

## Evaluation of certain veterinary drug residues in food

Eighty-eighth report of the Joint FAO/WHO Expert Committee on Food Additives



Food and Agriculture Organization of the <u>United Nations</u>





The World Health Organization (WHO) was established in 1948 as a specialized agency of the United Nations serving as the directing and coordinating authority for international health matters and public health. One of WHO's constitutional functions is to provide objective and reliable information and advice in the field of human health, a responsibility that it fulfils in part through its extensive programme of publications. The Organization seeks through its publications to support national health strategies and address the most pressing public health concerns of populations around the world. To respond to the needs of Member States at all levels of development, WHO publishes practical manuals, handbooks and training material for specific categories of health workers; internationally applicable guidelines and standards; reviews and analyses of health policies, programmes and research; and state-of-the-art consensus reports that offer technical advice and recommendations for decision-makers. These books are closely tied to the Organization's priority activities, encompassing disease prevention and control, the development of equitable health systems based on primary health care, and health promotion for individuals and communities. Progress towards better health for all also demands the global dissemination and exchange of information that draws on the knowledge and experience of all WHO Member States and the collaboration of world leaders in public health and the biomedical sciences. To ensure the widest possible availability of authoritative information and guidance on health matters, WHO secures the broad international distribution of its publications and encourages their translation and adaptation. By helping to promote and protect health and prevent and control disease throughout the world, WHO's books contribute to achieving the Organization's principal objective - the attainment by all people of the highest possible level of health.

The WHO Technical Report Series makes available the findings of various international groups of experts that provide WHO with the latest scientific and technical advice on a broad range of medical and public health subjects. Members of such expert groups serve without remuneration in their personal capacities rather than as representatives of governments or other bodies; their views do not necessarily reflect the decisions or the stated policy of WHO.

To purchase WHO publications, please contact: WHO Press, World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland (tel. +41 22 791 3264; fax: +41 22 791 4857; email: bookorders@who.int; http://www.who.int/bookorders).

### WHO Technical Report Series 1023

# Evaluation of certain veterinary drug residues in food

Eighty-eighth report of the Joint FAO/WHO Expert Committee on Food Additives

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



Food and Agriculture Organization of the United Nations



Evaluation of certain veterinary drug residues in food: eighty-eighth report of the Joint FAO/WHO Expert Committee on Food Additives

(WHO technical report series; no. 1023)

ISBN 978-92-5-132120-1 [FAO] ISBN 978-92-4-121032-4 [WHO] ISSN 0512-3054 WHO and FAO, 2020

#### © World Health Organization and Food and Agriculture Organization of the United Nations, 2020

Some rights reserved. This work is available under the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 IGO licence (CC BY-NC-SA 3.0 IGO; https://creativecommons.org/licenses/by-nc-sa/3.0/igo/).

Under the terms of this licence, you may copy, redistribute and adapt 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 the World Health Organization (WHO) or the Food and Agriculture Organization of the United Nations (FAO) endorse any specific organization, products or services. The use of the WHO or FAO logo is not permitted. If you adapt the work, then you must license your work under the same or equivalent Creative Commons licence. If you create a translation of this work, you should add the following disclaimer along with the suggested citation: "This translation was not created by the World Health Organization (WHO) or the Food and Agriculture Organization of the United Nations (FAO). WHO and FAO are not responsible for the content or accuracy of this translation. The original English edition shall be the binding and authentic edition".

Any mediation relating to disputes arising under the licence shall be conducted in accordance with the mediation rules of the World Intellectual Property Organization http://www.wipo.int/amc/en/mediation/rules.

Suggested citation. Evaluation of certain veterinary drug residues in food: eighty-eighth report of the Joint FAO/WHO Expert Committee on Food Additives. Geneva: World Health Organization and Food and Agriculture Organization of the United Nations; 2020 (WHO technical report series; no. 1023). Licence: CC BY-NC-SA 3.0 IGO.

Cataloguing-in-Publication (CIP) data. CIP data are available at http://apps.who.int/iris.

Sales, rights and licensing. To purchase WHO publications, see http://apps.who.int/bookorders. To submit requests for commercial use and queries on rights and licensing, see http://www.who.int/about/licensing.

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.

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 WHO or FAO concerning the legal or development 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, whether or not these have been patented, does not imply that they are endorsed or recommended by WHO or FAO 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 and FAO 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 and FAO 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 policies of WHO or FAO.

Design: Rania Spatha (http://www.raniaspatha.com)

Printed in Malta.

## Contents

List of participants	iv
List of abbreviations	vi
1. Introduction	1
1.1 Declarations of interests	2
1.2 Modification of the agenda	2
2. General considerations	3
2.1 Matters of interest arising from previous sessions of CCRVDF	3
2.2 Comments on the parallel review process	3
2.3 Report on JECFA/JMPR Residue Definition Working Group	4
2.4 General considerations about the use of scientific literature in risk assessment 2.5 Toxicological profiling of compounds and less-than-lifetime dietary	7
exposure assessment	8
2.6 Combined exposure to multiple chemicals	9
2.7 Microbiological effects on the safety evaluation of veterinary drug residues in food	12
3. Comments on residues of specific veterinary drugs	15
3.1 Diflubenzuron	15
3.2 Ethion	27
3.3 Flumethrin	29
3.4 Fosfomycin	36
3.5 Halquinol	51
3.6 lvermectin	58
3.7 Selamectin	71
4. Future work and recommendations	81
Acknowledgements	83
References	85
Annex 1	
Reports and other documents resulting from previous meetings of the Joint FAO/WHO Expert Committee on Food Additives	95
Annex 2	
Recommendations on the substances on the agenda	109
Annex 3	
Meeting agenda	115

### **List of participants**

Eighty-eighth meeting of the Joint FAO/WHO Expert Committee on Food Additives Rome, 22–31 October 2019

#### World Health Organization (WHO) members

- Professor (Emeritus) Alan R. Boobis, National Heart and Lung Institute, Imperial College London, London, United Kingdom of Great Britain and Northern Ireland (United Kingdom) (Co-Chair)
- Dr Carl E. Cerniglia, Director, Division of Microbiology, National Center for Toxicological Research, Food and Drug Administration, Jefferson, United States of America
- Mr G.J. (Johan) Schefferlie, Medicines Evaluation Board, Veterinary Medicinal Products Unit, Utrecht, The Netherlands (WHO Rapporteur)

#### Food and Agriculture Organization of the United Nations (FAO) members

- Dr Alan Chicoine, Department of Veterinary Biomedical Sciences, Western College of Veterinary Medicine, University of Saskatchewan, Saskatoon, Canada (FAO Rapporteur)
- Mr Peter Cressey, Senior Scientist, Institute of Environmental Science and Research Limited, Christchurch Science Centre, Christchurch, New Zealand
- Dr Pascal Sanders, ANSES [French Agency for Food, Environmental and Occupational Health & Safety] Laboratoire de Fougères, Fougères, France
- Dr Stefan Scheid, BVL Federal Office of Consumer Protection and Food Safety, Department of Veterinary Medicines, Berlin, Germany (Chair)

#### **FAO** experts

- Professor Benjamin U. Ebeshi, Department of Pharmaceutical & Medicinal Chemistry, Faculty of Pharmacy, Niger Delta University, Bayelsa State, Nigeria
- Dr Holly Erdely, Residue Chemistry Team, Division of Human Food Safety, FDA Center for Veterinary Medicine, Rockville, United States of America
- Dr Anke Finnah, German Federal Office of Consumer Protection and Food Safety, Berlin, Germany

Mr Samuel Fletcher, United Kingdom Veterinary Medicines Directorate, Surrey, United Kingdom

Professor Susanne Rath, University of Campinas, Department of Analytical Chemistry, São Paulo, Brazil

Dr Rainer Reuss, Safe Work Australia, Canberra, Australia

#### **WHO experts**

Professor Silvana Lima Górniak, Department of Pathology, School of Veterinary Medicine and Animal Sciences, University of São Paulo

#### WHO temporary adviser

Dr Mayumi Ishizuka, Laboratory of Toxicology, Faculty of Veterinary Medicine, Hokkaido University, Sapporo, Japan

### Secretariat

- Ms Gracia Brisco, Food Standards Officer, Joint FAO/WHO Food Standard Programme, Food and Agriculture Organization of the United Nations, Rome, Italy (Codex Secretariat)
- Dr Hilary Cadman, Cadman Editing Services, Bellingen, Australia (WHO technical editor)
- Dr Vittorio Fattori, Food Safety and Quality Unit, Agriculture and Consumer Protection Department, Food and Agriculture Organization of the United Nations (FAO Secretariat)
- Dr Kevin Greenlees, Senior Advisor for Science and Policy, Center for Veterinary Medicine, US Food and Drug Administration, Maryland, United States of America (Chair of Codex Committee on Residues of Veterinary Drugs in Foods)
- Dr Markus Lipp, Senior Food Safety Officer, Scientific Advice and Joint FAO/WHO Expert Committee on Food Additives (JECFA) Secretary, Agriculture and Consumer Protection Department, Food and Agriculture Organization of the United Nations, Rome, Italy (FAO Secretariat)
- Mr Soren Madsen, Joint FAO/WHO Meeting on Pesticide Residues (JMPR) and JECFA Secretariat, Department of Food Safety and Zoonoses (FOS), World Health Organization, Switzerland (WHO Secretariat)

## List of abbreviations

95/95 UTL	95/95 upper tolerance limit; upper limit of the one-sided 95%
	confidence interval over the 95th percentile of residue
	concentrations
ADI	acceptable daily intake
AGAL	Australian Government Analytical Laboratories
ARfD	acute reference dose
AUC	area under the concentration-time curve
AUC	area under the concentration-time curve from time 0 extrapolated
0	to infinite time
AUC <sub>0-100</sub>	area under the concentration–time curve from time 0 to time of
	limit of quantification
bw	body weight
CAC	Codex Alimentarius Commission (Codex)
CAS	Chemical Abstracts Service
CCPR	Codex Committee on Pesticide Residues
CCRVDF	Codex Committee on Residues of Veterinary Drugs in Foods
CIFOCOss	FAO/WHO Chronic Individual Food Consumption Database –
	Summary statistics
5-CL	5-chloro-8-hydroxyquinoline or 5-chloroquinolin-8-ol (CHQ)
7-CL	7-chloro-8-hydroxyquinoline
5-CLG	5-chloro-8-hydroxyquinoline glucuronide conjugate
5-CLS	5-chloro-8-hydroxyquinoline sulfate conjugate
C <sub>max</sub>	maximum concentration
CNS	central nervous system
5,7-DCL	5,7-dichloroquinolin-8-ol (DCHQ)
5,7-DCLG	5,7-dichloroquinolin-8-ol glucuronide conjugate
5,7-DCLS	5,7-dichloroquinolin-8-ol sulfate
DNA	deoxyribonucleic acid

## 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\_24811