold	1998	32
Betal quid, pan masala and areca nut chewing	1994	36
Biobank project	2003	194
Bisphenol A	1997	6
in canned food	2001	8
Bisphenol A diglycidyl ether (BADGE)	1996	35
	1997	8
Boron in drinking water and food	1995	6
Bracken	1993	33
Breast implants		
Polyurethan coated	1994	36
PIP hydrogel	2000	11
	2002	16

Breast milk, PCBs in	2001	19
Bromate	1993	50
Brominated flame retardants in fish from the Skerne-Tees river system	2003	8
Bromine	2000	17
Bromodichloromethane	1994	22
Bromoform	1994	23, 33
1,3-Butadiene	1992	41, 58
	1998	33
Butylated hydroxyanisole	1992	16
Caffeine, Reproductive effects of	2001	22
Cancer incidence near municipal solid waste incinerators in Great Britain	2000	104
Canned foods, Bisphenol A in	2001	8
Captan	1993	35, 50
Carbaryl	1995	30, 64
Carcinogenic air pollutants, Quantification of risk	2002	128
Carcinogenicity of 2,3,7,8-tetrachlorodibenzo(p)dioxin (TCDD)	2001	136
Carcinogenicity studies in rats, Minimum duration of	2001	142
	2002	130
Carrageenan	1991	14
	1993	12
	1997	11
Cell lines expressing human xenobiotic metabolising enzymes in mutagenicity testing	1995	38
Cell transformation assays	1994	26
Childhood cancer		
and paternal smoking	1997	68
Hazard proximities in Great Britain (from 1953 to 1980)	1997	110
Chlorinated drinking water	1991	32
	1992	55
Chlorinated drinking water and reproductive outcomes	1998	8
	2001	23
Chlorine	1993	33
Chlorine and chlorine dioxide as flour treatment agents	1996	7, 36
Chlorobenzenes	1997	12

2-Chlorobenzylidene malonitrile (CS)	1998	34
and CS Spray	1999	7
	1999	51
Chlorodibromomethane	1994	23
Chloroform	1994	22, 32
Chromium picolinate	2003	141
Chrysotile-substitutes, Carcinogenic risks	1998	50
Chymosin	1991	16
	2000	16
	2002	10
Classification of chemicals on the basis of mutagenic properties	1992	43
COC guidelines		
Review of	2001	142
Revision of	2002	134
COC template	2002	129
COM template	2002	87
Comet Assay	1995	39
	1998	35
Comfrey	1992	19
	1994	7
Committee procedures		
Reviews of risk procedures used by Government advisory committees dealing with food	2000 2001	22, 110 106
Code of Practice for scientific advisory committees: 2nd Round of Consultation	2000 2001 2002	12, 106 9, 106 129
Review of committee procedures in the light of the Phillips enquiry	2001 2002	14, 139 86
Horizon scanning	2003	16, 137, 193
Proposal to hold meetings in open session	2002	20
	2003	17, 194
Contaminants in soil	2001	10
Coumarin	1998	29, 41
Cyclamate	1995	6

Dental amalgam	1997	13
Deoxenivalenol (DON)	1991	50
Dibenzo(a,l)pyrene	2001	17
In air pollution	2003	189
1,3-Dichloropropan-2-ol	2003	128, 190
and 2,3-dichloropropan-1-ol	2001	99
	2001	137
Dichlorvos	2001	99
	2002	83
Diesel exhaust	1991	47
Update on carcinogenicity from 1990	1996	62
Dietary restriction and carcinogenesis in rats	1991	51
Di-2-ethylhexyl adipate	1991	17, 28
Diethyl-m-toluamide (DEET)	2002	8
	2003	128
Diethylstilboestrol	1993	38
Di-isopropylnaphthalenes in food packaging made from recycled paper and board:	1998	9
	2000	14
	2002	9
Conclusion on mutagenicity studies using the mouse lymphoma assay (MLA)	2000	62
Dimethoate	1992	39
Dimethyldicarbonate	1992	24, 37
Dimetridazole	2002	84
2,4-Dinitrophenol	2003	14
Dioxins		
2,3,7,8-Tetrachlorodibenzo-*p*-dioxin	1993	49
	1995	15, 64
	1998	19, 45
	1999	49
Carcinogenicity of	2001	136
Dioxins and dioxin-like PCBs		
In marine fish and fish products	1999	31
Consideration of the TDI	2000	26
	2001	10
Dietary exposure	2000	13

In free range eggs	2000	14
In fish oil – urgent advice	2002	9
Dithiocarbamates in latex products	1994	18
DNA adduct inducing chemicals, Joint Meeting of COM and COC on the significance of low level exposures	1996	48
DNA gyrase inhibitors	1992	42, 58
Dominant Lethal Assay	1994	26
Drinking Water		
Arsenic in,	1999	59
Benz(a)pyrene in,	1994	32
Boron in,	1994	35
Chlorinated,	1995	6
	1991	32
Reproductive outcomes of,	1992	55
	1998	8
Fluoranthene in,	1994	34, 70
	1995	33
Trihalomethanes in,	1994	22, 32, 69
	1995	35
Early identification of non-genotoxic carcinogens	2000	106
ECETOC Monograph on Aneuploidy	1997	78
ECETOC workshop on use of T25 in chemical carcinogen evaluation	2001	141
Emulsifier YN (Ammonium Phosphatides)	1994	7
Enrofloxacin	1992	56
	1993	50
Environmental Tobacco Smoke (ETS) and lung cancer	1997	88
	2003	191
Enzymes – Amano 90	2000	15
	2001	12
– Chymosin	1999	16
	2000	16
	2002	10

	2003	8
– Immobilised lipase from Rhizopus niveus	1994	9
	1998	13
– Lipase D	2000	16
	2001	12
– Newlase	2000	17
analytical method to detect rhizoxin	2000	11
– Xylanase preparation from Aspergillus niger	2001	13
EPA risk assessment guideline: supplemental data for assessing susceptibility from early life exposure to carcinogens	2003	195
Epoxidised soya bean oil	1994	8
	1999	16
Erythritol	2003	9
Erythrosine	1991	29
Ethanol, acetaldehyde and alcoholic beverages	2000	62
Ethanol intake, effects on pregnancy, reproduction and infant development	1995	8
Evaluation of sensible drinking message	1995	58
Evidence for an increase in mortality rates from intrahepatic cholangiocarcinoma in England and Wales 1968-1996	2000	107
Flunixin, flunixin-meglumine, meglumine	2002	89
Florfenicol	1993	12
Fluoranthene in drinking water	1994	34, 70
	1995	33
Fluoride	1995	35
Fluorine, bromine and iodine	2000	17
Fluorine (fluoride): 1997 Total Diet Study	2001	23
	2002	19
Flunixin, meglumine and flunixin-meglumine	2003	129
Food additives		
Hyperactivity and,	2000	27
and behaviour	2002	11
Food and food ingredients		
adverse reactions to,	2000	10
Food chemical exposure assessment	2002	12
Food Intolerance	1997	17
	1999	16

Food Standards Agency funded research and surveys	2000	18
Food Standards Agency review of scientific committees	2001	24
French Maritime Pine bark extract	1998	10
	1999	16
	2000	19
Fumonisins	1993	48
in maize meal	2003	15
Furocoumarines in the diet	1994	25, 39
Gallates	1992	37
Gellan Gum	1993	13
Genetic susceptibility	2000	110
to cancer	1998	35
Genotype and environment interaction on susceptibility to cancer	2001	142
	2002	132
Guar gum	1991	14
Health effects in populations living close to landfill sites	2000	19
	2001	15
Hemicellulase		
Enzyme in bread-making	1999	19
from *Aspergillus niger*	1994	8
Preparations for use in breadmaking	1995	9
Hexachlorobutadiene contamination at Weston Quarries	2000	20
	2003	10
Historical control data in mutagenicity studies	1996	47
Hormesis	2003	196
Hydrocarbon propellants	1994	9
Hydroquinone and phenol	1994	20
	1995	34
	2000	60
Hyperactive children's support group	1996	9
Hyperactivity and food additives	2000	27
Additional analyses on research project results	2001	16
Hypospadias and maternal nutrition	1999	19
ICH guidelines:		
Genotoxicity: A standard battery for genotoxicity testing of pharmaceuticals (S2B) and consideration of the mouse		

lymphoma assay	1997	75
	1998	50
Consideration of neonatal rodent bioassay	1997	112
Testing for carcinogenicity of pharmaceuticals		
IGHRC paper on uncertainty factors	2001	17
	2002	129
ILSI/HESI research programme on alternative cancer models: results of Syrian hamster embryo cell transformation assay	2002	87
Imidocarb	1992	38, 57
Impurities in the pesticide 1-methylcyclopropene	2003	191
In vitro mammalian cell mutation assays	2003	137
In vitro micronucleus test	1994	26
	1996	47
(IWGT meeting)	2002	88
In vivo gene mutation assays using transgenic animal models	1996	45
In-vivo mutagenicity at high doses, Significance of	2002	89
Increase in mortality rates from intrahepatic cholangiocarcinoma in England and Wales 1968-1998	2001	138
Infant food, metals and other elements in	1999	27
International workshop on the categorisation of mutagens	2001	108
Intrahepatic cholangiocarcinoma	2003	192
Iodine	1992	25
	2000	17
in cows' milk	1997	17
	1999	20
	2002	20
	2003	10
ISO Water quality standard: Determination of the genotoxicity of water and waste water using the *umu* test	1997	69
Joint COC/COM symposium on genetic susceptibility to cancer	1998	35
Joint COM/COC on the significance of low level exposures to DNA adduct inducing chemicals	1996	48
Joint meeting of COT/COC/COM on use of genomics and proteomics in toxicology	2001	24, 109 143
	2002	14
Kava kava – urgent advice	2002	14
Lactic acid producing cultures	1991	14

Landfill sites		
and congenital anomalies	1998	13
Health effects of populations living close to,	2000	19
	2001	15
Leukaemia		
Advice on three paediatric cases in Camelford, North Cornwall	1996	57
and drinking water in South West England	1997	105
Lindane	1995	33
Long chain polyunsaturated fatty acid for use in infant formula	1997	19
Longevity of carcinogenicity studies: consideration of a database prepared by the Pesticides Safety Directorate	2000	109
Lung cancer and Environmental Tobacco Smoke (ETS)	1997	88
Lupins	1995	10
Malachite Green	1993	14
	1995	12
	1999	47
and Leucomalachite Green in Farmed fish	1999	23
Malathion	2002	84, 126
	2003	132
Male reproductive system, Adverse trends	2003	21
Man made mineral fibres	1994	38
	1996	65
Refractory ceramic fibres	1995	68
Mathematical modelling – Applications in toxicology	1999	27
Mechanism of carcinogenicity in humans	1995	57
Mercury in fish and shellfish	2002	17
	2003	12
Metals and other elements		
in infant food	1999	27
	2003	12
in the 2000 Total Diet Study	2003	12
Methylcyclopentadienyl manganese tricarbonyl	1995	12
	1999	28
1-Methylcyclopropene, Impurities in	2003	191
Microbial enzyme	1991	17
Mineral hydrocarbons	1993	15

Moniliformin in maize and maize products	1998	14
3-Monochloro-propane 1,2-diol (3-MCPD)	1999	48
	2000	61, 102
Mouse lymphoma assay, Presentation by Dr Jane Cole	1997	77
Mouse carcinogenicity bioassay	1997	70, 117
Mouse Spot Test	1992	44
Multielement survey		
in various items in the diet	1998	15
of wild fungi and blackberries	1999	28
Multiple Chemical Sensitivity	1999	30
	2000	21
Municipal solid waste incinerators in Great Britain, Cancer incidence near	2000	104
Mycotoxins	1991	31, 48
Natural toxins	1992	44, 59
Newlase	2000	17
anayltical method to detect rhizoxin	2002	11
Nicotine from nicotine patches, Possible nitration of	2002	86
Nickel leaching from kettle elements into boiled water	2003	13
Nicotine from nicotine patches, Possible nitrosation of	2002	86
Nitrate metabolism in man	1998	16
Nitrosamines: potency ranking in tobacco smoke	1995	71
Nitrous oxide	1995	14
N-Nitroso compounds	1992	59
Non-genotoxic carcinogens, Early identification of	2000	106
Non-Hodgkin's lymphoma	1993	51
Novel fat	1992	18
Novel oils for use in infant formulae	1995	14
Ochratoxin A	1997	20
	1998	17
Ohmic heating	1991	19
Olestra	1993	35
Olfactory neuroblastomas: possible association in dentists and dental nurses	2003	197
Omethoate	1992	38
Openness (see also Committee procedures)	1999	30
	2002	20
	2003	194

Organochlorines and breast cancer	1995	96
	1999	62
	2003	196
Organophosphates	1999	30
Organophosphorus esters	1998	17
Oxibendazole	1995	36
	1996	41
Ozone	1999	50
(review of animal carcinogenicity data)	1999	71
p-53 tumour suppressor gene	1993	39
PAH concentrations in food: interim pragmatic guideline limits for use in emergencies	2001	18
PAHs in shellfish	2001	18
Passive smoking	1993	52
Paternal exposure to chemicals, possibility of paternal exposure inducing cancer in offspring	1991	36
Patulin	1991	49
PAVA (Nonivamide): Use as an incapacitant spray	2001	25
	2002	18, 85
PCBs in breast milk	2001	19
Peanut allergy	1996	10
	1997	23
	1998	18
Pediatric leukaemia cases in Camelford, North Cornwall	1996	57
Perchloroethylene (see tetrachloroethylene)		
Peroxisome proliferators	1992	45
Phenol	2003	132
tolerable daily intake (oral)	2002	15
2-Phenylphenol	1992	39
	1997	64
	2003	133
Phosphine	2001	103
and metal phosphides	1997	65
Phosphorus, parathyroid hormone and bone health	2003	21
Phthalates in infant formulae	1996	10

Phytoestrogens		
in soya-based infant formulae	1998	18
	1999	35
and health, report	2002	20
	2003	17
Platinum-based fuel catalyst for diesel fuel	1996	12
Polychlorinated biphenyls (PCBs)	1994	21, 37
	1997	23
Effects on play behaviour	2002	17
PCDDs, PCDFs and PCBs in marine fish and fish products	1999	31
Polycyclic aromatic hydrocarbons	1994	19, 34
	1995	32
	1996	67
Advice on dibenzo(a,l)pyrene	2002	127
In air pollution	2003	135, 192
In the 2000 Total Diet Study	2002	16
Pragmatic guideline limits for use in emergencies	2000	27
Polyurethane	1991	46
Polyurethane coated breast implants	1994	36
Potassium and sodium ferrocyanides	1994	10
Potatoes genetically modified to produce *Galanthus nivalis* Lectin	1999	34
Presentation on initial preliminary results of meta-analysis of alcohol and breast cancer	2001	142
Prioritisation of carcinogenic chemicals	1994	41
Propoxur	1991	47
Propylene carbonate	1992	26
Prostate cancer	2002	134
	2003	197
Ranking of carcinogens: comparison of method using some air pollutants	2001	40
Quantification of risk associated with carcinogenic air pollutants	2002	128
RCEP study of long term effects of chemicals	2001	20
Refractory ceramic fibres	1995	68
Report on phytoestrogens and health	2002	20
Reproductive effects of caffeine	2001	22

Research		
and surveys, Food Standards Agency funded	2000	18
priorities and strategy, Department of Health	1996	9, 44, 75
Risk assessment of carcinogens, Revised guidance	2003	197
Risk assessment of in vivo mutagens (and genotoxic mutagens)	2001	107
Risk Assessment of Mixtures of Pesticides (and similar substances)	2000	25
	2002	19
Risk assessment strategies		
Guidelines for exposure assessment practice for human health	2003	19
Physiologically-based pharmacokinetic modelling	2003	19
Uncertainty factors: their use in human health risk assessment by UK government	2003	20
Risk procedures used by the Government's Advisory Committees dealing with food safety	2000	22, 110
Risks associated with exposure to low levels of air pollution	2003	193
Salmonella assay, Use of	1991	35
SCF Guidelines on the Assessment of Novel Foods	1996	13
Sellafield	1991	35
Sensible drinking message, Evaluation of	1995	58
SHE cell transformation assay	1996	46
Shellfish		
poisoning, amnesic	2001	7
PAHs in,	2001	18
Short and long chain triacyl glycerol molecules (Salatrims)	1997	39
	1999	36
Short-term carcinogenicity tests		
ILSI/HESI research programme on alternative cancer models	1997	114
using transgenic animals	1999	73
	2002	131
Significance of *in-vivo* mutagenicity at high doses	2003	139
Single cell protein	1996	14
Soil, Contaminants in	2001	10
Soluble fibre derived from guar gum	1996	15
	1997	46

Sterigmatocystin	1998	19
Strategy for investigating germ cell mutagens	2003	138
Sucralose	1993	34
	1994	24
	2000	23
Sudan I found in chilli powder	2003	16
Sulphur dioxide	1991	19, 30
Surveys: guidelines for project officers	2001	22
Terephthalic acid	2001	105
	2003	14
and isophthalic acids in food	2000	24
T_{25} to estimate carcinogenic potency	1995	72
Test strategies and evaluations	1993	39
	1994	25
	1995	37
	1996	44, 75
	1997	75, 112
	1998	34, 50
	1999	51, 72
	2000	63
	2001	107
	2002	87, 129
	2003	137-139
		194-196
2,3,7,8-Tetrachlorodibenzo-*p*-dioxin (TCDD)	1993	49
	1995	15, 64
	1998	45
	1999	49
	2001	136
Tetrachloroethylene	1996	37, 68
	1997	47
Thalidomide	1997	62
Thiabendazole	1991	20
	1995	20
	1996	40
	1997	50

Thiamphenicol	1992	26
Threshold for benzene induced carcinogenicity, Consideration of evidence for	1998	32
Thresholds for aneuploidy inducing chemicals	1995	37
	1996	42
Tobacco induced lung carcinogenesis: the importance of p53 mutations	2001	107
Toltrazuril	1992	57
Toxic equivalency factors for dioxin analogues	1998	19
Transgenic animal models, Use in short terms tests for carcinogenicity	2001	142
Transgenic mouse models	1997	114
Trichloroethylene	1996	39, 71
Trihalomethanes in drinking water	1994	22, 32, 69
	1995	35
Tryptophan and eosinophilia-myalgia syndrome	2003	21
Type I caramel	1991	30
Unlicensed traditional remedies	1994	10
Uncertainty factors, IGHRC paper on	2001	17
	2002	129
Validation of short-term carcinogenicity tests using transgenic animals, Presentation on	1999	73
Vitamin A	1993	22
Vitamin B6	1997	51
	1998	20
Vitamins and minerals, *Ad hoc* expert group (EVM)	1997	6
Wild fungi and blackberries, Multielement survey of	1999	28
Xylanase preparation from Aspergillus niger	2001	13
Zearalenone	1998	29

ANNEX 6

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.

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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.

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

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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).

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