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FAO JECFA Monographs 2

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Joint FAO/WHO Expert Committee on Food Additives

66th meeting 2006

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FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS
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(66TH MEETING)
Rome, 22 – 28 February, 2006

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ABBREVIATIONS

ADI	Acceptable daily intake
AOAC	AOAC International
AUC	Area under the curve
BW or bw	Body weight
CAC	Codex Alimentarius Commission
CAS	Chemical Abstracts Service
CCRVDF	Codex Committee on Residues of Veterinary Drugs in Foods
Cl	Clearance rate
Cmax	Maximum concentration
CR	Renal clearance
CV	Coefficient of variation
Cv_r	Repeatability
Cc_R	Reproducibility
ECD	Electron capture detector
EDI	Estimated daily intake
EMEA	European Medicines Agency
FAO	Food and Agriculture Organization of the UN
FDA	US Food and Drug Administration
GC	Gas chromatography
GLP	Good laboratory practice
H or h	Hour
HPLC	High pressure liquid chromatography
IM	Intramuscular
IR	Infrared
IU	International Unit
IUPAC	International Union of Pure and Applied Chemistry
IV	Intravenous
JECFA	Joint FAO/WHO Expert Committee on Food Additives
JMPR	Joint Committee on Pesticide Residues
Kg or kg	Kilogram (10^3grams)
LC	Liquid chromatography
LOD	Limit of detection
LOQ	Limit of quantitation
µg	microgram (10^{-6}grams)
mg	milligram (10^{-3}grams)
min	Minimum or minute
MGA	Melengestrol acetate
mL or ml	milliliter
MIC	Minimum Inhibitory Concentration
MRL	Maximum Residue Limit
MRM	Multiple reaction monitoring
MS	Mass spectrometry
MW or mw	Molecular weight
N	Negative
NA or na	Not analyzed or not applicable
NADA	New Animal Drug Application
NC or nc	Not calculated
ND	Not detected
NICI	Negative ion chemical ionization
NOEL	No effect level
NQ	Non quantifiable
P	Positive
QA	Quality assurance
QC	Quality control
RfD	Acute reference dose
RP	Reverse phase
SC	Subcutaneous (injection)
SD	Standard deviation
S/N	Signal to noise ratio
SPE	Solid phase extraction
SD	Standard deviation
s.e.	Standard error
$t_{½}$	Half life
TR	Total residue
TLC	Thin layer chromatography
TMDI	Theoretical maximum daily intake
TRR	Total radiolabelled residues
TRS	Technical Report Series
TSP	Thermospray
USP	United States Pharmacopoeia
UV	Ultraviolet
Vd	Volume of distribution
WHO	World Health Organization

INTRODUCTION

The monographs in this volume of the FAO JECFA Monographs on the residues of, statements on, or other parameters of the veterinary drugs on the agenda were prepared by the invited experts for the sixty-sixth meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA) held in Rome, Italy, 22-28 February, 2006. This was the seventeenth meeting of JECFA convened specifically to consider residues of veterinary drugs in food animals. The Committee has evaluated residues of veterinary drugs in food animals at the 12th, 26th, 27th, 32nd, 34th, 36th, 38th, 40th, 42nd, 43rd, 45th, 47th, 48th, 50th, 52nd, 54th, 58th, 60th, and 62nd meetings (Ref. 1-15 and 19-22, respectively). The tasks for the Committee were to further elaborate principles for evaluating the safety of residues of veterinary drugs in food and for establishing acceptable daily intakes (ADIs) and recommend maximum residue limits (MRLs) for substances on the agenda when they are administered to food producing animals in accordance with good veterinary practice in the use of veterinary drugs. The enclosed monographs provided the scientific basis for the recommendations of MRLs.

There are two significant items in this volume of the FAO JECFA Monographs to bring to the attention of readers. First, this volume is the first in a new format for the presentation of monographs from meetings of the Committee. Second, this was the first meeting of JECFA subsequent to the completion of the workshop to update the principles and methods of risk assessment for MRLs for pesticides and veterinary drugs, held jointly by FAO/RIVM/WHO, in Bilthoven, The Netherlands, 7 - 11 November, 2005. Specifically, the Committee decided to implement one of the more significant recommendations in the workshop report – the concept of using median residue values to estimate daily intakes of residues of veterinary drugs in food for chronic exposure intake estimates (Ref. 24).

Background

In response to the growing use of veterinary medicines in food animal production systems internationally and the potential implications for human health and fair trading practices, a Joint FAO/WHO Expert Consultation on Residues of Veterinary Drugs was convened in Rome, November 1984 (Ref. 16). Among the major recommendations of this consultation were the establishment of the Codex Committee on Residues of Veterinary Drugs in Foods (CCRVDF) and the periodic convening of an appropriate expert body to provide independent scientific advice to this Committee and to member countries of FAO and WHO. At its first session in Washington, DC in November 1986, the CCRVDF reaffirmed the need for such a scientific body and made a number of recommendations and suggestions to be considered by JECFA (Ref. 17). In response to these recommendations, the 32nd JECFA meeting was devoted entirely to the evaluation of residues of veterinary drugs in food – a new responsibility to the Joint FAO/WHO Expert Committee on Food Additives. Sixteen such meetings of JECFA have been held prior to this meeting of JECFA.

66th Meeting of JECFA

This present volume in its new format contains monographs of the residue data on six of the nine substances originally scheduled for the meeting. No data were provided for two substances and one substance was for review of toxicological data only and no residue monograph was prepared. The monographs are prepared in a uniform format consistent with the data provided and the specific request for risk assessment by CCRVDF. The format includes identity of substance, residues in food and their evaluation, metabolism studies, tissue residue depletion studies, methods of residue analysis, a final appraisal of the study results, and if appropriate, recommendations on MRLs. There is one unique report in this

particular volume. It was noted in the editing of the monograph for melengestrol acetate at the 62nd JECFA that an inconsistency in the approach to recommend MRLs using appropriate biological activity of the pertinent metabolites was detected that could not be fully corrected. To address the unresolved issues, the corrected accounting of the biologically active residues was completed in this monograph without any additional data provided to JECFA. A summary of the recommendations on compounds on the agenda and further information required is included in Annex 1. In addition, a summary of JECFA evaluations of residues of veterinary drugs in foods from the 32nd meeting to the present 66th meeting is found in Annex 2. ***The monographs and general considerations on risk assessment principles of this volume must be considered in context of the full report of the meting, which will be published in the WHO Technical Report Series No. 939.***

On-line edition of Residues of some veterinary drugs in animals and foods (FAO Food and Nutrition paper Number 41)

The monographs and statements that have been published in the FAO Food and Nutrition Paper 41 (sixteen volumes since 1988) are available online at www.fao.org/es/esn/jecfa/archive_en.stm. The search interface is available in five languages (Arabic, Chinese, English, French and Spanish) and follows searching for compounds, functional classes, ADI and MRL status. For each veterinary drug assessed by JECFA an excerpt is available that summarizes the opinion of JECFA with respect to the ADI and MRLs. The on-line edition will be updated to include the monographs contained in this volume.

Contact and Feedback

More information on the work of the Committee is available from the FAO homepage of JECFA at www.fao.org/ag/agn /jecfa/index_en.stm. Readers are invited to address comments and questions on this publication and other topics related to the work of JECFA to:

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