

GENERAL REMARKS

Since the beginning in 1971 of the *IARC Monographs Programme on the Evaluation of the Carcinogenic Risk of Chemicals to Man*, now the *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans*, some 834 agents have been evaluated, some of them more than once. These monographs and evaluations were published in Volumes 1–70 of the series. During recent years, the volume of biological data that could be relevant to an evaluation process has increased enormously and there has been growing concern that many of the older evaluations are becoming out of date and may require re-evaluation.

In 1979, re-evaluations were made for 54 chemicals, complex mixtures or occupational exposure circumstances for which cancer epidemiological data existed. The results of the meeting were published as Supplement 1 (IARC, 1979). In February 1982 there was another re-evaluation of data on 155 chemicals, groups of chemicals and exposures to complex mixtures that had been considered in Volumes 1–29 of the *IARC Monographs*, for which there were some data on human carcinogenicity. Those re-evaluations were published in Supplement 4 (IARC, 1982). Supplement 4 was subsequently updated as a result of two Working Group meetings, one in December 1986 of which the outcome was Supplement 6 (IARC, 1987a) and another in March 1987, which produced Supplement 7 (IARC, 1987b). The aim of the December 1986 Working Group was to summarize and bring up to date the findings from tests for genetic and related effects for all of the agents that had been evaluated in Volumes 1–42 of the *Monographs* and for which some cancer epidemiological data were available.

The objectives of Supplement 7 were two-fold. The first was to summarize and bring up to date the data on cancer epidemiology and experimental carcinogenesis for all 189 agents that had been evaluated in Volumes 1–42 of the *Monographs* and for which some cancer epidemiological data were available. The second objective was to make overall evaluations of carcinogenicity to humans for all 628 agents that had been evaluated in Volumes 1–42 of the *Monographs*.

Although the number of compounds re-evaluated in this Volume 71 of the *IARC Monographs* is smaller than in previous updatings, the undertaking was more extensive. A total of 121 organic compounds, most of them industrial chemicals, were selected for re-evaluation. Four of these compounds were treated as full length monographs, of the kind to be found in standard volumes of the *IARC Monographs*, i.e., all relevant data were reviewed. These four compounds (acrylonitrile, 1,3-butadiene, chloroprene and dichloromethane) were selected because there was a large quantity of new data and there was specific, widespread interest in having them re-evaluated.

For a number of other chemicals, the starting point for these reviews was the last full summary and evaluation. The summarized statements prepared previously were incorporated with data published since the previous evaluation. These 'mini-monographs' were prepared for those chemicals for which new epidemiological data and/or experimental carcinogenicity data were available that required review and acceptance by the full plenary meeting of invited experts, because changes in the classifications were anticipated.

A third group of chemicals consisted of those for which there was no new epidemiological evidence and, although there might be new experimental carcinogenicity data, these were, in the judgement of the secretariat, unlikely to lead to any change in the evaluation and classification. In these up-dated monographs the previous summary statements, in so far as they existed, are restated and new data are described. In all cases, however, there was a need to describe the toxicity and disposition data, since this was not consistently done in monographs published before the early 1990s.

The full monographs and the mini-monographs appear in Part 1 and Part 2, respectively, and the monograph updates are in Part 3 of this volume. Some of the chemicals were combined into single monographs because there was a close relationship between them. The monograph on 1,3-butadiene also contains the available data on 1,2:3,4-diepoxbutane because this is an important metabolite and a full consideration of the effects of exposure to 1,3-butadiene could not be made without frequent reference to this metabolite, to which human exposure from environmental sources could not be confirmed. Three α -chlorinated toluenes (benzyl chloride, benzal chloride and benzotrichloride) appear in a single mini-monograph along with benzoyl chloride, which is not an α -chlorinated toluene but is inextricably associated with them in industrial processes. Another mini-monograph is on the polychlorophenols and their sodium salts (and contains data on five of them), this forming a natural grouping of the chemicals, as does the combination of *ortho*-, *meta*- and *para*-xylenes.

During the first half of an *IARC Monographs* working group meeting, participants are allocated to specialist subgroups, which review drafts on chemistry and exposure, cancer epidemiology, experimental carcinogenicity and disposition (absorption, distribution, metabolism, excretion) and toxicology. For Volume 71, the same allocation to these subgroups was made, but in addition there was a multidisciplinary subgroup that reviewed all draft documents proposed for update. Wherever this subgroup concluded that a more detailed examination of any particular section was required, that section was passed on to the relevant specialist subgroup and on the recommendation of that specialist subgroup may have been brought to plenary session to consider whether any change in evaluation was appropriate. By this process, an update may have advanced to mini-monograph status. If, however, no such in-depth review was recommended, then the up-dated monograph was reviewed only by the multidisciplinary subgroup and was not reviewed in plenary session by the entire working group.

To minimize repetition in this very large undertaking, certain changes in procedure were introduced. One relates to occupational exposure data in the United States that are

available from the National Occupational Exposure Survey (NOES); another relates to the presentation of data on genetic and related effects. In the case of NOES data, reference is made in each Monograph to this General Remarks section for a short description of the survey. In the case of genetic and related effects data, the experimental evidence is tabulated (unless no new evidence has emerged since the last evaluation) and described in the accompanying text. Previously, there was also a presentation of genetic activity profiles, which summarize pictorially the genetic data already described in the text and in the tables. Since these profiles are now available on the worldwide web, it has been decided to inform readers of the *Monographs* how to access them, but not to print them in this or future volumes.

National Occupational Exposure Survey

Information on the extent of occupational exposure in the United States is available from the National Occupational Exposure Survey (NOES) conducted by the United States National Institute for Occupational Safety and Health (NIOSH). NOES was a nationwide observational survey conducted in a sample of 4490 establishments from 1981 to 1983. The target population was defined as employees working in establishments or job sites in the United States of America employing eight or more workers in a defined list of Standard Industrial Classifications. Generally, these classifications emphasized coverage of construction, manufacturing, transportation, private and business service and hospital industries. The NOES had little or no sampling activity in agriculture, mining, wholesale/retail trade, finance/real estate or government operations. NOES addressed recordable potential exposure that had to meet two criteria: (1) a chemical, physical or biological agent or trade name product had to be observed in sufficient proximity to an employee such that one or two physical phases of that agent or product were likely to come into contact or enter the body of the employee; and (2) the duration of the potential exposure had to meet the minimum duration guidelines, i.e. it must have presented a potential exposure for at least 30 min a week (on an annual average) or be used at least once per week for 90% of the weeks of the work year (NOES, 1997).

Genetic Activity Profiles

The Genetic and Related Effects data presented in the *Monographs* are also available in the form of Graphic Activity Profiles (GAP) prepared in collaboration with the United States Environmental Protection Agency (EPA) (see also Waters *et al.*, 1987) using software for personal computers that are Microsoft Windows[®] compatible. The EPA/IARC GAP software and database may be downloaded free of charge from www.epa.gov/gapdb.

References

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