Changes to legislation: *Commission Regulation (EU) 2018/782 is up to date with all changes known to be in force on or before 28 December 2020. There are changes that may be brought into force at a future date. Changes that have been made appear in the content and are referenced with annotations. (See end of Document for details) View outstanding changes*

Commission Regulation (EU) 2018/782 of 29 May 2018 establishing the methodological principles for the risk assessment and risk management recommendations referred to in Regulation (EC) No 470/2009 (Text with EEA relevance)

COMMISSION REGULATION (EU) 2018/782

of 29 May 2018

establishing the methodological principles for the risk assessment and risk management recommendations referred to in Regulation (EC) No 470/2009

(Text with EEA relevance)

THE EUROPEAN COMMISSION,

Having regard to the Treaty on the Functioning of the European Union,

Having regard to Regulation (EC) No 470/2009 of the European Parliament and of the Council of 6 May 2009 laying down Community procedures for the establishment of residue limits of pharmacologically active substances in foodstuffs of animal origin, repealing Council Regulation (EEC) No 2377/90 and amending Directive 2001/82/EC of the European Parliament and of the Council and Regulation (EC) No 726/2004 of the European Parliament and of the Council[(1)], and in particular Article 13(2)(a) thereof,

Whereas:

(1) Regulation (EC) No 470/2009 provides that, except in cases where the Codex Alimentarius procedure applies, any pharmacologically active substance intended for use in the Union in veterinary medicinal products which are to be administered to food-producing animals shall be subject to an opinion of the European Medicines Agency ('Agency') on the maximum residue limits ('MRLs') of pharmacologically active substances used or intended to be used in veterinary medicinal products. The Agency's opinion should consist of a scientific risk assessment and risk management recommendations.

(2) Regulation (EC) No 470/2009 empowers the Commission to adopt measures establishing the methodological principles for the risk assessment and risk management recommendations regarding the establishment of the MRLs of pharmacologically active substances.

(3) In order to provide legal certainty, clarity and predictability with regard to the process of the establishment of MRLs, it is appropriate that the criteria against which the Agency appraise the applications are provided for in this Regulation.

(4) The methodological principles for the risk assessment and risk management recommendations should aim to ensure a high level of human health protection, whilst also ensuring that human health, animal health and animal welfare are not negatively affected by the lack of availability of appropriate veterinary medicinal products.

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(5) Taking into account the requirements set out in Article 6 of Regulation (EC) No 470/2009, the detailed rules on the methodological principles for the scientific risk assessment part of the Agency's opinion should be laid down in this Regulation.

(6) Taking into account the requirements set out in Article 7 of Regulation (EC) No 470/2009, the detailed rules on the methodological principles for the risk management recommendations part of Agency's opinion should be laid down in this Regulation. In the risk management recommendations, the Agency is also required to consider the availability of alternative substances and other legitimate factors, such as the technological aspects of food and feed production or the feasibility of controls. Therefore it is appropriate to lay down rules on that requirement.

(7) The measures provided for in this Regulation are in accordance with the opinion of the Standing Committee on Veterinary Medicinal Products,

HAS ADOPTED THIS REGULATION:

Article 1

Subject matter

1 This Regulation sets out the methodological principles for the scientific risk assessment and risk management recommendations referred to in Articles 6 and 7 of Regulation (EC) No 470/2009 that shall be applied by the Agency when preparing opinions on the MRLs of pharmacologically active substances which may be permitted in food of animal origin under that Regulation.

2 The methodological principles for the scientific risk assessment are set out in Annex I.

3 The methodological principles for the risk management recommendations are set out in Annex II.

Article 2

Definitions

For the purposes of this Regulation, in addition to the definitions set out in Regulation (EC) No 470/2009, the following definitions shall apply:

— ‘major metabolites’ means metabolites comprising ≥ 100 μg/kg or ≥ 10 % of the total residue in a sample collected from the target animal species in the metabolism study,

— ‘marker residue’ means a residue whose concentration is in a known relationship to the concentration of total residue in an edible tissue,

— ‘dairy starter cultures’ means prepared cultures of microorganism employed in the manufacture of a variety of dairy products including butter, cheese, yoghurt and cultured milk.

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Article 3

Entry into force

This Regulation shall enter into force on the twentieth day following that of its publication in the *Official Journal of the European Union*.

This Regulation shall be binding in its entirety and directly applicable in all Member States.

Done at Brussels, 29 May 2018.

For the Commission

The President

Jean-Claude JUNCKER

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ANNEX I

Methodological principles for the scientific risk assessment referred to in Article 6 of Regulation (EC) No 470/2009

I.GENERAL PRINCIPLES

I.1. Safety and residue tests for the establishment of maximum residue limits ('MRLs') shall be carried out in conformity with the provisions related to Good Laboratory Practice ('GLP') as laid down in Directive 2004/10/EC of the European Parliament and of the Council.[(2)]

If data are available that have not been generated under GLP conditions, the potential impact of this shall be addressed.

I.2. Use of experimental animals in safety and residue tests shall comply with Directive 2010/63/EU of the European Parliament and of the Council[(3)].

I.3. Documentation presented in relation to safety and residue tests shall name the laboratory where the work was performed and shall be signed and dated. Summaries of any studies that are not accompanied by the raw data shall not be accepted as valid documentation.

Design, methods and conduct of the studies, name and qualifications of investigator, place and period of time during which the study was undertaken shall be clear from the test reports. The experimental techniques shall be described in such detail as to allow them to be reproduced, and the investigator shall establish their validity. All abbreviations and codes, irrespective of whether they are internationally accepted or not, shall be accompanied by a key.

I.4. Where applicable, all observed results from the studies submitted shall be evaluated by an appropriate statistical method and be discussed in conjunction with the other available studies. The results of all studies shall be presented in a form that facilitates their review.

I.5. Test reports shall include the following information (where applicable):

(a) chemical identification of the test pharmacologically active substance, including the isomer ratio and the enantiomers, if appropriate;

(b) purity of the test substance;

(c) formulation of the administered drug and method of dose preparation;

(d) stability, including stability in vehicle and feed when so administered;

(e) mode of dose administration (dose (expressed in mg/kg body weight), frequency of dosing, and duration of treatment);

(f) for administration of the test substance other than in the diet or drinking water: the characteristics of the vehicle, including toxicological characteristics;

(g) species, strain and source of test animals used, use of specific pathogen free animals, sex of the dosed animals, age of the animals at the beginning of the dosing, number of dosed animals;

(h) dose levels and route and frequency of administration (with dosage in mg/kg bodyweight/day), test period, parameters followed, frequency of observation; conditions of animal husbandry including environmental conditions, water and food consumption (especially for drugs administered in drinking water and/or feed);

(i) sampling time points;

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(j) description of toxic signs with the inclusion of time of onset, degree and duration (for safety tests), where appropriate;

(k) results of the clinical observations, gross necropsy, histopathology and of all other parameters investigated (for safety tests), where appropriate;

(l) where appropriate, an estimate of a no observed (adverse) effect level ('NO(A)EL') or lowest observed (adverse) effect level ('LO(A)EL') or lower bound of the benchmark dose ('BMDL') (for safety tests);

(m) weight of dosed animals;

(n) milk and egg production (if applicable);

(o) specific activity and radio-purity of labelled substances (for residues tests);

(p) sample collection, sample size, and sample storage;

(q) analytical methods: a complete description of the procedure, including preparation of analytical samples, instrumentation and data derived from standards, control tissues, fortified tissues and tissues with incurred residues; validation data for the analytical method shall be provided, including limit of detection, limit of quantification, linearity in and around the relevant range of concentrations, stability, accuracy, precision and susceptibility to interferences;

(r) raw data of all test results including those of the analytical method used to determine the residues in the edible tissues or products, methods of calculation.

I.6. Biological substances other than those identified in Article 1(2)(a) of Regulation (EC) No 470/2009 of the European Parliament and of the Council[(4)] shall be:

(a) subject to a normal MRL where the biological substance is chemical-like insofar as it could be produced by chemical synthesis and so presents similar concerns to chemical substances and can be expected to leave residues in the same way as chemical substances (e.g. cytokines, hormones);

(b) evaluated on a case-by-case basis where the biological substance is chemical-unlike insofar as being more complex than chemically synthesised pharmacologically active substances and so may contain multiple chemical types whose residues may generally be cells, amino acids, lipids, carbohydrates, nucleic acids and their breakdown products.

I.7. For chemical-unlike biological substances, a report describing the scientific basis for the request on whether a full MRL evaluation is required or not shall be required together with the following information:

(a) the nature of the biological substance (e.g. cell, tissue, live or killed organism) and a comparison with similar biological substances to which consumers are known to be routinely exposed;

(b) a description of the mechanism of action underlying the substances therapeutic effect and, if available, information on its potency;

(c) the fate of the substance in the treated animal (i.e. is it bioavailable, are residues expected in food commodities);

(d) any activity that the substance may have in the human gut (are the residues inactive or do they produce local effects);