



## Reply to Letter to the Editor

## Classification schemes for carcinogenicity based on hazard identification serve science and society



Editor,

A recent article by Boobis et al. (2016) emphasizes the importance of using established, rigorous methods to evaluate carcinogenicity. We agree that a uniform classification scheme can support efforts to take scientifically-based measures to reduce exposure to carcinogens. However, the scheme that Boobis et al. advocate is largely silent about the important role of epidemiological data, while key methodological aspects do not reflect the current state of science. Moreover, Boobis et al. inappropriately conflate the scientific evaluation of hazards with the broader socio-political process of risk management, in sharp contrast to prominent recommendations for advancing risk assessment and systematic review (NRC, 1983, 1994, 2009; US EPA, 2012).

Hazard classification is based on a critical evaluation of scientific findings. Epidemiological studies, including observed relationships of exposure to response, are a central part of the evidence evaluated. On the other hand, dose-response assessments that extend beyond the range of observations are developed “using a combination of data, science policy decisions and models” (US EPA, 2012). As a result, such risk estimates differ widely across regulatory contexts, even for the same chemical and based on the same underlying observational study data (Holman et al., 2016). Moreover, public health measures take account of a range of other factors besides the dose-response relationship. This is illustrated by the example of tobacco smoking and second-hand tobacco smoke, both classified as “carcinogenic to humans” by the IARC Monographs reflecting the strength of scientific evidence. Subsequent cancer control measures considered their different dose-response relationships, based on observations in a wealth of epidemiological studies, but also the different nature of exposures (personal versus workplace, voluntary versus involuntary) as well as a range of economic, legal and other factors. Hazard identification, incorporating the “real-world” exposures measured in epidemiological studies, thus provides a vital platform for the subsequent steps of risk assessment and management.

In place of hazard assessment, Boobis et al. advocate an evaluation approach that rests heavily on identifying “modes of action.” This approach, although characterised as “modern”, does not reflect the current state of science documented in recent scientific consensus reports, that instead provide “precautionary lessons” on mode of action analyses or endorse “toxicity pathways” (US

EPA, 2012; NRC, 2007). Indeed, the NRC (2007) indicate that scientific data “call into question” the previous controversial assertion on the human relevance of rodent cancers induced by diethylhexylphthalate (IARC, 2000, 2013; Klaunig et al., 2003; NRC, 2008; Rusyn and Corton, 2012). These and other “lessons learned” were taken into account when IARC modernized the formal procedures, first introduced in 1991, to up- or down-grade carcinogen hazard evaluations when human data are less than sufficient (IARC, 2006). Although cancer mechanisms remain of high interest, the possibility of taking scientifically-informed actions to mitigate risk in the absence of mechanistic knowledge is an essential cornerstone of public health. In the modern era, this is best illustrated by actions to reduce tobacco smoking: these were initiated without a full understanding of the pertinent mechanisms, yet have resulted in significant long-term reductions in the incidence of cancer. Furthermore, it is important to note that the suggestion by Boobis et al. for “further evaluation including full risk assessment” before taking action to mitigate risk from a carcinogenic hazard is a political stance, not a scientific one.

Far from “stigmatizing” products or creating “health scares” as Boobis et al. claim, echoing the tobacco industry (UCSF, 2016), carcinogen classification schemes provide an unbiased review of scientific evidence and remain a necessary and valuable foundation for cancer prevention. The IARC Monographs pioneered evaluation of carcinogenic chemicals and have extended and adapted to encompass physical, biological and lifestyle exposures (Saracci and Wild, 2015). The Programme continues to be acknowledged as a leader worldwide in objective, systematic cancer hazard evaluations (NRC, 2011), incorporating the latest scientific understanding and conducted in the light of strict management of conflicts of interest.

## References

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