FLASH INFO

CODEX ALIMENTARIUS

New Risk-Based Approach for Veterinary Drug Residues Resulting from Carryover

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Executive Summary

Recent developments within the Codex Alimentarius framework, particularly during CCRVDF28, mark significant progress in addressing veterinary drug residues arising from unintended carryover in animal feed.

In recent years, this issue has gained prominence due to increasing detections reported through systems such as the **RASFF**, reflecting both the structural nature of cross-contamination and the improved sensitivity of analytical methods. These findings have, in some cases, led to regulatory actions and trade disruptions, particularly where no Codex MRLs are established, highlighting the risk of disproportionate measures and potential trade barriers.

In response, Codex is advancing a risk-based approach integrating Action Levels (ALs), the Residue Risk Score (RRS), and the Risk Management Decision Tool (RMDT). As part of this work, Action Levels have been proposed for eggs, notably **220 µg/kg for nicarbazin (DNC)** and **100 µg/kg for lasalocid**, to support the interpretation of residue findings associated with carryover.

This framework enables a more proportionate interpretation of analytical results, strengthening consumer protection while improving consistency and predictability in international trade.

For competent authorities responsible for food safety oversight, this approach provides practical guidance to interpret low-level residue detections in a risk-based manner, differentiate between carryover and potential misuse, avoid disproportionate regulatory actions and unnecessary trade restrictions, and support harmonized decision-making aligned with Codex principles.

Further work is needed to expand the range of substances covered, refine exposure assessment methodologies, and strengthen the scientific basis of the approach through data collection and international collaboration.

Background and Context

Food safety systems for products of animal origin have historically relied on the establishment of Maximum Residue Limits (MRLs), which are derived from toxicological evaluations and intended to ensure that residues resulting from the proper use of veterinary drugs remain within safe levels. This approach has proven effective in managing risks associated with **intentional administration of veterinary medicinal products** in target species.

However, the increasing sophistication of food production systems has revealed the limits of this paradigm. In particular, the phenomenon of *carryover*, defined as the unintended transfer of trace amounts of veterinary drugs from medicated feed to non-target feed, has emerged as a **structural and unavoidable feature** of modern feed manufacturing and distribution systems.

This issue is not primarily the result of non-compliance, but rather of the inherent complexity of feed production chains. Even under strict application of Good Manufacturing Practices (GMP) and HACCP-based controls, complete elimination of cross-contamination remains technically difficult. As a result, trace residues may be detected in products derived from animals that have not been treated.

The growing importance of this issue is closely linked to advances in analytical technologies, particularly high-sensitivity methods such as LC-MS/MS, which are capable of detecting residues at extremely low concentrations. These technological improvements, while strengthening surveillance capacity, have also led to an increase in detection events that challenge existing regulatory frameworks.

At the international level, monitoring systems and scientific assessments have documented multiple occurrences of such residues, particularly in eggs and poultry products. These findings have raised significant **regulatory and trade-related questions**, especially in cases where no Codex MRLs exist for the matrix concerned.

In this context, reliance on a strict compliance-based interpretation may lead to disproportionate measures, including product rejection or trade disruption, even in situations where the actual risk to consumers is negligible. This has underscored the need for a more flexible and scientifically grounded approach.

Recognizing these challenges, the **Codex Alimentarius**, through the Codex Committee on Residues of Veterinary Drugs in Foods (CCRVDF), has undertaken dedicated work to develop a harmonized framework capable of addressing carryover situations in a consistent and risk-based manner.

A Paradigm Shift: Risk-Based Approach

The framework developed by the Codex represents a fundamental shift in regulatory philosophy. Rather than relying exclusively on predefined limits, it introduces a **stepwise decision-making system** that takes into account the actual exposure of consumers and the context in which residues are detected.

At the core of this approach is the recognition that not all detections of residues necessarily imply a public health concern. By incorporating scientific risk assessment into the decision process, the framework allows authorities to differentiate between negligible-risk situations and those requiring intervention.

This system is built around three interconnected components: Action Levels, which serve as operational screening thresholds; the Residue Risk Score, which provides a quantitative assessment of exposure; and the Risk Management Decision Tool, which translates these elements into structured decision pathways. Together, these tools enable a more coherent and proportionate response to carryover-related findings.

Residue Risk Score (RRS): Calculation and Interpretation

The Residue Risk Score (RRS) is a central element of the new framework, providing a quantitative measure of the potential risk to consumers based on dietary exposure.

$$RRS = \frac{EDI}{ADI}$$

The RRS is calculated as the ratio between the Estimated Daily Intake (EDI) of a residue and the Acceptable Daily Intake (ADI), which represents the maximum amount of a substance that can be ingested daily over a lifetime without appreciable health risk.

The estimation of exposure (EDI) takes into account the concentration of the residue in food, the level of consumption of the food commodity, and the body weight of the consumer. Where appropriate, additional correction factors may be incorporated to reflect processing effects or bioavailability.

The interpretation of the RRS is straightforward yet robust: a value less than or equal to one indicates that exposure remains within acceptable limits, while a value exceeding one suggests the need for further risk management actions. This approach ensures that decisions are directly linked to the actual magnitude of exposure rather than solely to the presence of a residue.

Risk Management Decision Tool (RMDT)

The Risk Management Decision Tool operationalizes the risk-based approach by providing a structured pathway for decision-making. It integrates the use of Action Levels and the RRS into a coherent framework that guides authorities from detection to final decision.

Step	Condition / Question	Outcome / Decision	Action / Interpretation
1	Detection of residue exceeding Codex AL or no AL	Proceed to risk assessment	Calculate RRS
2	RRS > 1	Food safety concern	Apply national risk management strategy
3	RRS ≤ 1	No food safety concern	Accept for human consumption
4	If RRS ≤ 1: If the detected residues exceed 10×AL or lowest Codex MRL in food from target animals?	Further differentiation	Assess carryover vs misuse

5	NO	Likely carryover	No additional action
6	YES	Not likely carryover	Trace back investigation

This decision tree illustrates how screening thresholds and risk assessment are combined to ensure that actions taken are proportionate to the level of risk identified. It also provides a practical mechanism for distinguishing between carryover and potential misuse.

Practical Applications Adopted

As part of its recent work, CCRVDF has proposed specific Action Levels for substances frequently associated with carryover, particularly in eggs. These include nicarbazin (expressed as DNC) and lasalocid, for which reference values have been established to support interpretation and decision-making (notably 220 µg/kg for nicarbazin (DNC) and 100 µg/kg for lasalocid).

These values are not intended to replace MRLs but rather to complement existing frameworks by addressing situations where no MRL is applicable. They serve as operational benchmarks, allowing authorities to rapidly assess whether a detected residue is likely to result from unintended transfer and whether further evaluation is required.

Conclusion

The developments within the CCRVDF reflect ongoing efforts to evolve food safety management toward more science-based and context-sensitive approaches. By incorporating exposure assessment, operational thresholds, and structured decision tools, the proposed Codex framework provides elements to support the interpretation of residue findings associated with carryover.

This approach aligns with broader trends in international food safety governance, where increasing attention is given to proportionality, transparency, and the integration of risk analysis into decision-making processes. At the same time, it maintains the objective of ensuring a high level of consumer protection while contributing to greater consistency in international trade practices.

The effective adoption of this framework will depend on several factors, including the availability of reliable occurrence and consumption data, the capacity of competent authorities to apply risk-based tools, and the development of clear implementation guidance. Continued work within Codex, including the refinement of methodologies and expansion to additional substances, will be important to support its practical application and facilitate harmonized use across countries.

Reference

Guidelines on recommended risk-based actions to address the detection of residues of a veterinary drug in food caused by unavoidable and unintentional carryover of veterinary drugs in animal feed where there is no applicable Codex MRL. REP26/RVDF28-Appendix VI