

Environmental Health Criteria 109

Summary report on the evaluation of short-term tests for carcinogens

Please note that the layout and pagination of this web version are not identical with the printed version.



INTERNATIONAL PROGRAMME ON CHEMICAL SAFETY

ENVIRONMENTAL HEALTH CRITERIA 109

SUMMARY REPORT ON THE EVALUATION OF
SHORT-TERM TESTS FOR CARCINOGENS
(COLLABORATIVE STUDY ON *IN VIVO* TESTS)

This report contains the collective views of an international group of experts and does not necessarily represent the decisions or the stated policy of the United Nations Environment Programme, the International Labour Organisation, or the World Health Organization.

Published under the joint sponsorship of
the United Nations Environment Programme,
the International Labour Organisation,
and the World Health Organization

World Health Organization
Geneva, 1990

The International Programme on Chemical Safety (IPCS) is a joint venture of the United Nations Environment Programme, the International Labour Organisation, and the World Health Organization. The main objective of the IPCS is to carry out and disseminate evaluations of the effects of chemicals on human health and the quality of the environment. Supporting activities include the development of epidemiological, experimental laboratory, and risk-assessment methods that could produce internationally comparable results, and the development of manpower in the field of toxicology. Other activities carried out by the IPCS include the development of know-how for coping with chemical accidents, coordination of laboratory testing and epidemiological studies, and promotion of research on the mechanisms of the biological action of chemicals.

WHO Library Cataloguing in Publication Data

Summary report on the evaluation of short-term tests for
carcinogens : (collaborative study on *in vivo* tests).

(Environmental health criteria ; 109)

1.Carcinogens - analysis 2.Mutagens - analysis
3.Mutagenicity tests 4. Evaluation studies I.Series

ISBN 92 4 157109 8 (NLM Classification: QZ 202)
ISSN 0250-863X

The World Health Organization welcomes requests for permission to reproduce or translate its publications, in part or in full. Applications and enquiries should be addressed to the Office of Publications, World Health Organization, Geneva, Switzerland, which will be glad to provide the latest information on any changes made to the text, plans for new editions, and reprints and translations already available.

(c) World Health Organization 1990

Publications of the World Health Organization enjoy copyright protection in accordance with the provisions of Protocol 2 of the Universal Copyright Convention. All rights reserved.

The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the Secretariat of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries.

The mention of specific companies or of certain manufacturers' products does not imply that they are endorsed or recommended by the World Health Organization in preference to others of a similar nature that are not mentioned. Errors and omissions excepted, the names of proprietary products are distinguished by initial capital letters.

CONTENTS

SYNOPSIS

1. INTRODUCTION

2. THE COLLABORATIVE STUDY ON SHORT-TERM IN VIVO TESTS FOR MUTAGENS AND CARCINOGENS (CSSTT/2) 1983-85

3. OVERALL AIMS OF THE STUDY AND CRITERIA FOR THE SELECTION OF AN APPROPRIATE SHORT-TERM IN VIVO TEST

3.1. The use of short-term tests for the primary identification of genotoxic chemicals

3.2. The use of short term in vivo assays for assessing the hazard associated with exposure to in vitro genotoxins

3.3. The role of short-term in vitro tests in research into the mechanisms of cancer

3.4. Assays for the detection of germ cell mutagens

4. CRITERIA FOR THE SELECTION OF THE FOUR TEST CHEMICALS

4.1. Activity of the four test chemicals in short-term in vitro tests

4.2. Summary of carcinogenicity data on the test chemicals

5. SOURCE AND PURITY OF THE TEST CHEMICALS

6. SHORT-TERM IN VIVO ASSAYS

- 6.1. Cytogenetic assays
- 6.2. Assays in rodent liver cells
- 6.3. Miscellaneous assays
- 6.4. The mouse spot test
- 6.5. Mammalian germ cell studies
- 6.6. Drosophila assays

7. RESULTS

- 7.1. Benzo [a] pyrene and pyrene
 - 7.1.1. Cytogenetic studies
 - 7.1.2. Liver-specific assays
 - 7.1.3. Miscellaneous assays
 - 7.1.4. Mouse spot tests
 - 7.1.5. Mammalian germ cell assays
 - 7.1.6. Drosophila assays
- 7.2. 2-Acetylaminofluorene and 4-acetylaminofluorene
 - 7.2.1. Cytogenetic studies
 - 7.2.2. Liver-specific assays
 - 7.2.3. Miscellaneous assays
 - 7.2.4. Mouse spot tests
 - 7.2.5. Mammalian germ cell assays
 - 7.2.6. Drosophila assays
- 7.3. Summary of the *in vivo* genotoxicity of the four chemicals

8. ASSESSMENT OF THE PERFORMANCE OF THE ASSAYS

- 8.1. Cytogenetic assays
 - 8.1.1. Chromosome aberrations
 - 8.1.2. Micronuclei
 - 8.1.3. Sister chromatid exchange
- 8.2. Liver assays
 - 8.2.1. Initiation and promotion
 - 8.2.2. Unscheduled DNA synthesis and S-phase analysis
 - 8.2.3. DNA strand breaks
 - 8.2.4. Cytogenetics
- 8.3. Miscellaneous assays
 - 8.3.1. Specific carcinogenicity assays
 - 8.3.2. Supplementary assays
 - 8.3.3. Immunotoxicity assays
 - 8.3.4. Host-mediated assays and urine mutagenicity tests
- 8.4. Mouse spot tests
- 8.5. Assays in mammalian germ cells
 - 8.5.1. Dominant lethal and unscheduled DNA synthesis assay
 - 8.5.2. Sperm abnormality tests
- 8.6. Drosophila assays

9. SELECTION OF THE MOST EFFECTIVE *IN VIVO* ASSAYS IN RELATION TO THEIR PERFORMANCE

- 9.1. Assays that are not considered appropriate for routine *in vivo* testing of chemicals for genotoxic activity
- 9.2. Assays that satisfy some or all of the criteria for an acceptable *in vivo* short-term test
 - 9.2.1. Assays currently in general use
 - 9.2.2. Assays that show promise for future development
- 9.3. The detection of germ cell mutagens
- 9.4. Influence of route of administration of the test chemicals

10. CONCLUSIONS

REFERENCES

ETUDE COLLECTIVE POUR L'EVALUATION ET LA VALIDATION DES EPREUVES DE COURTE
DUREE RELATIVES AUX CANCEROGENES

ESTUDIO EN COLABORACION SOBRE EVALUACION Y COMPROBACION DE PRUEBAS A CORTO
PLAZO PARA SUSTANCIAS CARCINOGENAS

PARTICIPANTS IN THE COLLABORATIVE STUDY

- Dr I. Adler, Mammalian Genetics Institute, Association for
Radiation and Environmental Research, Neuherberg, Federal
Republic of Germany
- Dr R. Albanese, Pharmaceuticals Division, Imperial Chemical
Industries PLC, Macclesfield, Cheshire, England
- Dr J.W. Allen, Genetic Toxicology Division, US Environmental
Protection Agency, Research Triangle Park, North
Carolina, USA
- Dr J.A. Allen, Department of Mutagenesis and Cell Biology,
Huntingdon Research Centre Ltd., Huntingdon, Cambridge-
shire, England
- Dr O. Andersen, Odense University, Institute of Community
Health, Department of Environmental Medicine, Odense,
Denmark
- Dr D. Anderson, British Industrial Biological Research
Association, Carshalton, Surrey, United Kingdom
- Dr J. Arany, Institut d'Hygiène et d'Epidémiologie,
Brussels, Belgium
- Dr J. Ashby, Central Toxicology Laboratory, Imperial Chemi-
cal Industries PLC, Macclesfield, Cheshire, United
Kingdom
- Dr R.A. Baan, Medical Biological Laboratory TNO, Rijswijk,
Netherlands
- Dr P. Bannasch, Cytopathology Department, Institute of
Experimental Pathology, German Cancer Research Centre,
Heidelberg, Federal Republic of Germany
- Dr G.C. Becking, International Programme on Chemical Safety,
World Health Organization, Research Triangle Park, North
Carolina, USA
- Dr B. Beije, Department of Genetic and Cellular Toxicology,
Wallenberg Laboratory, Stockholm University, Stockholm,
Sweden
- Dr J. Benes, Institute of Nuclear Biology and Radiochemis-
try, Prague, Czechoslovakia
- Dr E. Bermudez, Department of Genetic Toxicology, Chemical
Industry Institute of Toxicology, Research Triangle Park,
North Carolina, USA
- Dr H.C. Birnboim, Department of Experimental Oncology,
Ottawa Regional Cancer Centre, Ottawa, Ontario, Canada
- Dr J.B. Bishop, Cellular and Genetic Toxicology Branch,
Toxicology Research and Testing Program, National Insti-
tute of Environmental Health Sciences, Research Triangle
Park, North Carolina, USA
- Dr D.H. Blakey, Mutagenesis Section, Environmental Health
Centre, Department of National Health and Welfare,
Tunney's Pasture, Ottawa, Ontario, Canada
- Dr R. Braum, Central Institute for Genetics and for Research
on Cultivated Plants, Academy of Science of the German
Democratic Republic, Gatersleben, German Democratic
Republic
- Dr G. Bronzetti, National Research Council, Institute of
Mutagenesis and Differentiation, Pisa, Italy
- Dr B.E. Butterworth, Chemical Industry Institute of Toxi-
cology, Research Triangle Park, North Carolina, USA

- Dr P.S. Chauhan, Bio-Medical Group, Bhabha Atomic Research Centre, Bombay, India
- Dr I. Chouroulinkov, Unité de Cancérogénèse Expérimentale et de Toxicologie Génétique (E.R. 304) I.R.S.C.-C.N.R.S., Villejuif, France
- Dr M.G. Clare, Shell Research Ltd, Sittingbourne, Kent, United Kingdom
- Dr R.D. Combes, School of Biological Sciences, Portsmouth Polytechnic, Portsmouth, United Kingdom
- Dr C. Coton, Mammalian Genetics Laboratory, Department of Biology, European Nuclear Centre, Mol, Belgium
- Dr R. Crebelli, Higher Institute of Health, Viale Regina Elena, Rome, Italy
- Dr B.J. Dean, Upchurch, Sittingbourne, Kent, United Kingdom
- Dr G.M. Decad, Department of Materials Toxicology, IBM Corporation, San Jose, California, USA
- Dr F.J. de Serres, National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina, USA
- Dr D.J. Doolittle, Toxicology Research, Bowman Gray Technical Center, R.J. Reynolds Co., Winston-Salem, North Carolina, USA
- Dr U.H. Ehling, Mammalian Genetics Institute, Association for Radiation and Environmental Research, Neuherberg, Federal Republic of Germany
- Dr B.M. Elliott, Genetic Toxicology Section, Imperial Chemical Industries PLC, Macclesfield, Cheshire, United Kingdom
- Dr R. Fahrig, Fraunhofer Institute for Research on Toxicology and Aerosols, Hannover, Federal Republic of Germany
- Dr R. Forster, Life Science Research, Rome Toxicology Centre, Pomezia, Rome, Italy
- Dr K. Fujikawa, Drug Safety Evaluation Laboratories, Central Research Division, Takeda Chemical Industries Ltd, Osaka, Japan
- Dr C. Furihata, Department of Molecular Oncology, Institute of Medical Science, University of Tokyo, Tokyo, Japan
- Dr S.M. Galloway, Merck Sharp & Dohme Research Laboratories, West Point, Pennsylvania, USA
- Dr W.M. Generoso, Biology Division, Oak Ridge National Laboratory, Oak Ridge, Tennessee, USA
- Dr H.P. Glauert, McArdle Laboratory for Cancer Research, University of Wisconsin, Madison, Wisconsin, USA
- Dr U. Graf, Toxicology Institute, Zurich Federal Polytechnic and University, Zurich, Switzerland
- Dr B.L. Harper, Division of Environmental Toxicology, University of Texas Medical Branch, Galveston, Texas, USA
- Dr G.G. Hatch, Toxicology Division, Northrop Services Inc., Environmental Sciences, Research Triangle Park, North Carolina, USA
- Dr M. Hayashi, Biological Safety Research Centre, National Institute of Hygienic Sciences, Tokyo 158, Japan
- Dr R.M. Hicks, School of Pathology, Middlesex Hospital Medical School, London, United Kingdom
- Dr J.M. Hunt, Department of Pathology and Laboratory Medicine, University of Texas Medical School, Houston, Texas, USA
- Dr N. Inui, Biological Research Centre, Japan Tobacco Inc., Kanagawa, Japan
- Dr M. Ishidate, Jr., Biological Safety Research Centre, National Institute of Hygienic Sciences, Tokyo, Japan
- Dr V.I. Ivanov, Institute of Medical Genetics, Academy of

- Medical Sciences, Moscow, USSR
- Dr J.C. Jensen, National Food Institute, Institute of Toxicology, Copenhagen, Denmark
- Dr D. Jenssen, Department of Genetic Toxicology, Wallenberg Laboratory, University of Stockholm, Stockholm, Sweden
- Dr B.J. Kilbey, Institute of Animal Genetics, University of Edinburgh, Edinburgh, United Kingdom
- Dr I. Kimber, Central Toxicology Laboratory, Imperial Chemical Industries PLC, Macclesfield, Cheshire, United Kingdom
- Dr U. Kliesch, Mammalian Genetics Institute, Association for Radiation and Environmental Research, Neuherberg, Federal Republic of Germany
- Dr A.D. Kligerman, Environmental Health Research and Testing Inc., Research Triangle Park, North Carolina, USA
- Dr D. Kornbrust, Merck Sharp & Dohme Research Laboratories, Department of Safety Assessment, West Point, Pennsylvania, USA
- Dr C. Lasne, Unité de Cancérogénèse Expérimentale et de Toxicologie Génétique (ER-304) I.R.S.C.-C.N.R.S., Villejuif, France
- Dr A. Léonard, Mammalian Genetics Laboratory, Department of Biology, European Nuclear Centre, Mol, Belgium
- Dr C.A. Luke, Medical Department, Brookhaven National Laboratory, Upton, New York, USA
- Dr J.T. MacGregor, US Department of Agriculture, Western Regional Research Center, Berkeley, California, USA
- Dr A.M. Malashenko, Scientific Research Laboratory of Experimental Biological Models of the Academy of Medical Sciences of the USSR, Moscow Region, USSR
- Dr C. Malaveille, International Agency for Research on Cancer, Lyon, France
- Dr B.H. Margolin, Biometry and Risk Assessment Program, National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina, USA
- Dr D. McGregor, Developmental Toxicology, Inveresk Research International Ltd, Musselburgh, United Kingdom
- Dr A.L. Meyer, Shell Research Ltd, Sittingbourne, Kent, United Kingdom
- Dr J.C. Mirsalis, Cellular and Genetic Toxicology Department, SRI International, Menlo Park, California, USA
- Dr N. Nashed, Johann Wolfgang Goethe-Universität, Frankfurt am Main, Federal Republic of Germany
- Dr S.B. Neal, Toxicology Division, Lilly Research Laboratory, Greenfield, Indiana, USA
- Dr A. Neuhäuser-Klaus, Mammalian Genetics Institute, Association for Radiation and Environmental Research, Neuherberg, Federal Republic of Germany
- Dr D.A. Pagano, Cellular and Genetic Toxicology Branch, Toxicology Research and Testing Program, National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina, USA
- Dr F. Palitti, Evolutionary Genetics Centre of the National Research Council, Genetics and Molecular Biology Department, University City, Rome, Italy
- Dr S. Parodi, Chemical Carcinogenesis Laboratory, National Cancer Research Institute, Genoa, Italy
- Dr M. Pereira, Health Effects Research Laboratory, US Environmental Protection Agency, Cincinnati, Ohio, USA
- Dr J. Pot-Deprun, Unité de Cancérogénèse Expérimentale et Toxicologie Génétique (ER-304) I.R.S.C.- C.N.R.S. Laboratoires de Recherche Appliquée sur le Cancer,

Villejuif, France

- Dr G.S. Probst, Toxicology Division, Lilly Research Laboratories, Greenfield, Indiana, USA
- Dr C. Ramel, Wallenberg Laboratory, University of Stockholm, Stockholm, Sweden
- Dr K. Randerath, Baylor College of Medicine, Department of Pharmacology, Houston, Texas, USA
- Dr H.S. Rosenkranz, Department of Environmental Health Sciences, Case Western Reserve University, Cleveland, Ohio, USA
- Dr P. Russo, National Cancer Research Institute, Genoa, Italy
- Dr M.F. Salamone, Moe-Biohazard Laboratory, Rexdale, Ontario, Canada
- Dr C.B. Salocks, Department of Materials Toxicology, IBM Corporation, San Jose, California, USA
- Dr J. Schöneich, Central Institute for Genetics and for Research on Cultivated Plants, Academy of Science of the German Democratic Republic, Gatersleben, German Democratic Republic
- Dr A.G. Searle, Medical Research Council Radiobiology Unit, Harwell, Didcot, United Kingdom
- Dr G.A. Sega, Biology Division, Oak Ridge National Laboratory, Oak Ridge, Tennessee, USA
- Dr M.D. Shelby, Cellular and Genetic Toxicology Branch, Toxicology Research and Testing Program, National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina, USA
- Dr H. Shibuya, Laboratory of Genetic Toxicology, Hatano Research Institute, Food and Drug Safety Center, Kanagawa, Japan
- Dr T. Shibuya, Laboratory of Genetics, Hatano Research Institute, Food and Drug Safety Center, Kanagawa, Japan
- Dr R.H. Stevens, Radiation Research Laboratory, Department of Radiation, University of Iowa, Iowa, USA
- Dr G.D. Stoner, Department of Pathology, Medical College of Ohio, Toledo, Ohio, USA
- Dr J.A. Styles, Central Toxicology Laboratory, Imperial Chemical Industries PLC, Macclesfield, Cheshire, United Kingdom
- Dr K.E. Suter, Preclinical Research, Toxicology Department, Sandoz Limited, Basel, Switzerland
- Dr A. D. Tates, Department of Radiation Genetics and Chemical Mutagenesis, State University of Leiden, Leiden, Netherlands
- Dr R.R. Tice, Medical Department, Brookhaven National

预览已结束，完整报告链接和二维码如下：

https://www.yunbaogao.cn/report/index/report?reportId=5_30762

