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Purpose

Some feed manufacturing facilities use medications (drugs) in the production of feed products. This document describes the policy the Canadian Food Inspection Agency (CFIA) will use to determine if these facilities have developed and are using the necessary procedures and controls intended to mitigate the risks associated with the use of medications in their facility, such as the carryover of medications between feed batches.

Applicability and scope

Facilities manufacturing or handling livestock feeds, and medicating ingredients or medicated feeds.

Regulatory requirements

In Canada, the use of drugs in livestock feeds is regulated under two sets of legislation: the <u>Food and Drugs Act</u> and <u>Food and Drug Regulations</u>, which are administered by <u>Health Canada's Veterinary Drugs Directorate</u>, and the <u>Feeds Act</u> and <u>Feeds Regulations</u>, which are administered by the CFIA. Livestock is defined as cattle, sheep, horses, chickens, turkeys, geese, ducks, swine, rabbits, fish, mink and foxes.

The <u>Compendium of Medicated Ingredient Brochures</u> (CMIB) is a listing of drug premixes that have been approved and assigned a Drug Identification Number (DIN) by Health Canada. These premixes can be used without veterinary oversight in livestock feeds, as long as they are used in accordance with the CMIB (e.g., for the approved species, at the approved level).

Desired outcome

Control and management of medication residues in feeds that are not intended to contain them contributes to safe feed, prudent use of medications, as well as food safety. This includes controls to ensure the appropriate dosage of the correct medications in medicated livestock feeds and to control cross-contamination with medicated feeds with other feeds.

Cross-contamination of feeds occurs when substances, including medications which according to the formulation are not intentionally included in the feed, have been carried over from previous use of the same equipment. This carryover can be minimized through the use of effective equipment and good manufacturing practices, but cannot be completely eliminated without physical cleaning of the equipment.

If carryover is not properly managed, cross-contamination with medicated feeds can:

- harm species that are sensitive to the drug residues they consume
- contribute to antimicrobial resistance
- lead to drug residues in food products

The CFIA recognizes that the prevention of comingling or cross-contamination of feeds with medications through the use of dedicated equipment, or equipment cleanout, is not always practical. The Agency also considers the risk associated with unintentional medication residues acceptable in cases where there is no negative impact on animal or human health.

Considering these factors, the CFIA has developed guidelines to permit the production of medicated and non-medicated feeds in cross-utilized equipment, where feeds containing medications are followed only by feeds intended to contain those same medications, or by feeds where residual levels of the carryover medications present an acceptable risk. The CFIA's assessment of acceptable production sequences involving medications considers whether the medication residue(s) are appropriate for the species and class of animal affected.

Medication sequencing guideline for management of drug carryover

The Medication Sequencing Guideline for Management of Drug Carryover is used by CFIA inspection staff to assess the acceptability of feed production sequences involving medications. The guideline considers whether the medication residue(s) is (are) appropriate for the species and class of animal feed affected. It provides a listing of each approved drug, and identifies the types of feed (by species and class of animals) in which it is acceptable to have residual levels of that drug.

With a few exceptions, the information in the guideline reflects the intended uses detailed in the CMIB. The most notable set of exceptions are the result of a joint project between the CFIA and Health Canada designed to quantify the risks associated with carryover of individual drug residues, and to identify flexibilities or restrictions for production sequences where appropriate.

In cases where the order of feed production through common equipment occurs in an acceptable sequence, specific cleanout of the equipment is not required. In cases where the feed cannot be manufactured in an acceptable production order, the equipment involved must be cleaned (by flushing or other physical cleanout) using validated procedures. Information regarding acceptable procedures for validating equipment cleanout is available in Acceptable Validation Testing Procedures for Equipment Clean-out Procedures.

Associated documents

The following documents are used in association with the **Medicated Sequencing Guideline for Management of Drug Carryover:**

- Feeds Act and Regulations
- Feed Compliance Verification System Procedural Manual
- Compendium of Medicated Ingredient Brochures
- Veterinary Prescription Checklist
- Regulatory Guidance documents
- Validation Studies for Modification of Sequencing Guidelines
- Measurement of Feed Carryover Level; and
- Acceptable Validation Testing Procedures for Equipment Clean-out Procedures

Medication sequencing guideline for management of drug carryover

For use by CFIA inspection staff as a guide in assessing the adequacy of written clean out procedures for cross-utilized equipment used to manufacture and handle medicated feeds containing different medications or medicated and non-medicated feeds in commercial feed mills, feed retail outlets and on-farm feed mills. This document is a risk management tool used by CFIA inspection staff as a guide in verifying compliance with domestic requirements under the Feeds Act and Regulations associated with managing drug residue cross-contamination (14 (b) 19(1)(j)&(k)). Sequencing requirements related to other programs for such things as export (for example the Canadian Ractopamine-Free Pork Certification Program) or private certification are not included in this guide and may be more stringent.

For the most part, these guidelines reflect the intended uses detailed in the <u>Compendium of Medicating Ingredient Brochures</u> (CMIB) which are based on the submissions from the drug companies to Health Canada for approval, with the following exceptions:

- 1. Concerns related to residues of sulfamethazine in barbecue hogs has limited sequencing as a viable drug management strategy in commercial feed mills and feed retail outlets for this medication to swine starter rations (swine <20kg) with labelled withdrawal times of at least 7 days. For on-farm situations, greater sequencing flexibility remains as the livestock producer will have access to information on the feeding practices for the animals on the farm and be able to determine whether a residue might be present in animals receiving feeds that contain residual levels of sulfamethazine.
- 2. Health Canada and the CFIA are conducting a joint **Drug Carryover Risk Project** to evaluate the risks associated with carryover drug residues for both approved and unapproved uses in order to provide additional guidance on management strategies supporting the development of production sequences that will result in the manufacture of feeds that do not negatively impact on either animal or human health. This version of the Medication Sequencing Guideline includes the results of evaluations to date, e.g., where scientifically justified, carryover levels of medications such as chlortetracycline hydrochloride, lasalocid sodium, and lincomycin are now considered acceptable in certain additional species or production classes of animal for which the

- drug is not approved in the CMIB. Updates to the Medication Sequencing Guideline will continue to be made as the evaluation of additional drugs is completed.
- 3. In the absence of safety evaluations, Emergency Drugs Release (EDRs) can only be sequenced when both feeds contain the same medications stipulated on the EDR.

Remarks

- This guide requires that inspection staff consider concentration of medications in feeds when
 assessing sequencing procedures to verify that carryover does not result in the feeds
 (unintentionally) containing treatment levels of medications (for example, a complete feed
 might safely follow a medicated complete feed but it may not be safe for that same complete
 feed to follow a medicated premix or other medicated feed containing high concentrations of
 the same drug).
- 2. Market Ready is defined as follows:
 - for feeds manufactured in commercial feed mills feeds labelled for consumption by finishing animals, growing swine, laying hens and lactating animals producing milk intended for human consumption or where the labelling does not specify the stage of production (e.g. swine ration).
 - o for feeds manufactured on-farm feeds intended for feeding to animals that produce food for human consumption (meat, milk, eggs) within the withdrawal period for the drug being fed. Special caution needs to be used when culling sows or selecting BBQ hogs, etc. to make sure that animals that have consumed a feed containing a medication that has a withdrawal period are fed non-medicated feed for a period equal to the withdrawal period for that medication prior to being shipped.

Medication sequencing guideline for management of drug carryover				
Medication	Brand name (DIN)	MIB Code	Approved for	May follow with feeds for
Amprolium	Amprol Feed Premix (140503)	АМР	1. Broiler and replacement chickens, turkeys (not laying birds or breeders) 2. Calves (not replacement, not market ready)	 Turkeys up to 16 weeks of age Chickens up to 18 weeks Calves (not replacement, not market ready)
Avilamycin	1. Surmax 100 Premix (02421062) 2. Surmax 200 Premix (02436760)	AVI	 Broiler chickens (not laying birds) Swine (less than 14 weeks of age) 	1. Broiler chickens 2. Swine (less than 14 weeks of age)
Bacitracin methylene disalicylate	1. BMD 110 G Medicated Premix (2206099) 2. Bacitracin MD Premix (2408317)	BACN-	 Broiler chickens Pregnant and Lactating Swine 	1. Broiler chickens and replacement hens (layers and breeding hens not in lay) 2. Swine 3. Turkeys (meat birds)
Bacitracin zinc	 Albac 110 Zinc Bacitracin Premix (2237196) Zinc Bacitracin 110 (824186) 	BACN-	 Chicks and Broiler Chickens Swine 	1. Broiler chickens and replacement hens (layers and breeding hens not in lay) 2. Turkeys – meat birds 3. Swine
Bambermycins	Flavomycin 4 Antibiotic Premix (577235)	BAM	Broiler chicken and turkeys (not layers, breeders or replacement birds)	 Chickens – meat birds up to market weight Turkeys - meat birds up to 12 weeks

Medication sequencing guideline for management of drug carryover				
Medication	Brand name (DIN)	MIB Code	Approved for	May follow with feeds for
Chlortetracycline hydrochloride	 Aureomycin 220G Granular Medicated Premix (2242693) Chlor 50 (641804) Chlor 100 (698210) Deracin 22% granular premix (2407558) 	СТС	 Turkeys (not market ready) Swine (not market ready) Beef and non-lactating dairy cattle (not market ready) Lambs (not market ready) 	 Chickens (not market ready - meat) Turkeys (not market ready) Lambs (not market ready) Swine (not market ready) Beef and non-lactating dairy cattle (not market ready)
Chlortetracycline hydrochloride, sulfamethazine, and procaine penicillin	 Aureo S-P 250 G Granular Medicated Premix (2242661) Aureomix 625 G Granular Medicated Premix (2242706) Chlor 250 Medicated Premix (641979) Super Chlor 250 (657220) Super Chlorosol 250 Premix (2172658) 	CSP	Swine	1. Swine (starter swine (<20 kg) feeds with a minimum 7 day withdrawal or onfarm feed mills only) 2. Chickens – meat Table Note 1 (on-farm feed mills only, not breeding, not market ready) 3. Turkeys – meat Table Note 1 (on-farm feed mills only, not breeding, not market ready)
Clopidol	Coyden 25 Anticoccidial Premix (656925)	CLO	Broiler and replacement layer chickens (not birds for breeding)	Chickens (up to 16 weeks)

Medication sequencing guideline for management of drug carryover				
Medication	Brand name (DIN)	MIB Code	Approved for	May follow with feeds for
Decoquinate	 Deccox 6% Premix (867349) Deccox-M Premix (2312379) 	DEC	1. Broiler chickens 2. Cattle (not lactating dairy cattle producing milk for food) 3. Lambs (not lactating ewes producing milk for food)	II Sheen (not lactating I
Diclazuril	Clinacox 0.5% Premix (2246048)	DCLZ	Broiler chickens and growing turkeys	 Chickens - meat birds up to market weight. Growing turkeys (up to 14 weeks in age).
Emamectin benzoate	Slice 0.2% Premix (02328216)	EMA	Atlantic salmon (not breeding stock)	Atlantic salmon (not breeding stock)
Fenbendazole	Safe-Guard Premix 20% (617598)	FEN	 Swine Cattle (not market ready) Turkey (not breeding, not market ready) 	 Swine Cattle (not market ready) Turkey (not breeding, not market ready)
Florfenicol	1. Nuflor 4% Premix (02339579) 2. Aquaflor 50% Medicated Premix (02231742)	FLOR	1. Swine (not breeding stock, not market ready) 2. Salmon (not market ready or for release as stocker fish)	stock, not market ready)
Halofuginone hydrobromide	Stenorol Premix (2031124)	HAL	Chickens - meat birds raised for slaughter (not market ready)	Chickens - meat birds raised for slaughter (not market ready)

Table note 1: Additional flexibility as a result of the Drug Carryover Risk Project

Medication sequencing guideline for management of drug carryover				
Medication	Brand name (DIN)	MIB Code	Approved for	May follow with feeds for
Ivermectin	 Ivomec Premix For Swine (1913085) Ivomec 0.04% Premix For Swine (2225204) 	IVR	Swine (not market ready)	Swine (not market ready)
Lasalocid sodium	1. Avatec 20 Lasalocid Sodium Premix (2321920) 2. Bovatec 20 Lasalocid Sodium Premix (2321939)	LAS	 Broiler chickens - up to market weight Turkeys - meat birds up to market weight Cattle Lambs 	·
Lubabergon	Experior Lubabegron Premix (02482016)	LBGF	Beef cattle (steers and heifers fed in confinement)	Beef cattle (steers and heifers)
Lincomycin	 Lincomix 44 Premix (813559) Lincomix 110 Premix (813648) Lincomycin 44 Premix (2085844) Lincomycin 110 Premix (2089874) Lincomycin 44 G Premix (2091097) Lincomycin 110 G Premix (2089882) 	LINC	Swine (not breeding swine)	 Swine Table Note 1 (not breeding swine) Chickens- meat birds up to market weight Turkeys Table Note 1 (not breeding turkeys)

Ме	Medication sequencing guideline for management of drug carryover				
Medication	Brand name (DIN)	MIB Code	Approved for	May follow with feeds for	
Lincomycin and spectinomycin	1. L-S 20 Premix (813907) 2. Lincomycin- Spectinomycin 4.4% G Premix (2209098)	LISP	Swine (not breeding swine, not market ready)	Swine Table Note 1 (not breeding swine, not market ready)	
Maduramicin ammonium	Cygro 1% Premix (2243809)	MAD	 Broiler chickens and turkeys (not layers, not market ready) Not feeds containing tiamulin 	 Chickens - meat birds raised for slaughter (not market ready) Turkeys - meat birds raised for slaughter (not market ready) Not feeds containing tiamulin 	
Melengestrol acetate	MGA 100 Premix (813826)	MGAF	Feedlot heifers	Beef cattle - heifers only (181 kg or more, not market ready)	
Monensin sodium	 Coban Premix (2231172) Rumensin Premix (2231173) Monensin Premix (2243232) 	MOS	1. Broiler chickens and turkeys (not replacement or layers) 2. Cattle 3. Sheep (not lactating ewes 4. Goats (not lactating nannies) 5. Not feeds containing tiamulin	 Chickens - meat birds up to market weight Turkeys raised for slaughter up to market weight Cattle Table Note 1 Swine Table Note 1 Lambs, ewes and rams Table Note 1 Goats (not lactating nannies) Not feeds containing tiamulin 	

Medication sequencing guideline for management of drug carryover				
Medication	Brand name (DIN)	MIB Code	Approved for	May follow with feeds for
Morantel tartrate	Banminth II 20% Premix (327042)	MORF	Swine Cattle	Cattle (not market ready) Swine (not market ready)
Narasin	Monteban 100 Premix (2431696)	NAR	Broiler chickens Swine (not breeders or replacements) Not feeds containing tiamulin	 Chickens - meat birds up to market weight Table Note 1 Beef cattle Table Note 1 Swine Table Note 1 Not feeds containing tiamulin
Neomycin sulfate and Oxytetracycline dihydrate	Neo-Terramycin 50/50 (02325098)	NEOTC	Pigs (not breeding, not market ready)	Pigs (not breeding, not market ready)
Narasin and nicarbazin	Maxiban Premix (1902687)	NRNC	 Broiler chickens (not breeding hens in production) Not feeds containing tiamulin 	 Chickens - meat birds raised for slaughter Not feeds containing tiamulin
Nicarbazin	Nicarb 25% Premix (140546)	NIC	Chickens (not layers or breeding hens)	Chickens up to 18 weeks of age Turkeys Table Note 1 meat birds
Oxytetracycline hydrochloride	Terramycin-Aqua Oxytetracycline Dihydrate Medicated Premix (2421216)	ОТС	Salmonids (not market ready)	Salmonids (not market ready)

Medication sequencing guideline for management of drug carryover				
Medication	Brand name (DIN)	MIB Code	Approved for	May follow with feeds for
Oxytetracycline hydrochloride	1. Terramycin-50 (2246806) 2. Terramycin-100 (2246807) 3. Terramycin-200 (2246808) 4. Oxysol 110 (780774) 5. Oxysol 220 (2223902) 6. Oxysol 440 (685224) 7. Oxytetracycline 50 premix (637513) 8. Oxytetracycline 100 premix (654787) 9. Oxytetracycline 200 premix (719315)	отс	 Turkeys (not market ready) Swine (not market ready) Beef cattle (not market ready) Calves (not market ready) Lambs (not market ready) 	 Chickens (not market ready - meat) Turkeys (not market ready) Lambs (not market ready) Swine (not market ready) Cattle (not lactating dairy cows, not market ready)
Penicillin	Penicillin G Procaine 110 (1989944)	PEN	Broiler chickens	 Chickens Table Note 1 — (not breeding, not laying) Swine Turkeys - (not breeding)
Piperazine	Piperazine 52 (236667)	PID	1. Chickens 2. Turkeys 3. Swine	1. Turkeys 2. Chickens 3. Swine
Poloxalene	Bloat-Guard (1911643)	POX	Cattle	Cattle

Medication sequencing guideline for management of drug carryover				
Medication	Brand name (DIN)	MIB Code	Approved for	May follow with feeds for
Pyrantel tartrate	Pro-Banminth Premix (491799)	PYRF	Swine intended for slaughter (not market ready)	Swine intended for slaughter (not market ready)
Ractopamine hydrochloride	 Paylean 20 Premix (2268973) Engain 20 (2426447) Optaflexx 100 Premix (2295091) Actogain 100 (2426242) 	RAC	 Finishing turkeys (not breeders) Finishing swine ≥70 kg (not breeding or replacement) Confined finishing cattle (greater than 400 kg, not lactating dairy cattle and calves to be processed for veal) 	 Finishing swine ≥7 0 kg (not breeding or replacement) Finishing heavy toms or hens turkeys for the last 14 days prior to slaughter (not breeding) Cattle (greater than 400 kg fed in confinement 28-42 days prior to slaughter, not lactating dairy cattle and calves to be processed for veal)
Robenidine hydrochloride	Robenz Medicated Premix (2242975)	ROB	 Broiler chickens (not market ready) Turkeys (not older than 8 weeks of age, not market ready) Weaned and growing rabbits (not market ready, not breeding animals) 	 Chickens - meat birds raised for slaughter (not market ready) Turkeys - meat birds raised for slaughter under 8 weeks of age Weaned and growing rabbits (not breeding rabbits, not market ready)

Medication sequencing guideline for management of drug carryover				
Medication	Brand name (DIN)	MIB Code	Approved for	May follow with feeds for
Salinomycin sodium	 Coxistac 6% Premix (884545) Coxistac 12% Premix (2237631) Posistac 6% Premix (603724) Sacox 120 Medicated Premix (2230508) Salinomycin 60 Premix (2237431) Bio-Cox 120 G Plus Premix (2246692) 	SAL	 Broiler chickens (not replacement or breeders) Swine (not breeders) Beef cattle (not replacement or breeding animals, not calves < 220 kg) Rabbits (not market ready) Not feeds containing tiamulin 	 Swine Table Note 1 (not breeding swine) Weaned and growing rabbits – not breeding animals, not market ready Chickens - meat birds up to market weight Beef cattle (not replacement or breeding animals, not calves <220 kg) Not feeds containing tiamulin
Semduramicin sodium	Aviax Medicated Premix 5% (2229543)	SEMD	1. Broiler chickens (not replacement or breeders, not marker ready) 2. Not feeds containing tiamulin	 Chickens - meat birds raised for slaughter (not market ready) Not feeds containing tiamulin
Sulfadimethoxine and Ormetoprim	Romet 30 Medicated Premix (2242954)	SMOR	Salmonids (not market ready or for release as stocker fish, not for smolt)	Salmonids (not market ready or for release as stocker fish, not for smolt)
Sulfadiazine and Trimethoprim	 Uniprim Oral Powder (02241375) Uniprim Oral Granules (02320835) Tribrissen 40% Powder (02146037) 	SZTM	 Horses (not market ready (meat)) Salmon (not market ready or for release as stocker fish, not for smolt) 	 Horses (not market ready (meat)) Salmon (not market ready or for release as stocker fish, not for smolt)

Table note 1: Additional flexibility as a result of the Drug Carryover Risk Project

Medication sequencing guideline for management of drug carryover				
Medication	Brand name (DIN)	MIB Code	Approved for	May follow with feeds for
Tiamulin	 Denagard Medicated Premix (860735) Tiamulin 1.78% Premix (2242446) Denagard 10% GF Premix (2393301) Tamulin HF 10% Premix (2444364) 	TIA	1. Swine (not market ready or gilts/sows within four weeks after service) 2. Not feeds containing polyether ionophores (monensin, salinomycin, narasin, lasalocid, maduramicin and semduramicin)	1. Swine (not market ready or gilts/sows within four weeks after service) 2. Not feeds containing polyether ionophores (monensin, salinomycin, narasin, lasalocid, maduramicin and semduramicin)
Tilmicosin	 Pulmotil Premix (2240124) Tilmovet Premix (2349507) Tilmicosin 200 Premix (2461099) 	TIL	1. Swine (not market ready, not boars used for breeding) 2. Feedlot beef cattle (not market ready, not pre-ruminant calves or replacement or breeding cattle) 3. Rabbits (not market ready, not breeding animals)	1. Swine (not market ready, not boars used for breeding) 2. Feedlot beef cattle (not market ready, not pre-ruminant calves or replacement or breeding cattle) 3. Rabbits (not market ready, not breeding animals)
Tylosin phosphate	 Tylan 10 Premix (103624) Tylan 40 Premix (474444) Tylan 100 Premix (2242023) Tylosin 10 Premix (713481) Tylosin 40 Premix (800422) Pharmasin 100 Premix (2397846) 	TYL	 Broiler chickens Swine Beef cattle (not replacement, breeding or lactating cattle) 	1. Swine 2. Beef cattle (not replacement, breeding or lactating cattle) 3. Chickens - meat birds up to market weight

Table note 1: Additional flexibility as a result of the Drug Carryover Risk Project

Medication sequencing guideline for management of drug carryover				
Medication	Brand name (DIN)	MIB Code	Approved for	May follow with feeds for
Tylvalosin tartate	Aivlosin 17% Premix (2419491)	TYLV	Swine (not male or female breeding swine, including pregnant and lactating sows)	Swine (not male or female swine intended for breeding including pregnant and lactating sows)
Virginiamycin	 Stafac 22 (1908359) Stafac 44 (1908367) Stafac 500 (1908340) Virginiamycin 44 Premix (2215691) Vmax 44 (02484323) Vmax 500 (0248331) 	VMY	1. Broiler chickens (not replacement or breeding animals) 2. Swine 3. Cattle (fed in confinement for slaughter)	 Swine Chickens (meat birds up to market weight) Beef cattle (not veal, not replacement, breeding or lactating cattle)
Zilpaterol hydrochloride	Zilmax Premix (2324121)	ZIL	Beef cattle greater than 450 kg (on-farm only, not market ready, not calves to be processed for veal or animals intended for breeding)	Beef cattle greater than 450 kg (on-farm only, not market ready, not calves to be processed for veal or animals intended for breeding)
Zoalene	Zoamix Medicated Premix (656917)	ZOAF	 Chickens up to 14 weeks of age Turkeys up to 7 weeks of age 	Chickens up to 14 weeks of age Turkeys up to 7 weeks of age