Instructions to Authors

Instructions to Authors for the Preparation of Drafts for IARC Monographs

This document should be read in conjunction with the Preamble to the IARC Monographs, which describes the scientific principles and procedures used in developing a Monograph, the types of evidence considered and the scientific criteria that guide the evaluations.

These instructions were prepared by staff of the IARC Monographs programme and are provided to authors preparing the first drafts of an IARC Monograph (members of the Working Group). Authors are also provided with details and instructions specific to each Monograph topic as appropriate, and are advised to consult a recent copy of the IARC Monographs. The outline for each Monograph is provided to each author and defines the detailed structure of the Monograph and individual writing assignments.

While individual authors (Working Group Members) prepare the preliminary drafts, the final Monograph and resulting evaluation is a consensus document that is reviewed and validated by the entire Working Group.

Table of contents

Section 1. Exposure data................................................................. 2
Section 2. Cancer in humans.......................................................... 5
Section 3. Cancer in animals........................................................... 8
Section 4. Mechanistic and other data ........................................... 11
Section 5. Summaries................................................................. 16
Section 6. Evaluation ................................................................. 18
Section 1. Exposure data

Section 1 identifies the agent, describes its measurement, main uses, and production volume and summarizes the prevalence and level of human exposure worldwide. Methods of measurement and regulations are noted where relevant. Information is obtained from research studies, government reports and other publicly available sources, with all statements of scientific fact substantiated by a fully referenced article, report or web site. *The data should present a representative overview, but all the available data are not comprehensively reviewed.*

1.1 Identification of the agent (half a page for a single chemical; 2–3 pages for mixtures, occupations or industries)

The agent being evaluated is unambiguously identified. For chemicals, provide the Chemical Abstracts Service Registry Number, the latest primary name and the IUPAC systemic name and other names in common usage. Briefly describe physical and chemical properties relevant to occurrence, identification and biological activity and occurrence (e.g. liquid, solid or gaseous state; volatility, etc. for chemicals; composition, crystal structure and morphology for minerals; energy transfer for radiation, etc.). For a mixture, describe the main components, their sources and their relative proportions. Note impurities, contamination, bioaccumulation or transformations that may have an impact on the carcinogenicity evaluation (e.g. dioxin contamination of 2,4,5-T, or weathering of polychlorinated biphenyls in the environment). For an occupation or industry, describe the nature of the work and the agents involved with a focus on exposure to potential carcinogens. If the material tested in animals or in-vitro systems is different from that to which humans are likely to be exposed, note the relevant differences.

1.2 Production & use (1–2 pages; *may be modified or omitted if covered in 1.1.*)

1.2.1 Production

When relevant, indicate production quantities and countries where the agent is produced. Note if nationally or internationally classified as of high production volume. Indicate production processes with significant potential for occupational exposure. If significant exposures have occurred historically, note when production or exposure began and describe important changes in production processes, volume, or locations.

1.2.2 Uses

Describe the principal uses; if possible, indicate the amount or proportion attributed to each. Include minor or historical uses with significant exposure potential or that may aid interpretation of available epidemiological studies. A tabular summary may aid presentation if major and minor uses are numerous.
1.3 Measurement and analysis (up to 1 page + 1 optional table; may be omitted or modified according to relevance for the agent.)

An overview of analytical methods for research and regulatory purposes is provided as appropriate for the agent and specified in the Monograph outline. Describe in terms accessible to general readers the measurement methods for media that are important sources of human exposure. Address sampling issues (e.g. location, duration, personal versus environmental) pertinent to estimating population exposure. A tabular summary with standard references may optionally be used for multiple analytical methods or sample matrices. NB: Technical details of chemical analyses are no longer required.

1.4 Occurrence and exposure (up to 5 pages each of text and tables for 1.4.1, 5 pages and 1 table for 1.4.2)

Quantitative information regarding the prevalence and level of exposure is summarized for a concise overview of human exposure worldwide.

1.4.1. Exposures

Briefly describe the principal sources of population exposure (e.g. air, drinking-water, food, personal habits, or workplace). For those sources that are significant, representative exposure data from research studies, government reports and web sites, and other citable, publicly available sources are tabulated. It is important to search for and include data from low- and middle-income countries to the extent possible. Where data are lacking for important regions or countries, this is noted.

Organize tabulated data by source (environmental medium, occupation, use of the agent, etc.) and then by world region and country. Provide the year of sampling, mean or median, and range of exposure and other relevant parameters, such as the number of samples, sample duration, measurement method or type of site as appropriate (sample tables for environmental and occupational exposure are provided to the authors). The Monograph outline may provide a more specific or detailed organizational approach.

NB: Current exposures are of primary interest, but historical exposures may be as relevant for interpreting epidemiological studies and when agents are persistent or have long-term effects (cf. previous Monograph – if available). Data regarding environmental media, plants or wildlife that are not important sources of direct human exposure can be excluded. Similarly, data concerning remote, unpopulated sites (“background” exposures) may not be pertinent.

1.4.2 Exposure assessment and biological markers

When pertinent for the interpretation of studies of cancer in humans, describe and assess strengths and limitations of exposure measurement methods used in pertinent epidemiological studies. Such methods might include, for example, questionnaires, expert assessment, job-exposure matrices, exposure modelling, or biological markers. A table may be included to summarize methods and their strengths and limitations.
1.5 Regulations and guidelines (up to 1 page and 1 optional table; may be omitted if not applicable)

If regulations or guidelines have been established for the agent, the approach taken is described in a brief narrative. The applicable populations, the media concerned, and the basis on cancer risk, other health risks, or environmental considerations may be relevant. National and international bans on production, use, and trade are noted. If exposure limits have been established, these may optionally be tabulated if informative for the interpretation of existing or historical exposure levels (Section 1.4).
Section 2. Cancer in humans

Section 2 summarizes all of the pertinent epidemiological studies and identifies tumour sites for which there is sufficient, limited or inadequate evidence of carcinogenicity in humans.

Instructions at a glance

1. Section 2 is a systematic review of original research. Generally only analytical epidemiological studies (typically cohort and case–control studies) are included.

2. The literature search will be conducted using the HAWC Literature Search tool (a collaborative workspace for conducting risk assessments for human health; https://hawcproject.org/). Initial searches will be provided by the IARC secretariat and further refined by the Working Group.

3. Text is written in Word and submitted electronically via the IARC Monographs Online Publication System. Included studies are described individually, providing essential details about the study and the key results. Information given in the tables does not need to be repeated in the text.

4. Tables for Section 2 are constructed using the IARC Table Builder linked to the IARC Monographs Online Publication System.

5. Your assignment should be prepared before the meeting according to the deadline provided to you.

The Working Group conducts a systematic review of original research. Normally only analytical epidemiological studies (typically cohort and case–control studies) are included. When multiple publications are available for a single study, only the most recent or most informative publication is described in detail. Well-conducted quantitative meta-analyses may also be reviewed. Case reports and descriptive studies (correlation or ecological studies) should be reviewed only when they are the only information available or when they add materially to other evidence. Narrative reviews, commentaries and letters that do not provide relevant original data are not reviewed or cited.

Identifying the relevant information

Searching the literature

The Working Group identifies relevant peer-reviewed literature through comprehensive searches of relevant databases (e.g. PubMed). Additional studies may be identified by hand searching or from past Monographs, government documents, authoritative reviews or, expert knowledge of the literature. The HAWC Literature Search tool documents the search topics, terms, sources, and identified studies.
terms are drafted by the IARC secretariat and further refined by the Working Group. Further detail on these topics and associated search terms is available at https://hawcproject.org/.

Instructions on how to use the HAWC Literature Search tool can be found in this video.

**Screening and organizing the results**

The Working Group screens the retrieved literature for relevance. The IARC secretariat can assist with the initial screen focused on exclusion of studies that do not address the agent or cancer in humans. Other exclusion criteria (e.g. ecological studies and case reports) used by the Working Group are documented in HAWC (https://hawcproject.org/) using tags.

The Working Group considers all included studies. Using the literature tagging function in HAWC (https://hawcproject.org/), the Working Group organizes the studies by cancer site and/or study design, and by additional sub-topics according to the monograph outline. Studies may fall into more than one topic or category. Default tags for included and excluded studies are provided by the IARC secretariat and if necessary may be further refined by the Working Group.

Literature trees (in https://hawcproject.org/) document the number of studies identified, screened, excluded and categorized per category of evidence.

See page 8 of the Preamble to the IARC Monographs for further guidance about the types of studies included.

**Summarizing the evidence**

Once tagging is complete, the IARC secretariat reviews the results and may refine the outline and writing assignments, considering the extent of relevant evidence and needed expertise.

**Text**

Text is written in Word and uploaded electronically via the IARC Monographs Online Publication System. Included studies are described individually, providing essential details about the study (design, location, number of subjects) and the key results. The level of detail should be proportionate to the importance of the study and give only the minimum detail needed to evaluate the particular study in the context of all of the studies presented. Information given in the tables does not need to be repeated in the text unless it is especially important for interpreting the results. When there are multiple publications on a single study, previous papers may be briefly indicated in the text as Working Group comments or in the comments field of the table.

Less informative studies may be either described in a brief, summary style giving key characteristics and results of the studies or in the aggregate.
For each study or group of studies, it is important to include an expert assessment of the strengths and limitations as well as important points of interpretation, which should be indicated in square brackets [ ]. Study strengths and limitations are noted in the tables (see below).

Subsections describing a number of studies may have a brief introduction describing the included literature, the reasons for exclusions, if any, and highlighting important issues of interpretation.

**Tables**

Tables for Section 2 are constructed using the IARC Table Builder linked to the IARC Monographs Online Publication System. Please fill in all of the fields provided for descriptive information and results for each study.
**Section 3. Cancer in animals**

Section 3 summarizes all the pertinent carcinogenicity bioassays, classifies the evidence relevant to carcinogenicity in experimental animals into one of four defined categories (sufficient, limited, inadequate or suggesting lack of carcinogenicity), and identifies tumour sites for those agents for which the evidence for carcinogenicity will be sufficient in humans.

In this section, only published (or accepted for publication) sources of information in the peer-reviewed literature can be used (also see the Preamble). Exceptionally, publicly available data from government agency reports are also considered. Studies of doubtful quality may also be summarized for discussion by members of the Working Group assigned to this section.

**Summarizing the evidence**

**Tables of study design and results**

Study design and results of all pertinent individual studies will be presented in table format using the table template provided, including:

- Species, strain (sex) [note if unspecified], age at start if unusual, duration, reference
- Route, dosing regimen, numbers of male and female animals/group at start
- Number of each tumour type/effective number of animals (incidence) and percentage, tumour multiplicity if provided
- Statistical significance of differences between groups, and statistical method used; if not provided, $P$ values should be calculated by the Working Group and given in square brackets.
- Comments should include limitations of the study; survival data (if important); if any of the above items is not reported.

**Text**

For each study, indicate:

- Number of males and of females in each experimental and control group
- Strain
- Route of administration of test substance
- Treatment of controls (untreated, vehicle, “positive”)
- Doses as quoted in the original paper (conversions to SI units will be added by the Secretariat)
• Dosing schedules
• Duration of treatment
• Duration of observation
• Histological types of tumours in treated and control animals
• Increased/decreased incidence of each tumour type of interest (both benign and malignant) in treated compared to control animals; dose-response. Tumours with a low spontaneous incidence rate should also be reported if above incidence range in historical controls.
• Tumours at unusual sites, with early onset, etc…

Precancerous lesions and non-neoplastic histopathological lesions that may be relevant to interpretation of tumour incidence, i.e., in the same target organ, should also be described.

The author's interpretation may be included if you consider it necessary, but it must be clearly identified as such.

Strengths and weaknesses of study should be presented in square brackets: [inadequate duration, no controls, underpowered study, inadequate reporting of exposure or results, high mortality]

Preferred outline

For each agent:

3.1. Mouse
  3.1.1 Oral administration
  3.1.2 Skin application
  3.1.3 Subcutaneous administration
  3.1.4 Inhalation
  3.1.5 Intratracheal administration
  3.1.6 Intrapleural administration
  3.1.7 Intraperitoneal administration
  3.1.8 Intravenous administration
  3.1.9 Transplacental and perinatal
  3.1.10 Other routes of exposure
  3.1.11 Administration with known carcinogens or other agents
  3.1.12 Carcinogenicity of metabolites

3.2 Rat
  3.2.1 Oral administration…

3.3 Hamster …
3.4 Dog …
3.5 Monkey …
3.6 etc…

*Checklist for quality control:* might include the following standards:

- Were adequate numbers of animals used?
- Were they allocated randomly to groups?
- Was the schedule of exposure adequate?
- Was the agent clearly defined or characterized?
- Was the duration of exposure adequate?
- Was survival acceptable?
- Was the duration of observation adequate?
- Was the study adequately reported?
- Were appropriate comparisons and statistical methods used? (See also Preamble)
Section 4. Mechanistic and Other Data

Section 4 summarizes data on mechanisms of carcinogenesis for the agent under consideration drawn from representative studies in humans, animals, and in vitro, and judged to be important by the Working Group.

Rationale

Mechanistic data may provide evidence of carcinogenicity, and can play a role in up- or downgrading an evaluation based on cancer findings in animals or humans (see Appendix 1). Important determinations in the evaluation of mechanistic data are:

- Is there strong evidence of an operative carcinogenic mechanism(s)?
- Is the evidence from exposed humans, human in-vitro systems, or animals?
- Does the mechanism only operate in animals?
- Does the agent belong to a class of agents evaluated as Group 1 or Group 2A (e.g. as in Monograph Volume 100F)?

In a style of a review article, Section 4 of the Monograph summarizes human and animal evidence and data gaps informative for addressing these questions, covering:

- Toxicokinetics (metabolites, enzymes involved, kinetic factors, etc.)
- Carcinogenic mechanisms, based on 10 key characteristics of carcinogens (see Table 1)
- Other relevant evidence (e.g. structure–activity relationships, susceptibility, target organ toxicity).

The approach to identifying, screening, organizing and summarizing these data is presented below. Two online tools facilitate this approach: the Literature Search (https://hawcproject.org/), and the IARC Table Builder.

Identifying the relevant information

Step 1. Searching the literature: With support from the IARC secretariat, the Working Group identifies relevant studies through comprehensive searches of peer-reviewed literature, supplemented by manual searching (e.g. of past IARC Monographs or other authoritative reviews). Databases (e.g. PubChem) and peer-reviewed government reports can also be searched. The HAWC Literature Search tool (https://hawcproject.org/) documents the search terms (covering the agent, metabolites, toxicokinetics, and mechanisms), sources, and results.

Step 2. Screening and organizing the results: The Working Group screens the retrieved literature for relevance, with assistance from the IARC secretariat.
The Working Group organizes the relevant literature by mechanistic topic, noting if human or animal, in vivo or in vitro, using literature tags in the HAWC Literature Search tool (https://hawcproject.org/). Authoritative, balanced review articles are identified. Literature trees document the number of studies identified, excluded and categorized per mechanistic topic and species.

**Step 3. Summarizing the evidence:** The Working Group summarizes the extent of data available, addressing the range of study designs and doses tested, whether effects are observed at the physiological, cellular or molecular level, and any consistencies or differences in results within and across experimental paradigms. Emphasis is given to human data, where they exist. Gaps in evidence are identified.

Although based on comprehensive searches and review, the *Monograph* includes only information relevant to making the evaluation and does not necessarily cite all retrieved studies. The length is similar to a review article, i.e. 25–50 pages of combined text, tables, figures and references in Section 4. Authoritative, balanced reviews may be cited in lieu of numerous supporting references.

**Section outline**

4.1 Toxikokinetic data: Evidence on absorption, distribution, metabolism and elimination is described in sub-sections 4.1.1 Humans and 4.1.2 Experimental systems. Evidence for the metabolic fate, including metabolites and the enzymes involved in the activation and detoxification, are presented. A metabolic schema may indicate the relevant pathways, products and whether supporting evidence is from humans and/or experimental animals. Kinetic factors that may affect dose–response relationships or cross-species comparisons (e.g. uptake, deposition, half-life in tissues, protein binding, metabolic activation) are presented.

4.2 Mechanisms of carcinogenesis: Representative data on the 10 key characteristics in Table 1 is presented. An expert Working Group convened by IARC concluded that Group 1 carcinogens commonly show one or more of these 10 key characteristics. These characteristics can provide a basis for systematically collating and analysing mechanistic information. The evidence for these characteristics may be grouped into mechanistic categories, using the colours in Table 1 as one example. Within each group, subsections summarize evidence from (1) humans and (2) experimental systems. Evidence is further organized (as appropriate) by species, sex, strain, target organ, and end-point. Tabular presentations capture the experimental system, dose (exposure), and result. Separate tables may depict evidence for each mechanistic category and metabolites. Information in tables is not repeated in text, although essential design details and key results of influential studies can be highlighted. When considered supportive of evidence in humans or higher organisms, non-mammalian studies (e.g. data from plants, lower eukaryotes) can be synthetically summarized, and representative studies cited, but results not detailed in tables.

4.3 Data relevant to comparisons across agents and end-points: If important to the evaluation, structure-activity relationships, any additional high-throughput/output data, etc., are summarized.
4.4 Cancer susceptibility: Cancer studies addressing differential susceptibility due to toxicokinetic or mechanistic factors (e.g. genetic polymorphisms, metabolic differences, etc.) are summarized.

4.5 Other adverse effects: If data on other topics are limited, relevant evidence confirming distribution to, or effects at, tumour sites is briefly summarized. Any targets of toxicity not addressed in sections 4.1–4.4, including reproduction or development, can be identified in a paragraph, if relevant to cancer hazard identification.

4.6 Summary of mechanistic evidence. A tabular summary developed in the IARC Table Builder gives key conclusions, identifying references and if human and/or animal, in vivo and/or in vitro.

5.4 Mechanistic and other relevant data. Summary statements on the entirety of Section 4 covering toxicokinetics, major mechanisms, and other relevant data highlight key supporting evidence and gaps, and address:

- Is there strong/moderate/weak evidence (i.e. from human or animal data) of an operative carcinogenic mechanism(s)?
- Does the agent belong to a class of agents evaluated in Group 1 or Group 2A? and
- Does the mechanism(s) of carcinogenicity only operate in animals?

6. Evaluation and rationale. Mechanistic and other evidence judged to be relevant to an evaluation of carcinogenicity and of sufficient importance to affect the overall evaluation is highlighted (see Table 1).
Appendix 1. Role of mechanistic data in the overall evaluation

Group 1
- Sufficient evidence in humans OR
- Sufficient evidence in animals AND strong evidence in exposed humans that the agent acts through a relevant mechanism
- Clearly belongs, based on mechanistic considerations, to a class of agents for which one or more members have been classified in Group 1

Group 2A
- Limited in humans AND sufficient in animals
- Inadequate in humans AND sufficient in animals AND strong evidence that the carcinogenesis is mediated by a mechanism that also operates in humans
- Clearly belongs, based on mechanistic considerations, to a class of agents for which one or more members have been classified in Group 2A

Group 2B
- Limited in humans AND less than sufficient in animals
- Inadequate in humans BUT sufficient in animals
- Inadequate in humans AND less than sufficient in animals AND supporting evidence from mechanistic and other relevant data

Group 3
- Inadequate in humans AND inadequate/limited in animals
- Inadequate in humans AND sufficient in animals AND strong evidence that the mechanism of carcinogenicity in animals does not operate in humans
### Table 1. Key characteristics of carcinogens

<table>
<thead>
<tr>
<th>Characteristica</th>
<th>Example of relevant evidence</th>
<th>Commonly linked characteristicsb</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Electrophilic or ability to undergo metabolic activation</td>
<td>Parent compound or metabolite with an electrophilic structure (e.g. epoxide, quinone, etc.), formation of DNA and protein adducts</td>
<td>2, 3, 4, 7, 8, 9</td>
</tr>
<tr>
<td>2. Genotoxic</td>
<td>DNA damage (DNA strand breaks, DNA–protein crosslinks, unscheduled DNA synthesis), intercalation, gene mutations, cytogenetic changes (e.g. chromosome aberrations, micronucleus formation)</td>
<td>1, 3, 4, 5, 10</td>
</tr>
<tr>
<td>3. Alter DNA repair or cause genomic instability</td>
<td>Alterations of DNA replication or repair (e.g. topoisomerase II, base-excision or double-strand break repair)</td>
<td>1, 2, 4, 6, 7, 9, 10</td>
</tr>
<tr>
<td>4. Epigenetic alterations</td>
<td>DNA methylation, histone modification, microRNAs</td>
<td>1, 6, 10</td>
</tr>
<tr>
<td>5. Oxidative stressor</td>
<td>Oxygen radicals, oxidative stress, oxidative damage to macromolecules (e.g. DNA, lipids)</td>
<td>2, 6, 8, 10</td>
</tr>
<tr>
<td>6. Induce chronic inflammation</td>
<td>Elevated white blood cells, myeloperoxidase activity, altered cytokine and/or chemokine production</td>
<td>3, 4, 5, 7, 8, 10</td>
</tr>
<tr>
<td>7. Immunosuppressant</td>
<td>Decreased immnosurveillance, immune system dysfunction</td>
<td>1, 3, 6, 8, 9</td>
</tr>
<tr>
<td>8. Modulate receptor-mediated effects</td>
<td>Receptor in/activation (e.g. ER, PPAR, AhR) or modulation of exogenous ligands (including hormones)</td>
<td>1, 5, 6, 7, 10</td>
</tr>
<tr>
<td>9. Immortalization</td>
<td>Inhibition of senescence, cell transformation</td>
<td>1, 3, 7, 10</td>
</tr>
<tr>
<td>10. Alter cell proliferation, cell death and nutrient supply</td>
<td>Increased proliferation, decreased apoptosis, changes in growth factors, energetics and signalling pathways related to cellular replication or cell-cycle control, angiogenesis</td>
<td>2, 3, 4, 5, 6, 8, 9</td>
</tr>
</tbody>
</table>

aColours in this column indicate characteristics for which an individual Working Group or Committee member or group of members work together to identify data and draft the initial language.

bSome mechanisms can cause cancer without other mechanisms, but generally it is the combined effect of multiple mechanisms that will be the root cause. Any of the 10 characteristics in this table could interact with any other, but there are some common interactions that are highlighted in the column (e.g. oxidative stress, DNA damage and chronic inflammation when combined provides stronger evidence for a cancer mechanism than would oxidative stress alone).
**Section 5. Summaries**

Section 5 combines summaries of the data reviewed in Sections 1 to 4. Each subgroup (members of the Working Group assigned to a particular Section) is responsible for writing the summary of the text they reviewed. Summaries are composed *during the meeting*, and are the product of the entire subgroup and, subsequently, of the entire Working Group.

**Overall comments**

Summaries are the sections most read in the entire volume. In that sense, it is extremely important to provide essential and relevant information, and yet remain concise.

The summaries should not contain studies or other elements that have not been mentioned before, in the main text.

Summaries must be understandable by the lay public. Avoid technical jargon.

No references should be quoted.

**Section 5.1**

The agent and its use are briefly described. Human exposure is summarized on the basis of the data on production, use and occurrence.

**Section 5.2**

A concise summary should be provided of the epidemiological studies considered to be of adequate quality for use in making an evaluation of carcinogenicity to humans. Those considered uninformative and not used in making the evaluation need not be brought forward to the description of studies in the summary.

A statement should be made of the type and number of studies (cohort, case–control) and whether an association was found between the exposure and the occurrence of cancer at different sites and under what circumstances. Quantitative data are not given. Any limitations should be mentioned.

References should not be cited, but information such as geographical location should be given to allow the reader to identify a study.

**Section 5.3**

A concise summary should be provided of those studies considered to be of adequate quality for use in making an evaluation of carcinogenicity to animals. Studies with critical weaknesses and not used in making the evaluation need not be brought forward to the summary.
A statement should be made of the number of experiments, the species and by what routes the agent has been tested adequately and with what qualitative results, including the main organ sites at which tumours were observed. Studies in which tumours were produced following single doses should be identified. Dose–response relationships should be noted. Several studies of the same type and/or with concordant results may be summarized together. Any limitations should be mentioned. Studies in which the agent was given in combination with known carcinogens should be summarized only briefly. Studies on preneoplastic lesions may be described if relevant to the evaluation. Cancer bioassays with major metabolites may be summarized.

Section 5.4

Information on biological effects in humans relevant to an evaluation of carcinogenicity is summarized, e.g. kinetic and metabolic considerations, evidence of DNA binding, persistence of DNA lesions or genetic damage in exposed people. Similarly, data on kinetics and metabolism in experimental animals are given only if considered relevant. The results of tests for genetic and related effects are summarized for exposed humans, other mammalian species, cultured human and mammalian cells and non-mammalian systems. Other mechanistic considerations may be included.
Section 6. Evaluation

Section 6 is a statement of the Working Group’s evaluations of the strength of the evidence for carcinogenicity arising from data from humans and experimental animals, using standard terms (see the Preamble). Mechanistic and other evidence judged to be relevant to an evaluation of carcinogenicity and of sufficient importance to affect the overall evaluation is highlighted. Finally, the body of evidence is considered as a whole, in order to reach an overall evaluation of the carcinogenicity of the agent to humans, and the agent is classified in one of four groups:

- **Group 1**: Carcinogenic to humans
- **Group 2A**: Probably carcinogenic to humans
- **Group 2B**: Possibly carcinogenic to humans
- **Group 3**: Not classifiable as to its carcinogenicity to humans
- **Group 4**: Probably not carcinogenic to humans

The rationale used by the Working Group to achieve its overall evaluation is summarized.

*Last update 04/12/2014*