Metabolism and Residues Kinetics (MRK) EWG

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Introduction

To obtain approval of a veterinary medicinal product for use in food-producing animals, knowledge of the residues that occur in tissues and other foodstuffs from treated animals is required, as well as knowledge of how these residues compare to the metabolites seen in toxicity tests with laboratory animals. The potential value of harmonized guidance was recognized in the early 2000s, with the MRK EWG being set up in 2005, firstly to compare the requirements across VICH regions, and then to develop guidelines.

Guidelines adopted

Between 2005 and 2011, four MRK guidelines were developed (GL46 to 49). They lay out the data needed to characterize and quantify residues in muscle, fat, liver, kidney, milk and eggs of terrestrial, food-producing species. These were supplemented in 2018 and 2019 by two further guidelines focusing specifically on studies for products intended for use in honey bees (GL56) and aquatic species (GL57).

Guidelines under development

A need for entirely new MRK guidelines has not been identified. The EWG is currently working on an update to GL49 in response to comments from stakeholders. Certain aspects of the guideline were difficult to follow, in particular Annex 3, which presents an example protocol, including calculations, to validate the analytical method for quantifying residues. The group is reviewing a reworked version of the Annex, verifying the calculations and correcting inconsistencies regarding the underlying statistics.

New topics

While the ongoing revision of GL49 is focused on Annex 3, the EWG is discussing whether a case should be developed for reviewing other areas of this guideline.

The group has also agreed that an update to GL47 would be beneficial, for example to provide additional information relevant to *in vitro* metabolism studies. A concept paper formally proposing this work is under development.

In the longer term, there may be an update to GL46, particularly to provide further guidance relevant to total residue studies in fish.

Key benefits of the harmonized guidelines

The MRK series of guidelines was developed to facilitate mutual acceptance of metabolism and residue data by national and regional regulators. As such, the guidelines benefit regulators and industry by providing clarity on the required studies; they benefit industry by providing a single set of requirements acceptable across VICH regions; they benefit consumers by assuring that any residues from veterinary medicinal products will not represent a safety concern.

The six metabolism and residues kinetics guidelines:

VICH GL46 Studies to evaluate the metabolism and residue kinetic of veterinary drugs in food-producing animals: metabolism study to determine the quantity and identify the nature of residues

VICH GL47 Studies to evaluate the metabolism and residue kinetic of veterinary drugs in food-producing animals: comparative metabolism studies in laboratory animals

VICH GL48 Studies to evaluate the metabolism and residue kinetic of veterinary drugs in food-producing animals: marker residue depletion studies to establish product withdrawal periods

VICH GL49 Studies to evaluate the metabolism and residue kinetic of veterinary drugs in food-producing animals: validation of analytical methods used in residue depletion studies

VICH GL56 Studies to evaluate the metabolism and residue kinetic of veterinary drugs in food-producing animals: study design recommendations for residue studies in honey for establishing MRLs and withdrawal periods

VICH GL57 Studies to evaluate the metabolism and residue kinetic of veterinary drugs in food-producing animals: marker residue depletion studies to establish product withdrawal periods in aquatic species

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