Safety Expert Working Group

Chairperson: Tong Zhou (US FDA)

Introduction

The Safety EWG was established in 1996 and originally chaired by Dr. Margaret Miller, USA. The Safety EWG's mandate was to determine the complete package of toxicological studies needed to establish an Acceptable Daily Intake (ADI) for residues of veterinary drugs. During that time, a task force was formed to address the potential effects of microbiologically active residues on the human gastrointestinal microflora. The task force developed a decision tree approach for the determination of a microbiological ADI. The Safety EWG was reestablished under the chairmanship of Dr. Kevin Greenlees (US FDA) around 2009 to address new issues and review use and application of existing guidelines. From 2021 to 2022, the Safety EWG was led by Dr. Charli Long (US FDA). Starting 2022, the Safety EWG has been chaired by Dr. Tong Zhou (US FDA).

Guidelines adopted

The Safety Working Group has been very active in developing internationally harmonised guidelines for data that may allow a regulatory authority to derive an ADI for the residues of veterinary drugs in food. Currently adopted guidelines include:

- GL22 Studies to evaluate the safety of residues of veterinary drugs in human food: Reproduction studies. May 2004.
- GL23(R) Studies to evaluate the safety of residues of veterinary drugs in human food: Genotoxicity testing. October 2014.
- GL28 Studies to evaluate the safety of residues of veterinary drugs in human food: Carcinogenicity testing. February 2005.
- GL31 Studies to evaluate the safety of residues of veterinary drugs in human food: Repeat-dose toxicity testing. May 2004.
- GL32 Studies to evaluate the safety of residues of veterinary drugs in human food: Developmental toxicity testing. May 2004.
- GL33 Studies to evaluate the safety of residues of veterinary drugs in human food. General Approach to Testing. February 2009.
- GL36(R2) Studies to evaluate the safety of residue of veterinary drugs in human foods: General approach to establish a microbiological ADI. February 2019.
- GL37 Studies to evaluate the safety of residues of veterinary drugs for human food: Repeat-dose chronic toxicity testing. May 2004.
- GL54 Studies to evaluate the safety of residues of veterinary drugs for human food: General approach to establish an acute reference dose (ARfD). November 2016.

Key scientific issues resolved

Current products of the Safety EWG have addressed the studies needed to generate data that may be used to derive an ADI for residues of a veterinary drug. The guidelines address the toxicological ADI based on systemic/developmental/reproductive endpoints of toxicity, genotoxicity and carcinogenicity testing, and the microbiological ADI based on microbiological endpoints (potential effects on the human intestinal microflora).

Key benefits of the harmonized guidelines

They allow data developed for any of the VICH member nations as well as non-VICH member nations to serve the data requirements of any of the other members. This offers considerable savings to industry and greatly reduces the number of animal studies necessary, as the studies do not need to be repeated for each regulatory authority.

Guidelines under development/revision

The Safety EWG has completed revisions of two guidelines, which are now in step 4 for public consultation:

VICH GL22(R) - provide the current recommendations for addressing reproductive toxicity;

VICH GL23(R) - provide current recommendations for assessing genotoxicity.

New topics

The following may be topics for future discussions:

- Safety evaluation of biologicals/biotherapeutics - do the current guidelines apply?
- Guidance for addressing thresholds/points of departure for non- genotoxic carcinogens
- Modernization of toxicity testing/new approach methods (NAMs)/incorporating 3Rs (replacement, reduction, refinement) developments
- Reassessment of existing guidelines
  chronic studies – duration and clarification of the rat as the default
  carcinogenicity studies – clarification of need, and 1 or 2 species

EWG Composition

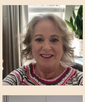

C. Bergman
EU/EMA


A. Kamp-Koetter
EU/
AnimalhealthEurope


M. Ozawa
Japan/JMAFF


A. Kangawa
Japan/JVPA


L. You
US/FDA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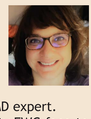
E. Freeman
US/AHI


T. Zhou
US/FDA

S. Fletcher was replaced by N O'Brien in August 2024 as the UK/VMD expert.
M. Escribano on behalf of S. Fletcher participated in the VICH Safety EWG face-to-face meeting in November 2023.
J. van Benthem (EU) and T. Nohmi (Japan/JMAFF) retired from the Safety EWG in August 2024.

VICH

Amsterdam
November 2024