



Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment (COC)

COC Guidance Statement G11

A case for change: the challenge to develop a better approach to assessing risk of cancer caused by chemicals

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COC Guidance Statement G11

COMMITTEE ON CARCINOGENICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT

A case for change: the challenge to develop a better approach to assessing risk of cancer caused by chemicals

The challenge – a call to action

1. The purpose of this exceptional COC guidance document is to facilitate a change in the current paradigm for carcinogenic risk assessment in order to achieve the best possible protection of public health using all available evidence and appropriate methodologies.
2. The current testing and risk assessment approach for chemicals often focusses on a binary outcome of carcinogen or non-carcinogen with respect to cancer, which then governs potential use, or not, of the chemical. This binary outcome does not allow consideration of the potential for risk of cancer following exposure in use.
3. The COC is keen to identify approaches which allow better prediction of human cancer risk, which is not necessarily achieved with the current approach that often relies on long-term animal studies.
4. Therefore, the Committee invites interested parties to contact the Secretariat with proposals for approaches in this area, or to present case studies where alternative methodology has been used to select candidate compounds before full regulatory testing.

Introduction

5. The COC recognises many ongoing activities to improve risk assessment of chemicals including assessment of potential carcinogenicity. With these developments, the COC considers that current guidance, and in some sectors regulatory requirements, on assessing risks of cancer should not consider the two-year rodent study to be the 'gold standard' nor that long-term, or potentially any,

animal studies should be absolutely required. Instead other modalities should be evaluated alongside current practice.

6. The COC's overarching guidance statement on [“A strategy for the Risk Assessment of Chemical Carcinogenicity” \(COC Guidance Statement G01- version 5.0\)](#) was last updated in 2020. At that time, it was noted by the COC that carcinogenic classification schemes underpinned by the use of the 2-year rodent bioassay were no longer wholly adequate, and that alternative approaches should be considered that focus on data more relevant for risk of cancer in humans than for the identification of carcinogens per se.

7. Over the last few years, the COC has discussed possible changes to the [guidance statements on hazard identification](#), and on [alternative methods](#). These discussions included 2 workshops focussing on advances in carcinogenic risk assessment in agrochemicals (in November 2022) and cosmetics (in November 2023).

8. It is intended that this guidance should act as a living resource to encourage and facilitate state of the art carcinogenic risk assessment that will support risk managers in decision making and meet regulatory and societal expectations.

Concerns regarding status quo

9. A lot of work conducted on chemicals with respect to cancer focusses on classification of whether a substance is a carcinogen or not, which is often governed by regulatory requirements, for example, carcinogens cannot be used in certain product types, or for product labelling, for example under CLP. The provenance of this hazard classification scheme, along with its limitations has been extensively discussed by Boobis and others ([1](#)). In itself, classification of carcinogenic hazard does not inform on the potential risk of cancer following exposure to a specific chemical, which is the more relevant aspect to consider in protecting human health. Indeed, it increasingly appears that certain classifications of carcinogens make it more difficult to present clear and helpful messages to the public about cancer risk, and may undermine the desire to take relevant action to protect public health.

10. The COC and some published papers draw attention to the limitations of long-term animal carcinogenicity assays both for classification and risk assessment of chemicals. Limitations include that some of the findings are not relevant to human health risk, a significant number of animals are used, it takes a long time, and in some cases potential for carcinogenicity can be identified from data already available. (For example, from investigative work undertaken before a long-term study is conducted, see references [1 to 9](#)).

11. There is now growing consensus that there are additional and/or better tools for assessing potential for risk of cancer in humans from chemicals. This includes

better use of existing data or data from development of compounds and incorporation of new approach methodologies (NAMs) as they develop into the assessment process. However, there are some concerns around the definition, identification, verification and validation of these NAMs, that act as a barrier to adoption in a regulatory environment. The Committee cautions against comparing NAMs with existing animal studies, and instead recommends consideration of their use in the context of human health and risk.

12. The COC is aware that there are challenges to regulators in changing the approach to dealing with risk of cancer from chemicals. There is always a risk that the public may perceive any change as a reduction in protection, especially if there appears to be less testing. It is essential therefore not only to ensure that any new approach is as good or better than the current one at protecting public health, but also to be able to demonstrate this to the public.

13. An additional concern is the likely difficulty with changing from a binary 'carcinogen' or 'non-carcinogen' classification approach. It could make communication with the public around cancer risk more challenging. However, at the moment what is being communicated to the public may be inadequate and potentially misleading, so this should not prevent progress, but rather emphasises the importance of transparency and clear communication around advances in cancer risk assessment.

14. Wider barriers to changing how potential risk of cancer from chemicals is assessed include current regulatory requirements which might prevent some industry partners from exploring alternatives. The COC is aware that significant work is undertaken by industry in advance of undertaking long-term animal studies for regulatory submission, to optimise the outcomes of such studies (for example gaining more information than whether a compound is a carcinogen or not); the data from this work could support progress to move away from the subsequent animal studies and the regulatory burden while maintaining health protection. Interested industry sectors invite parallel submissions of conventional data along with data from other approaches for regulatory approval, but this is not a requirement and there may be hesitation from industry in supplying such data. The COC is also interested in submission of approaches where compounds were not progressed due to identification of potential for cancer before any long-term animal studies were conducted.

15. Skills and expertise within industry and regulators to assess data from other approaches may be limited, resulting in uncertainty should conventional information not be supplied as well.

Lessons from 2 workshops

16. The COC hosted 2 workshops to discuss how progress can be made in assessing the risk of cancer from chemicals. The first explored the issues from the perspective of the pesticides sector, where use of animal data including the long-term rodent carcinogenicity assay is a regulatory requirement. The second focussed on the cosmetics and personal care industry where use of substances tested on animals for the purposes of cosmetic use after 2013 has been banned, so no new animal data are being used for risk assessments.

17. Across the 2 workshops it was clear that activities are ongoing to improve carcinogenic risk assessment and move away from the long-term animal carcinogenicity study. In the pesticide sector, programs like the “Rethinking Carcinogenicity Assessment for Agrochemicals Project (ReCAAP)” are demonstrating how other data including from shorter animal studies can sufficiently address the potential for cancer risk (6). This also follows work by ICH¹ in the pharmaceuticals sector which has moved towards a weight of evidence approach for carcinogenicity assessment and in some cases, a sponsor may be able to gain regulatory agreement to not conduct a 2-year rat carcinogenicity study ([ICH guideline S1B\(R1\) on testing for carcinogenicity of pharmaceuticals Step 5 \(europa.eu\)](#)). The COC notes that the ReCAAP project focusses on ensuring health protection at predicted levels of exposure, while the ICH approach is focussed on whether a compound is carcinogenic or not, but only requiring the long-term animal test to be conducted where it is not possible to determine this from shorter-term tests.

18. Some challenges in the cosmetics and personal care sectors specifically were highlighted in the second workshop, where it was noted that few ingredients are in use that have been developed following the animal testing ban. Work is continuing in the area and as exploration is made of alternative approaches for testing for other complex endpoints, this is likely to support developments for assessment of carcinogenicity.

19. The workshops highlighted that determination of whether a compound is a carcinogen or not, was not particularly helpful to assessment of risk. Both workshops suggested a need for demonstration of effectiveness of alternative approaches to aid regulatory change; recognised barriers to uptake of such approaches, including a lack of international harmonisation and legislation; and acknowledged the need for courage to submit dossiers with supplementary non-conventional data or without drawing on historical conventional data to lead the way and provide assurance to others in the same or different sectors that effective cancer risk assessment can be undertaken without (long-term) animal data.

¹ International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use

20. Alongside scientific developments, the workshops flagged the importance of clear communication of developments in the field recognising the sensitivity around cancer risk compared to some other types of toxicity, as public risk perception will be an important consideration for risk management.

Challenge to action – submission of approaches

21. The COC is keen to encourage continued evaluation of different scientifically robust approaches to assessing cancer risks to humans from chemicals, using data from real life examples and studies.

22. It is acknowledged that this will require effort and investment from industry colleagues, from regulators, assessors and from other interested parties. The reward for this effort should clearly be improved risk assessment for humans, in terms of earlier and more reliable assurance of safety or identification of potential for carcinogenicity, as well as reduced use of animals. It may ultimately lead to changes in the assessment requirements for chemicals, including reduced cost and facilitate faster and more chemicals assessed for their ability to increase the risk of cancer.

23. The Committee invites interested parties to contact the Secretariat (via COC@ukhsa.gov.uk) with proposals for approaches in this area, or to present cases studies where alternative methodology has been used to select candidate compounds before full regulatory testing. All such submissions to the Committee will be reviewed to support development of future COC guidance; where underpinning data are confidential the Committee would be informed by this but would not publish the data.

Conclusions

24. In the interest of enabling progress to maximise the effectiveness of carcinogenic risk assessment of chemicals, this guidance sets out the Committee's invitation to industry, regulators, academia and other interested parties to provide ideas regarding approaches to risk assessment for potential carcinogenicity in humans. These submissions should be weight of evidence assessments from multiple inputs (not individual assays) and provide the evidence supporting how this approach allows conclusions on risk assessment for carcinogenicity to be reached.

25. The COC is particularly keen to move away from suggesting there can be binary conclusions on whether a chemical is carcinogenic or not, and instead enable an appropriate human health risk assessment of the potential for cancer at relevant exposure levels.

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