Matrix Ranking for Prioritising Testing of Veterinary Medicine Residues

[A + B] × [C + D + E + F] = **Substance Total Score**

Nature of the hazard

The more serious the potential adverse effect, the higher the score.

Toxicological data are assessed as part of the authorisation process of a veterinary medicine. In this, potential adverse effects caused by exposure to a substance are identified. The more serious the potential adverse effect identified, especially if it is irreversible, the higher the score.

Typical evidence base: The most recent evaluations by the European Medicines Agency's (EMA) Committee on Medicinal Products for Veterinary Use (CVMP), the Joint FAO/WHO Meeting on Food Additives (JECFA), the European Food Safety Authority (EFSA) or other evaluations by international risk assessment bodies.

Scores	
0	No reported adverse effects
1	Reversible adverse pharmocological or microbiological effects
2	Reversible organ toxicity
3	Evidence of allergic reactions in animals in safety testing
4	Non-genotoxic carcinogen. Irreversible organ toxicity.
5	Irreversible effects including neurotoxicity, reproductive toxicity and immunotoxicity
6	Carcinogenic in rodent bio-assays with mode of action relevant to humans (e.g. genotoxic *in vivo*)

Potency

The lower the dose that can cause the adverse effect, the higher the score.

Most substances will cause adverse effects if we eat or absorb enough. The MR assessment is based on the Acceptable Daily Intake (ADI – expressed in µg/kg bw/day) or No Observable (Adverse) Effect Level (NO(A)EL) if no ADI is available.

Typical evidence base: Identical to the evidence used for Hazard (A).

See also the general rules (below) to be considered when scoring a substance for hazard and potency.

Scores	
0	> 10 µg/kg/bw/day
1	>0.1 - 10 µg/kg/bw/day
2	>0.001 - 0.1 µg/kg/bw/day
3	<0.001 µg/kg/bw/day

Estimate of the proportion of meat and animal products consumed that comes from animals which may have been treated

The higher the proportion of food that might come from a treated animal, the higher the score.

Some medicines are used only in a single species, while others are used in several, increasing the chance of exposure.

Typical Evidence Base: Standard Food Basket reports, Marketing Authorisations or label instructions (if black market) for veterinary medicines by species (provided that they relate to countries which exports that species to the UK)

Benchmark taken for % of diet: National Diet and Nutrition Survey 2008/9 – 2011/12 - Mean g/week for men in 19 - 64 age group.

Scores	
0	<2.5%
1	2.5% - 20%
2	20% - 50%
3	>50%

Estimate of frequency of dosing / percentage of animals within the herd treated when the product is administered correctly

Some medicines are used over a whole herd, while others are used to treat individual animals. Additionally, (e.g. for some endoparasites) sheep flocks might be treated a number of times during the year.

Typical evidence base: Label instructions on formulated medicines, reports from veterinarians on how medicines are used in the field, endemic diseases in countries with export to the UK for which the medicine is a popular treatment (data from veterinarians, FVO reports, climate-dependant diseases).

Scores	
0	<2.5%
1	2.5% - 20%
2	20% - 50%
3	50% - 100%

Evidence for high exposure groups, based on consumption of the species in which the medicine may be used

Where there are consumer groups who might be at particular risk a higher score is allocated.

Some groups might ingest a higher amount of a particular residue because of their pattern of consumption of foods. Higher scores will be allocated if there is a significant age or sex-related difference in consumption compared with the benchmark in Category C. Higher scores may also be allocated based on other strong anecdotal or circumstantial evidence.

Typical evidence base: Dietary groups within the population where their major source of protein comes from a single species or animal product.

Scores	
0	No evidence for high exposure groups
1	Unlikely to be high exposure groups
2	Likely to be high exposure groups
3	Strong evidence for high exposure groups

Evidence for detectable residues, or suspicion of misuse coupled with insufficient residue monitoring data.

Where residues above legal or other limits have been detected, a higher score is allocated.

The greater the number of non-compliant residues for the particular substance, the higher the score allocated. Highest score may be allocated when either a residue has been confirmed for a substance for which no safe concentration has been identified; or no residue testing has been carried out.

Typical evidence base : Residue monitoring reports, RASFF notifications, FVO reports (including conclusions on the effectiveness of controls on VMP sales and prescription), ready on-line access to formulations and dosing instructions for unapproved species applications. (e.g. Alibaba.com, for China).

Overall Substance Score

(A+B) x (C+D+E+F)

A	Hazard
B	Potency
C	Diet
D	Frequency
E	Exposure
F	Evidence

Matrix Ranking Principles

In 'Matrix Ranking', specific criteria and weightings were developed, against which candidate substances were assessed. The Committee hopes stakeholders see this as an open and transparent system for prioritising the sampling.

Scoring Hazard (A) and Potency (B) – General Rules

- The hazard scored in 'A' must relate to the potency score given in 'B'.
- For any substance, in most cases the scores for hazard (A) and potency (B) will be based on the sum of the toxicological effect (A) and related potency (B) which give the highest resulting score. Generally this means that the score will be based on the highest score for hazard and this is likely to be the most critical effect of the substance.
- In the first instance the hazard score is based on the most sensitive no-observed-adverse-effect-level (NOAEL - often a body-weight effect). However, if a more critical adverse effect (e.g. adverse reproductive effects) occurs within 5-fold of the most sensitive NOAEL, the more critical effect will be used to derive the hazard score.
- When the critical effects are only applicable at levels too high to be relevant (cut-off point nominally chosen as more than 5-fold of the most sensitive NOAEL) then the more sensitive effect will be used for arriving at a score.

These rules may not cover all eventualities. Where scientific judgement is applied, the reasoning for any deviations from the application of these rules will be supplied.

Matrix ranking system developed by the Veterinary Residues Committee with the assistance and advice of the Veterinary Medicines Directorate and the Food Standards Agency.