

Pesticide residues in food — 2005

**Joint FAO/WHO Meeting on
Pesticide Residues**

EVALUATIONS 2005

Part II — Toxicological

IPCS International Programme on Chemical Safety



**Food and Agriculture
Organization of the United
Nations**



**World Health
Organization**

Pesticide residues in food — 2005

Toxicological evaluations

**Sponsored jointly by FAO and WHO
With the support of the International Programme
on Chemical Safety (IPCS)**

**Joint Meeting of the
FAO Panel of Experts on Pesticide Residues
in Food and the Environment
and the
WHO Core Assessment Group**

Geneva, Switzerland, 20–29 September 2005

The summaries and evaluations contained in this book are, in most cases, based on unpublished proprietary data submitted for the purpose of the JMPR assessment. A registration authority should not grant a registration on the basis of an evaluation unless it has first received authorization for such use from the owner who submitted the data for JMPR review or has received the data on which the summaries are based, either from the owner of the data or from a second party that has obtained permission from the owner of the data for this purpose.

WHO Library Cataloguing-in-Publication Data

Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group (2005 : Geneva, Switzerland) Pesticide residues in food – 2005 : toxicological evaluations / Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group, Geneva, Switzerland, 20–29 September 2005.

Sponsored jointly by FAO and WHO with the support of the International Programme on Chemical Safety (IPCS).
Cover title: Pesticide residues in food 2005 : evaluations. Part 2, Toxicological.

1. Pesticide residues – toxicity. 2. No-observed-adverse-effect level. 3. Food contamination. I. FAO Panel of Experts on Pesticide Residues in Food and the Environment. II. WHO Core Assessment Group on Pesticide Residues. III. Title. IV. Title: Toxicological evaluations. V. Title: Pesticide residues in food 2005 : evaluations. Part 2, Toxicological.

ISBN 92 4 166521 1

(NLM classification: WA 240)

ISBN 978 92 4 166521 6

This report contains the collective views of two international groups of experts and does not necessarily represent the decisions nor the stated policy of the Food and Agriculture Organization of the United Nations or the World Health Organization.

The preparatory work for the toxicological evaluations of pesticide residues carried out by the WHO Expert Group on Pesticide Residues for consideration by the FAO/WHO Joint Meeting on Pesticide Residues in Food and the Environment is actively supported by the International Programme on Chemical Safety 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 assessing the risk to human health and the environment to exposure from 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, the Food and Agriculture Organization of the United Nations, WHO, the United Nations Industrial Development Organization, and the Organisation for Economic Co-operation and Development (Participating Organizations), following recommendations made by the 1992 United Nations Conference on the 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.

© World Health Organization 2006

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 3264; fax: +41 22 791 4857; e-mail: bookorders@who.int). Requests for permission to reproduce or translate WHO publications – whether for sale or for noncommercial 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 expressed 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.

This publication 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.

Printed in: United Kingdom

TABLE OF CONTENTS

	Page
List of participants.....	vii
Abbreviations	xi
Introduction	xiii
Toxicological evaluations	
Acephate.....	3
Azocyclotin**	17
Benalaxyl**	39
Carbendazim.....	87
Chlorpropham.....	107
Clofentezine**	115
Cyhexatin**	149
Dimethanamid-P/racemic dimethenamid*	189
Ethoxyquin	241
Fenhexamid*	255
Imazalil.....	303
Indoxacarb*	315
Novaluron*	357
Propamocarb**	417
Sulfuryl fluoride*	453
Annex 1. Reports and other documents resulting from previous Joint Meetings of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Groups on Pesticide Residues	523

* First full evaluation

** Evaluated within the periodic review programme of the Codex Committee on Pesticide Residues

**2005 Joint Meeting of the FAO Panel of Experts on
Pesticide Residues in Food and the Environment
and the WHO Core Assessment Group**

Geneva, 20–29 September 2005

PARTICIPANTS

FAO Panel of Experts on Pesticide Residues in Food and the Environment

Dr Ursula Banasiak, Federal Institute for Risk Assessment, Thielallee 88-92, D-14195 Berlin, Germany

Tel.: (49 30) 8412 3337; Fax: (49 30) 8412 3894; E-mail: u.banasiak@bfr.bund.de

Dr Eloisa Dutra Caldas, University of Brasilia, College of Health Sciences, Pharmaceutical Sciences Department, Campus Universitário Darci Ribeiro, 70919-970 Brasília/DF, Brazil

Tel.: (55 61) 307 3671; Fax: (55 61) 273 0105; E-mail: eloisa@unb.br

Dr Stephen Funk, Health Effects Division, United States Environmental Protection Agency, 1200 Pennsylvania Ave NW, 7509C, Washington, DC 20460, USA (*Vice-Chairman*)

Tel.: (1 703) 305 5430; Fax: (1 703) 305 0871; E-mail: funk.steve@epa.gov

Mr Denis J. Hamilton, Principal Scientific Officer, Biosecurity, Department of Primary Industries and Fisheries, PO Box 46, Brisbane, QLD 4001, Australia

Tel.: (61 7) 3239 3409; Fax: (61 7) 3211 3293; E-mail: denis.hamilton@dpi.qld.gov.au

Dr Bernadette C. Ossendorp, Centre for Substances and Integrated Risk Assessment, National Institute of Public Health and the Environment (RIVM), Antonie van Leeuwenhoeklaan 9, PO Box 1, 3720 BA Bilthoven, Netherlands

Tel.: (31 30) 274 3970; Fax: (31 30) 274 4475; E-mail: bernadette.ossendorp@rivm.nl

Dr Yukiko Yamada, Director, Food Safety and Consumer Policy Division, Food Safety and Consumer Affairs Bureau, Ministry of Agriculture, Forestry and Fisheries, 1-2-1

Kasumigaseki, Tokyo 100-8950, Japan

Tel.: (+81 3) 3502 8111 (ext. 3060)/(+81 3) 3591 4963 (direct); Fax: (+81 3) 3597 0329; E-mail: yukiko_yamada@nm.maff.go.jp

Toxicological Core Assessment Group

Professor Alan R. Boobis, Experimental Medicine & Toxicology, Division of Medicine, Faculty of Medicine, Imperial College London, Hammersmith Campus, Duane Road, London W12 0NN, England (*Chairman*)

Tel.: (44 20) 8383 3221; Fax: (44 20) 8383 2066; E-mail: a.boobis@imperial.ac.uk

Dr Les Davies, Senior Advisor Toxicology, Office of Chemical Safety, Therapeutic Goods Administration, Australian Department of Health and Ageing, PO Box 100, Woden, ACT 2606, Australia

Tel.: (61 2) 6829 3204; Fax: (61 2) 6289 3299; E-mail: les.davies@health.gov.au

Dr Vicki L. Dellarco, United States Environmental Protection Agency, Office of Pesticide Programs (7509C), Health Effects Division, 1200 Pennsylvania Avenue NW, Washington, DC 20460, USA (*WHO Rapporteur*)

Tel.: (1 703) 305 1803; Fax: (1 703) 305 5147; E-mail: dellarco.vicki@epa.gov

Dr Helen Hakansson, Institute of Environmental Medicine, Karolinska Institute, Unit of Environmental Health Risk Assessment, Box 210, Nobels väg 13, S-171 77 Stockholm, Sweden

Tel.: (46 8) 5248 7527; Fax: (46 8) 3438 49; E-mail: Helen.Hakansson@ki.se

Dr Angelo Moretto, Dipartimento Medicina Ambientale e Sanità Pubblica, Università di Padova, Via Giustiniani 2, 35128 Padova, Italy

Tel.: (39 049) 821 1377/2541; Fax: (39 049) 821 2550/2542; E-mail: angelo.moretto@unipd.it

Dr Roland Solecki, Safety of Substances and Preparations — Coordination and Overall Development, Federal Institute for Risk Assessment, Thielallee 88-92, D-14195 Berlin

Tel.: (49 30) 8412 3232; Fax: (49 30) 8412 3260; E-mail: r.solecki@bfr.bund.de

Dr Maria Tasheva, National Center of Public Health Protection (NCPHP), 15, Iv. Ev. Geshov boulevard, 1431 Sofia, Bulgaria

Tel.: (3592) 954 11 97; Fax: (3592) 954 11 97; E-mail: mtasheva@aster.net

Secretariat

Dr Arpad Ambrus, Central Service for Plant Protection and and Soil Conservation, Plant and Soil Protection Directorate, Budaörsi ut 141-145, H-1118 Budapest, Hungary (*FAO Consultant*)

Tel.: (36 1) 309 1003; Fax: (36 1) 246 2955; E-mail: ambrus.arpad@ontsz.hu

Dr Hong Chen, Coordinator, IR-4 Project, Rutgers University, 681 US Highway #1 South , North Brunswick, NJ 08902-3390, USA (*FAO Consultant*)

Tel. (1 732) 932 9575 ext 627; Fax: (1 732) 932 8481 ; E-mail: hchen@AESOP.Rutgers.edu

Mr Bernard Declercq, 13 impasse du court Riage, 91360 Epinay sur Orge, France (*FAO Consultant*)

Tel.: (33 1) 64488369; Fax: (33 1) 64488369; E-mail: bernard-declercq@wanadoo.fr

Dr Ian C. Dewhurst, Pesticides Safety Directorate, Mallard House, King's Pool 3 Peasholme Green, York YO1 7PX, England (*WHO Temporary Adviser*)

Tel.: (44 1904) 455 890; Fax: (44 1904) 455 711; E-mail: ian.dewhurst@psd.defra.gsi.gov.uk

Dr Salwa Dogheim, Central Laboratory of Residue Analysis of Pesticides and Heavy Metals in Food, Agriculture Research Center, Ministry of Agriculture, 7 Mahalla Street, Heliopolis, Cairo, Egypt (*FAO Consultant*)

Tel.: (2012) 215 5201; Fax: (2012) 418 2814 ; E-mail: s.dogheim@link.net

Dr Ronald David Eichner, 13 Cruikshank Street, Wanniasa ACT 2903, Australia (*FAO Editor*)

Tel.: (61 2) 629 62118; Fax: (61 2) 629 46564; E-mail: eichners@tpg.com.au

Dr Roberto H. Gonzalez, University of Chile, College of Agricultural Sciences, PO Box 1004, Santiago, Chile (*FAO Consultant*)

Tel.: (56 2) 978 5812/978 5714; Fax: (56 2) 541 7055 ; E-mail: rgonzale@abello.dic.uchile.cl and rgonzale@uchile.cl

Dr P.K. Gupta, Director, Toxicology Consulting Services Inc., C-44 Rajinder nagar, Bareilly 243 122 (UP), India (*WHO Temporary Adviser*)

Tel.: (91 581) 2300 628/ mobile 0935 9104 922; Fax: E-mail: drpkg_brly@sancharnet.in

Dr Yibing He, Pesticide Residue Division, Institute for the Control of Agrochemicals, Ministry of Agriculture, Building 22, Maizidian Street, Chaoyang District, Beijing 100026, China (*FAO Consultant*)

Tel.: (86 10) 659 36997; Fax: (86 10) 641 94017; E-mail: heyibing@agri.gov.cn

Mr Yasuo Kitamura, Agricultural Chemicals Inspection Station, 2-772 Suzuki-Cho, Kodaira-Shi, Tokyo, 187-0011 Japan (*FAO Consultant*)

Tel.: (+81 42) 383 2151; Fax: (+8142) 385 3361; E-mail: kitamura@acis.go.jp

Dr H. Jeuring, Chairman, Codex Committee on Pesticide Residues, Senior Public Health Officer Food, Food and Consumer Product Safety Authority, PO Box 19506, 2500 CM The Hague, Netherlands (*WHO Temporary Adviser*)

Tel.: (31 70) 448 4848; Fax: (31 70) 448 4747; E-mail: hans.jeuring@vwa.nl

Dr Manfred Luetzow, Consultant, Feldhofweg 38, CH-5432 Neuenhof, Switzerland (*FAO Consultant*)

Tel.: (41 56) 406 2357; Fax: (41 56) 406 2359; E-mail: manfred.luetzow@luetzow.ch

Mr David Lunn, Programme Manager (Residues-Plants), Dairy and Plant Products Group, New Zealand Food Safety Authority, PO Box 2835, Wellington, New Zealand (*FAO Consultant*)

Tel.: (644) 463 2654; Fax (644) 463 2675; E-mail: dave.lunn@nzfsa.govt.nz

Dr Dugald MacLachlan, Australian Quarantine and Inspection Service, Australian Department of Agriculture, Fisheries and Forestry, Edmond Barton Building, Kingston, ACT 2601, Australia (*FAO Consultant*)

Tel.: (61 2) 6272 3183; Fax: (61 2) 6271 6522; E-mail: dugald.maclachlan@affa.gov.au

Dr Jeronimas Maskeliunas, Food Standards Officer, Joint FAO/WHO Food Standards Programme, Food and Nutrition Division, Food and Agriculture Organization of the United Nations, Viale delle Terme di Caracalla, 00100 Rome, Italy (*FAO Staff Member*)

Tel.: (39 06) 570 53967; Fax: (39 06) 570 54593; E-mail: Jeronimas.Maskeliunas@fao.org

Dr Heidi Mattock, 9 rue Jules Verne, 67400, Illkirch-Graffenstaden, France (*WHO Editor*)

Tel.: (33 388) 66 07 34; E-mail: heidimattock@yahoo.com

Dr Douglas B. McGregor, Toxicity Evaluation Consultants, 38 Shore Road, Aberdour, KY3 0TU, Scotland (*WHO Temporary Adviser*)
Tel.: (44 1383) 860901; Fax: (44 1383) 860901; E-mail: mcgregortec@btinternet.com

Dr Utz W. Mueller, Team Leader, AgVet Chemical Review, Office of Chemical Safety Therapeutic Goods Administration, Australian Department of Health and Ageing, PO Box 100 MDP 88, Woden ACT 2606, Australia (*WHO Temporary Adviser*)
Tel (+61 2) 6289 3220 ; Fax (+61 2) 6289 3299 ; Email Utz.Mueller@health.gov.au

Dr Rudolf Pfeil, Pesticides and Biocides Division, Federal Institute for Risk Assessment, Thielallee 88-92, D-14195 Berlin, Germany (*WHO Temporary Adviser*)
Tel.: (49 30) 8412 3828; Fax: (49 30) 8412 3260; E-mail: r.pfeil@bfr.bund.de

Mr Derek Renshaw, Food Standards Agency, Aviation House 125 Kingsway, London WC2B 6NH, England (*WHO Temporary Adviser*)
Tel.: (44 20) 7276 8505; Fax: (44 20) 7276 8513; E-mail: derek.renshaw@foodstandards.gsi.gov.uk

Dr Atsuya Takagi, Section Researcher, Division of Toxicology, Biological Safety Research Centre, National Institute of Health Sciences, 1-18-1 Kamiyoga, Setaga-ku, Tokyo 158-8501, Japan (*WHO Temporary Adviser*)
Tel.: (81 3) 3700 1141 (ext 406); Fax: (81 3) 3700 9647; E-mail: takagi@nihs.go.jp

Dr Prakashchandra V. Shah, United States Environmental Protection Agency, Mail Stop: 7509C, 1200 Pennsylvania Avenue NW, Washington DC 20460, USA (*WHO Temporary Adviser*)
Tel.: (1 703) 308 1846; Fax: (1 703) 305 7775; E-mail: Shah.PV@epa.gov

Dr Angelika Tritscher, WHO Joint Secretary, International Programme on Chemical Safety World Health Organization, 1211 Geneva 27, Switzerland (*WHO Joint Secretary*)
Tel.: (41 22) 791 3569; Fax: (41 22) 791 4848; E-mail: tritschera@who.int

Dr Gero Vaagt, Senior Officer, Pesticide Management Group, Plant Protection Service, Plant Production and Protection Division, Food and Agriculture Organization of the United Nations, Viale delle Terme di Caracalla, 00100 Rome, Italy (*Acting FAO Joint Secretary*)
Tel.: (39 06) 570 55757; Fax: (39 06) 570 56347; E-mail: gero.vaagt@fao.org

Dr Christiane Vleminckx, Toxicology Division, Scientific Institute of Public Health, FPS - Public Health, Food Chain Safety and Environment, Rue Juliette Wytsman, 16B-1050 Brussels, Belgium (*WHO Temporary Adviser*)
Tel.: (32 2) 642 5351; Fax: (32 2) 642 5224; E-mail: c.vleminckx@iph.fgov.be

Dr Gerrit Wolterink, Centre for Substances & Integrated Risk Assessment, National Institute of Public Health and the Environment (RIVM), Antonie van Leeuwenhoeklaan 9, PO Box 1, 3720 BA Bilthoven, Netherlands (*WHO Temporary Adviser*)
Tel.: (31 30) 274 4531; Fax: (31 30) 274 4475; E-mail: Gerrit.Wolterink@rivm.nl

Abbreviations used

ADI	acceptable daily intake
ARfD	acute reference dose
AUC	area under the curve of concentration–time
bw	body weight
CAS	Chemical Abstracts Service
DMSO	dimethylsulfoxide
ECG	electrocardiogram
F ₀	parental generation
F ₁	first filial generation
F ₂	second filial generation
FOB	functional observational battery
GLP	good laboratory practice
HPLC	high-performance liquid chromatography
IPCS	International Programme on Chemical Safety
ISO	International Organization for Standardization
IUPAC	International Union of Pure and Applied Chemistry
LC ₅₀	median lethal concentration
LD ₅₀	median lethal dose
LOAEL	lowest-observed-adverse-effect level
MS	mass spectrometry
MCV	mean corpuscular volume
MCH	mean corpuscular haemoglobin
MCHC	mean corpuscular haemoglobin concentration
MRL	maximum residue level
NOAEC	no-observed-adverse-effect concentration
NOAEL	no-observed-adverse-effect level
NMR	nuclear magnetic resonance
OECD	Organisation for Economic Co-operation and Development
ppm	parts per million
T ₃	triiodothyronine
T ₄	thyroxine
TSH	thyrotropin
TLC	thin-layer chromatography
TMDI	theoretical maximum daily intake
QA	quality assurance
WHO	World Health Organization
w/v	weight for volume
w/w	weight for weight

Introduction

The toxicological monographs and monograph addenda contained in this volume were prepared by a WHO Core Assessment Group that met with the FAO Panel of Experts on Pesticide Residues in Food and the Environment in a Joint Meeting on Pesticide Residues (JMPR) in Geneva, Switzerland, on 20–29 September 2005.

Five of the compounds evaluated by the Core Assessment Group at the Meeting, dimethanamid-P/racemic dimethanamid, fenhexamid, indoxacarb, novaluron and sulfuric fluoride, were evaluated for the first time. The other 10 substances had been evaluated at previous meetings. For five of these, only information received since the previous evaluations is summarized in ‘monograph addenda’. Of these, acephate, imazalil and carbendazim were evaluated for establishment of an acute reference dose. The appropriate earlier documents on the five compounds should be consulted in order to obtain full toxicological profiles. Toxicological monographs were prepared on azocyclotin, benalaxyl, clofentezine, cyhexatin and propamocarb, summarizing new data and, where relevant, incorporating information from previous monographs and addenda. Reports and other documents resulting from previous Joint Meetings on Pesticide Residues are listed in Annex 1.

The report of the Joint Meeting has been published by the FAO as *FAO Plant Production and Protection Paper 183*. That report contains comments on the compounds considered, acceptable daily intakes established by the WHO Core Assessment Group, and maximum residue limits established by the FAO Panel of Experts. Monographs on residues prepared by the FAO Panel of Experts are published as a companion volume, as *Evaluations 2005, Part I, Residues*, in the FAO Plant Production and Protection Paper series.

The toxicological monographs and addenda contained in this volume are based on working papers that were prepared by temporary advisers before the 2005 Joint Meeting. A special acknowledgement is made to those advisers.

The preparation and editing of this volume was made possible by the technical and financial contributions of the lead institutions of the International Programme on Chemical Safety (IPCS), which supports the activities of the JMPR. 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 Central Unit of the IPCS concerning the legal status of any country, territory, city or area or of its authorities, nor 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 IPCS in preference to others of a similar nature that are not mentioned.

Any comments or new information on the biological properties or toxicity of the compounds included in this volume should be addressed to: Joint WHO Secretary of the Joint FAO/WHO Meeting on Pesticide Residues, International Programme on Chemical Safety, World Health Organization, 20 Avenue Appia, 1211 Geneva, Switzerland.