

MARCH 20, 2015

expert reaction to carcinogenicity classification of five pesticides by the International Agency for Research on Cancer (IARC)

The International Agency for Research on Cancer has classified five pesticides as either probably or possible carcinogenic to humans.

Prof. Andreas Kortenkamp, Professor in Human Toxicology at Brunel University London, said:

“IARC have carefully assessed new evidence about the cancer hazards of pesticides, and have now classified 5 pesticides as either ‘probably’ or ‘possibly’ carcinogenic to humans. The authorities in the EU must now consider whether existing measures are sufficient to protect consumers and pesticide applicators from cancer risks. This will be particularly important for the widely used weedkiller glyphosate, now classified as probably carcinogenic to humans. Home gardeners especially should exercise the utmost care when they use weedkillers that contain glyphosate.”

Dr Oliver Jones, Senior Lecturer in Analytical Chemistry at RMIT University in Melbourne, said:

“The main thing in this new assessment is that two pesticides not previously assessed by the IARC (Glyphosate and Diazinon) have been reviewed and classified as ‘probably carcinogenic to humans’. Malathion has been upgraded to the same status, while Parathion and Tetrachlorvinphos are now classified as ‘possibly carcinogenic’.

“This sounds scary and IARC evaluations are usually very good, but to me the evidence cited here appears a bit thin.

“The study itself says that for all compounds, the evidence of human carcinogenicity was limited or considered inadequate. Aside from this, Tetrachlorvinphos is banned in the EU anyway, while use of Diazinon and Parathion is severely restricted. Glyphosate and Malathion are quite widely used but are also extensively studied, including by the US Environmental Protection Agency which still allows their use.

“People might be interested to know that there are over 70 other things IARC also classifies as ‘probably carcinogenic’, including night shifts. In the highest category of known carcinogens are ‘alcoholic beverages’ and ‘solar radiation’ (sunlight) – along with plutonium.

“So yes, pesticides can be dangerous, but are many other common things which are also dangerous in sufficient amounts or over long periods of time – the dose makes the poison. While absence of evidence is not evidence of absence this does seem to me to be a precautionary rather than a reactionary change.

“From a personal perspective, I am a vegetarian so I eat a lot of vegetables and I’m not worried by this report.”

Prof. Alan Boobis, Professor of Biochemical Pharmacology at Imperial College London, said:

“IARC bases its conclusions on an evaluation of the human and experimental data, leading to hazard identification. They ask: is a substance carcinogenic? And if so, how good is the evidence in humans?”

“The IARC process is not designed to take into account how a pesticide is used in the real world – generally there is no requirement to establish a specific mode of action, nor does mode of action influence the conclusion or classification category for carcinogenicity.

“The IARC process is not a risk assessment. It determines the potential for a compound to cause cancer, but not the likelihood. Exposure assessment in epidemiological studies on the effects of pesticides is notoriously difficult. Agricultural workers, the most commonly studied group, are almost never exposed to just a single pesticide and it is very difficult to establish cause and effect.

“The UK Committee on Carcinogenicity has evaluated possible links between pesticide exposure and cancer on several occasions. It has found little evidence for such a link. At most, the evidence was inconsistent and was considered insufficient to call for regulatory action.

“These conclusions of IARC are important and should be taken into account when evaluating these pesticides, but that must also take into account how the pesticides are used in the real world. In my view this report is not a cause for undue alarm.”

Prof. Sir Colin Berry, Emeritus Professor of Pathology at Queen Mary University of London, said:

“I have served on a number of regulatory bodies for the UK, EU and WHO and I am well used to sifting wheat from chaff in the analysis of pesticides. What is missing in this new assessment is balance in the consideration of the studies.

“There are over 60 genotoxicity studies on glyphosate with none showing results that should cause alarm relating to any likely human exposure. For human epidemiological studies there are 7 cohort and 14 case control studies, none of which support carcinogenicity.

“The authors have included non-Hodgkin lymphoma (NHL), but that diagnosis is no longer used in pathology because it’s far too imprecise. Even if you do include NHL there are still 7 studies, only one of which is positive – and that one is not a good study in my view.

“The weight of evidence is against carcinogenicity.

“The authors of the one study cited as ‘positive’ say the following: *‘Because 26 pesticides were evaluated for their association with NHL and its subtypes, some chance finding could have occurred. Our results showed pesticides from different chemical and functional classes were associated with an excess risk of NHL and NHL subtypes, but not all members of any single class of pesticides were associated with an elevated risk of NHL or NHL subtypes.’*

“This assessment has looked at a group of 43 diseases lumped into one category, multiple pesticides with very different chemistry, and has failed to include critical data. There is nothing here to suggest that the variety of genetic changes in these diseases could be caused by these pesticides. This appears to be a rather selective review.”

Prof. David Coggon, Professor of Occupational and Environmental Medicine at the University of Southampton, said:

“IARC monographs do not present new primary research. Rather they rigorously and systematically review the available evidence from published peer-reviewed studies in animals and humans in order to classify chemicals according to their cancer hazard (i.e. their potential to cause cancer at some level of exposure) in animals and in humans.

“Given the large number of epidemiological studies that have been carried out on pesticides and cancer, many of them looking at multiple types of malignancy, it is to be expected that some positive associations will occur simply by chance. Thus, when evaluating the epidemiological evidence, one is looking for a consistent pattern of increased risk for one or more tumour types, which is unlikely to be explained by biases (often unavoidable) in the study methods. It is clear from the summary table in the Lancet report that clear and consistent evidence of this type was not found for any of the pesticides that were considered.

“In contrast, studies in laboratory animals were judged to show clear evidence of carcinogenicity for four of the five compounds. In this circumstance, what matters for the management of risk is whether the potential to cause cancer in animals might translate into a material risk of cancer in humans at the levels of exposure which could occur as a consequence of their use as pesticides. A judgement on this will depend on the mechanism by which the cancer in animals might have occurred (could it represent a genotoxic effect, or is there good evidence that another mechanism is involved?). If the mechanism is thought to be non-genotoxic, is it one which might occur in humans, would it only be expected to cause cancer at exposures above a threshold level, and if so, might human exposures exceed that threshold?

“Regulatory risk assessment for pesticides, both in the EU and the USA, routinely considers evidence on potential carcinogenicity, both from animal studies (including some that may not have been published in the peer-reviewed literature, but which have been conducted to specified exacting standards) and also, where available, from epidemiological research. The approach adopted is precautionary. Where there are any indications that a compound might cause cancer, it will not be approved for use unless there is good evidence that it is not genotoxic and that no risk of cancer would occur from the levels of exposure that could occur in a worst case scenario. Risk assessments are reviewed periodically, and particularly if new evidence emerges to suggest a previously unrecognised problem.

“The IARC report does not raise immediate alarms. However, I would expect regulatory authorities around the world to take note of this new evaluation,

and to consider whether it indicates a need to review their risk assessments for any of the pesticides that they currently approve.”

Prof. Tony Dayan, Emeritus Toxicologist, said:

“The new assessment by IARC continues their practice of making a comprehensive review of published information about each compound. Its assessments have always tended to be influenced more by laboratory toxicity data from rigorously controlled experiments than by reports of human experience, with its common problems of poor reproducibility and the well-known problems of trying to combine analyses of disparate clinical reports in which it is difficult to distinguish the possible effects of the compound in question and the many other substances and factors to which we are exposed in ordinary life.

“In the present report the classification of glyphosate and malathion as carrying a Class IIA risk of causing cancer in humans reflects a variety of laboratory results with a small number of studies in man of varied quality and mixed conclusions. Detailed analysis of the nature and quality of the evidence overall does not support such a high level classification, which at the most should be Class IIB.”

‘Carcinogenicity of tetrachlorvinphos, parathion, malathion, diazinon, and glyphosate’ by the International Agency for Research on Cancer Monograph Working Group published in *The Lancet Oncology* on Friday 20 March.

Declared interests

Prof. Dayan:

I have been involved in the registration and regulatory assessment of pesticides in the past, including malathion and glyphosate. I have consulted for a number of pesticide manufacturers but not for about 10 years.

Prof. Boobis:

I have no consultancies or grants from pesticide companies. I do participate in the WHO/FAO JMPR meetings and I have funding from Public Health England which sometimes requires us to review adverse health effects of pesticides for advisory committees such as COC, COT or COM.