

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 World Health Organization, the International Labour Organization or the United Nations Environment Programme.

Harmonization Project Document No. 5

SKIN SENSITIZATION IN CHEMICAL RISK ASSESSMENT

This project was conducted within the IPCS project on the Harmonization of Approaches to the Assessment of Risk from Exposure to Chemicals.

Published under the joint sponsorship of the World Health Organization, the International Labour Organization and the United Nations Environment Programme, and produced within the framework of the Inter-Organization Programme for the Sound Management of Chemicals.

The **International Programme on Chemical Safety (IPCS)**, established in 1980, is a joint venture of the United Nations Environment Programme (UNEP), the International Labour Organization (ILO) and the World Health Organization (WHO). The overall objectives of the IPCS are to establish the scientific basis for assessment of the risk to human health and the environment from exposure to chemicals, through international peer review processes, as a prerequisite for the promotion of chemical safety, and to provide technical assistance in strengthening national capacities for the sound management of chemicals.

The **Inter-Organization Programme for the Sound Management of Chemicals (IOMC)** was established in 1995 by UNEP, ILO, the Food and Agriculture Organization of the United Nations, WHO, the United Nations Industrial Development Organization, the United Nations Institute for Training and Research and the Organisation for Economic Co-operation and Development (Participating Organizations), following recommendations made by the 1992 UN Conference on Environment and Development to strengthen cooperation and increase coordination in the field of chemical safety. The purpose of the IOMC is to promote coordination of the policies and activities pursued by the Participating Organizations, jointly or separately, to achieve the sound management of chemicals in relation to human health and the environment.

WHO Library Cataloguing-in-Publication Data

Skin sensitization in chemical risk assessment.

(IPCS harmonization project document ; no. 5)

1.Radiodermatitis. 2.Dermatitis, Allergic contact. 3.Chemicals - toxicity. 4.Risk assessment.
I.International Programme on Chemical Safety. II.Series.

ISBN 978 92 4 156360 4

(NLM classification: WR 160)

© **World Health Organization 2008**

All rights reserved. Publications of the World Health Organization can be obtained from WHO Press, World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland (tel.: +41 22 791 2476; fax: +41 22 791 4857; e-mail: bookorders@who.int). Requests for permission to reproduce or translate WHO publications—whether for sale or for non-commercial distribution—should be addressed to WHO Press, at the above address (fax: +41 22 791 4806; e-mail: permissions@who.int).

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 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. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

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.

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

TABLE OF CONTENTS

FOREWORD	1
ACKNOWLEDGEMENTS.....	2
LIST OF CONTRIBUTORS	3
LIST OF ACRONYMS AND ABBREVIATIONS	6
SKIN SENSITIZATION IN CHEMICAL RISK ASSESSMENT: REPORT OF A WHO/IPCS INTERNATIONAL WORKSHOP FOCUSING ON DOSE–RESPONSE ASSESSMENT.....	8
<i>H. Van Loveren, A. Cockshott, T. Gebel, U. Gundert-Remy, W.H. De Jong, J. Matheson, H. McGarry, L. Musset, M.K. Selgrade, and C. Vickers</i>	
APPENDIX A: ABSTRACTS.....	21
The use of human data when conducting dermal sensitization quantitative risk assessments for fragrance ingredients.....	22
<i>A.M. Api</i>	
Application of the local lymph node assay (LLNA) for respiratory sensitizers	29
<i>J.H.E. Arts, W.H. De Jong, H. Van Loveren, and C.F. Kuper</i>	
Information derived from sensitization test methods: test sensitivity, false positives, and false negatives	32
<i>D. Basketter</i>	
Skin sensitization—a regulatory overview	36
<i>A. Cockshott</i>	
Quantification, potency, and risk assessment: induction versus elicitation.....	40
<i>G.F. Gerberick</i>	
Uncertainty factors and risk assessment for skin sensitizers	46
<i>P. Griem</i>	
Hazard identification (human data)	54
<i>J.D. Johansen</i>	
Clinical experience informing risk assessment.....	58
<i>C. Lidén</i>	

Perspective of the United States Environmental Protection Agency’s Office of Pesticide Programs on assessment of dermal sensitization risk using hexavalent chromium as a case-study	63
<i>T.F. McMahon and J. Chen</i>	
New approaches for skin sensitization hazard identification: (Q)SARs/expert systems	66
<i>G. Patlewicz</i>	
New approaches for hazard identification: the development of in vitro methods for predicting contact sensitization potential.....	71
<i>C.A. Ryan</i>	
Sensitization potency of chemicals.....	76
<i>M. Takeyoshi</i>	
New approaches to hazard identification: non-radioactive alternatives	80
<i>H.-W. Vohr</i>	

FOREWORD

Harmonization Project Documents are a family of publications by the World Health Organization (WHO) under the umbrella of the International Programme on Chemical Safety (IPCS) (WHO/ILO/UNEP). Harmonization Project Documents complement the Environmental Health Criteria (EHC) methodology (yellow cover) series of documents as authoritative documents on methods for the risk assessment of chemicals.

The main impetus for the current coordinated international, regional and national efforts on the assessment and management of hazardous chemicals arose from the 1992 United Nations Conference on Environment and Development (UNCED). UNCED Agenda 21, Chapter 19, provides the “blueprint” for the environmentally sound management of toxic chemicals. This commitment by governments was reconfirmed at the 2002 World Summit on Sustainable Development and in 2006 in the Strategic Approach to International Chemicals Management (SAICM). The IPCS project on the Harmonization of Approaches to the Assessment of Risk from Exposure to Chemicals (Harmonization Project) is conducted under Agenda 21, Chapter 19, and contributes to the implementation of SAICM. In particular, the project addresses the SAICM objective on Risk Reduction and the SAICM Global Plan of Action activity to “Develop and use new and harmonized methods for risk assessment”.

The IPCS Harmonization Project goal is *to improve chemical risk assessment globally, through the pursuit of common principles and approaches, and, hence, strengthen national and international management practices that deliver better protection of human health and the environment within the framework of sustainability*. The Harmonization Project aims to harmonize global approaches to chemical risk assessment, including by developing international guidance documents on specific issues. The guidance is intended for adoption and use in countries and by international bodies in the performance of chemical risk assessments. The guidance is developed by engaging experts worldwide. The project has been implemented using a stepwise approach, first sharing information and increasing understanding of methods and practices used by various countries, identifying areas where convergence of different approaches would be beneficial and then developing guidance that enables implementation of harmonized approaches. The project uses a building block approach, focusing at any one time on the aspects of risk assessment that are particularly important for harmonization.

The project enables risk assessments (or components thereof) to be performed using internationally accepted methods, and these assessments can then be shared to avoid duplication and optimize use of valuable resources for risk management. It also promotes sound science as a basis for risk management decisions, promotes transparency in risk assessment and reduces unnecessary testing of chemicals. Advances in scientific knowledge can be translated into new harmonized methods.

This ongoing project is overseen by a geographically representative Harmonization Project Steering Committee and a number of ad hoc working groups that manage the detailed work. Finalization of documents includes a rigorous process of international peer review and public comment.

ACKNOWLEDGEMENTS

IPCS thanks the workshop chair (Ursula Gundert-Remy) and rapporteur (Henk Van Loveren) as well as the following Planning Group members for their assistance in workshop preparations: Amanda Cockshott, Peter Evans, Laurence Musset, and MaryJane Selgrade.

Full workshop participants were Kristiina Alanko, Helsinki, Finland; Klaus Ejner Andersen, Odense, Denmark; Josje H.E. Arts, Zeist, Netherlands; Jonathan Chen, Washington, DC, United States of America (USA); Amanda Cockshott, Bootle, United Kingdom; Wim H. De Jong, Bilthoven, Netherlands; Jeanne Duus Johansen, Hellerup, Denmark; Tom Gebel, Dortmund, Germany; An Goossens, Leuven, Belgium; Ursula Gundert-Remy, Berlin, Germany; Paul Harvey, Sydney, Australia; Abigail Jacobs, Silver Spring, MD, USA; Carola Lidén, Stockholm, Sweden; Joanna M. Matheson, Bethesda, MD, USA; Tim McMahon, Research Triangle Park, NC, USA; MaryJane Selgrade, Research Triangle Park, NC, USA; Masahiro Takeyoshi, Saitana, Japan; Henk Van Loveren, Bilthoven, Netherlands; and Marilyn L. Wind, Bethesda, MD, USA.

The following workshop participants employed by a commercial entity with an interest in the workshop topic were observers during the final plenary session of the workshop on “Agreement of workshop conclusions and recommendations”: Anne Marie Api, Woodcliff Lake, NJ, USA; Peter Griem, Sulzbach, Germany; Erwin L. Roggen, Bagsvaerd, Denmark; Cindy Ryan, Cincinnati, OH, USA; and Hans-Werner Vohr, Wuppertal-Elberfeld, Germany.

The following workshop participants representing organizations were observers during the final plenary session of the workshop on “Agreement of workshop conclusions and recommendations”: Laurence Musset, Paris, France (Organisation for Economic Co-operation and Development); David Basketter, Sharnbrook Beds, United Kingdom (European Centre for Toxicology & Ecotoxicology of Chemicals); Michael P. Holsapple, Washington, DC, USA (International Life Sciences Institute); Grace Tier-Patlewicz, Ispra, Italy (European Commission/Joint Research Centre); and Pauline McNamee, Egham, United Kingdom (The European Cosmetic Toiletry and Perfumery Association).

The WHO Secretariat consisted of Carolyn Vickers, Geneva, Switzerland; and Helen McGarry, Bootle, United Kingdom.

LIST OF CONTRIBUTORS

Workshop Report

Amanda Cockshott
Health and Safety Executive, Bootle, United Kingdom

Wim H. De Jong
National Institute of Public Health and the Environment (RIVM), Bilthoven, Netherlands

Tom Gebel
Federal Institute for Occupational Safety and Health, Dortmund, Germany

Ursula Gundert-Remy
Federal Institute for Risk Assessment (BfR), Berlin, Germany

Joanna Matheson
Consumer Product Safety Commission, Bethesda, Maryland, USA

Helen McGarry
Health and Safety Executive, Bootle, United Kingdom

Laurence Musset
Environment Directorate, Organisation for Economic Co-operation and Development, Paris, France

MaryJane K. Selgrade
Environmental Protection Agency, Research Triangle Park, North Carolina, USA

Henk Van Loveren
National Institute of Public Health and the Environment (RIVM), Bilthoven, Netherlands

Carolyn Vickers
International Programme on Chemical Safety, World Health Organization, Geneva, Switzerland

Abstracts

Anne Marie Api
Research Institute for Fragrance Materials, Inc. (RIFM), Woodcliff Lake, New Jersey, USA

J.H.E. Arts
TNO Quality of Life, Zeist, Netherlands

David Basketter

Unilever Safety and Environmental Assurance Centre, Sharnbrook, Bedford, United Kingdom

Jonathan Chen

Antimicrobials Division, Office of Pesticide Programs, Environmental Protection Agency, Washington, DC, USA

Amanda Cockshott

Health & Safety Executive, Merseyside, United Kingdom

W.H. De Jong

National Institute for Public Health and the Environment (RIVM), Bilthoven, Netherlands

Jeanne Duus Johansen

National Allergy Research Centre, Gentofte Hospital, University of Copenhagen, Copenhagen, Denmark

G. Frank Gerberick

The Procter & Gamble Company, Cincinnati, Ohio, USA

Peter Griem

Corporate Product Safety, Clariant Produkte (Deutschland) GmbH, Sulzbach, Germany

C.F. Kuper

TNO Quality of Life, Zeist, Netherlands

Carola Lidén

Stockholm Centre for Public Health and Karolinska Institutet, Stockholm, Sweden

Timothy F. McMahon

Antimicrobials Division, Office of Pesticide Programs, Environmental Protection Agency, Washington, DC, USA

Grace Patlewicz

European Chemicals Bureau, Joint Research Centre, European Commission, Ispra, Italy

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_29505

