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Comments on IARC Monographs preamble (and other items)

Title. In my opinion title is wrong since IARC working groups perform qualitative evaluations of the carcinogenic potential (which is a part of hazard) and not quantitative assessment of risks.

Data considered for evaluation. Since publication of the first volume in 1972, IARC policy was to evaluate only data from open literature. This position could be considered correct enough up to 1979. Indeed, in that year EPA guidelines for carcinogenicity testing were set up in order to avoid false results (see the case of Industrial Biotest Laboratory data that are worldwide considered as invalid). Since 1980s this is, however, a gap for IARC with respect to well designed and performed long-term assay in small rodents sponsored by chemical industry and subjected to quality assurance and, unfortunately, to confidentiality.

Thus, evaluations made by IARC working groups and those performed by national or multistate or international advisory committees on the same substance, also in the same year, often differ. This is due to existence of a lot of confidential data that are better evaluable than those reported in a paper published on Journals, which not always warrant quality nor are completely evaluable.

On the other hand, another expression of WHO, like Joint Meetings of FAO-WHO on pesticide use and residues, takes into account all the data existing and their technical reports briefly summarize such confidential information.

Finally, cases of publication of false results sometimes occur also in the open literature and on highly quoted Journals.

Groups for qualitative classification of carcinogenicity towards humans. IARC classification consider groups 1, 2A, 2B, 3 and 4. Groups 2A and 2B could be considered by a non expert similar enough whereas agents classified in these two groups are rather different. Indeed, in E.U., for example, where the classification is: category 1, 2 and 3, agents classified as carcinogenic for humans (cat. 1) or probably carcinogenic for humans (cat. 2) are treated in the same manner, with the same risk phrases (R 45 or R49) to protect workers from carcinogenic risk. On the contrary, agents classified in category 3 (possibly carcinogenic for humans, where the true risk could be rather small or in certain cases relevant) are labelled with R40 phrase (limited evidence of carcinogenicity) and no protection for worker is required.

To improve the comprehension by non experts, it would sound better to eliminate 2A and 2B in the IARC classification and use a classification similar to that adopted by E.U. or by Italy.

Quantitative risk assessment Any time it is possible, the estimate, with its uncertainty, of the excess number of tumors caused by daily exposure lifetime to a well defined dose of a carcinogenic agent should be calculated since the qualitative classification in groups is useful to alert about hazards but the risks related could be trivial as well as high enough. These considerations are also valid for the qualitative approach by E.U. that labels hazardous chemicals with **risk** phrases which are really **alert** phrases. Mathematical models with some biological correction are available as well as software for such calculations (see for example that of U.S. EPA, i.e. BMDS 1.3.2, that people can easily download without charge from EPA web site through internet). In other terms, at least the potency of the carcinogenic effect by a specific agent should be calculated.

Extrapolation of carcinogenicity data from animals to humans. In the preamble of IARC Monographs, statements about the impossibility to translate to humans the excess tumors induced in particular organs are not present. On the contrary, E.U. and Italian (National Toxicology Advisory Committee, where I worked over 20 years) have well defined the conditions that do not allow extrapolation from animals to humans. Examples are tumors induced only in particular strains of a rodent species or only in one sex with clearly demonstrated species-specific effects due to peculiar gene, metabolic and mechanistic profiles.

E.U. does not classify in such instances whereas Italian approach leads to classify the carcinogenic agent in category 4 (not classifiable as to carcinogenicity to humans) and subcategory 4b (tumors induced in animals whose meaning for humans is doubtful: further experimentation is not needed).

Declassification of many chemicals on this basis begun at earliest 1990s in Italy and Europe, and many years later in the U.S.A.

Anyway, I always read with great interest each IARC Monograph and appreciate the effort by IARC to give sounded information.

Compensation was or will be received for this comment neither by me nor by my organization.

Best regards

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