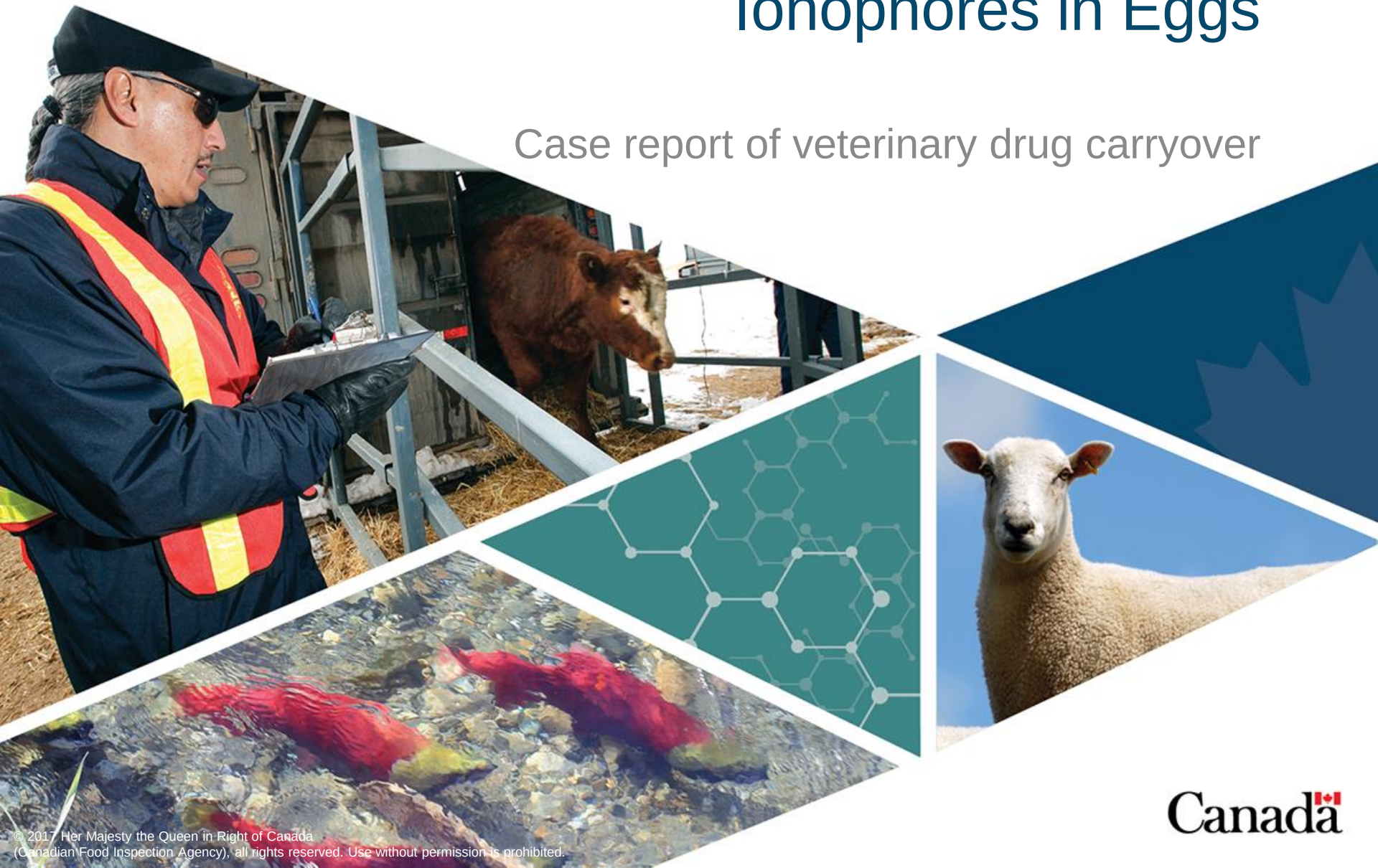
Canadian Food Inspection Agency | Agence canadienne d'inspection des aliments

Ionophores in Eggs

Case report of veterinary drug carryover



Canada

Feed Manufacturing in Canada

- Medicated feed accounts for ~30% of all complete feeds
- On-farm and in commercial feed mills
  - Single species using few medications vs
  - Multispecies using a variety of medications
- Equipment is cross-utilized for medicated and non-medicated feeds
- Opportunity for cross-contamination

Ionophores in Eggs

- 2004-2007 Detectable residues ranging from 0.3 to 94 ppb in approximately 10 per cent of all eggs tested (domestic and imported)
  - lasalocid, monensin, narasin, and salinomycin
- Since they are not approved for use in laying hens, Canada has no MRL for these drugs in eggs
- Any detectable residue in eggs was considered to be an adulteration and a violation
- The scientific literature and surveillance reports from other jurisdictions confirmed that this was not an issue unique to Canada

Analytical Capabilities

- CFIA and its contract labs, at the time, had LOQs for ionophores ranging from
  - 0.2 to 0.5 ppb in eggs
  - 1 to 2 ppm in feed
  - 3 to 4 orders of magnitude less sensitive.
- Non-detectable residues of ionophores in feed from carryover cross-contamination were resulting in detectable residues in eggs

Risk Assessment

- Health Canada conducted a risk assessment of the detected residues and conservative exposures were found to be a fraction of the ADI
- Recommendations:
  1. Improve analytical capabilities for feed residue monitoring
  2. Ensure that there is no deliberate unapproved use and actions to ensure that cross-contamination is eliminated as much as possible at the feed mills to minimize carryover

Response to Recommendation 1: Address Analytical Sensitivity

- CFIA lab responsible for feed drug residue analysis developed and validated a LC-MS/MS method for ionophore residues
  - LOQs of 10 ppb in feed
- Additionally, methods for other in-feed drug residues were also reviewed and more sensitive methods have since been developed for a number of analytes.
- The CFIA aims to develop feed drug residue methods with LOQs of 1-2 % of the lowest approved use rate in feed.

Response to Recommendation 1: Address Analytical Sensitivity

- Realizing the reduced LOQs would result in residue detections that may not represent an immediate risk to animal health or food safety the CFIA and Health Canada developed:
  1. Risk-based feed maximum levels (MLs) considering unintentional exposure due to cross-contamination for non-target livestock species
  2. Risk-based food MLs for liver and eggs from non-target livestock species.

Response to Recommendation 1: Address Analytical Sensitivity

Table 1: Maximum Limits (MLs) for lasalocid, monensin, narasin, nicarbazin, and salinomycin in feed, eggs, and liver for non-target species

Drug	Feed ML (ppm)	Egg ML (ppm)	Liver ML (ppm)
Lasalocid	0.5 (layers) 1.0 (others)	0.03	0.01
Monensin	1.0	0.025	0.01
Narasin	1.0	0.01	0.005
Nicarbazin	2.0	0.15	0.05
Salinomycin	0.5 (horses) 0.9 (turkeys) 1.0 (others)	0.01	0.035

Response to Recommendation 1: Address Analytical Sensitivity

- Feed MLs
  - Consider animal health
    - e.g., horse and turkey sensitivity to residues of salinomycin
  - Residue transfer to be protective of food MLs
    - e.g., lasolocid transfers to eggs more readily
- Food MLs
  - The magnitude of the food MLs for unintentional exposure from carryover cross-contamination represent a much smaller fraction of the ADI than would be considered for an MRL developed for an approved use of a drug.

Response to Recommendation 2 Management of Cross-Contamination

- CFIA developed the "Medication Sequencing Guideline for Management of Drug Carryover" as a risk management tool.

- Guidance for the feed industry to manage the order of production of medicated feed and non-medicated feed to limit incidents of carryover residues to feed for species where low-level residues would result in food violations.

https://inspection.canada.ca/animal-health/livestock-feeds/inspection-program/medication-sequencing/eng/1389362488069/1389362490053

Response to Recommendation 2 Management of Cross-Contamination

- Sequencing was limited based on the scope of the drug approval with some additional considerations:
  - Withdrawal times (i.e., finishing market animals).
  - Animal health concerns where cautions are indicated (e.g. ionophores and horses).
  - Drug incompatibilities (e.g. tiamulin and ionophores)
- When a valid production sequence is not possible, feed mills are expected to use a validated flushing or physical cleanout processes to eliminate carryover.

Response to Recommendation 2 Management of Cross-Contamination

- Additional sequencing flexibility was requested by the Feed Industry as the volumes of flushing materials generated presented handling, storage, and disposal challenges.
- The CFIA and Health Canada continued to assess the risk of additional sequencing options using data in the peer reviewed literature and information available from foreign drug approvals.
- The risk assessment framework is available to address new data or issues on a case-by-case basis

Summary

- Exposure to carryover cross-contamination of feeds with medications can result in detectable residues in foods of animal origin
- Good manufacturing practices should be followed to minimize to magnitude and frequency of occurrence
- Risk-based approaches for the mitigation and evaluation of residues in feeds for and foods derived from non-target livestock are needed

THANK YOU