MRLs for some “chemical-unlike” biological substances

Published by AGRINFO on 06 Jun 2025

EU adds five “chemical-unlike” biological substances to list of authorised pharmacologically active substances in food-producing animals

Commission Regulation (EU) 2025/1101 of 3 June 2025 amending Regulation (EU) 2018/782 concerning the assessment by the European Medicines Agency of maximum residue limits for chemical-unlike biological substances

Commission Implementing Regulation (EU) 2025/1102 of 3 June 2025 amending Regulation (EU) No 37/2010 as regards chemical-unlike biological substances

Commission Implementing Regulation (EU) 2025/1103 of 3 June 2025 amending Implementing Regulation (EU) 2017/12 as regards the requirements for applications and requests for the establishment of a no MRL required classification for chemical-unlike biological substances

Update

The European Union (EU) has amended its rules on evaluating biological substances used in veterinary medicines to allow the European Medicines Agency (EMA) to determine when there is no maximum residue level (MRL) required for “chemical-unlike” biological substances. It has also authorised the following five substances for use in certain food-producing animals with the classification "no MRL required":

- bovine casein hydrolysate (bCNH)
- probiotic components including bacteria and yeasts
- recombinant bovine IL-8 (His-tag) for intrauterine use in cattle
- stem cells
- naked unmodified dsRNA.

Impacted products

Cattle, beef, bees, all food-producing animals

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What is changing?

The EMA has assessed five “chemical-unlike” (see Background) biological substances that can be used in food-producing animals. It has concluded they do not pose a risk for health, and can be included in the list of authorised pharmacologically active substances in Regulation 37/2010, classified as “no MRL required”. The substances are as follows.

For all food-producing animals:

- probiotic components including bacteria and yeasts
- stem cells.

For cattle:

- bovine casein hydrolysate (bCNH) produced from sodium caseinate hydrolysed with trypsin, heat treated
- recombinant bovine IL-8 (His-tag).

For bees:

- Varroa destructor calmodulin gene-specific double-stranded interfering RNA EP15 (naked unmodified dsRNA).

Why?

The EMA must assess the use of pharmacologically active substances in food-producing animals and set the appropriate MRLs. Chemical-unlike substances are evaluated on a case-by-case basis. In most cases, the residues of chemical-unlike biological substances fall into groups of substances that are normal constituents of food, such as amino acids, lipids, and carbohydrates, and do not pose risks to public health. Consequently, such chemical-unlike biological substances can be classified as “no MRL required”.

Regulation 2018/782 establishes the risk assessment principles used by the EMA. Regulation 2025/1101 amends these principles to allow the EMA to classify substances as “no MRL required” (new Section I.7 of Annex I).

The Annex to Regulation 37/2010 sets out pharmacologically active substances that may be used in veterinary medicines, and their MRLs in food of animal origin. Regulation 2025/1102 adds the five “chemical-unlike” biological substances in the Annex, Table 1.

Regulation 2025/1103 updates the requirements (Regulation 2017/12) that must be met by applicants requesting “chemical-unlike” biological substances to be classified as “no MRL

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required".

Timeline

The three Regulations apply from **24 June 2025**.

Background

Regulation 470/2009 requires that MRLs for pharmacologically active substances intended for use in veterinary medicinal products administered to food-producing animals in the EU are subject to an opinion by the EMA.

The risk assessment undertaken depends on the type of biological substance:

- "chemical-like" substances, which could be produced by chemical synthesis and raise similar concerns, are subject to a normal MRL evaluation
- "chemical-unlike" substances, which are more complex and may contain multiple chemical types, are evaluated on a case-by-case basis.

Resources

Regulation 470/2009 laying down Community procedures for the establishment of residue limits of pharmacologically active substances in foodstuffs of animal origin

Commission Regulation 2018/782 establishing the methodological principles for the risk assessment and risk management recommendations referred to in Regulation (EC) No 470/2009

Commission Regulation 37/2010 on pharmacologically active substances and their classification regarding maximum residue limits in foodstuffs of animal origin

Commission Implementing Regulation 2017/12 regarding the form and content of the applications and requests for the establishment of maximum residue limits

Sources

Commission Regulation 2025/1101 concerning the assessment by the European Medicines Agency of maximum residue limits for chemical-unlike biological substances

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Commission Implementing Regulation 2025/1102 as regards chemical-unlike biological substances

Commission Implementing Regulation 2025/1103 as regards the requirements for applications and requests for the establishment of a no MRL required classification for chemical-unlike biological substances

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