# IARC MONOGRAPHS



## 1,1,1-TRICHLOROETHANE AND FOUR OTHER INDUSTRIAL CHEMICALS

VOLUME 130

IARC MONOGRAPHS ON THE IDENTIFICATION OF CARCINOGENIC HAZARDS TO HUMANS

International Agency for Research on Cancer



# IARC MONOGRAPHS

## 1,1,1-TRICHLOROETHANE AND FOUR OTHER INDUSTRIAL CHEMICALS

VOLUME 130

This publication represents the views and expert opinions of an IARC Working Group on the Identification of Carcinogenic Hazards to Humans, which met remotely, 7–22 October 2021

LYON, FRANCE - 2022

IARC MONOGRAPHS ON THE IDENTIFICATION OF CARCINOGENIC HAZARDS TO HUMANS

International Agency for Research on Cancer



### IARC MONOGRAPHS

In 1969, the International Agency for Research on Cancer (IARC) initiated a programme on the evaluation of the carcinogenic hazard of chemicals to humans, involving the production of critically evaluated monographs on individual chemicals. The programme was subsequently expanded to include evaluations of carcinogenic hazards associated with exposures to complex mixtures, lifestyle factors and biological and physical agents, as well as those in specific occupations. The objective of the programme is to elaborate and publish in the form of monographs critical reviews of data on carcinogenicity for agents to which humans are known to be exposed and on specific exposure situations; to evaluate these data in terms of cancer hazard to humans with the help of international working groups of experts in carcinogenesis and related fields; and to identify gaps in evidence. The lists of IARC evaluations are regularly updated and are available on the internet at <a href="https://monographs.iarc.who.int/">https://monographs.iarc.who.int/</a>.

This programme has been supported since 1982 by Cooperative Agreement U01 CA33193 with the United States National Cancer Institute, Department of Health and Human Services. Additional support has been provided since 1986 by the European Commission Directorate-General for Employment, Social Affairs, and Inclusion, initially by the Unit of Health, Safety and Hygiene at Work, and since 2014 by the European Union Programme for Employment and Social Innovation "EaSI" (for further information please consult: <a href="https://ec.europa.eu/social/easi">https://ec.europa.eu/social/easi</a>). Support has also been provided since 1992 by the United States National Institute of Environmental Health Sciences, Department of Health and Human Services. The contents of this volume are solely the responsibility of the Working Group and do not necessarily represent the official views of the United States National Cancer Institute, the United States National Institute of Environmental Health Sciences, the United States Department of Health and Human Services, or the European Commission.



Co-funded by the European Union

Published by the International Agency for Research on Cancer, 150 cours Albert Thomas, 69372 Lyon Cedex 08, France ©International Agency for Research on Cancer, 2022 Online publication, August 2022

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.

*IARC Monographs* (and Corrigenda) are published online at <u>https://publications.iarc.fr</u>. To report an error, please contact: <u>imo@iarc.who.int</u>.

Distributed by WHO Press, World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland (tel.: +41 22 791 3264; fax: +41 22 791 4857; website: https://apps.who.int/bookorders; email: bookorders@who.int).

Permissions and rights: Some rights reserved. This work is available under the Creative Commons Attribution-NonCommercial-NoDerivs 3.0 IGO licence (CC BY-NC-ND 3.0 IGO; https://creativecommons.org/licenses/by-nc-nd/3.0/igo/). Under the terms of this licence, you may copy and redistribute the work for non-commercial purposes, provided the work is appropriately cited, as indicated below. In any use of this work, there should be no suggestion that WHO endorses any specific organization, products, or services. The use of the WHO logo is not permitted. Any mediation relating to disputes arising under the licence shall be conducted in accordance with the mediation rules of the World Intellectual Property Organization.

To submit requests for adaptations or commercial use and queries on rights and licensing, see the IARC Publications website (<u>https://publications.iarc.fr/Rights-And-Permissions</u>).

Third-party materials: If you wish to reuse material from this work that is attributed to a third party, such as tables, figures or images, it is your responsibility to determine whether permission is needed for that reuse and to obtain permission from the copyright holder. The risk of claims resulting from infringement of any third-party-owned component in the work rests solely with the user.

General disclaimers: 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 WHO 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.

All reasonable precautions have been taken by WHO to verify the information contained in this publication. However, the published material is being distributed without warranty of any kind, either expressed or implied. The responsibility for the interpretation and use of the material lies with the reader. In no event shall WHO or contributing agencies be liable for damages arising from its use.

The IARC Monographs Working Group alone is responsible for the views expressed in this publication.



About the cover: Worker applying a yellow epoxy protective resin to a floor. 1,1,1-Trichloroethane, *N*-methylolacrylamide, and isophorone are used in commercial resins.

Source: © AdobeStock.com/Doralin

How to cite: IARC (2022). 1,1,1-Trichloroethane and four other industrial chemicals. *IARC Monogr Identif Carcinog Hazards Hum*. 130:1–368.

### IARC Library Cataloguing-in-Publication Data

Names: IARC Working Group on the Identification of Carcinogenic Hazards to Humans.

Title: 1,1,1-Trichloroethane and four other industrial chemicals.

Description: Lyon: International Agency for Research on Cancer, 2022. | Series: IARC monographs on the identification of carcinogenic hazards to humans, ISSN 1017-1606; v. 130. | "This publication represents the views and expert opinions of an IARC Working Group on the Identification of Carcinogenic Hazards to Humans, which met remotely, 7–22 October 2021." | Includes bibliographical references.

Identifiers: ISBN 9789283201700 (pbk.) | ISBN 9789283201977 (ebook)

Subjects: MESH: Carcinogens--toxicity. | Neoplasms--chemically induced. | Trichloroethanes--adverse effects. | Phenylhydrazines--adverse effects. | Diphenylamine--adverse effects. | Acrylamides--adverse effects. | Cyclohexanones--adverse effects. | Risk Factors.

Classification: NLM W1



This volume of the *IARC Monographs* provides evaluations of the carcinogenicity of five industrial chemicals: 1,1,1-trichloroethane, 1,2-diphenylhydrazine, diphenylamine, *N*-methylolacrylamide, and isophorone.

1,1,1-Trichloroethane was used extensively until the 1990s as a solvent, metal degreaser, chemical intermediate. Since the Montreal Protocol on Substances that Deplete the Ozone Layer, production and use have dwindled, and it is now mostly used as a chemical feedstock in closed systems and for "essential uses". Poorly documented non-essential uses might occur in low-income and middle-income countries.

1,2-Diphenylhydrazine was primarily used as an intermediate in the manufacture of benzidine dyes, which has ceased in the USA and European Union, although production might occur elsewhere. Additional uses include as an intermediate in drug manufacture.

Diphenylamine, *N*-methylolacrylamide, and isophorone are High Production Volume chemicals and intermediates used for a wide range of industrial applications. The use of diphenylamine in agrochemicals to prevent fruit scalding is prohibited in the European Union, but ongoing in the USA and elsewhere. Isophorone has been detected in numerous polymer-based products from food packaging to aquatic inflatables, and in food items, possibly because of agrochemical contamination or migration from packaging.

For all agents, data were sparse regarding exposure levels (apart from 1,1,1-trichloroethane, for which data were available mainly on exposures pre-dating the adoption of the Montreal Protocol), but indicated that exposures are higher in occupational situations than in the general population.

An *IARC Monographs* Working Group reviewed evidence from cancer studies in humans (available for 1,1,1-trichloroethane), cancer bioassays in experimental animals, and mechanistic studies to assess the carcinogenic hazard to humans of exposure to these agents and concluded that:

- 1,1,1-Trichloroethane is probably carcinogenic to humans (Group 2A)
- 1,2-Diphenylhydrazine, diphenylamine, *N*-methylolacrylamide, and isophorone are possibly carcinogenic to humans (Group 2B).



© AdobeStock.com/Doralin