Food Safety
AUTHORITY OF IRELAND

Report of the Scientific Committee
of the Food Safety Authority of Ireland

2014

Risk-Based Approach to Developing the National Residue Sampling Plan

(For Veterinary Medicinal Products and Medicated Feed Additives in Domestic Animal Production)

Report of the Scientific Committee
of the Food Safety Authority of Ireland

Risk-Based Approach to Developing the National Residue Sampling Plan

(For Veterinary Medicinal Products and Medicated Feed Additives in Domestic Animal Production)

Published by:
Food Safety Authority of Ireland
Abbey Court, Lower Abbey St
Dublin 1

Advice Line: 1890 336677
Tel: +353 1 8171300
Fax: +353 1 8171301
info@fsai.ie
www.fsai.ie

ISBN 1-904465-93-5

Abbreviations used within this report:

CVMP	Committee for Medical Products for Veterinary Use
DAFM	Department of Agriculture, Food and the Marine
EFSA	European Food Safety Authority
EMA	European Medicines Agency
FEEDAP	Panel on Additives and Products or Substances used in Animal Feed
FSAI	Food Safety Authority of Ireland
FSIS	Food Safety and Inspection Service
MI	Marine Institute
MRL	Maximum Residue Limits
NFRD	National Food Residue Database
RASFF	Rapid Alert System for Food and Feed
USDA	United States Department of Agriculture

Risk-Based Approach to Developing the National Residue Sampling Plan

(For Veterinary Medicinal Products and Medicated Feed Additives in Domestic Animal Production)

CONTENTS

SUMMARY

A ranking system for veterinary medicinal products and medicated feed additives has been developed as a tool to be applied in a risk-based approach to the residue testing programme for foods of animal origin in the National Residue Control Plan.

There have been a number of developments over the last decade at European Union level, at Member State level and internationally towards a risk-based approach to developing residue testing programmes. Within the EU, consideration has been given to part of the residue testing programme being undertaken at a national level using a risk-based approach. In recently-published European Food Safety Authority Opinions, risk ranking of both biological hazards and chemical hazards are central to proposals for a new approach to meat inspection.

In the context of food sampling and residue testing for the National Residue Control Plan, there is firstly, the risk to human health from residues of chemical substances in food and secondly, the issue of non-compliance with regulations relating to residues in food due to improper farm practices; both these elements are included in the developed risk-ranking of substances. Three characteristics of substances that may occur as residues in food are included in the developed risk-ranking system: 'Potency', as measured by the acceptable daily intake value assigned to each substance; 'Usage', as measured by the three factors of number of doses, use on individual animals or for group treatment, and withdrawal period; 'Residue Occurrence', as measured by non-compliant samples in the National Residue Control Plan. For both number of doses and non-compliant samples, data for the five-year period 2008 to 2012 have been used.

The risk-ranking system for substances has been developed for beef cattle, sheep and goats, pigs, poultry and dairy cattle using a scoring system applied to the various parameters described above to give an overall score based on the following equation:

'Potency' ×' Usage' (no. doses + individual/group use + withdrawal period) × 'Residue Occurrence'

Applying this risk-ranking system, the following substances are ranked very highly: antimicrobials such as Amoxicillin (for all species except pigs), Oxytetracycline (for all species except poultry), Sulfadiazine with Trimethoprim (for pigs and poultry) and Tilmicosin (for poultry); antiparasitic drugs, such as the benzimidazoles Triclabendazole (for beef and dairy cattle), Fenbendazole/Oxfendazole (for sheep/goats and dairy cattle) and Albendazole (for dairy cattle), the avermectin Ivermectin (for beef cattle), and anti-fluke drugs Closantel and Rafoxanide (for sheep/goats); the anticoccidials Narasin, Nicarbazin and Toltrazuril (for poultry).

The risk-ranking system described is a relatively simple system, designed to provide a basis for selecting the veterinary medicinal products and medicated feed additives that might be prioritised for residue testing. However, there are a number of limitations associated with the system and this risk-ranking of substances represents only one component of a total risk-based approach to designing the residue testing programme for the annual National Residue Control Plan. Other factors which should be taken into account are issues of regulatory concern, such as evidence of misuse of particular veterinary medicinal products and medicated feed additives and changes in the specifications for particular veterinary medicinal products and medicated feed additives, such as new maximum residue limits that would affect the occurrence of non-compliant samples. In addition, the importance of multi-analyte residue testing methods and dietary exposure need to be considered.

BACKGROUND

A working group on the topic *Application of a risk-based approach to developing the national residues sampling plan* was established during the lifetime of the previous *Food Additives, Chemical Contaminants and Residues Sub-Committee* of the Scientific Committee, Food Safety Authority of Ireland (FSAI).

The previous sub-committee was established in January 2008 following discussions between personnel from the FSAI, Ashtown Food Research Centre, Teagasc and the Department of Agriculture, Food and the Marine (DAFM). A total of five meetings of the working group were held during the period January 2008 to September 2009 and the membership consisted of personnel from the FSAI, DAFM, Ashtown Food Research Centre, Teagasc and the Marine Institute (MI).

The context for the working group's activities was the following:

a) Developments at an EU level towards a risk-based approach for the 'national' component of the National Residue Control Programme in the proposed replacement of Council Directive 96/23/EC, including the *Reflection Paper* exercise

b) A Food for Health Research Initiative (FHRI) funded project at Ashtown Food Research Centre, Teagasc entitled 'Food safety – monitoring and surveillance' (2008-2012) for which one objective was *to develop a risk-based approach for monitoring and surveillance of chemical contaminants in foods consumed in Ireland through prioritisation of substances based on toxicity, incidence and usage*

c) Concerns expressed over a number of years by agencies/laboratories involved in sampling and testing for the Irish National Residue Control Plan that these activities should be better focused, based on risk

The working group undertook the following tasks:

a) Consideration of systems used in other countries to develop risk-based sampling, such as the UK Veterinary Residues Committee (VRC) *Matrix Ranking for Prioritising Testing of Veterinary Medicine Residues* and the United States Department of Agriculture Food Safety and Inspection Service (USDA FSIS) *Design of the Domestic Scheduled Sampling Plan for Veterinary Drugs*

b) Consideration of the outputs from the database on usage of veterinary medicines and feed additives, developed within the FHRI funded research project on 'Food safety – monitoring and surveillance', including systems to validate usage data

c) Consideration of additional information to be used in a risk-based ranking, such as (a) seasonal variation in usage of veterinary medicines and feed additives, (b) use of medicated feed additives and pre-mixes, (c) data on non-compliant samples for prohibited substances determined in Ireland and in other Member States, (d) toxicological parameters and relative weightings to be given to such parameters for assessing the risk from exposure to substances in food

The working group identified the following issues to be addressed:

a) The potential need to adjust the relative weightings (used in other systems) to better reflect Irish agricultural practices
b) The potential need to include a factor relating to 'future disease in humans' (as is used in the USDA system), particularly relating to potential impact of antimicrobial usage in agriculture on development of antimicrobial-resistant pathogens in animals and humans
c) The interpretation of sales data for veterinary medicines and feed additives to reflect actual usage at farm level
d) Gaps in the database on usage of veterinary medicines and medicated feed additives due to importation of products from other Member States for use in Ireland but which are not listed in the veterinary formulary for Ireland
e) The potential need to include an additional factor relating to 'regulatory concern', which would take into account the potency of a substance versus its effect
f) The need to consider data from countries with broadly similar agricultural production systems to Ireland when assessing data from the Rapid Alert System for Food and Feed (RASFF) system for Member States
g) The need to exclude certain usages of veterinary medicines and feed additives where these are primarily used on younger animals that do not enter the food chain close to such usages

The Scientific Committee, at its meeting on 16th March 2012, allocated a request for advice from the FSAI to the Chemical Safety Sub-committee on the topic: *Application of a risk-based approach to developing the national residues sampling plan* (Appendix I). This document constitutes the response to that request for advice.

INTRODUCTION

The aim of the working group's activities is to develop a ranking system for chemical substances in foods of animal origin that may be applied to a risk-based approach to developing the National Residue Control Plan (and, potentially, other national sampling plans for chemical residues and contaminants in food/feed).

The National Residue Control Plan refers to the testing programme for substances and residues thereof in animals and animal products that is required to be carried out by each Member State according to the provisions laid down in Council Directive 96/23/EC. This Directive specifies the monitoring plans for the detection of residues or substances, the official control measures to be undertaken by the competent authority in each Member State, and the measures to be taken in the event of an infringement. In the Annexes to the Directive are detailed the substances to be covered by the control plan (Annex I), the types of substances to be covered for each type of food-producing animal (Annex II), the sampling strategy to be adopted, i.e. targeted sampling (Annex III), and the sampling levels and frequency for each type of food-producing animal, including the proportion of samples to be taken from live animals in the case of prohibited substances (Annex IV). The range of substances covered by the provisions of Council Directive 96/23/EC, as detailed in Annex I, are shown in Table 1.

The chemical substances to be included in the ranking system initially are licensed veterinary medicinal products and medicated feed additives, corresponding to Groups B1 and B2 in Annex I of Council Directive 96/23/EC. Subsequently, it is intended that the ranking system will be extended to prohibited substances and contaminants, corresponding to Group A and Group B3 in Annex I of Council Directive 96/23/EC.

In the case of veterinary medicinal products, these are assessed by the Committee for Medicinal Products for Veterinary Use (CVMP) of the European Medicines Agency (EMA). The CVMP is responsible for conducting the initial assessment of veterinary medicines for which an EU-wide marketing authorisation is sought. Assessments conducted by the CVMP are based on purely scientific criteria and determine whether or not the medicines concerned meet the quality, safety and efficacy requirements, in accordance with EU legislation. A core activity of the CVMP is the establishment of maximum residue limits (MRLs) for veterinary medicines that are permissible in foods of animal origin; MRLs must be established for all pharmacologically active substances contained in a veterinary medicine before it can be granted a marketing authorisation. MRLs for veterinary medicinal products are established by Commission Regulation (EU) No 37/2010, and as amended by subsequent regulations. Table 2 of Commission Regulation (EU) No 37/2010 lists those substances together with the stilbenes, thyreostats, steroids, resorcylic acid lactones, beta-agonists, malachite green, carbadox, olaquindox and nifursol that are currently prohibited within the EU for use on animals destined for human food. Current legislation forbids the presence of residues of these substances in food.

In the case of medicated feed additives, particularly coccidiostats and histomonostats, these are evaluated by the Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) of the European Food Safety Authority (EFSA) and, after a favourable opinion of the EFSA, medicated feed additives are authorised for inclusion in feed for specific animal species with specific conditions, including MRLs and post market monitoring if deemed necessary, according to Regulation (EC) No 1831/2003. All authorised medicated feed additives are listed in the *European Union Register of Feed Additives*.

Sampling and testing for residues of veterinary medicinal products and medicated feed additives is undertaken in each European Member State as prescribed by Council Directive 96/23/EC which describes the measures to monitor certain substances and residues thereof in live animals and animal products. To ensure appropriate and comparable performance of testing in Member States, Commission Decision 2002/657/EC describes how Council Directive 96/23/EC should be implemented concerning the performance of analytical methods and the interpretation of results. In Ireland, the overall responsibility for the National Residue Control Plan resides with the FSAI and implementation of the sampling and testing programme is undertaken by DAFM and a number of laboratories.

RISK-RANKING OF SUBSTANCES

There have been a number of developments over the last decade at European Union level, at Member State level and internationally towards a risk-based approach to developing residue testing programmes.

Within the EU, it was considered that the highly prescriptive approach as outlined in Council Directive 96/23/EC was not completely satisfactory. As part of the *Reflection Paper* exercise carried out in 2003, consideration was given to part of the residue testing programme being undertaken at a national level using a risk-based approach (European Commission 2003, 2004). More recently in 2010, the European Commission asked EFSA to produce opinions on a risk-based approach to meat inspection, including chemical residues and contaminants in all species of food-producing animals. A series of six Opinions have been published by EFSA dealing with the public health hazards to be covered by inspection of meat of bovine animals, sheep and goats, pigs, poultry, domestic solipeds, and farmed game (EFSA, 2011, 2012, 2013a, 2013b, 2013c, 2013d). In these Opinions, risk-ranking of both biological hazards and chemical hazards are central to the proposals for the new approach to meat inspection.

At individual country level, e.g. within the EU in the UK and internationally in the USA, risk-ranking systems have been used for a number of years to prioritise substances for residue testing. In the UK, the VRC developed the *Matrix Ranking for Prioritising Testing of Veterinary Medicine Residues* (Veterinary Residues Committee, 2011; Clare and Price, 2012) and in the USA, the Food Safety Inspection Service, USDA developed the *Design of the Domestic Scheduled Sampling Plan for Veterinary Drugs* (FSIS, 2011) for their national residue surveillance programmes. Both of these systems use the categories of nature of a substance, usage of a substance, residue occurrence and dietary exposure for risk-ranking of substances but use different parameters for each of these categories. The various parameters used to define the categories are shown below.

Category	Parameter in VRC system	Parameter in FSIS system
Nature of a substance	• Nature of the hazard • Potency of the substance (ADI)	• Acute or chronic toxicity concerns • Impact on new and existing human disease
Usage of a substance	• Exposure (no. of species of animal treated) • Exposure (no. of treatments per animal)	• Relative number of animals treated • Withdrawal time
Residue occurrence	• Evidence for detectable residues	• U.S. NRP historical testing information on violations • Regulatory concern (information on misuse)
Dietary exposure	• Exposure (contribution of food to diet) • Exposure (consumer groups subject to high exposure, due to diet)	• Estimated relative consumption

Both of these risk-ranking systems use coding systems for the various parameters and scoring systems based on, more or less complex, mathematical equations to determine overall scores for the individual substances and consequent ranking.

COMPONENTS OF THE SYSTEM

The first step in developing a risk-based approach to food sampling and residue testing for the National Residue Control Plan is to consider what should be addressed. Firstly and primarily, there is the **risk to human health** from residues of chemical substances in food. Secondly, there is the **issue of non-compliance** with regulations relating to residues in food due to improper farm practices, e.g. inappropriate use of veterinary medicinal products and medicated feed additives, potential abuse of prohibited substances, and use of feed of insufficient quality in terms of chemical contaminants. Both of these elements need to be considered and included in the developed risk-based system.

Characteristics of Substances

The second step is to identify those substance characteristics that need to be included in a ranking system for chemical substances. Three characteristics of substances that may occur as residues in food are essential elements in a risk-ranking system: the 'Potency' of the substance, the 'Usage' of the substance and the occurrence of 'Residues' of the substance in food. A further characteristic of Dietary Exposure is commonly included in risk-ranking systems, e.g.in the VRC and FSIS systems referred to previously. While the characteristic of Dietary Exposure is not included in the risk-ranking system developed here, it is expected that it be considered in the application of the risk-ranking system (see below).

For the risk-ranking system developed here, measures of these three characteristics have been applied to the list of veterinary medicinal products and medicated feed additives used in each species of food-producing animal.

Potency

In the case of veterinary medicinal products and medicated feed additives, an appropriate measure for the potency of the substance is the acceptable daily intake (ADI) value. The ADI is the amount of a substance in food that can be ingested on a daily basis over a lifetime without an appreciable health risk. The ADI is expressed as mg of the substance per kilogram bodyweight per day (mg/kg bw/day). The higher the ADI for a substance, the lower is its potential adverse effect on human health. Therefore, ADI values provide a measure of safety during long-term exposure to repeated ingestion of substances in foods. The ADI value is calculated by extrapolation from animal experiments and the use of safety factors to deal with inter and intra species variations.

Usage

Obtaining an accurate measure of the usage of veterinary medicinal products and medicated feed additives for each species of food-producing animal is complex. Not only is it difficult to obtain accurate information on the overall quantity of each substance used for each species of animal, of importance also for predicting likelihood of residue occurrence may be factors such as how the substance is used, e.g. route of administration, number of doses given to animals, whether the substance is used typically on individual animals or as a total herd/flock treatment, how close to slaughter or milking the substance is used, etc.

Data provided from the Veterinary Medicinal Products and Feed Additives Database (VetFAD), developed within the *Safe and Healthy Foods* research project, are used as the basis for determining usage of each substance. The database provides data for each substance broken down by annual gross sales data for each commercial product. From these data, combined with specified dosage for each product and animal population data, an estimate of total number of doses of the substance for each animal category may be estimated. The estimated total number of doses for each substance for each species of food-producing animal is used as the primary measure of 'usage' in the risk-ranking system. In order to improve the reliability of these data on 'usage', the results for a five-year period of the VetFAD are used in the risk-ranking system. Because the product sales data, on which the primary measure of 'usage' is based, are commercially sensitive, the numbers of doses for the substances is graded as 'Lowest', 'Low', 'Medium' and 'High' in this document.

The second characteristic of 'usage' included in the risk-ranking system is whether the substance is used typically for individual animal treatment or for herd/flock treatment. It is considered that if all animals in a herd/flock are treated with the substance, there may be a greater likelihood overall that the substance will occur as a residue in food. However, it should be considered also that an increased likelihood of residues being present in edible tissues does not necessarily mean that such residues would be at non-compliant levels, i.e. exceeding MRLs.

The third characteristic of usage included in the risk-ranking system is the withdrawal period specified for the product/substance. The withdrawal period is defined as the time required after administration of a veterinary medicinal product or medicated feed additive to an animal needed to assure that residues of the substance in food are below the specified MRL. Because veterinary medicinal products and medicated feed additives are marketed as products with different specified dosages and routes of administration, e.g. injection, oral powder, pour-on, feed additive, etc., the withdrawal periods specified for the individual products are variable. To use this information in the risk-ranking system, a compromise of selecting a typical withdrawal period for each substance is used. The typical withdrawal period for the substance is considered to be related to the likely persistence of the substance in edible tissues, with products/substances having longer withdrawal periods being expected to have more persistent residues.

Residue Occurrence

There are limited data available for the occurrence of residues of veterinary medicinal products and medicated feed additives in food. The annual testing of foods of animal origin undertaken in the National Residue Control Programme provides the most comprehensive data for residues in food. These data, published each year by DAFM and included in Teagasc's *National Food Residue Database*, provide information on residues of veterinary medicinal products and feed additives in food only where the specified MRLs are exceeded, i.e. non-compliant samples. In order to obtain reliable data on residue occurrence, the results for a rolling five-year period of the National Residue Control Programme are used in the risk-ranking system. In addition, all data on non-compliant samples, both from the routine targeted sampling and from the suspect sampling, are included for the risk-ranking system.

DEVELOPMENT OF THE RISK-RANKING SYSTEM

Data for the three characteristics of 'potency', 'usage' (2008-2012) and 'residue occurrence' (2008-2012) to be used in the risk-ranking system are shown in Tables 2 to 6, covering the major species of food-producing animals. Currently, data for a majority of classes of veterinary medicinal products and medicated feed additives are included, but data for further substances will be added when available. In the case of fish, 'usage' data for veterinary medicinal products and medicated feed additives are not currently available, but the risk-ranking system will be applied to fish when such data become available.

For beef cattle, a total of 61 veterinary medicinal products and medicated feed additives licensed for use are included in the risk-ranking. For sheep and goats, a total of 36 veterinary medicinal products and medicated feed additives are included, together with flubendazole which is not approved for use in these species but for which a non-compliant sample was found in National Residue Control Plan testing. For pigs, a total of 39 veterinary medicinal products and medicated feed additives licensed for use are included in the risk-ranking. For poultry, a total of 21 veterinary medicinal products and medicated feed additives licensed for use are included, together with diclofenac and ivermectin which are not approved for use in poultry but for which non-compliant samples were found in National Residue Control Plan testing. For dairy cattle, a total of 51 veterinary medicinal products and medicated feed additives are included, together with closantel, ivermectin, nitroxynil and rafoxanide which are not approved for use in animals producing milk for human consumption but for which non-compliant samples were found in National Residue Control Plan testing. It should be noted that MRLs in milk were approved for some of these substances (closantel, nitroxynil) during 2012.

The coding system shown in Table 7 is applied to the data in Tables 2 to 6, for the purposes of the risk-ranking system. For ADI values, a four-point coding system is applied with 1 being assigned to substances having the highest ADI values (> 0.1 mg/kg bw/day), i.e. least potent substances, and 4 being assigned to substances having the lowest ADI values (<0.001 mg/kg bw/day), i.e. most potent substances. For number of doses, a four-point coding system is applied with 1 being assigned to substances having the lowest number of doses per year and 4 being assigned to substances having the highest number of doses per year. For use on individual animals or groups (herds/flocks), a two-point coding system is applied with 1 being assigned to substances used on individual animals and 2 being assigned to substances used for treatment of herds/flocks or to substances used for both individual animal and herd/flock treatment. For withdrawal period, a four-point coding system is applied with 1 being assigned to substances with a withdrawal period of < 10 days and 4 being applied to substances with a withdrawal period of > 100 days, except in the case of poultry and dairy cattle where the figures range from < 5 days to > 20 days. For non-compliant results, a four-point coding is applied with 1 being assigned to substances for which no non-compliant samples were determined in National Residue Control Plan testing 2008-2012 and 4 being assigned to substances for which greater than five non-compliant results were determined in National Residue Control Plan testing 2008-2012. The values obtained from applying the coding system are shown in Tables 8 to 12.

These coded values are used to develop scores for the individual substances. The scoring system developed for risk-ranking the substances combines the elements of potency (ADI) with usage (number of doses, plus individual or group usage, plus withdrawal period) and with residue occurrence (number of non-compliant samples in National Residue Control Plan testing). To give relatively equivalent weighting to the three characteristics of 'potency', 'usage' and 'residue' occurrence in scoring substances, the coded values for the three components contributing to 'usage' (number of doses, individual/group use, withdrawal period) are summed. The overall score for a substance is obtained by multiplying the coded values for 'potency', 'usage' and 'residue occurrence', according to the following equation:

'Potency' × 'Usage' (no. doses + individual/group use + withdrawal period) × 'Residue Occurrence'

The overall scores for the substances are shown in Tables 8 to 12, together with the consequent ranking for each substance. Since the parameters of ADI, use on individual animals or herd/flock treatment and withdrawal period are constant and, for any 5-year period, the number of non-compliant samples is fixed, the only variable from year to year is the number of doses. Change in the number of doses from year to year might result in slightly different scoring, and consequent ranking, for individual substances, but the overall ranking over the five-year period 2008-2012 may be expected to be broadly similar for each substance. For the purposes of clarity, only the scores for number of doses used in 2012 are shown in Tables 8 to 12; where a different number of doses for a particular substance, resulting in a different score for this parameter, occurs in some years of the period 2008 to 2012, this is shown in Tables 2 to 6.

DISCUSSION

The risk-ranking system described is a relatively simple system, designed to provide a basis for selecting the veterinary medicinal products and medicated feed additives that might be prioritised for residue testing.

The ADI values are considered to provide a good basis for the relative potency of the various substances. For 'usage' data, VetFAD provides good information on the number of doses of each veterinary medicinal product and medicated feed additive used in the various species. This measure of usage is qualified by whether the substance is used on individual animals or for herd/flock treatment to increase the ranking of substances that are more likely to occur as residues in food of animal origin. In addition, inclusion of data on withdrawal period increases the ranking of substances for which longer withdrawal is required and for which, therefore, there is more likelihood of residues occurring in edible tissues. The results of National Residue Control Plan testing provide some measure of the occurrence of residues in food of animal origin.

However, these data are at best only an indication of 'potency', 'usage' and 'residue occurrence' characteristics for veterinary medicinal products and medicated feed additives and, as such, provide only a general ranking of substances for each animal species. There is little basis for developing more quantitative systems for risk-ranking, such as using weighting factors for the various characteristics or applying more complex equations for scoring substances.

To provide an overview of the substance ranking system, the substances have been categorised into five groupings, A – E, for each species, corresponding to five broad categories of risk for occurrence as residues in food (Tables 13-17). The purpose of this categorisation is to place substances with broadly similar likelihood of occurrence as residues in food into groups and to avoid over-reliance on the quantitative scoring and consequent ranking.

Looking at the results of the ranking, the following substances are ranked very highly:

- The antimicrobials Amoxicillin (for all species except pigs), Oxytetracycline (for all species except poultry), Sulfadiazine with Trimethoprim (for pigs and poultry) and Tilmicosin (for poultry)
- Antiparasitic drugs, such as the benzimidazoles Triclabendazole (for beef and dairy cattle), Fenbendazole/ Oxfendazole (for sheep/goats and dairy cattle) and Albendazole (for dairy cattle), the avermectin Ivermectin (for beef cattle), and anti-fluke drugs Closantel and Rafoxanide (for sheep/goats)
- The anticoccidials Narasin, Nicarbazin and Toltrazuril (for poultry); the organophosphorus compound Phoxim is also ranked very highly for poultry and this ranking should be considered in the context of the substance being used as an environmental spray in poultry houses and the estimated number of doses for exposure which may not be accurate

At a slightly lower ranking are the following substances:

- Antimicrobials such as the penicillins Procaine benzylpenicillin (for pigs and dairy cattle) and Ampicillin, Cloxacillin and Penethamate (for dairy cattle), Sulfadimidine (for poultry and dairy cattle), the fluoroquinolones Enrofloxacin (for beef cattle and poultry) and Marbofloxacin (for beef cattle), the macrolides and lincosamides Tilmicosin and Tylosin (for beef cattle) and Erythromycin and Lincomycin (for poultry)
- Antiparasitic drugs, such as the avermectins Ivermectin (for sheep/goats and pigs) and Eprinomectin (for dairy cattle), and the synthetic pyrethroid Deltamethrin (for dairy cattle)
- The anti-inflammatory drug, Prednisolone, and the bronchodilator, Clenbuterol (for dairy cattle)

Limitations of the Risk-Ranking System

An evaluation of the limitations in the model described here for risk-ranking of substances identifies a number of inherent uncertainties in the data used.

In the case of 'potency':

- ADI values have been well-established, based on animal experimentation, and may be considered to be an appropriate indicator for the absence of a potential adverse effect of the substances on human health. However, there is an inherent uncertainty in the derivation of an ADI value, particularly in the appropriateness of the safety factors used in deriving the ADI value

In the case of 'usage', there are inherent uncertainties in each of the three parameters used:

- Sale of product data, from which the number of doses used on each particular species is derived, is at best only an approximate measure of the amount of substance used
- 'Usage' on individual animals or for herd/flock treatment is inexact and is based on best available knowledge and product use information and advice
- Withdrawal period data involve identifying a typical withdrawal period for the substance and where multiple products, doses and routes of administration are involved for a substance, such a typical withdrawal period has a high level of inherent uncertainty

In the case of 'residue occurrence':

- The data available from the National Residue Control Programme provide only the number of non-compliant samples determined from the testing programme; there is no information available on samples found to contain residues at levels at or below MRLs and, therefore, no overall information on the occurrence of residues of a particular substance in edible tissues
- Changes in the MRLs assigned to particular substances, e.g. anticoccidials used on poultry and anthelmintics used on dairy cattle) make historical non-compliance data poor for prediction purposes

In summary, the limitations associated with the parameters used in the risk-ranking model contribute to an overall high level of uncertainty in the risk-ranking model as a tool for identifying those substances that should be prioritised for residue testing. This weakness in the risk-ranking model requires that it be re-evaluated on an ongoing basis to establish whether it is providing an appropriate tool for prioritising substances for residue testing. In addition, particular steps should be taken to reduce the uncertainty in the risk-ranking model such as (a) a structured veterinary medicinal product and medicated feed additive usage survey with primary producers to supplement the product sales data, and (b) more comprehensive reporting from the residue testing in the National Residue Control Plan to include quantitative data for both compliant and non-compliant samples.

Application of the Risk-ranking System

The risk-ranking of substances according to the model proposed here provides a tool that may be used in developing the residue testing programme for the annual National Residue Control Plan. The risk-ranking of substances resulting from application of the model is not intended to constitute the plan, as it represents only one component of a total risk-based approach to be applied by those responsible for designing the residue testing programme.

Already in designing the residue testing programme, the competent authority takes account of a range of issues that provide a risk-based approach in implementation of the National Residue Control Plan. These issues, which may be described as "regulatory concern" include (a) knowledge of potential misuse of particular veterinary medicinal products and medicated feed additives, (b) animals constituting an increased risk for residues, e.g. cull cows and emergency slaughter animals, (c) use of additional substances under the 'cascade' usage, and (d) experience from other countries with similar agricultural practices.

There are a number of risk management issues that need to be considered when applying this risk-ranking system to prioritising substances for residue testing:

- The risk-ranking system is limited to veterinary medicinal products and medicated feed additives that are approved for use on food animal species in Ireland and, as such, would not select for inclusion in the National Residue Control Plan substances that are not authorised for use. Where there is evidence of misuse of particular veterinary medicinal products and medicated feed additives, e.g. in the case of Diclofenac and Ivermectin in poultry production, such substances might be prioritised for residue testing independent of their ranking using the risk-ranking model proposed here
- Where there are changes in the specifications for particular veterinary medicinal products and medicated feed additives, for example the new MRLs assigned to nicarbazin from 2010 onwards, the prioritisation of such substances for residue testing might be adjusted to other than would be indicated from use of the risk-ranking model proposed here
- Because many of the methods commonly applied in residue testing are multi-analyte methods, it may be appropriate to include testing for substances ranked as of lower priority where testing for a higher priority substance uses a common method of analysis
- In designing an overall residue testing plan across multiple species, the relative contribution of a particular food type to the diet might be used to determine the relative numbers of samples of that food type to be included in the residue testing plan. Such an approach introduces the issue of dietary exposure to the residue testing plan, e.g. data from the FSAI Total Diet Study (FSAI, 2011) might be used to determine the numbers of samples of each food type to be included in a residue testing plan (Table 18)

These, and other issues should be considered, together with the risk-ranking of substances according to the model proposed here, when developing the residue testing plan for the National Residue Control Plan.

RECOMMENDATIONS

To deal with some of the limitations and uncertainties in the model described here for risk-ranking of substances, a number of recommendations are made towards supporting and improving the model and towards extending its applicability as a tool for developing the residue testing programme for the annual National Residue Control Plan.

- The risk-ranking model should be re-evaluated on an ongoing basis to establish whether it is providing an appropriate tool for prioritising substances for residue testing.
- Regarding the availability in future years of current data on residue occurrence and on usage of veterinary medicinal products and medicated feed additives, it is important that the relevant databases are operational into the future, i.e. the National Food Residue Database (NFRD) and the VetFAD databases, respectively.
- In the case of residue occurrence data, the risk-ranking of substances would be much improved if quantitative information on the actual measured amount of each residue in each sample, whether compliant or non-compliant, were provided from the National Residue Control Plan testing to the NFRD.
- In the case of usage data, the risk-ranking of substances would be much improved if more complete information on sales of product, withdrawal periods and usage for individual or herd/flock treatment were supplied, possibly via mandatory reporting of such data by the veterinary medicinal product and medicated feed additive manufacturing companies. In addition, a structured veterinary medicinal product and medicated feed additive usage survey with primary producers should be undertaken, possibly as part of the Teagasc farm survey activity, to supplement the product sales data obtained from manufacturing companies.
- This model for risk-ranking of substances, modified as required for different classes of substances, should be extended to cover other classes of substances included in the residue testing programme for the annual National Residue Control Plan, such as prohibited substances and contaminants, and to other residue monitoring programmes related to food. Such an extension of the application of the model for risk-ranking of substances would follow on an evaluation (road-testing) of the performance of the current model for veterinary medicinal products and medicated feed additives in the designing of the residue testing programme for the annual National Residue Control Plan.

REFERENCES

EFSA Panels on Biological Hazards (BIOHAZ), on Contaminants in the Food Chain (CONTAM), and on Animal Health and Welfare (AHAW); Scientific Opinion on the public health hazards to be covered by inspection of meat (swine). *EFSA Journal* 2011;9(10):2351, 198 pp.

EFSA Panels on Biological Hazards (BIOHAZ), on Contaminants in the Food Chain (CONTAM), and on Animal Health and Welfare (AHAW); Scientific Opinion on the public health hazards to be covered by inspection of meat (poultry). *EFSA Journal* 2012;10(6):2741, 179 pp.

EFSA BIOHAZ Panel (EFSA Panel on Biologicial Hazards), 2013. Scientific Opinion on the public health hazards to be covered by inspection of meat (solipeds). *EFSA Journal* 2013;11(6):3263, 161 pp.

EFSA BIOHAZ Panel (EFSA Panel on Biological Hazards), 2013. Scientific Opinion on the public health hazards to be covered by inspection of meat from farmed game. *EFSA Journal* 2013;11(6):3264, 181 pp.

EFSA BIOHAZ Panel (EFSA Panel on Biological Hazards), 2013. Scientific Opinion on the public health hazards to be covered by inspection of meat from sheep and goats. *EFSA Journal* 2013;11(6):3265, 186 pp.

EFSA BIOHAZ Panel (EFSA Panel on Biological Hazards), 2013. Scientific Opinion on the public health hazards to be covered by inspection of meat (bovine animals). *EFSA Journal* 2013;11(6):3266, 261 pp.

European Commission, Enterprise Directorate-General/Health and Consumer Protection Directorate-General, 2003, Reflection Paper on Residues in foodstuffs of animal origin, 20pp.

European Commission, Enterprise Directorate-General/Health and Consumer Protection Directorate-General, 2004, Reflection Paper on Residues in foodstuffs of animal origin – Summary of comments, 8pp.

Food Safety and Inspection Service, USDA, 2011, *United States National Residue Program - 2011 Scheduled Sampling Plans*, pp. 18-45.

Food Safety Authority of Ireland, 2011, *Report on a Total Diet Study carried out by the Food Safety Authority of Ireland in the period 2001 – 2005*, pp. 120.

G. Clare and S. Price, 2012, *Matrix ranking for prioritising testing of veterinary medicine residues*, Veterinary Residues Committee, VRC. Poster presented at the British Toxicology Society Annual Congress, March 2012.

Veterinary Residues Committee, 2011, *Annual Report on Surveillance for Veterinary Residues in Food in the UK 2010*, pp. 42-44, 50.

Table 1. The Range of Substances covered in the National Residue Control Plan (Annex I of Council Directive 96/23/EC)

GROUP A – Substances having anabolic effect and unauthorised substances
(1) Stilbenes, stilbene derivatives, and their salts and esters
(2) Antithyroid agents
(3) Steroids
(4) Resorcylic acid lactones including zeranol
(5) Beta-agonists
(6) Compounds included in Annex IV to Council Regulation (EEC) No 2377/90 (*now Table 2 of Commission Regulation 37/2010*)
GROUP B – Veterinary drugs & contaminants
(1) Antibacterial substances, including sulphonamides, quinolones
(2) Other veterinary drugs
(a) Anthelmintics
(b) Anticoccidials, including nitroimidazoles
(c) Carbamates and pyrethroids
(d) Sedatives
(e) Non-steroidal anti-inflammatory drugs (NSAIDs)
(3) Other substances and environmental contaminants
(a) Organochlorine compounds, including PCBs
(b) Organophosphorus compounds
(d) Chemical elements
(d) Mycotoxins
(e) Dyes
(f) Others

Table 2. Data on Potency (ADI), Usage (number of doses 2008-2012; Use on Individual Animals or Groups; Withdrawal Period) and Residue Occurrence (National Residue Control Plan Non-compliant Samples 2008-2012) for Beef Cattle

Veterinary medicine - active ingredient	ADI[1] (mg/kg bw/d)	Number of doses[2] 2008 - 2012	Use on individual animals or groups[3]	Withdrawal period (days)[4]	Number of non-compliant samples in the National Residue Control Plan 2008 - 2012[5]
Abamectin	0.0025	Medium	G	35	
Albendazole	0.005	High	G	14	
Amitraz	0.003	Topical	G	4	
Amoxicillin	0.0005	Medium	I & G	28	6
Ampicillin	0.0005	Low	I & G	28	
Benzylpenicillin	0.0005	- (a)	I	7	2
Carprofen	0.01	Lowest	I	21	
Cefalexin	0.054	Medium (b)	I	15	
Cefalonium	0.02	Medium	I	21	
Cefapirin	0.1	Low	I	4	
Cefoperazone	0.75	Lowest	I	2	
Cefquinome	0.0038	Low	I	5	
Ceftiofur	0.3	Medium (b)	I	8	
Chlortetracycline	0.003	Aerosol	G	5	1
Clavulanic acid	0.05	Medium	I	42	
Clenbuterol	0.0000042	Lowest	I	14	
Closantel	0.03	Medium	I & G	49	
Cloxacillin	0.0005	Medium	I	28	
Cyhalothrin	0.005	Lowest (c)	I & G	14	
Cypermethrin	0.015	High	I & G	14	
Danofloxacin	0.024	Lowest	I	8	1
Deltamethrin	0.01	Medium	I & G	18	
Dexamethasone	0.015	Medium (b)	I	21	
Dihydrostreptomycin	0.025	Medium	I	21	
Doramectin	0.0005	Low (c)	I & G	63	
Enrofloxacin	0.002	Medium (b)	I	14	1
Eprinomectin	0.005	Low	G	15	
Fenbendazole	0.007	Medium	I & G	28	
Florfenicol	0.003	Medium (b)	I	44	
Flumethrin	0.0018	Low	I & G	5	
Flunixin	0.006	Low	I	7	

Veterinary medicine - active ingredient	ADI[1] (mg/kg bw/d)	Number of doses[2] 2008 - 2012	Use on individual animals or groups[3]	Withdrawal period (days)[4]	Number of non-compliant samples in the National Residue Control Plan 2008 - 2012[5]
Gamithromycin	0.01	Low (a)	I	64	
Gentamicin	0.004	Lowest	I	90	
Imidocarb	0.01	Low	I	213	
Ivermectin	0.001	High	I & G	49	3
Levamisole	0.006	Medium	I & G	14	
Lincomycin	0.01	Lowest	I	2	
Marbofloxacin	0.04	Medium	I	5	8
Meloxicam	0.00125	Low (a)	I	15	
Metamizole	0.01	Low (a)	I	28	
Moxidectin	0.0015	Medium (b)	I & G	108	
Nafcillin	0.0075	- (a)	I	28	
Neomycin	0.16	Low	I	28	
Nitroxynil	0.005	Medium (d)	I & G	60	
Oxfendazole	0.007	Medium	I & G	28	
Oxyclozanide	0.03	High (b)	I & G	28	
Oxytetracycline	0.003	Medium; Aerosol	I & G	28	25
Penethamate	0.0005	Low	I	7	
Permethrin	0.05	Medium	G	7	
Pirlimycin	0.1	Lowest	I	23	
Procaine benzylpenicillin	0.0005	Medium	I	7	
Rafoxanide	0.002	Medium	I & G	60	
Streptomycin	0.025	Low	I	12	
Sulfadiazine	0.05	Medium	I	25	
Sulfadimidine	0.05	Lowest	I	14	2
Tilmicosin	0.004	Low	I	60	1
Tolfenamic acid	0.01	Lowest	I	12	
Triclabendazole	0.0015	High (c)	I & G	56	1
Trimethoprim	0.004	Low	I	25	
Tulathromycin	0.05	Low (a)	I	49	1
Tylosin	0.006	Medium (b)	I	28	2

Veterinary medicine - active ingredient	ADI[1] (mg/kg bw/d)	Number of doses[2] 2008 - 2012	Use on individual animals or groups[3]	Withdrawal period (days)[4]	Number of non-compliant samples in the National Residue Control Plan 2008 - 2012[5]

NOTES

[1]**ADI values:** Value of 0.0005 mg/kg bw/d (microbiological ADI) entered for penicillin antibiotics for which no specific ADI value set; value of 0.05 mg/kg bw/d used for sulphonamides (JECFA value).

[2]**Number of doses:** Number of individual animal doses derived from data on veterinary medicinal products and medicated feed additives containing the active ingredient (VetFAD database). Data for 2012 shown; where number of doses are lower/ higher in other years of the period 2008-2012, this is shown as follows:

(a) For some years, no. of doses was "Lowest"
(b) For some years, no. of doses was "Low"
(c) For some years, no. of doses was "Medium"
(d) For some years, no. of doses was "High"

[3]**Use on individual animals or groups:** I = used on individual animals; G = used on groups of animals; I & G = used on individual animals and on groups of animals.

[4]**Withdrawal period:** Withdrawal period selected as the most representative for the substance, e.g. generally related to an injection product and one containing only the single substance.

[5]**Non-compliant samples:** Number of non-compliant samples for beef cattle from the National Residue Control Plan for the period 2008-2012, including both 'Targeted' and 'Suspect' sampling.

Table 3. Data on 'Potency' (ADI), 'Usage' (number of doses 2008-2012; use on individual animals or groups; withdrawal period) and Residue Occurrence (National Residue Control Plan non-compliant samples 2008-2012) for Sheep and Goats

Veterinary medicine - active ingredient	ADI[1] (mg/kg bw/d)	Number of doses[2] 2008 - 2012	Use on individual animals or groups[3]	Withdrawal period (days)[4]	Number of non-compliant samples in the National Residue Control Plan 2008 - 2012[5]
Abamectin	0.0025	Low (c)	G	16	
Albendazole	0.005	High	G	10	
Amitraz	0.003	Topical	G	24	
Amoxicillin	0.0005	Medium	I	21	1
Ampicillin	0.0005	Lowest	I	18	
Benzylpenicillin	0.0005	- (a)	I	7	
Chlortetracycline	0.003	Aerosol	G	5	
Closantel	0.03	High	I & G	28	12
Cypermethrin	0.015	Medium (b); Topical	G	8	
Cyromazine	0.02	- (c)	I & G	28	
Decoquinate	0.075	High (c)	G	0	
Deltamethrin	0.01	Low	I & G	7	
Diclazuril	0.03	Medium	G	0	
Dicyclanil	0.007	Medium (a)	I & G	40	
Dihydrostreptomycin	0.025	Medium	I	28	
Doramectin	0.0005	Low (c)	I & G	63	
Fenbendazole	0.007	Medium	I & G	14	2
Flubendazole[6]	0.012	-			1
Flugestone acetate	0.00003	Low (a)	I	14	
Ivermectin	0.001	High	I & G	42	
Levamisole	0.006	High (c)	I & G	18	
Mebendazole	0.0125	Medium	G	14	
Monepantel	0.03	Lowest (b)	G	7	
Moxidectin	0.0015	High (c)	I & G	82	
Nitroxynil	0.005	Medium (d)	I & G	60	1
Oxfendazole	0.007	Medium	I & G	21	1
Oxyclozanide	0.03	High (b)	I & G	28	
Oxytetracycline	0.003	Medium; Aerosol	I	21	3
Procaine benzylpenicillin	0.0005	Medium	I	5	
Rafoxanide	0.002	Medium	I & G	60	4

Veterinary medicine - active ingredient	ADI[1] (mg/kg bw/d)	Number of doses[2] 2008 - 2012	Use on individual animals or groups[3]	Withdrawal period (days)[4]	Number of non-compliant samples in the National Residue Control Plan 2008 - 2012[5]
Spectinomycin	0.25	Lowest	I	10	
Streptomycin	0.025	Lowest	I	21	
Sulfadiazine	0.05	- (a)	I	18	
Sulfadimidine	0.05	Lowest	I	14	
Tilmicosin	0.004	Lowest (b)	I	42	
Toltrazuril	0.002	Lowest	I	42	
Triclabendazole	0.0015	High	I & G	56	

NOTES

[1]**ADI values:** Value of 0.0005 mg/kg bw/d (microbiological ADI) entered for penicillin antibiotics for which no specific ADI value set; value of 0.05 mg/kg bw/d used for sulphonamides (JECFA value).

[2]**Number of doses:** Number of individual animal doses derived from data on veterinary medicinal products and medicated feed additives containing the active ingredient (VetFAD database). Data for 2012 shown; where number of doses are lower/ higher in other years of the period 2008-2012, this is shown as follows:

(a) For some years, no. of doses was "Lowest"
(b) For some years, no. of doses was "Low"
(c) For some years, no. of doses was "Medium"
(d) For some years, no. of doses was "High"

[3]**Use on individual animals or groups:** I = used on individual animals; G = used on groups of animals; I & G = used on individual animals and on groups of animals.

[4]**Withdrawal period:** Withdrawal period selected as the most representative for the substance, e.g. generally related to an injection product and one containing only the single substance.

[5]**Non-compliant samples:** Number of non-compliant samples for sheep and goats from the National Residue Control Plan for the period 2008-2012, including both 'Targeted' and 'Suspect' sampling.

[6]**Flubendazole:** According to Commission Regulation 37/2010, Flubendazole is not approved for use in sheep and goats.

Table 4. Data on 'Potency' (ADI), 'Usage' (number of doses 2008-2012; use on individual animals or groups; withdrawal period) and Residue Occurrence (National Residue Control Plan non-compliant samples 2008-2012) for Pigs

Veterinary medicine - active ingredient	ADI[1] (mg/kg bw/d)	Number of doses[2] 2008 - 2012	Use on individual animals or groups[3]	Withdrawal period (days)[4]	Number of non-compliant samples in the National Residue Control Plan 2008 - 2012[5]
Amitraz	0.003	Topical	G	1	
Amoxicillin	0.0005	Medium	I & G	14	
Ampicillin	0.0005	Lowest	I	18	
Apramycin	0.04	Lowest	G	14	
Azaperone	0.0008	Low	I	10	
Benzylpenicillin	0.0005	- (a)	I	7	
Cefquinome	0.0038	Low (a)	I	3	
Ceftiofur	0.3	Low	I	5	
Chlortetracycline	0.003	High (c)	G	15	
Colistin	0.0625	Lowest	I & G	1	
Danofloxacin	0.024	Lowest	I	3	
Dexamethasone	0.015	Low (a)	I	4	
Dihydrostreptomycin	0.025	Low	I	18	
Doxycycline	0.003	Lowest	G	6	
Enrofloxacin	0.002	Low	I	10	1
Fenbendazole	0.007	Low (c)	G	10	
Florfenicol	0.003	Medium (b)	I & G	18	
Flubendazole	0.012	Medium (b)	G	7	
Flunixin	0.006	Low (a)	I	24	
Ivermectin	0.001	High (c)	I & G	28	
Lincomycin	0.01	Medium; Premix	I & G	2	
Marbofloxacin	0.04	Medium (b)	I	2	1
Meloxicam	0.00125	Medium	I	5	
Oxytetracycline	0.003	Medium; Aerosol	I & G	21	2
Phenoxy-methylpenicillin	0.0005	High	G	1	
Procaine benzylpenicillin	0.0005	Medium	I	7	2
Spectinomycin	0.25	Medium (b); Additive	I & G	12	
Streptomycin	0.025	Lowest	I	18	
Sulfadiazine	0.05	Medium	I & G	20	6

Veterinary medicine - active ingredient	ADI[1] (mg/kg bw/d)	Number of doses[2] 2008 - 2012	Use on individual animals or groups[3]	Withdrawal period (days)[4]	Number of non-compliant samples in the National Residue Control Plan 2008 - 2012[5]
Sulfadimidine	0.05	Lowest	I	35	1
Tiamulin	0.032	Lowest (b)	I & G	2	
Tilmicosin	0.004	Low	I & G	14	
Tolfenamic acid	0.01	Lowest	I	3	
Toltrazuril	0.002	Low	I	77	
Trimethoprim	0.004	Medium (d)	I & G	20	1
Tulathromycin	0.05	Low (a)	I	33	
Tylosin	0.006	Medium	I & G	7	
Tylvalosin	0.22	Medium (b, d)	G	2	
Valnemulin	0.08	- (b, c)	G	1	

NOTES

[1]**ADI values:** Value of 0.0005 mg/kg bw/d (microbiological ADI) entered for penicillin antibiotics for which no specific ADI value set; value of 0.05 mg/kg bw/d used for sulphonamides (JECFA value).

[2]**Number of doses:** Number of individual animal doses derived from data on veterinary medicinal products and medicated feed additives containing the active ingredient (VetFAD database). Data for 2012 shown; where number of doses are lower/ higher in other years of the period 2008-2012, this is shown as follows:

(a) For some years, no. of doses was "Lowest"
(b) For some years, no. of doses was "Low"
(c) For some years, no. of doses was "Medium"
(d) For some years, no. of doses was "High"

[3]**Use on individual animals or groups:** I = used on individual animals; G = used on groups of animals; I & G = used on individual animals and on groups of animals.

[4]**Withdrawal period:** Withdrawal period selected as the most representative for the substance, e.g. generally related to an injection product and one containing only the single substance.

[5]**Non-compliant samples:** Number of non-compliant samples for pigs from the National Residue Control Plan for the period 2008-2012, including both 'Targeted' and 'Suspect' sampling.

Table 5. Data on 'Potency' (ADI), 'Usage' (number of doses 2008-2012; use on Individual animals or groups; withdrawal period) and 'Residue Occurrence' (National Residue Control Plan non-compliant samples 2008-2012) for Poultry

Veterinary medicine - active ingredient	ADI[1] (mg/kg bw/d)	Number of doses[2] 2008 - 2012	Use on individual animals or groups[3]	Withdrawal period (days)[4]	Number of non-compliant samples in the National Residue Control Plan 2008 - 2012[5]
Amoxicillin	0.0005	High	G	1	
Apramycin6	0.04	-	G	7	
Chlortetracycline	0.003	Low (a)	G	2	
Colistin	0.0625	Low (a)	G	1	
Diclofenac[7]	0.005	-			1
Doxycycline	0.003	Lowest	G	6	
Enrofloxacin	0.002	Medium	G	4	
Erythromycin	0.005	Low (a)	G	6	
Flubendazole	0.012	Low	G	7	
Flumequine	0.025	- (a, b)	G	2	
Ivermectin[7]	0.001	-			1
Lincomycin	0.01	Low (a)	G	7	
Monensin[8]	0.0125	High	G	3	
Narasin[8]	0.005	High	G	1	
Nicarbazin[8]	0.77	High	G	1	27
Phoxim[9]	0.004	Medium	G	25	
Spectinomycin	0.25	Low	G	7	
Sulfadiazine	0.05	High	G	5	
Sulfadimidine	0.05	Medium (d)	G	14	
Tilmicosin	0.004	Low (a)	G	12	
Toltrazuril[10]	0.002	Low	G	14	
Trimethoprim	0.004	High	G	5	
Tylosin	0.006	Low	G	1	

Veterinary medicine - active ingredient	ADI[1] (mg/kg bw/d)	Number of doses[2] 2008 - 2012	Use on individual animals or groups[3]	Withdrawal period (days)[4]	Number of non-compliant samples in the National Residue Control Plan 2008 - 2012[5]

NOTES

[1]**ADI values:** Value of 0.0005 mg/kg bw/d (nicrobiological ADI) entered for penicillin antibiotics for which no specific ADI value set; value of 0.05 mg/kg bw/d used for sulphonamides (JECFA value).

[2]**Number of doses:** Number of individual animal doses derived from data on veterinary medicinal products and medicated feed additives containing the active ingredient (VetFAD database). Data for 2012 shown; where number of doses are lower/ higher in other years of the period 2008-2012, this is shown as follows:

(a) For some years, no. of doses was "Lowest"
(b) For some years, no. of doses was "Low"
(c) For some years, no. of doses was "Medium"
(d) For some years, no. of doses was "High"

[3]**Use on individual animals or groups:** I = used on individual animals; G = used on groups of animals; I & G = used on individual animals and on groups of animals.

[4]**Withdrawal period:** Withdrawal period selected as the most representative for the substance, e.g. generally related to an injection product and one containing only the single substance.

[5]**Non-compliant samples:** Number of non-compliant samples for poultry from the National Residue Control Plan for the period 2008-2012, including both 'Targeted' and 'Suspect' sampling.

[6]**Apramycin:** Apramycin may be used on poultry with no MRL required.

[7]**Diclofenac, Ivermectin:** Diclofenac and Ivermectin are not approved for use in poultry.

[8]**Monensin, Narasin, Nicarbazin:** These anticoccidials are used in large quantities as medicated feed additives in poultry production but Number of Doses data are not available; based on their widespread use in poultry production, Number of Doses of "High" has been assigned to each substance for each of the years 2008-2012.

[9]**Phoxim:** Phoxim is applied as an environmental spray so Number of Doses data are not available; based on the Quantity of Substance Used data and comparison with other substances, a Number of Doses of "Medium" is estimated for Phoxim for each year in which it was used in poultry production.

[10]**Toltrazuril:** Toltrazuril is applied as an additive to drinking water for treatment of coccidiosis; based on the Quantity of Substance Used data and comparison with other substances, a Number of Doses of "Low" is estimated for Toltrazuril for each year in which it was used in poultry production.

Table 6. Data on 'Potency' (ADI), 'Usage' (number of doses 2008-2012; use on individual animals or groups; withdrawal period) and 'Residue Occurrence' (National Residue Control Plan non-compliant samples 2008-2012) for Dairy Cattle

Veterinary medicine - active ingredient	ADI[1] (mg/kg bw/d)	Number of doses[2] 2008 - 2012	Use on individual animals or groups[3]	Withdrawal period (days)[4]	Number of non-compliant samples in the National Residue Control Plan 2008 - 2012[5]
Albendazole	0.005	Medium	G	14	
Amitraz	0.003	Topical	G	4	
Amoxicillin	0.0005	Medium	I	4	1
Ampicillin	0.0005	Low	I	7	
Benzylpenicillin	0.0005	- (a)	I	7	
Carprofen[6]	0.01	Lowest	I	0	
Cefalexin	0.054	Low (c)	I	7	
Cefalonium	0.02	Medium (b)	I	21	
Cefapirin	0.1	Low (a)	I	4	
Cefoperazone	0.75	Lowest	I	4	
Cefquinome	0.0038	Low	I	5	
Ceftiofur	0.3	Low	I	2	
Chlortetracycline	0.003	Aerosol	G	5	
Clavulanic acid	0.05	Low	I	7	
Clenbuterol	0.0000042	Lowest	I	14	
Closantel[7]	0.03	-			15
Cloxacillin	0.0005	Low (a)	I	28	
Cyhalothrin	0.005	Lowest (c)	I & G	14	
Cypermethrin	0.015	Medium	I & G	0	
Danofloxacin	0.024	Lowest	I	5	
Deltamethrin	0.01	Low	I & G	18	
Dexamethasone	0.015	Low	I	7	
Dihydrostreptomycin	0.025	Medium	I	7	
Enrofloxacin	0.002	Low	I	5	
Eprinomectin	0.005	Low (a)	G	15	
Fenbendazole	0.007	Medium	I & G	14	
Flumethrin	0.0018	Low (a)	I & G	5	
Flunixin	0.006	Low (a)	I	7	
Gentamicin	0.004	Lowest	I	10	
Imidocarb	0.01	Low	I	21	
Ivermectin[8]	0.001	-			4
Kanamycin	0.008	Medium (b)	I	7	

Veterinary medicine - active ingredient	ADI[1] (mg/kg bw/d)	Number of doses[2] 2008 - 2012	Use on individual animals or groups[3]	Withdrawal period (days)[4]	Number of non-compliant samples in the National Residue Control Plan 2008 - 2012[5]
Lincomycin	0.01	Lowest	I	2	
Marbofloxacin	0.04	Low	I	3	
Meloxicam	0.00125	Low (a)	I	15	
Nafcillin	0.0075	- (a)	I	28	
Neomycin	0.16	Medium	I	7	
Nitroxynil[7]	0.005	-			14
Novobiocin	0.02	Medium	I	7	
Oxfendazole	0.007	Low	I & G	14	
Oxyclozanide	0.03	Medium (a)	I & G	28	
Oxytetracycline	0.003	Medium; Aerosol	I & G	10	
Penethamate	0.0005	Low	I	28	
Permethrin	0.05	Low	G	7	
Pirlimycin	0.1	Lowest	I	23	
Prednisolone	0.0002	Medium	I	7	
Procaine benzylpenicillin	0.0005	Medium	I	5	
Rafoxanide[7]	0.002	-			1
Streptomycin	0.025	Lowest	I	7	
Sulfadiazine	0.05	Low	I	5	
Sulfadimidine	0.05	Lowest	I	14	1
Tolfenamic acid	0.01	Lowest	I	12	
Triclabendazole[7]	0.0015	Medium (a)	I	37	4
Trimethoprim	0.004	Low (a)	I	5	
Tylosin	0.006	Low	I	21	

Veterinary medicine - active ingredient	ADI[1] (mg/kg bw/d)	Number of doses[2] 2008 - 2012	Use on individual animals or groups[3]	Withdrawal period (days)[4]	Number of non-compliant samples in the National Residue Control Plan 2008 - 2012[5]

NOTES

[1]**ADI values:** Value of 0.0005 mg/kg bw/d (microbiological ADI) entered for penicillin antibiotics for which no specific ADI value set; value of 0.05 mg/kg bw/d used for sulphonamides (JECFA value).

[2]**Number of doses:** Number of individual animal doses derived from data on veterinary medicinal products and medicated feed additives containing the active ingredient. Data for 2012 shown; where number of doses are lower/higher in other years of the period 2008-2012, this is shown as follows:

(a) For some years, no. of doses was "Lowest"
(b) For some years, no. of doses was "Low"
(c) For some years, no. of doses was "Medium"
(d) For some years, no. of doses was "High"

[3]**Use on individual animals or groups:** I = used on individual animals; G = used on groups of animals; I & G = used on individual animals and on groups of animals.

[4]**Withdrawal period:** Withdrawal period selected as the most representative for the substance, e.g. generally related to an injection product and one containing only the single substance.

[5]**Non-compliant samples:** Number of non-compliant samples for dairy cattle from the National Residue Control Plan for the period 2008-2012, including both 'Targeted' and 'Suspect' sampling.

[6]**Carprofen:** According to Commission Regulation 37/2010, no MRL is required for Carprofen in milk; therefore, a withdrawal period of "0" has been assigned.

[7]**Closantel, Nitroxynil, Rafoxanide, Triclabendazole:** According to Commission Regulation 37/2010, these substances were "not for use in animals producing milk for human consumption"; provisional MRLs were applied to Closantel, Nitroxynil and Triclabendazole in 2012.

[8]**Ivermectin:** According to Commission Regulation 37/2010, this substance is "not for use in animals producing milk for human consumption".

Table 7. Scoring System for Risk-ranking of Veterinary Medicinal Products and Medicated Feed Additives

Parameter	Score	Description
Potency		
Acceptable Daily Intake	1	> 0.1 mg/kg bw/day
	2	0.01 - 0.1 mg/kg bw/day
	3	0.001 - 0.01 mg/kg bw/day
	4	< 0.001 mg/kg bw/day
Usage		
Number of Doses	1	Lowest
	2	Low
	3	Medium
	4	High
Individual or Group	1	Used on individual animals
	2	Used on groups of animals or on individuals and on groups
Withdrawal Period	1	< 10 days (< 5 days for Poultry and Dairy Cattle)
	2	10 - 30 days (5 - 10 days for Poultry and Dairy Cattle)
	3	30 - 100 days (10 - 20 days for Poultry and Dairy Cattle)
	4	> 100 days (> 20 days for Poultry and Dairy Cattle)
Residue Occurrence (over a 5-year period)	1	Zero
Non-compliant samples	2	One or two
	3	Three to five
	4	Greater than five

Table 8. Risk-ranking Coding and Scoring for Substances in Beef Cattle

Veterinary medicine - active ingredient	ADI	Number of doses 2012	Use on individual animals or groups	Withdrawal period	Non-compliant samples in the National Residue Control Plan 2008-2012	Score	Rank
Abamectin	3	3	2	3	1	24	11
Albendazole	3	4	2	2	1	24	11
Amitraz	3		2	1	1	9	53
Amoxicillin	4	3	2	2	4	112	1
Ampicillin	4	2	2	2	1	24	11
Benzylpenicillin	4		1	1	2	16	27
Carprofen	3	1	1	2	1	12	41
Cefalexin	2	3	1	2	1	12	41
Cefalonium	2	3	1	2	1	12	41
Cefapirin	2	2	1	1	1	8	57
Cefoperazone	1	1	1	1	1	3	61
Cefquinome	3	2	1	1	1	12	41
Ceftiofur	1	3	1	1	1	5	59
Chlortetracycline	3		2	1	2	9	53
Clavulanic acid	2	3	1	3	1	14	40
Clenbuterol	4	1	1	2	1	16	27
Closantel	2	3	2	3	1	16	27
Cloxacillin	4	3	1	2	1	24	11
Cyhalothrin	3	1	2	2	1	15	34
Cypermethrin	2	4	2	2	1	16	27
Danofloxacin	2	1	1	1	2	12	41
Deltamethrin	3	3	2	2	1	21	18
Dexamethasone	2	3	1	2	1	12	41
Dihydrostreptomycin	2	3	1	2	1	12	41
Doramectin	4	2	2	3	1	28	9
Enrofloxacin	3	3	1	2	2	36	6
Eprinomectin	3	2	2	2	1	18	25
Fenbendazole	3	3	2	2	1	21	18
Florfenicol	3	3	1	3	1	21	18
Flumethrin	3	2	2	1	1	15	34
Flunixin	3	2	1	1	1	12	41
Gamithromycin	3	2	1	3	1	18	25
Gentamicin	3	1	1	3	1	15	34
Imidocarb	3	2	1	4	1	21	18
Ivermectin	4	4	2	2	3	96	2

Veterinary medicine - active ingredient	ADI	Number of doses 2012	Use on individual animals or groups	Withdrawal period	Non-compliant samples in the National Residue Control Plan 2008-2012	Score	Rank
Levamisole	3	3	2	2	1	21	18
Lincomycin	3	1	1	1	1	9	53
Marbofloxacin	2	3	1	1	4	40	5
Meloxicam	3	2	1	2	1	15	34
Metamizole	3	2	1	2	1	15	34
Moxidectin	3	3	2	4	1	27	10
Nafcillin	3		1	2	1	9	53
Neomycin	1	2	1	2	1	5	59
Nitroxynil	3	3	2	3	1	24	11
Oxfendazole	3	3	2	2	1	21	18
Oxyclozanide	2	4	2	2	1	16	27
Oxytetracycline	3	3	2	2	4	84	3
Penethamate	4	2	1	1	1	16	27
Permethrin	2	3	2	1	1	12	41
Pirlimycin	2	1	1	2	1	8	57
Procaine benzylpenicillin	4	3	1	1	1	20	24
Rafoxanide	3	3	2	3	1	24	11
Streptomycin	2	2	1	2	1	10	52
Sulfadiazine	2	3	1	2	1	12	41
Sulfadimidine	2	1	1	2	2	16	27
Tilmicosin	3	2	1	3	2	36	6
Tolfenamic acid	3	1	1	2	1	12	41
Triclabendazole	3	4	2	3	2	54	4
Trimethoprim	3	2	1	2	1	15	34
Tulathromycin	2	2	1	3	2	24	11
Tylosin	3	3	1	2	2	36	6

CODING SYSTEM

ADI (mg/kg bw/d), four point coding: > 0.1 = 1; 0.01 - 0.1 = 2; 0.001 - 0.01 = 3; < 0.001 = 4

Number of doses, four point coding: Lowest = 1; Low = 2; Medium = 3; High = 4

Use on individual animals or groups, two point coding: I (used on individual animals) = 1; G (used on groups of animals) or I & G (used on individual animals and on groups of animals) = 2

Withdrawal period, four point scale: < 10 days = 1; 10 - 30 days = 2; 30 - 100 days = 3; > 100 days = 4

Non-compliant results, four point coding: zero = 1; one or two = 2; three to five = 3; greater than five = 4

SCORING SYSTEM

'Potency' × 'Usage' (No. Doses + Individual/Group Use + withdrawal period) × 'Residue Occurrence'

Table 9. Risk-ranking Coding and Scoring for Substances in Sheep and Goats

Veterinary medicine - active ingredient	ADI	Number of doses 2012	Use on individual animals or groups	Withdrawal period	Non-compliant samples in the National Residue Control Plan	Score	Rank
Abamectin	3	2	2	2	1	18	17
Albendazole	3	4	2	2	1	24	11
Amitraz	3		2	2	1	12	25
Amoxicillin	4	3	1	2	2	48	4
Ampicillin	4	1	1	2	1	16	18
Benzylpenicillin	4		1	1	1	8	30
Chlortetracycline	3		2	1	1	9	29
Closantel	2	4	2	2	4	64	2
Cypermethrin	2	3	2	1	1	12	25
Cyromazine	2		2	2	1	8	30
Decoquinate	2	4	2	1	1	14	23
Deltamethrin	3	2	2	1	1	15	20
Diclazuril	2	3	2	1	1	12	25
Dicyclanil	3	3	2	3	1	24	11
Dihydrostreptomycin	2	3	1	2	1	12	25
Doramectin	4	2	2	3	1	28	8
Fenbendazole	3	3	2	2	2	42	5
Flubendazole	2				2	0	
Flugestone acetate	4	2	1	2	1	20	15
Ivermectin	4	4	2	3	1	36	7
Levamisole	3	4	2	2	1	24	11
Mebendazole	2	3	2	2	1	14	23
Monepantel	2	1	2	1	1	8	30

Veterinary medicine - active ingredient	ADI	Number of doses 2012	Use on individual animals or groups	Withdrawal period	Non-compliant samples in the National Residue Control Plan	Score	Rank
Moxidectin	3	4	2	3	1	27	9
Nitroxynil	3	3	2	3	2	24	11
Oxfendazole	3	3	2	2	2	42	5
Oxyclozanide	2	4	2	2	1	16	18
Oxytetracycline	3	3	1	2	3	54	3
Procaine benzylpenicillin	4	3	1	1	1	20	15
Rafoxanide	3	3	2	3	3	72	1
Spectinomycin	1	1	1	2	1	4	36
Streptomycin	2	1	1	2	1	8	30
Sulfadiazine	2		1	2	1	6	35
Sulfadimidine	2	1	1	2	1	8	30
Tilmicosin	3	1	1	3	1	15	20
Toltrazuril	3	1	1	3	1	15	20
Triclabendazole	3	4	2	3	1	27	9

CODING SYSTEM

ADI (mg/kg bw/d), four point coding: > 0.1 = 1; 0.01 - 0.1 = 2; 0.001 - 0.01 = 3; < 0.001 = 4

Number of doses, four point coding: Lowest = 1; Low = 2; Medium = 3; High = 4

Use on individual animals or groups, two point coding: I (used on individual animals) = 1; G (used on groups of animals) or I & G (used on individual animals and on groups of animals) = 2

Withdrawal period, four point scale: < 10 days = 1; 10 - 30 days = 2; 30 - 100 days = 3; > 100 days = 4

Non-compliant results, four point coding: zero = 1; one or two = 2; three to five = 3; greater than five = 4

SCORING SYSTEM

'Potency' × 'Usage' (No. Doses + Individual/Group Use + withdrawal period) × 'Residue Occurrence'

Table 10. Risk-ranking Coding and Scoring for Substances in Pigs

Veterinary medicine - active ingredient	ADI	Number of doses 2012	Use on individual animals or groups	Withdrawal period	Non-compliant samples in the National Residue Control Plan	Score	Rank
Amitraz	3		2	1	1	9	28
Amoxicillin	4	3	2	2	1	28	7
Ampicillin	4	1	1	2	1	16	19
Apramycin	2	1	2	2	1	10	26
Azaperone	4	2	1	2	1	20	11
Benzylpenicillin	4		1	1	1	8	30
Cefquinome	3	2	1	1	1	12	22
Ceftiofur	1	2	1	1	1	4	39
Chlortetracycline	3	4	2	2	1	24	9
Colistin	2	1	2	1	1	8	30
Danofloxacin	2	1	1	1	1	6	36
Dexamethasone	2	2	1	1	1	8	30
Dihydrostreptomycin	2	2	1	2	1	10	26
Doxycycline	3	1	2	1	1	12	22
Enrofloxacin	3	2	1	2	2	30	6
Fenbendazole	3	2	2	2	1	18	14
Florfenicol	3	3	2	2	1	21	10
Flubendazole	2	3	2	1	1	12	22
Flunixin	3	2	1	2	1	15	20
Ivermectin	4	4	2	2	1	32	5
Lincomycin	3	3	2	1	1	18	14
Marbofloxacin	2	3	1	1	2	20	11
Meloxicam	3	3	1	1	1	15	20
Oxytetracycline	3	3	2	2	2	42	2
Phenoxymethyl penicillin	4	4	2	1	1	28	7
Procaine benzylpenicillin	4	3	1	1	2	40	4
Spectinomycin	1	3	2	2	1	7	35
Streptomycin	2	1	1	2	1	8	30
Sulfadiazine	2	3	2	2	4	56	1
Sulfadimidine	2	1	1	3	2	20	11
Tiamulin	2	1	2	1	1	8	30
Tilmicosin	3	2	2	2	1	18	14
Tolfenamic acid	3	1	1	1	1	9	28

Veterinary medicine - active ingredient	ADI	Number of doses 2012	Use on individual animals or groups	Withdrawal period	Non-compliant samples in the National Residue Control Plan	Score	Rank
Toltrazuril	3	2	1	3	1	18	14
Trimethoprim	3	3	2	2	2	42	2
Tulathromycin	2	2	1	3	1	12	22
Tylosin	3	3	2	1	1	18	14
Tylvalosin	1	3	2	1	1	6	36
Valnemulin	2		2	1	1	6	36

CODING SYSTEM

ADI (mg/kg bw/d), four point coding: > 0.1 = 1; 0.01 - 0.1 = 2; 0.001 - 0.01 = 3; < 0.001 = 4

Number of doses, four point coding: Lowest = 1; Low = 2; Medium = 3; High = 4

Use on individual animals or groups, two point coding: I (used on individual animals) = 1; G (used on groups of animals) or I & G (used on individual animals and on groups of animals) = 2

Withdrawal period, four point scale: < 10 days = 1; 10 - 30 days = 2; 30 - 100 days = 3; > 100 days = 4

Non-compliant results, four point coding: zero = 1; one or two = 2; three to five = 3; greater than five = 4

SCORING SYSTEM

'Potency' × 'Usage' (No. Doses + Individual/Group Use + withdrawal period) × 'Residue Occurrence'

Table 11. Risk-ranking Coding and Scoring for Substances in Poultry

Veterinary medicine - active ingredient	ADI	Number of doses 2012	Use on individual animals or groups	Withdrawal period	Non-compliant samples in the National Residue Control Plan	Score	Rank
Amoxicillin	4	4	2	1	1	28	1
Apramycin	2		2	2	1	8	19
Chlortetracycline	3	2	2	1	1	15	13
Colistin	2	2	2	1	1	10	18
Diclofenac	3				2	0	
Doxycycline	3	1	2	2	1	15	13
Enrofloxacin	3	3	2	1	1	18	8
Erythromycin	3	2	2	2	1	18	8
Flubendazole	2	2	2	2	1	12	17
Flumequine	2		2	1	1	6	20
Ivermectin	4				2	0	
Lincomycin	3	2	2	2	1	18	8
Monensin	2	4	2	1	1	14	16
Narasin	3	4	2	1	1	21	5
Nicarbazin	1	4	2	1	4	28	1
Phoxim	3	3	2	4	1	27	3
Spectinomycin	1	2	2	2	1	6	20
Sulfadiazine	2	4	2	2	1	16	11
Sulfadimidine	2	3	2	3	1	16	11
Tilmicosin	3	2	2	3	1	21	5
Toltrazuril	3	2	2	3	1	21	5
Trimethoprim	3	4	2	2	1	24	4
Tylosin	3	2	2	1	1	15	13

CODING SYSTEM

ADI (mg/kg bw/d), four point coding: > 0.1 = 1; 0.01 - 0.1 = 2; 0.001 - 0.01 = 3; < 0.001 = 4

Number of doses, four point coding: Lowest = 1; Low = 2; Medium = 3; High = 4

Use on individual animals or groups, two point coding: I (used on individual animals) = 1; G (used on groups of animals) or I & G (used on individual animals and on groups of animals) = 2

Withdrawal period, four point scale: < 10 days = 1; 10 - 30 days = 2; 30 - 100 days = 3; > 100 days = 4

Non-compliant results, four point coding: zero = 1; one or two = 2; three to five = 3; greater than five = 4

SCORING SYSTEM

'Potency' × 'Usage' (No. Doses + Individual/Group Use + withdrawal period) × 'Residue Occurrence'

Table 12. Risk-ranking Coding and Scoring for Substances in Dairy Cattle

Veterinary medicine - active ingredient	ADI	Number of doses 2012	Use on individual animals or groups	Withdrawal period	Non-compliant samples in the National Residue Control Plan	Score	Rank
Albendazole	3	3	2	2	1	21	3
Amitraz	3		2	1	1	9	34
Amoxicillin	4	3	1	1	2	40	2
Ampicillin	4	2	1	1	1	16	13
Benzylpenicillin	4		1	1	1	8	39
Carprofen	3	1	1	1	1	9	34
Cefalexin	2	2	1	1	1	8	39
Cefalonium	2	3	1	2	1	12	23
Cefapirin	2	2	1	1	1	8	39
Cefoperazone	1	1	1	1	1	3	51
Cefquinome	3	2	1	1	1	12	23
Ceftiofur	1	2	1	1	1	4	50
Chlortetracycline	3		2	1	1	9	34
Clavulanic acid	2	2	1	1	1	8	39
Clenbuterol	4	1	1	2	1	16	13
Closantel	2				4	0	
Cloxacillin	4	2	1	2	1	20	6
Cyhalothrin	3	1	2	2	1	15	16
Cypermethrin	2	3	2	1	1	12	23
Danofloxacin	2	1	1	1	1	6	47
Deltamethrin	3	2	2	2	1	18	10
Dexamethasone	2	2	1	1	1	8	39
Dihydrostreptomycin	2	3	1	1	1	10	31
Enrofloxacin	3	2	1	1	1	12	23
Eprinomectin	3	2	2	2	1	18	10
Fenbendazole	3	3	2	2	1	21	3
Flumethrin	3	2	2	1	1	15	16
Flunixin	3	2	1	1	1	12	23
Gentamicin	3	1	1	2	1	12	23
Imidocarb	3	2	1	2	1	15	16
Ivermectin	4				3	0	
Kanamycin	3	3	1	1	1	15	16
Lincomycin	3	1	1	1	1	9	34
Marbofloxacin	2	2	1	1	1	8	39
Meloxicam	3	2	1	2	1	15	16

Veterinary medicine - active ingredient	ADI	Number of doses 2012	Use on individual animals or groups	Withdrawal period	Non-compliant samples in the National Residue Control Plan	Score	Rank
Nafcillin	3		1	2	1	9	34
Neomycin	1	3	1	1	1	5	49
Nitroxynil	3				4	0	
Novobiocin	2	3	1	1	1	10	31
Oxfendazole	3	2	2	2	1	18	10
Oxyclozanide	2	3	2	2	1	14	22
Oxytetracycline	3	3	2	2	1	21	3
Penethamate	4	2	1	2	1	20	6
Permethrin	2	2	2	1	1	10	31
Pirlimycin	2	1	1	2	1	8	39
Prednisolone	4	3	1	1	1	20	6
Procaine benzylpenicillin	4	3	1	1	1	20	6
Rafoxanide	3				2	0	
Streptomycin	2	1	1	1	1	6	47
Sulfadiazine	2	2	1	1	1	8	39
Sulfadimidine	2	1	1	2	2	16	13
Tolfenamic acid	3	1	1	2	1	12	23
Triclabendazole	3	3	1	3	3	63	1
Trimethoprim	3	2	1	1	1	12	23
Tylosin	3	2	1	2	1	15	16

CODING SYSTEM

ADI (mg/kg bw/d), four point coding: > 0.1 = 1; 0.01 - 0.1 = 2; 0.001 - 0.01 = 3; < 0.001 = 4

Number of doses, four point coding: Lowest = 1; Low = 2; Medium = 3; High = 4

Use on individual animals or groups, two point coding: I (used on individual animals) = 1; G (used on groups of animals) or I & G (used on individual animals and on groups of animals) = 2

Withdrawal period, four point scale: < 10 days = 1; 10 - 30 days = 2; 30 - 100 days = 3; > 100 days = 4

Non-compliant results, four point coding: zero = 1; one or two = 2; three to five = 3; greater than five = 4

SCORING SYSTEM

'Potency' × 'Usage' (No. Doses + Individual/Group Use + withdrawal period) × 'Residue Occurrence'

Table 13: Overall Ranking of Substances for Testing in Beef Cattle

Ranking Group	Veterinary Medicine (active ingredient)		Ranking Score
A	Amoxcillin Ivermectin	Oxytetracycline1 Triclabendazole	> 40
B	Marbofloxacin Enrofloxacin	Tilmicosin Tylosin	31 - 40
C	Doramectin Moxidectin Abamectin Albendazole Ampicillin Cloxacillin Nitroxynil Rafoxanide	Tulathromycin Deltamethrin Fenbendazole Florfenicol Imidocarb Levamisole Oxfendazole	21 - 30
D	Procaine benzylpenicillin Eprinomectin Gamithromycin Benzylpenicillin Clenbuterol Closantel Cypermethrin Oxyclozanide Penethamate Sulfadimidine Cyhalothrin Flumethrin Gentamicin Meloxicam	Metamizole Trimethoprim Clavulanic acid Carprofen Cefalexin Cefalonium Cefquinome Danofloxacin Dexamethasone Dihydrostreptomycin Flunixin Permethrin Sulfadiazine Tolfenamic acid	11 - 20
E	Streptomycin Amitraz[1] Chlortetracycline[1] Lincomycin Nafcillin	Cefapirin Pirlimycin Ceftiofur Neomycin Cefoperazone	< 10

[1] The usage of Amitraz, Chlortetracycline and Oxytetracycline as topical or aerosol preparations is not accounted for in the substance ranking.

Table 14: Overall Ranking of Substances for Testing in Sheep and Goats

Ranking Group	Veterinary Medicine (active ingredient)		Ranking Score
A	Rafoxanide Closantel Oxytetracycline[1]	Amoxicillin Fenbendazole Oxfendazole	> 40
B	Ivermectin		31 - 40
C	Doramectin Moxidectin Triclabendazole Albendazole	Dicyclanil Levamisole Nitroxynil	21 - 30
D	Flugestone acetate Procaine benzylpenicillin Abamectin Ampicillin Oxyclozanide Deltamethrin Tilmicosin	Toltrazuril Decoquinate Mebendazole Amitraz[1] Cypermethrin[1] Diclazuril Dihydrostreptomycin	11 - 20
E	Chlortetracycline[1] Benzylpenicillin Cyromazine Monepantel	Streptomycin Sulfadimidine Sulfadiazine Spectinomycin	< 10

[1] The usage of Amitraz, Chlortetracycline, Cypermethrin and Oxytetracycline as topical or aerosol preparations is not accounted for in the substance ranking.

[2] Non-allowed usage of Flubendazole in sheep and goats is not accounted for in the substance ranking; this substance has been determined as non-compliant samples in sheep and goats in the National Residue Control Plan 2008-2012.

Table 15: Overall Ranking of Substances for Testing in Pigs

Ranking Group	Veterinary Medicine (active ingredient)		Ranking Score
A	Sulfadiazine Oxytetracycline[1]	Trimethoprim	> 40
B	Procaine benzylpenicillin	Ivermectin	31 - 40
C	Enrofloxacin Amoxicillin Phenoxymethylpenicillin	Chlortetracycline[1] Florfenicol	21 - 30
D	Azaperone Marbofloxacin Sulfadimidine Fenbendazole Lincomycin[1] Tilmicosin Toltrazuril Tylosin	Ampicillin Flunixin Meloxicam Cefquinome Doxycycline Flubendazole Tulathromycin	11 - 20
E	Apramycin Dihydrostreptomycin Amitraz[1] Tolfenamic acid Benzylpenicillin Colistin Dexamethasone	Streptomycin Tiamulin Spectinomycin[1] Danofloxacin Tylvalosin Valnemulin Ceftiofur	< 10

[1] The usage of Amitraz, Chlortetracycline, Lincomycin, Oxytetracycline and Spectinomycin as aerosol preparations, feed premixes or feed additives is not accounted for in the substance ranking.

Table 16: Overall Ranking of Substances for Testing in Poultry

Ranking Group	Veterinary Medicine (active ingredient)		Ranking Score
A	Amoxicillin Nicarbazin[1] Phoxim Trimethoprim	Narasin Tilmicosin Toltrazuril	> 20
B	Enrofloxacin Erythromycin Lincomycin	Sulfadiazine Sulfadimidine	16 - 20
C	Chlortetracycline Doxycycline Tylosin	Monensin Flubendazole	11 - 15
D	Colistin Apramycin	Flumequine Spectinomycin	6 - 10
E			< 5

[1] Nicarbazin: High numbers of non-compliant results for Nicarbazin were recorded during the years 2008 to 2010; many of these results would not be non-compliant based on the new MRLs for Nicarbazin applied from 2010 onwards.

[2] Non-allowed usage of Diclofenac and Ivermectin in poultry is not accounted for in the substance ranking; these substances have been determined as non-compliant samples in poultry in the National Residue Control Plan 2008-2012.

Table 17: Overall Ranking of Substances for Testing in Dairy Cattle

Ranking Group	Veterinary Medicine (active ingredient)		Ranking Score
A	Triclabendazole Amoxicillin Albendazole	Fenbendazole Oxytetracycline	> 20
B	Cloxacillin Penethamate Prednisolone Procaine benzylpenicillin Deltamethrin	Eprinomectin Oxfendazole Ampicillin Clenbuterol Sulfadimidine	16 - 20
C	Cyhalothrin Flumethrin Imidocarb Kanamycin Meloxicam Tylosin Oxyclozanide Cefalonium	Cefquinome Cypermethrin Enrofloxacin Flunixin Gentamicin Tolfenamic acid Trimethoprim	11 - 15
D	Dihydrostreptomycin Novobiocin Permethrin Amitraz Carprofen Chlortetracycline Lincomycin Nafcillin Benzylpenicillin	Cefalexin Cefapirin Clavulanic acid Dexamethasone Marbofloxacin Pirlimycin Sulfadiazine Danofloxacin Streptomycin	6 - 10
E	Neomycin Ceftiofur	Cefoperazone	< 5

[1] Non-allowed usage of Closantel, Ivermectin, Nitroxynil, Rafoxanide in "*animals producing milk for human consumption*" is not accounted for in the substance ranking. These substances have been determined as non-compliant samples in dairy cattle in the National Residue Control Plan 2008-2012. In 2012, the EC published MRLs for some of these substances in milk.

Table 18. Food Consumption Data (From the FSAI's Total Diet Study)

Food Category	Total Population		Consumers Only	
	Mean consumption (g/day)	**Proportion of meat diet (%)**	**Mean consumption (g/day)**	**Proportion of meat diet (%)**
Beef and Beef Products	35.2	26.7	68.0	29.1
Lamb and Lamb Products	8.9	6.7	23.6	10.1
Pork and Pork Products	55.2	41.8	93.6	40.0
Poultry and Poultry Products	32.6	24.7	48.7	20.8
Milk and Dairy Products	335.3		1111.6	
Eggs	18.5		20.5	

APPENDIX I. REQUEST FOR ADVICE FROM THE FSAI

The Scientific Committee, at its meeting on 16th March 2012, allocated a request for advice from the FSAI to the Chemical Safety Sub-committee on the topic: *Application of a risk based approach to developing the national residues sampling plan*.

Background/Context

The concept of applying a formalised risk-based approach to sampling for the National Monitoring Programme for Foods of Animal Origin is currently being considered by the FSAI and DAFM. Such an approach will be particularly important when developing the anticipated component of sampling based on national priorities, which is expected to be contained in the replacement for Directive 96/23/EC on residue monitoring. There is need to consider the overall issue of applying a risk-based approach to sampling for chemical contaminants in food and to develop, test and validate appropriate systems for application. Such a risk-based approach would also have potential application for other chemical contaminants surveillance and monitoring programmes.

Currently, the Food and Health Research Initiative (FHRI) is funding a research project (2008 – 2012) in the thematic area of food safety – monitoring and surveillance entitled '*Safe and Healthy Foods*'. This project has, as one of its objectives, to develop a risk-based approach for monitoring and surveillance of chemical contaminants in foods consumed in Ireland through prioritisation of substances based on toxicity, incidence and usage. This element of the research is being carried out by Ashtown Food Research Centre, Teagasc.

Risk Management Questions

1. What systems are used elsewhere for risk-based approaches to sampling for residue surveillance and monitoring and how might these systems be adapted for the Irish situation?
2. What information and data are required to implement a risk-based approach to sampling for chemical contaminants?
3. What are the components required for a risk-based approach to sampling for chemical contaminants and how should such components be applied in a developed risk-based system?
4. How might a risk-based system, developed for application in the national component of the future monitoring programme for foods of animal origin, be applied for other chemical residue surveillance and monitoring programmes in Ireland?

Modification of the Request for Advice

The request for advice was modified by the Scientific Committee, with the agreement of the FSAI, at its meeting on 11th September 2012, as follows:

The chemical substances to be included in the ranking system initially include licensed veterinary medicinal products and medicated feed additives; subsequently, it is intended that the ranking system will be extended to prohibited substances and contaminants.

APPENDIX 2. MEMBERS OF THE SCIENTIFIC COMMITTEE OF THE FSAI

Prof. Albert Flynn (Chair)
University College, Cork

Dr Colette Bonner
Department of Health and Children

Prof. Martin Cormican
University College Hospital, Galway

Dr Geraldine Duffy
Teagasc

Prof. Peter Jones
University College, Cork

Prof. Brian McKenna
University College, Dublin

Dr Paul McKeown
Health Protection Surveillance Centre

Dr Michael O'Keeffe
Residue Specialist

Dr Dan O'Sullivan
Dept of Agriculture, Food and the Marine

Dr Margaret O'Sullivan
Health Service Executive

Mr Ray Parle
Health Service Executive

Ms Ita Saul
Our Lady's Childrens Hospital, Crumlin

Dr Paula Barry Walsh
Department of Agriculture, Food and the Marine

Dr Iona Pratt
Food Safety Authority of Ireland

APPENDIX 3. MEMBERS OF THE CHEMICAL SAFETY SUB-COMMITTEE OF THE FSAI

Dr Michael O'Keeffe (Chair)
Residue Specialist

Dr Dan O'Sullivan (Deputy Chair)
Dept of Agriculture, Food and the Marine

Dr Thomasina Barron
Dept of Agriculture, Food and the Marine

Dr Padraig Burke
Health Service Executive

Dr Claire Chambers
Chambers Toxicological Consulting

Dr Colman Concannon
Environmental Protection Agency

Ms Catherine Cosgrove
Health Service Executive

Dr Martin Danaher
Teagasc

Dr John Keegan
Health Service Executive

Dr Peadar Lawlor
Teagasc

Mr Gerry Lohan
Dept of Agriculture, Food and the Marine

Dr Evin McGovern
Marine Institute

Dr David McGrath
(Retired) Teagasc

Dr John Moriarty
Dept of Agriculture, Food and the Marine

Dr Iona Pratt
Food Safety Authority of Ireland

Dr Joe Silk
Marine Institute

NOTES

Food Safety
AUTHORITY OF IRELAND

Food Safety Authority of Ireland
Abbey Court, Lower Abbey Street,
Dublin 1

Udarás Sábháilteachta Bia na hEireann
Cúirt na Mainistreach, Sráid na Mainistrach íocht.,
Baile Átha Cliath 1

Advice Line: 1890 336677
Telephone: +353 1 817 1300
Facsimile: +353 1 817 1301
E-mail: info@fsai.ie
www.fsai.ie