



Stockfeed Guideline Document 2
Setting Animal Commodity MRLs Based On
Livestock Dietary Exposure
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Setting Animal Commodity MRLs Based On Livestock Dietary Exposure

Scope

This document describes the procedure used by the NRA to establish Maximum Residue Limits (MRLs) for animal tissues, milk and eggs to cover residues arising from animals consuming treated feed commodities.

Background

The use of agricultural chemical products can result in the presence of chemical residues in agricultural commodities that are subsequently fed to livestock. Measurable residues of the chemical may occur in the tissues, milk and eggs of livestock consuming the treated feed commodity as a normal part of the diet. The NRA routinely establishes MRLs for animal tissues, milk and eggs to cover the residues that may arise as a result of livestock consuming treated feed items.

Residues of agricultural or veterinary chemicals can also occur in animal tissues, milk and eggs as a result of direct application to the animal. This information document is concerned only with the procedure for setting animal commodity MRLs based on dietary exposure from approved/registered uses of chemical products.

The animal commodity MRLs are established following consideration of (i) the magnitude of the residue in potential animal feed commodities, (ii) the amount of each feed commodity consumed by the animal and (iii) the extent to which livestock dietary exposure to the chemical results in residues in edible tissues, milk and eggs (animal transfer studies and/or metabolism studies).

Proportion of feed commodities in the livestock diet

A full discussion of the assumed feeding percentages of common animal feed commodities can be found in the Stockfeed Guideline Document 1: Primary Feed Commodities as a Proportion of Livestock Diets. The feeding percentages outlined in Stockfeed Guideline Document 1 are used by NRA evaluators to estimate the anticipated livestock dietary exposure.

Anticipated livestock dietary exposure

The daily intake of a chemical by an animal (mg chemical/animal/day) consuming a single feed commodity, is determined by multiplying the maximum residue in the feed commodity (mg/kg, dry matter basis) by the daily consumption of the feed commodity (kg/animal/day).

Where there are multiple sources of exposure in the diet, the overall dietary exposure is calculated by summing the contribution of treated feed commodities to give a total consumption equivalent to 100% of the diet. Taking into account the maximum percentage feed levels identified in Stockfeed Guideline Document 1, the feed commodities with the highest MRLs are used first so as to determine the highest anticipated dietary exposure.

Animal transfer studies

The relationship between the level of chemical in the livestock diet and the level of the residue observed in edible tissues, milk and eggs is determined by evaluation of animal transfer studies. Animal transfer studies are conducted by administering daily doses of the chemical to animals at various dietary exposure levels. Contemporary animal transfer studies are normally conducted over a 28 day dosing period and may also include a withdrawal or depuration period.

The current NRA guideline¹ states that animal transfer studies should be conducted if the total livestock dietary exposure is greater than or equivalent to 0.1 ppm. There are, however, exceptions to this trigger value where the chemical may rapidly accumulate in the fat. In cases where a transfer study is not available, or the anticipated dietary exposure is greater than the highest feed level in the transfer study, then some extrapolation may be made from relevant metabolism studies.

Metabolism studies are typically conducted by administering multiple doses over a range of intervals between 2 to 14 days². Such studies would only be useful where the composition of the total radioactive residues was determined in edible tissues, milk and eggs or the total radioactive residues in edible tissues were very low. In most cases where metabolism studies are used to set animal MRLs, both situations would apply. If however, the metabolism studies showed that the active constituent had a propensity to accumulate in offal or fat, then an animal feeding study would be specifically requested.

Setting the required MRLs

The anticipated livestock dietary exposure is compared to the feeding levels in animal transfer and/or metabolism studies and the resulting residue levels in tissues, milk and eggs. MRLs for animal tissues, milk and eggs are established at levels that would cover the highest residues expected to occur from the estimated livestock dietary exposure.

A new term called the Maximum Feeding Level (MFL) will be reported for each chemical. This value is the feed level used to establish the animal commodity MRLs. The MFL is expressed in parts per million (ppm) which is equivalent to mg chemical/kg feed, on a dry matter basis. The value may also be expressed in mg chemical/kg bodyweight of animal, in which case it is called the Daily Dietary Intake for Livestock (DDIL). The DDIL allows the exposure for various species (e.g. cattle, sheep and pigs) to be compared on a bodyweight basis. The DDIL also allows different animal transfer studies (eg. meat and milk) to be compared, where animals of differing bodyweights have been used in the different studies.

Worked example

The methodology used by the NRA closely follows that used by the JMPR³.

¹ Residue Guideline No. 1- Animal transfer studies

² Other factors such as $t_{1/2}$ for a single dose would also be considered, to determine whether the feeding period in a continuous dose study was adequate to allow radioactivity in various tissues to have reached a plateau or steady-state.

³ Joint Meeting of the FAO Panel of Experts on Pesticide Residues and the Environment and the WHO Expert Group Expert Group on Pesticide Residues

Active X is applied to cereal grains (post-harvest only) and apples for control of insect pests. The anticipated residues in cereal grains and dry apple pomace are 5 mg/kg and 10 mg/kg respectively.

According to Stockfeed Guideline Document 1 cereal grains may contribute up to 100% of the dietary intake for cattle on a dry weight basis. Apple pomace may contribute up to 20% of the diet on a dry weight basis. Cattle are assumed to have a bodyweight of 500 kg and consume 20 kg dry matter per day. The following table can be constructed to summarise the anticipated dietary exposure for cattle:

| Feed commodity | % in the diet | kg feed/animal/day | Residue ^b (mg/kg) | mg Active X /animal/day | mg Active X/kg bw/day |
|-------------------|-----------------|--------------------|------------------------------|-------------------------|-----------------------|
| Apple pomace, dry | 20 | 4 | 10 | 40 | 0.08 |
| Cereal grains | 80 ^a | 16 | 5 | 80 | 0.16 |
| Total | 100 | 20 | - | 120 | 0.24 |

- Cereal grains may contribute up to 100% of the diet. In this example the feed commodity with the highest anticipated residue (apple pomace, dry) is fed up to its maximum proportion (20%) and the remainder of the diet (80%) is comprised of cereal grains.
- The residue level may be the MRL or the highest or median residue observed in supervised residue trials, as deemed appropriate.

In an animal transfer study lactating cattle were dosed orally with Active X for 28 consecutive days at rates equivalent to 6.25, 18.75 and 62.5 ppm in the diet. The rates were equivalent to 0.25, 0.75 and 2.5 mg Active X/kg bw/day. The maximum residues observed in edible tissues and milk are shown below:

| Dose level, (mg Active X/kg bw/day) | Maximum residue of Active X (mg/kg) | | | | |
|-------------------------------------|-------------------------------------|--------|--------|-------|------|
| | Liver | Kidney | Muscle | Fat | Milk |
| 0.25 | 0.06 | 0.18 | 0.07 | <0.01 | 0.03 |
| 0.75 | 0.19 | 0.58 | 0.23 | <0.01 | 0.10 |
| 2.5 | 0.58 | 2.1 | 0.76 | 0.05 | 0.28 |

The anticipated dietary exposure for cattle was previously calculated to be 0.24 mg Active X /kg bw/day. The anticipated dietary exposure corresponds closely with the lowest dose level administered in the animal transfer study. The maximum residues observed following continuous feeding at 0.25 mg Active X/kg bw/day were 0.18 mg/kg for edible offal (liver and kidney), 0.07 mg/kg for muscle (ie. meat) and 0.03 mg/kg for milk. There was no preferential accumulation in fat.

Appropriate MRLs would be as follows:

| | |
|--------------------------|------------|
| Edible offal (mammalian) | 0.2 mg/kg |
| Meat (mammalian) | 0.1 mg/kg |
| Milks | 0.05 mg/kg |

The Maximum Feeding Level (MFL) is 6.25 ppm which is equivalent to a Daily Dietary Intake for Livestock (DDIL) of 0.25 mg Active X/kg bw/day.