Compendium of assessments of substances by the VRC's Matrix Ranking method

August 2013

Contents

Substance Groups in the National Surveillance Programme

Directive 96/23/EC

Group A (substances having an anabolic effect and unauthorised substances)

Antibiotics - Nitrofurans
Nitrofuran antibiotics are banned from use in food production in the EU and in many 3rd countries. They previously had many uses, for example as a feed/water additive to control bacterial infection in poultry flocks. They metabolise rapidly, and are measured in food as their tissue-bound metabolites. Examples include
Furazolidone (as its 3-amino-2-oxazolidinone (AOZ) metabolite)
Furaltadone (as its 3-amino-5-morpholinomethyl-2-oxazolidone (AMOZ) metabolite)
Nitrofurazone (as its semicarbazide metabolite)
Antibiotics - Chloramphenicol
Chloramphenicol is also now banned from use in food production in the EU and in most 3rd countries. It is a broad spectrum antibiotic, and prior to the ban was widely used across all species for a variety of treatments. It is used in human medicine, most commonly in eye drops for conjunctivitis.
Chloramphenicol
Antibiotics - Dapsone
Dapsone had fewer historical uses in veterinary medicine than chloramphenicol, but is now also banned within the EU for food production. It has an important use in human medicine for the treatment of leprosy and also for the treatment of some hypersensitivity skin conditions such as wheat allergies.
Dapsone
Growth Promoters - Stilbenes
The stilbene-derived substances are oestrogenic compounds which were used in the past for growth promotion in animals and sex-regulation in fish but are now prohibited in the EU and many 3rd countries. Examples include
Diethylstilboestrol
Dienestrol
Hexoestrol
Growth Promoters - Thyrostats
These substances reduce the activity of the thyroid gland, which can improve the apparent fattening rate of livestock by aiding water retention in the muscle. They are prohibited from use in food animals in the EU, but have some approved uses in pets to treat overactive thyroids. Examples include
Methimazole (Tapazole)
Thiouracil, and related substituted analogues
Mercaptobenzimidazole
Growth Promoters - Steroids and Hormones
Any natural or synthetic substance that is based upon the chemical structure of androgens (e.g. testosterone) or oestrogens (e.g. oestradiol). Many occur naturally in livestock, but their administration as growth promoters is banned within the EU, and in food production in 3rd countries for export to the EU. Growth promoters are approved and used in many non-EU countries for home-market production. Examples include
Stanozolol
Boldenone
Nandrolone (nortestosterone)

Growth Promoters - Gestagens and Progestagens
Synthetic variants of the hormone progesterone, these are similarly banned from food production within the EU, but approved and used in some 3rd countries for home-market production. Some have use in human medicine as contraceptives. Examples include
Medroxyprogesterone acetate
Chlormadinone acetate
Growth Promoters – Resorcyclic Acid Lactones
Compounds derived from fungal mycotoxins that have a chemical "backbone" of similar shape to oestradiol, and therefore similar oestragenic properties. Banned from food production within the EU but zeranol, particularly, is administered as an implant in cattle in some 3rd countries for home-market production. Examples include
Zeranol
Muscle Relaxants and Growth Promoters - β-Agonists
β-agonists relax smooth muscle, and are particularly used to widen the windpipe in respiratory diseases (especially in human medicine e.g. "Ventolin"), but they can also have a growth promoting effect. They have a restricted number of legal uses in EU food production for respiratory diseases and as a muscle relaxant in calving, but they are banned from use as growth promoters. They are approved for use as growth promoters in livestock in some 3rd countries for livestock production. Examples include
Clenbuterol Ractopamine Zilpaterol

Group B (veterinary drugs and contaminants)

Antibiotics - Aminoglycosides
Aminoglycosides are a well-proven and established class of antibiotics, usually biosynthesised from soil bacteria. They are generally administered to livestock as injectables (i.e. individual animals are treated, rather than as feed additives for an entire flock or herd). They are sometimes co-formulated with β-lactams (e.g. "PenStrep", containing penicillin and streptomycin). Examples include
Dihydrostreptomycin Streptomycin Neomycin Framomycin
Antibiotics - β-lactams
Includes penicillins and cephalosporins. One of the most common classes of antibiotics, both in veterinary and in human medicine. In veterinary medicine one of the most common applications is to treat mastitis in dairy cattle, but they have a variety of other uses in most species. Examples include
Amoxicillin Benzylpenicillin (Penicillin G) Ceftiofur Cephapirin
Antibiotics - Lincosamides
Similar in mode of action and use to macrolides. Examples include
Lincomycin
Antibiotics - Macrolides
A class of antibiotic based upon a common chemical "backbone" of a large lactone ring structure. They inhibit the synthesis of bacterial proteins. In veterinary medicine, they are particularly given to non-ruminant food animals such as poultry and pigs, as well as for pets. Examples include
Tilmicosin Tylosin
Antibiotics - Peptolides and Polypeptides
Historically used as prophylactic feed additives, until the EU ban on such feed additives (human-use antibiotics and antibiotics for the purpose of growth promotion), completed in 2006. Now that this use is no longer available, no longer used in the EU. Examples include
Virginiamycin Bacitracin
Antibiotics - Quinolones and Fluoroquinolones
Broad spectrum antibiotics with widespread uses in both human medicine and livestock / aquaculture medicine. Four "generations" of quinolones have been developed. Latter-generation drugs are restricted to human use, to minimise the risk of resistance developing. Examples that have veterinary uses include
Enrofloxacin Flumequine Oxolinic acid

Antibiotics - Sulphonamides and Trimethoprim

The first antibiotic drugs, developed in the 1930's for human use that still have many uses in veterinary medicine, particularly for poultry, rabbits and pigs. Sulphonamides are frequently co-formulated with Trimethoprim to potentiate their effect. Examples include

Sulphadiazine
Sulphamethazine (Sulfadimidine)
Sulphaquinoxaline

Antibiotics - Tetracyclines

Broad spectrum antibiotics, widely used in veterinary medicine for all species (including aquaculture). Can be administered to individual animals by injection, or as a feed additive to a whole flock or herd. Tetracyclines are low-cost, and available from a variety of generic manufacturers as most are now off-patent. Examples include

Chlortetracycline
Oxytetracycline
Tetracycline

Antibiotics - Carbadox and Olaquindox

Previously used as a feed additive, particularly to control dysentery in pigs, but now banned from use in food animals in the EU following concern over carcinogenicity. Permitted in some countries for their home-production.

Carbadox
Olaquindox

Anticoccidials

A variety of medicines are available to treat coccidiosis (an intestinal parasite) in poultry and rabbits. They are generally administered as feed additives. In conventional poultry production, treatment for coccidiosis is almost universal, with different medicines being given at different stages of the birds' lives. Non-medicated feed is then used in the days prior to slaughter, to allow any residues in the meat to deplete. Anticoccidials encompass a number of chemical classes and potencies, with many being ionophores (molecules that can carry ions through the cell membrane). Examples of anticoccidials include

Diclazuril
Lasalocid
Monensin
Salinomycin
Nicarbazin

Anthelmintics - Avermectins and Moxidectin

Anthelmintics are used to treat parasites; either internal (worms) or external (lice, mites). Avermectins are analogues of avermectin B1a, which was isolated from soil bacteria in the 1970s. Each is licensed for specific uses; these include sheep / cattle dips and pour-ons, treatments for liver fluke, and sea-lice in farmed fish. As with all anthelmintics, parasites can build resistance and so different drugs are sometimes rotated. Examples include

Doramectin
Emamectin
Ivermectin
Moxidectin

Anthelmintics – Benzimidazoles and Levamisole
Benzimidazoles are generally used as de-wormers, either for large livestock animals (e.g. albendazole, fenbendazole) or for poultry (flubendazole) or rabbits. They are also commonly used in dogs, cats and other companion animals. Thiabendazole also has a use as a pesticide (anti-fungal), and so there is an additional route for residues to enter the diet via fruit and vegetables. Examples include
Albendazole Flubendazole Thiabendazole Triclabendazole
Anthelmintics – Salicylanides and Phenol Derivatives
There are a variety of other treatments for worms, flukes, and external parasites, particularly for sheep and cattle. They are available as injectables, or pour-ons and drenches. There are often restrictions on the collection of milk following treatment of dairy cattle, to prevent residues in the milk and some are not licensed for use in lactating animals at all. Examples include
Oxyclozanide Closantel Nitroxynil
Anti-parasites / Antibiotics - Nitroimidazoles
Nitroimdazoles are banned from use in food production in the EU and in most 3rd countries. They previously had many uses, for example as feed additives to control blackspot in poultry and game birds, or dysentery in pigs. Some (e.g. carnidazole) still have use in racing pigeons, and some (e.g. metronidazole) are used in human medicine. Examples include
Dimetridazole Metronidazole Ronidazole
Antiparasitics - Pyrethroids
Pyrethroids are common insecticides used in agriculture and household products, but also have a use to treat external parasites (fleas, ticks, lice) in veterinary medicines. Approved uses include as pour-ons for sheep and to control sea-lice in farmed fish. Examples include
Cypermethrin Deltamethrin Permethrin
Antiparasitics – Carbamates and Organophosphates
Some carbamate and organophosphate insecticides also have veterinary uses to treat external parasites, although their use is much rarer now than in previous years. They tend to now be used in wound dressings or dusts, as very targeted treatments. Blanket organophosphate sheep dipping, for example, has fallen from favour due to fears of operator exposure. Organophosphates and carbamates inhibit acetylcholine esterase (i.e. inhibit nerve transmission), and have a relatively higher mammalian toxicity than many other classes of veterinary residues. Examples include
Carbaryl Methomyl Diazinon Malathion Chlorfenvinphos

Antiparasitics - Organochlorines
Organochlorines were one of the first treatments to be developed for external parasites, and were used in many early dips and drenches, but now have no approved use. They are environmentally persistent, accumulating in fatty tissue, and with sufficiently sensitive test methods residues from historical use can be detected in most food types, particularly fish and animal fats. Examples include
DDT Lindane (gamma-HCH) Dieldrin Fusarium toxins
Antiparasitics - Dyes
Substances which were not developed specifically for medicinal use, but it has been found that they are effective for treating parasites such as fin-rot in farmed fish. They have not been authorised for use in veterinary medicinal products in the EU and therefore should not be used to treat farmed fish. Examples include
Malachite Green Crystal Violet
Antiparasitics - Amitraz
Amitraz is primarily a treatment for external parasites in pets, but also has an approved use in many countries as a sheep dip or pour-on. It has also been used to control mites in honey bees.
Amitraz
Antiparasitics - Bronopol
Bronopol is most commonly found in toothpaste. It has an approved use to control lice in farmed fish, but is much less commonly used in the UK than alternatives such as emamectin.
Bronopol
Corticosteroids
Similar in structure and action to steroids. Corticosteroids are banned as growth promoters, but are frequently co-formulated with other medicines (e.g. antibiotics) that are intended for injection, to reduce the swelling and inflammation around the injection site. They can also be used in a similar manner to NSAIDs to reduce swelling. Examples include
Betamethasone Dexamethasone Prednisolone
Non Steroidal Anti-inflammatory Drugs (NSAIDs)
NSAIDs are administered to relieve pain or swelling (arthritic or injuries) in large food animals such as cattle and horses. There are a wide variety of NSAIDs available for humans and for pets, but relatively few which are approved for use in food animals. Examples include
Phenylbutazone (banned for food animals within the EU) Flunixin Meloxicam
Sedatives and Tranquilisers
Sedatives are used to reduce stress in larger animals (pigs, cattle, horses) when they are transported. There are a wide range of sedatives that have been developed for human use, but very few which have an approved veterinary use. Examples include
Carazolol Chlorpromazine (now banned within the EU) Xylazine

1,4-dichlorobenzene

Reviewed 2013 (FSA)

	Rationale	Score
Hazard (A)	Increased hepatocellular adenomas and carcinomas in mice, and some (weak) evidence that it is genotoxic in mouse liver (IARC 1999).	6
Potency (B)	A TDI of 107 µg/kg bw/day was set on the basis of considering 1,4-dichlorobenzene to not be genotoxic (WHO 2003).	0
Diet (C)	Only used in honey production – low % in diet.	0
Use (D)	When used, 100% of frames are treated	3
High Exposure (E)	No evidence for high exposure groups for honey	0
Detectable residues (F)	Seldom included in EU testing schemes. Used in UK apiaries for storage of hive frames over winter (mothballs – e.g. "Para-Moth") but should not be used during production season, limited knowledge on potential use in 3rd countries.	1
Total	(A+B) x (C+D+E+F)	24

IARC (1999). Dichlorbenzenes. In: IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Volume 73: Some Chemicals that cause Tumours of the Kidney or Urinary Bladder in Rodents and Some Other Substances. International Agency for Research on Cancer, Lyon, France. Available at http://monographs.iarc.fr/ENG/Monographs/vol73/mono73-13.pdf

WHO (2003). Dichlorobenzenes in drinking water. Background document for development of WHO Guidelines for Drinking-water Quality. World Health Organization. Available at http://www.who.int/water_sanitation_health/dwq/chemicals/dichlorobenzenes.pdf

17ß-oestradiol

Reviewed 2013 (FSA)

	Rationale	Score
Hazard (A)	Carcinogenic in humans and possibly mutagenic (VPC 2006)	6
Potency (B)	No threshold for mutagenicity/carcinogenicity identified (VPC 2006)	3
Diet (C)	Beef cattle and veal calf use, but not dairy (natural sources not considered for ranking purposes) (clenbuterol residues sought in poultry, but use is unlikely – other beta-agonists would be preferred)	2
Use (D)	Administered as an implant, so individual animals treated, but on farms where used likely to be given to all young cattle in the herd.	2
High Exposure (E)	No evidence for high exposure groups for beef	0
Detectable residues (F)	No RASFFs / residues detected (excluding those attributed to natural sources). Used in domestic production in territories which have split domestic/EU-export production systems e.g. USA but including in some e.g. Brazil where medicine controls have been criticised by FVO thus undermining confidence in the effective segregation of the split production	2
Total	(A+B) x (C+D+E+F)	54

VPC (2006). Risks associated with the use of hormonal substances in food-producing animals. Report of the Veterinary Products Committee, June 2006. Available at: http://www.vmd.defra.gov.uk/vpc/pdf/WG_Hormones_report.pdf

http://ec.europa.eu/food/fvo/audit_reports/details.cfm?rep_id=3209, accessed 26 October 2015

Albendazole

Reviewed 2013 (VMD)

	Rationale	Score
Hazard (A)	ADI is based on teratogenic effects	5
Potency (B)	ADI of 5 µg/kg is based on a NOEL of 5 mg/kg from a teratogenicity study with a safett factor of 1000	1
Diet (C)	Cattle, sheep and dairy	3
Use (D)	Oral suspension used in cattle and sheep for treatment of GI roundworm, lungworm, tapeworm and adult liver fluke. 100% of the herd is likely to be treated.	3
High Exposure (E)	Dairy uses = milk powder, thus infant formula milk	2
Detectable residues (F)	One sample above MRL in corned beef in 2012.	2
Total	(A+B) x (C+D+E+F)	60

Albendazole: Summary Report (1) - Committee for Veterinary Medicinal Products (1998)

Bromopropylate

Reviewed 2013 (FSA)

	Rationale	Score
Hazard (A)	Liver enlargement	2
Potency (B)	ADI of 30 µg/kg bw/ day (WHO 1994, Australian Department of Health and Aging Office of Chemical Safety 2012)	0
Diet (C)	Only used in honey production – low % in diet.	0
Use (D)	Anti-varroal, so all hives would be treated.	3
High Exposure (E)	No evidence for high exposure groups for honey	0
Detectable residues (F)	Seldom included in EU testing schemes. Limited knowledge on potential use in 3rd countries.	1
Total	(A+B) x (C+D+E+F)	8

Australian Department of Health and Aging Office of Chemical Safety (2012). ADI list: Acceptable Daily Intakes for agricultural and veterinary chemicals. Current as of 31 December 2012. Accessed at: http://www.health.gov.au/internet/main/publishing.nsf/Content/ocs-adi-list.htm

WHO (1994). Pesticide residues in food – 1993 evaluations. Part II - Toxicology. World Health Organization, WHO/PCS/94.4, nos 855-874 on INCHEM. Available at http://www.inchem.org/documents/jmpr/jmpmono/v93pr03.htm

Chloramphenicol

Reviewed 2013 (FSA)

	Rationale	Score
Hazard (A)	Can cause rare cases of the very serious blood disorder, aplastic anaemia. Also genotoxic in vivo. (WHO 2005)	6
Potency (B)	The aplastic anaemia is an idiosyncratic reaction with no known dose-response relationship or threshold. The genotoxicity may also not have a threshold. Therefore, no safe dose can be defined. (WHO 2005)	3
Diet (C)	Dairy (mastitis treatment in milking cows), shellfish, poultry and eggs.	3
Use (D)	Weighted categorisation: for dairy cows, only individual animals are treated, but for aquaculture it would be the entire pond.	1
High Exposure (E)	Dairy uses = milk powder, thus infant formula milk.	2
Detectable residues (F)	40 RASFFs 2012 & 2013	3
Total	(A+B) x (C+D+E+F)	81

WHO (2005). Chloramphenicol. In: *Toxicological Evaluation of Certain Veterinary Drug Residues in Food*. Prepared by the sixty-second meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA).WHO Food Additives Series: 53. World Health Organization, Geneva. Available at http://www.inchem.org/documents/jecfa/jecmono/v53je03.htm

Clenbuterol (hydrochloride)

Reviewed 2013 (VMD)

	Rationale	Score
Hazard (A)	Pharmocological effects of Beta agonists such as bronchodilation.	1
Potency (B)	pharmacological ADI of 0.25 µg/kg bw based on a NOEL of 2.5µg/day in a 60 kg human - this was determined as the most relevant ADI for risk assessment	1
Diet (C)	Beef cattle and veal calf use, but not dairy (natural sources not considered for ranking purposes) (clenbuterol residues sought in poultry, but use is unlikely – other beta-agonists would be preferred).	2
Use (D)	Used as an injection to relax the uterus in cattle at the time of parturition. Used as bronchiodilator in horses and is administered orally. Administered on an individual basis	0
High Exposure (E)	No evidence for high exposure groups for beef.	0
Detectable residues (F)	One RASFF for horse meat in 2012 containing clenbuterol at >10 x the MRL.	2
Total	(A+B) x (C+D+E+F)	8

Clenbuterol hydrochloride: Summary report (1) - Committee for Veterinary Medicinal Products (2000)

Clopidol (meticlorpindol, methylchloropindol)

Reviewed 2013 (FSA)

Criterion	Rationale	Score
Hazard (A)	Effects on testes following chronic dosing (SCAN 1982)	4
Potency (B)	An ADI of 15 µg/kg bw was previously set (SCAN 1982). Authorisations for clopidol were withdrawn in 2002 due to data limitations (Commission Regulation (EC) No 2205/2001).	0
Diet (C)	Poultry and eggs.	1
Use (D)	Poultry, so entire flock medicated.	3
High Exposure (E)	No evidence for high exposure groups for poultry.	0
Detectable residues (F)	48 RASFFs 2012 & 2013. Cheap. Authorised and reported widely used in most non-EU poultry-producing countries.	3
Total	(A+B) x (C+D+E+F)	28

SCAN (1982). Report of the Scientific Committee for Animal Nutrition on the use of Lerbek in feedingstuffs for poultry. Opinion expressed 17 November 1982. Available at: http://ec.europa.eu/food/fs/sc/oldcomm6/antibiotics/20_en.pdf

Crystal violet

Reviewed 2013 (FSA)

	Rationale	Score
Hazard (A)	Mutagenic in vitro (Aidoo et al. 1990), carcinogenic in rats and mice (Littlefield and Gaylor 1989, Littlefield et al. 1985). Prudent to assume it may be a genotoxic carcinogen	6
Potency (B)	There may not be a threshold to effects	3
Diet (C)	Farmed fish and shellfish	1
Use (D)	Aquaculture, so whole pond would be treated.	3
High Exposure (E)	Some consumers rely on fish for their protein (ethical avoidance of meat).	1
Detectable residues (F)	2 RASFFs in 2012 & 2013, despite widespread testing, so likely << 1% of samples tested. Anecdotal use in Vietnam, and theoretical substitute for Malachite Green, but no firm reports.	2
Total	(A+B) x (C+D+E+F)	63

Aidoo A, Gao N, Neft RE, Schol HM, Hass BS, Minor TY, Heflich RH (1990). Evaluation of the genotoxicity of gentian violet in bacterial and mammalian cell systems. Teratog Carcinog Mutagen 10, 449-462

Littlefield NA, Blackwell B-N, Hewitt CC, Gaylor DW (1985). Chronic toxicity and carcinogenicity studies of gentian violet in mice. Fundam Appl Toxicol 5, 902-912

Littlefield NA, Gaylor DW (1989). Chronic toxicity/carcinogenicity studies of gentian violet in Fischer 344 rats: two-generation exposure. Food Chem Toxicol 27, 239-247

Cypermethrin

Reviewed 2013 (VMD)

	Rationale	Score
Hazard (A)	Reversible neurotoxicity.	2
Potency (B)	ADI of 15 µg/kg bw	0
Diet (C)	Cypermethrin is a synthetic pyrethroid insecticide which is applied topically for the control of ectoparasites such as fleas, ticks, lice and blow flies. For use in all ruminants bovine, ovine and caprine. Also used as a parasiticide in salmon	3
Use (D)	It is likely that 100% of the herd or the fish pen will treated at one time.	3
High Exposure (E)	Some consumers rely on fish for their protein (ethical avoidance of meat).	1
Detectable residues (F)	No RASSFs, but residues seldom tested. Limited knowledge on veterinary product availability, but agricultural grade cypermethrin is widely available and theoretically easy to misuse, and has been so in years past in the UK for both sheep and salmon use.	2
Total	(A+B) x (C+D+E+F)	18

Cypermethrin: Summary report (2) - Committee for Veterinary Medicinal Products (2001)

Danofloxacin

Reviewed 2013 (FSA)

	Rationale	Score
Hazard (A)	Arthropathy in dogs (EMEA 1999)	4
Potency (B)	ADI = 24 µg/kg bw (EMEA 1999)	0
Diet (C)	Product approvals / MRLs for all species.	3
Use (D)	Weighted categorisation: for fish and poultry, entire flock will be treated, for large animals it may be administered to treat individuals.	2
High Exposure (E)	Some consumers rely on fish for their protein (ethical avoidance of meat).	1
Detectable residues (F)	No RASFFs. Included in many EU countries' surveillance schemes as a "standard" quinolone. No evidence from exporting countries suggesting misuse.	0
Total	(A+B) x (C+D+E+F)	24

EMEA (1999). Danofloxacin (extension to pigs): summary report 2. Committee for Veterinary Medicinal Products, European Agency for the Assessment of Medicinal Products. Available at: http://www.ema.europa.eu/docs/en_GB/document_library/Maximum_Residue_Limits_-_Report/2009/11/WC500013514.pdf

Dexamethasone

Reviewed 2013 (VMD)

Criterion	Rationale	Score
Hazard (A)	The target organs are the thymus and adrenal gland, at 0.1 mg/kg a day for 90-days, thymus involution and morphological changes occurred in the adrenal gland. Marginal decrease in white blood cells occurred at a dose of 0.003 mg/kg bw/day	4
Potency (B)	ADI of 0.015 µg/kg bw based on a NOEL of 0.0015 mg/kg bw/day in rats. At the next higher dose level there was increases in hepatic tyrosine amino transferase.	2
Diet (C)	Used in the treatment of metabolic diseases (eg. Ketosis) in ruminants and inflammatory diseases in a number of animal species. MRLs for bovine, caprine and porcine. Also co-formulated with injectable antibiotics for dairy cattle, to reduce swelling around injection site.	3
Use (D)	Administered on an individual basis.	0
High Exposure (E)	Dairy uses = milk powder, thus infant formula milk.	2
Detectable residues (F)	One RASFF in 2013 for beef containing >10 x the MRL, and a RASFF in 2010 for horse meat. Previous UK prosecution for black-market international trade in dairy injectables.	2
Total	(A+B) x (C+D+E+F)	42

Dexamethasone: Summary report (1) - Committee for Veterinary Medicinal Products (1997)

Diazinon

Reviewed 2013 (FSA)

Criterion	Rationale	Score
Hazard (A)	Neurotoxic (EMEA 1996); clinical signs and symptoms are largely reversible but poisoning with organophosphates may result in persistent neuropsychological deficits (COT 1999) or effects on neurodevelopment (WHO 2003)	5
Potency (B)	ADI = 2 µg/kg bw (EMEA 1996)	1
Diet (C)	Only used in sheep.	1
Use (D)	Entire flock dipped / pour-on.	3
High Exposure (E)	No evidence for high exposure groups for lamb.	0
Detectable residues (F)	Seldom included in EU testing schemes. Limited knowledge on potential use in 3rd countries.	1
Total	(A+B) x (C+D+E+F)	30

COT (1990). Organophosphates. Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment. Available at: http://cot.food.gov.uk/cotreports/cotwgreports/organophosphates

EMEA (1996). Diazinon (diampylate): summary report. Committee for Veterinary Medicinal Products, European Agency for the Evaluation of Medicinal Products. Available at: http://www.ema.europa.eu/docs/en_GB/document_library/Maximum_Residue_Limits_-_Report/2009/11/WC500013706.pdf

WHO (2003). Pesticide residues in food – 2002 evaluations. Part II – toxicological. World Health Organization, WHO/PCS/03.1. Available at: http://whqlibdoc.who.int/hq/2003/WHO_PCS_03.1.pdf

Diclofenac

Reviewed 2013 (VMD)

	Rationale	Score
Hazard (A)	Gastrointestinal effects such as vomiting and diarrhoea, indigestion, nausea, constipation and flatulence.	1
Potency (B)	ADI of 0.5 µg/kg bw based on an overall pharmacological and toxicological LOEL of 0.1 mg/kg bw and a safety factor of 200	1
Diet (C)	Beef, dairy and pig.	3
Use (D)	Administered on an individual basis.	0
High Exposure (E)	Dairy uses = milk powder, thus infant formula milk.	2
Detectable residues (F)	Seldom included in EU testing schemes. Limited knowledge on potential use in 3rd countries.	1
Total	(A+B) x (C+D+E+F)	12

Diclofenac: Summary report - Committee for Veterinary Medicinal Products (2003)

Difloxacin

Reviewed 2013 (FSA)

	Rationale	Score
Hazard (A)	Effects on cartilage of leg joints (EMEA 1997a)	4
Potency (B)	ADI = 10 µg/kg bw (EMEA 1997b)	1
Diet (C)	Product approvals / MRLs for all species.	3
Use (D)	Weighted categorisation: for fish and poultry, entire flock will be treated, for large animals it may be administered to treat individuals.	2
High Exposure (E)	Some consumers rely on fish for their protein (ethical avoidance of meat).	1
Detectable residues (F)	No RASFFs. Included in many EU countries' surveillance schemes as a "standard" quinolone. No evidence from exporting countries suggesting misuse.	0
Total	(A+B) x (C+D+E+F)	30

EMEA (1997a). Difloxacin: summary report. Committee for Veterinary Medicinal Products, European Agency for the Evaluation of Veterinary Medicinal Products. Available at http://www.ema.europa.eu/docs/en_GB/document_library/Maximum_Residue_Limits_-_Report/2009/11/WC500013811.pdf

EMEA (1997b), Difloxacin (modification): summary report 2. Committee for Veterinary Medicinal Products, European Agency for the Evaluation of Veterinary Medicinal Products. Available at http://www.ema.europa.eu/docs/en_GB/document_library/Maximum_Residue_Limits_-_Report/2009/11/WC500013813.pdf

Dimetridazole

Reviewed 2013 (FSA)

Criterion	Rationale	Score
Hazard (A)	Genotoxic in vitro, but unclear if this is expressed in vivo. Carcinogenic in rats by unclear mechanism. (EMEA 1996, COM 2002)	5[1]
Potency (B)	ADI of 4.6 µg/kg bw/day was previously suggested by one committee based on the view at that time by a majority of its members that dimetridazole was unlikely to be genotoxic in vivo, but was not adopted (SCAN 2000).	1[2]
Diet (C)	Blackspot in poultry and dysentery in pigs.	2
Use (D)	Administered to poultry flock or pig herd.	3
High Exposure (E)	No evidence for high exposure groups for poultry or pork.	0
Detectable residues (F)	Pig and poultry veterinary formulations easily available online (ref: alibaba.com, accessed 20/1/14) for delivery in mainland China, and appear big sellers. China has controls on EU export production (ref FVO report 2013) and clear segregation from domestic production, but China Animal Husbandry Group products are also deliverable to other countries in the region.	2
Total	(A+B) x (C+D+E+F)	42

COM (2002). Dimetridazole (DMZ). COM Statement COM/02/S4. Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment. Available at http://www.iacom.org.uk/statements/COM02S4.htm

EMEA (1996). Dimetridazole: summary report 3. Committee for Veterinary Medicinal Products, European Medicines Evaluation Agency. Available at http://www.ema.europa.eu/docs/en_GB/document_library/Maximum_Residue_Limits_-_Report/2009/11/WC500013885.pdf

SCAN (2000). Opinion of the Scientific Committee for Animal Nutrition on the use of dimetridazole in animal feedingstuffs. European Commission, Health & consumer Protection Directorate-General, Directorate C - Scientific Opinions. Available at http://ec.europa.eu/food/fs/sc/scan/out51_en.pdf

[1] If definitive evidence that dimetridazole is genotoxic in vivo is established the score would increase to the top score of 6.

[2] If definitive evidence that dimetridazole in genotoxic in vivo is established, and no threshold for this effect can be identified, the potency score would increase to 3.

Doramectin

Reviewed 2013 (FSA)

	Rationale	Score
Hazard (A)	Neurotoxicity, reversible symptoms such as pupil dilation, depression, ataxia, salivation [1.] (EMEA, 2006)	2
Potency (B)	ADI = 1.0 µg/kg bw/day (EMEA, 2006)	1
Diet (C)	Primarily used in sheep and cows, including dairy.	3
Use (D)	Antiparasitic, used to treat entire herd.	3
High Exposure (E)	Dairy uses = milk powder, thus infant formula milk.	2
Detectable residues (F)	Two RASFFs in prior 4 years, despite intensified testing of – particularly – corned beef following the ivermectin border rejections.	2
Total	(A+B) x (C+D+E+F)	30

EMEA, 2006 Doramectin (Modification of the MRLs): Summary Report 6. Committee for Medicinal Products for Veterinary Use (CVMP) EMEA/CVMP/126676/2006-final July 2006
NOAH, National Office of Animal Health Website, Compendium of Animal Medicines (www.noah.co.uk). (accessed September 2012).
COT, 2007 Recall of lamb containing excessive veterinary residues. Committee on Toxicity of Chemicals in Food, Consumer Products and Environment TOX/2007/25
RASFF Rapid Alert System for Food and Feed (www.ec.europa.eu/food/rapidalert/rasff_portal_database_en.htm) (accessed September 2012).

[1.] Hazard based on effect seen at lowest concentration (chronic exposure, 0.3 mg/kg bw to dogs). Other adverse effects seen, such as embryotoxicity in rabbits after exposure to 1.6 mg/kg bw, with higher concentrations (3.00 mg/kg) associated with teratogenicity.

Enrofloxacin / Ciprofloxacin

Reviewed 2013 (VMD)

Criterion	Rationale	Score
Hazard (A)	As for other Fluoroquinolone antibiotics.	5
Potency (B)	ADI of 0.3125 µg/kg - Effects on gut micro flora	1
Diet (C)	Cattle, dairy, pig, poultry	3
Use (D)	Administered as an oral solution in chicken, turkey cattle and by injection to cattle and pigs. Administered in the drinking water of poultry and rabbits.	3
High Exposure (E)	Some consumers rely on fish for their protein (ethical avoidance of meat).	1
Detectable residues (F)	Multiple RASFFs, including a finding of >10 x the MRL in turkey muscle in 2013 and a finding in eggs (no MRLs) in 2011.	3
Total	(A+B) x (C+D+E+F)	60

Enrofloxacin: Summary report (1) - Committee for Veterinary Medicinal Products (1996)

Erythromycin

Reviewed 2013 (FSA)

	Rationale	Score
Hazard (A)	Hypersensitivity reaction in humans treated medicinally, generally mild.	3
Potency (B)	ADI = 5 µg/kg (microbiological ADI) (EMEA 2000)	1
Diet (C)	EU MRLs for all food producing species. International use in chickens, turkeys and cattle, authorised for honeybees in China [ref. 2013 FVO report].	3
Use (D)	Can be formulated as a feed additive	3
High Exposure (E)	No evidence for high exposure groups for beef.	0
Detectable residues (F)	Seldom included in EU testing schemes. Limited knowledge on potential use in 3rd countries.	1
Total	(A+B) x (C+D+E+F)	28

EMEA (2000). Erythromycin: summary report 2. Committee for Veterinary Medicinal Products. European Agency for the Evaluation of Medicinal Products. Available at: http://www.ema.europa.eu/docs/en_GB/document_library/Maximum_Residue_Limits_-_Report/2009/11/WC500014184.pdf

Fipronil

Reviewed 2013 (VMD)

Criterion	Rationale	Score
Hazard (A)	Reversible neurotoxicity.	2
Potency (B)	ADI = 0.2 µg/kg	1
Diet (C)	Ticks in cattle.	1
Use (D)	If a tick treatment, 100% of herd is likely to be treated.	3
High Exposure (E)	No evidence for high exposure groups for beef.	0
Detectable residues (F)	Seldom included in EU testing schemes. Limited knowledge on potential use in 3rd countries.	1
Total	(A+B) x (C+D+E+F)	15

Fipronil EFSA Draft Assessment report. Volume 3, Annex B, B.6, January 2005

Florfenicol

Reviewed 2013 (FSA)

Criterion	Rationale	Score
Hazard (A)	Increased liver weight, atrophy of testes (EMEA 1996).	4
Potency (B)	Toxicological ADI = 10 µg/kg bw/day (also 3 µg/kg bw/day - microbiological ADI) (EMEA 1996)	1
Diet (C)	Cattle, dairy and farmed fish / aquaculture.	3
Use (D)	Weighted categorisation: fish and aquaculture the whole pond is treated, but cattle are treated individually.	2
High Exposure (E)	Some consumers rely on fish for their protein (ethical avoidance of meat).	1
Detectable residues (F)	Infrequently included in EU surveillance schemes as full MRL definition, and yet residues detected at ≥ 10 X MRL.	3
Total	(A+B) x (C+D+E+F)	45

EMEA (1996). Florfenicol: summary report 1. Committee for Veterinary Medicinal Products. European Agency for the Evaluation of Medicinal Products. Available at: http://www.ema.europa.eu/docs/en_GB/document_library/Maximum_Residue_Limits_-_Report/2009/11/WC500014274.pdf

Flumequine

Reviewed 2013 (FSA)

	Rationale	Score
Hazard (A)	Hepatotoxicity, tumours in mouse liver which are believed to be secondary to hepatotoxicity, and arthropathy. Disturbance of the ecology of the microflora in the large intestine. (EMEA 1999, WHO 2004)	4 for toxicity 1 for microbiological effects
Potency (B)	Toxicological ADI = 25 µg/kg bw/day Microbiological ADI = 8.25 µg/kg bw. (EMEA 1999)	0 or 1
Diet (C)	Product approvals / MRLs for all species	3
Use (D)	Administered to whole flock for poultry and aquaculture	3
High Exposure (E)	Some consumers rely on fish for their protein (ethical avoidance of meat).	1
Detectable residues (F)	No RASFFs. Included in many EU countries' surveillance schemes as a "standard" quinolone. No evidence from exporting countries suggesting misuse.	0
Total		28

EMEA (1999). Flumequine: summary report 2. Committee for Veterinary Medicinal Products, European Medicines Evaluation Agency. Available at http://www.ema.europa.eu/docs/en_GB/document_library/Maximum_Residue_Limits_-_Report/2009/11/WC500014315.pdf

WHO (2004). Flumequine. In: Toxicological Evaluation of Certain Veterinary Drug Residues in Food. Prepared by the sixty-second meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA).WHO Food Additives Series: 53. World Health Organization, Geneva. Available at http://whqlibdoc.who.int/publications/2004/9241660538_flumequine.pdf

Ivermectin

Reviewed 2013 (FSA)

	Rationale	Score
Hazard (A)	Reversible neurotoxicity (EMEA 2005).	2
Potency (B)	ADI = 10 µg/kg bw/day (EMEA 2005).	1
Diet (C)	Cattle, plus previous incidents (Scottish salmon mid-2000's) of illegal use in farmed fish.	2
Use (D)	The fact that residues have been detected in a highly homogenised product (corned beef) suggest that a high % of the cattle population are treated, otherwise the residues would be diluted out.	3
High Exposure (E)	Some consumers rely on fish for their protein (ethical avoidance of meat).	1
Detectable residues (F)	Detected in imported corned beef and beef above the EU advisory action level of 30 µg/kg (55 RASFFs since 2010)	3
Total		27

EMEA (2005). Ivermectin (modification of Maximum Residue Limits): summary report 5. Committee for Medicinal Products for Veterinary Use (CVMP). European Medicines Agency. Available at http://www.ema.europa.eu/docs/en_GB/document_library/Maximum_Residue_Limits_-_Report/2009/11/WC500014505.pdf

Lasalocid

Reviewed 2013 (VMD)

	Rationale	Score
Hazard (A)	Reversible pharmacological effect. Neurotoxicity effects are transient and without histopathological findings. No increase in incidence of neoplasm in chronic studies.	1
Potency (B)	Toxicological ADI = 2.5 µg/kg bw/day based on the NOEL of 0.5 mg/kg/day from the 2-year chronic oral toxicity study in rat and the maternal toxicity study in rabbits, applying a safety factor of 200 due to limited data in respect of neurotoxicity at higher dose levels.	1
Diet (C)	Antibiotic mainly active against gram positive microorganisms. Used as a feed additive given continuously to chickens and turkeys for prevention of coccidiosis caused by Eimeria spp. Used in the USA in sheep, cattle, rabbits, chickens and turkeys as an antococcidial and growth-promoting agent.	3
Use (D)	Medicated feed, so entire flock / herd is treated.	3
High Exposure (E)	No evidence for high exposure groups for poultry.	0
Detectable residues (F)	One 2012 RASFF for residues in poultry above the MRL. Included in most testing schemes, so incidence assumed as < 1%	2
Total	(A+B) x (C+D+E+F)	16

Lasalocid sodium: Summary report - Committee for Veterinary Medicinal Products (2004)

Levamisole

Reviewed 2013 (FSA)

Criterion	Rationale	Score
Hazard (A)	Agranulocytosis in individuals sensitised as a result of therapeutic use (EMEA 1996).	3
Potency (B)	ADI = 6 µg/kg bw/day based on a study in previously sensitised dogs (EMEA 1996)	1
Diet (C)	Cattle, sheep, pigs and poultry.	3
Use (D)	Administered on an individual basis.	0
High Exposure (E)	Dairy uses = milk powder, thus infant formula milk.	2
Detectable residues (F)	No RASFFs. Included in many EU countries' surveillance schemes as a "standard" . No information from 3rd countries suggests misuse. Other more modern anthelmintics have found more favour.	0
Total	(A+B) x (C+D+E+F)	20

EMEA (1996). Levamisole: summary report 2. Committee for Veterinary Medicinal Products, European Agency for the Evaluation of Medicinal Products. Available at: http://www.ema.europa.eu/docs/en_GB/document_library/Maximum_Residue_Limits_-_Report/2009/11/WC500014675.pdf

Maduramycin

Reviewed 2013 (VMD)

	Rationale	Score
Hazard (A)	Irreversible neurotoxicity and retinotoxicity.	5
Potency (B)	ADI = 1 µg/kg bw/day (The lowest NOAEL of 0.1 mg/kg bw/day is found in a chronic rat study and in a multi-generation study in rat).	1
Diet (C)	Primarily coccidiostat for poultry and rabbit, but also potential use for cattle.	2
Use (D)	Medicated feed, so entire flock / herd is treated.	3
High Exposure (E)	No evidence for high exposure groups for poultry.	0
Detectable residues (F)	Seldom included in EU testing schemes. Limited knowledge on potential use in 3rd countries.	1
Total	(A+B) x (C+D+E+F)	36

Summary: EFSA Journal 2011;9(1):1952; Scientific opinion on safety and efficacy of Cygro® 10G (maduramicin ammonium α) for chickens for fattening

Malachite Green / Leucomalachite Green

Reviewed 2013 (FSA)

Category	Rationale	Score
Hazard (A)	In vivo mutagen, and its metabolite leucomalachite green is regarded as a genotoxic carcinogen (COM/COC 2004)	6
Potency (B)	There may not be a threshold to effects	3
Diet (C)	Farmed fish and shellfish.	1
Use (D)	Aquaculture, so whole pond would be treated.	3
High Exposure (E)	Some consumers rely on fish for their protein (ethical avoidance of meat).	1
Detectable residues (F)	Residues detected at ≥ 10 X MRPL. 15 RASFFs since 2010.	3
Total	(A+B) x (C+D+E+F)	72

COM/COC (2004). Joint COM & COC Statement on mutagenicity and carcinogenicity of malachite green (MG) and leucomalachite green (LMG). Committees on Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. COM/04/S4 & COC/04/S7, December 2004. Available at: http://www.iacoc.org.uk/statements/jointcomcocstatementonmalachitegreenmgandleucomalachitegreenlmg.htm

Marbofloxacin

Reviewed 2013 (VMD)

	Rationale	Score
Hazard (A)	Irreversible organ toxicity. Please see comment on potency for more detail	4
Potency (B)	Toxicological ADI of 0.04 mg/kg bw/day based on a NOEL of 4 mg/kg from the 13 week dog study. Typical quinolone induced changes in the articular cartilage were observed at 40 mg/kg bw/day. Testicular atrophy was observed in 1/4 animals given 40 mg/kg and spermatic granuloma in 1/4 dogs. Microbiological ADI of 4.5 µg/kg bw/day. The ranking is based on the toxicological ADI.	0
Diet (C)	Oral or parenteral administration to cattle, including lactating dairy cattle for treatment of bovine respiratory diseases (MRLs for all tissues and milk). Parenteral administartion to pigs for the treatment of mastitis.	3
Use (D)	Administered by injection in cattle and pigs. Use of products should be based on susceptibility testing.	0
High Exposure (E)	Dairy uses = milk powder, thus infant formula milk.	2
Detectable residues (F)	Seldom included in EU testing schemes. Limited knowledge on potential use in 3rd countries. (one RASFF in 2009 for pork casings).	1
Total	(A+B) x (C+D+E+F)	24

Marbofloxacin: Summary report (1) - Committee for Veterinary Medicinal Products (1996)

Methylene blue (methylthionium chloride)

Reviewed 2013 (FSA)

Criterion	Rationale	Score
Hazard (A)	Developmental toxicity, methaemoglobinaemia, some evidence of carcinogenicity in male rats and mice and equivocal evidence of carcinogenicity in female mice, mutagenic in vitro (EMA 2011, NTP 2008)	5[3]
Potency (B)	No ADI has been set. As it is a possible mutagen there may be no threshold.	3
Diet (C)	Farmed fish and shellfish.	1
Use (D)	Aquaculture, so whole pond would be treated.	3
High Exposure (E)	Some consumers rely on fish for their protein (ethical avoidance of meat).	1
Detectable residues (F)	Seldom included in EU testing schemes. Limited knowledge on potential use in 3rd countries.	1
Total	(A+B) x (C+D+E+F)	48

EMA (2011). Assessment report: methylthionium chloride Proveblue. Committee for Medicinal Products for Human Use (CHMP). Available at: http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Public_assessment_report/human/002108/WC500107131.pdf

NTP (2008). NTP Technical Report on the Toxicology and Carcinogenesis Studies of Methylene Blue Trihydrate (CAS No. 7220-79-3) in F344/N Rats and B6C3F1 Mice (Gavage Studies). Technical Report Series, No. 540. National Toxicology Program, US Department of Health and Human Services, Public Health Service, National Institutes of Health. Available at http://ntp.niehs.nih.gov/ntp/htdocs/LT_rpts/tr540.pdf

[3] Methylene blue is mutagenic in vitro (gene mutations and chromosomal aberrations), but was negative in bone marrow and peripheral blood micronucleus assays in mice. If future data confirm that methylene blue is mutagenic in vivo, the score will increase to 6.

Metronidazole

Reviewed 2013 (FSA)

Criterion	Rationale	Score
Hazard (A)	Mutagenic in laboratory animals and humans; carcinogenic in rats and mice and some evidence for carcinogenicity in humans (EMEA 1997).	6
Potency (B)	There may be no threshold to effects (EMEA 1997).	3
Diet (C)	As dimetridazole, plus aquatic uses [ref Alibaba.com, accessed 28/5/14]	2
Use (D)	Administered to poultry flock or pig herd	3
High Exposure (E)	No evidence for high exposure groups for poultry or pork	0
Detectable residues (F)	Included in many testing schemes. No Residues detected in the non-statutory surveillance scheme in 2012 and no RASFFs in 2012. (RASFFs were raised for residues in raw poultry in 2008 and honey in 2011).	1
Total	(A+B) x (C+D+E+F)	54

EMEA (1997). Metronidazole: summary report. Committee for Veterinary Medicinal Product, European Agency for the Evaluation of Medicinal Products. Available at: http://www.ema.europa.eu/docs/en_GB/document_library/Maximum_Residue_Limits_-_Report/2009/11/WC500015087.pdf

Monensin

Reviewed 2013 (VMD)

	Rationale	Score
Hazard (A)	Clinical signs and clinico-pathologic findings were indicative of muscle related toxicity. Skeletal and cardiac muscle degeneration (inotropic activity via membrane current mechanisms) and heart/skeletal muscle (changes in sub cellular organelles/cell damage).	4
Potency (B)	Pharmacological ADI of 3.45 µg/kg Toxicological ADI of 7.6 µg/kg Microbiological ADI of 14.46 µg/kg CVMP concluded that the Pharmacological ADI is most relevant for consumer saftey.	1
Diet (C)	Polyether antibiotic intended for use in lactating dairy cattle.(MRLs in all tissues and milk), also feed additive coccidiostat for poultry	3
Use (D)	Weighted categorisation: for poultry, entire flock will be treated, for cattle, individual animals are treated	2
High Exposure (E)	Dairy uses = milk powder, thus infant formula milk	2
Detectable residues (F)	No RASFFs. Included in many EU countries' surveillance schemes as a "standard". No information from 3rd countries suggests misuse.	0
Total	(A+B) x (C+D+E+F)	35

Monensin (Cattle, including dairy cows): Summary report - Committee for Veterinary Medicinal Products (2007)

Monepantel

Reviewed 2013 (FSA)

Criterion	Rationale	Score
Hazard (A)	Effects on the liver, which may be related to cholestasis (EMA 2012)	2
Potency (B)	ADI = 30 µg/kg bw (EMA 2012)	0
Diet (C)	Anthelmintic for sheep and potential for cattle, including dairy	3
Use (D)	If a flukeworm problem, the entire herd would be treated	3
High Exposure (E)	Dairy uses = milk powder, thus infant formula milk.	2
Detectable residues (F)	New product, thus lack of evidence from residues testing. No specific intelligence on use, although Pfizer are predicting it to be a big seller as resistance grows to other classes of flukicide.	1
Total	(A+B) x (C+D+E+F)	18

EMA (2012). Monepantel (caprine and ovine species): European public MRL assessment report. Committee for Medicinal Products for Veterinary Use, European Medicines Agency. Available at http://www.ema.europa.eu/docs/en_GB/document_library/Maximum_Residue_Limits_-_Report/2012/03/WC500123497.pdf

Nalidixic acid

Reviewed 2013 (FSA)

	Rationale	Score
Hazard (A)	Carcinogenic in male rats (preputial gland), female rats (clitoral gland), and equivocal evidence of carcinogenicity in male mice (subcutaneous tissue neoplasms), but not genotoxic in in vitro tests. (NTP 1989)	4
Potency (B)	ADI not set	3
Diet (C)	Any use would be unlikely, as a superseded product and better quinolones are available. Most conceivable misuse would be in aquaculture.	1
Use (D)	For consistency with Flumequin, in potential aquaculture uses.	3
High Exposure (E)	Some consumers rely on fish for their protein (ethical avoidance of meat) – assuming aquaculture as most conceivable misuse.	1
Detectable residues (F)	Seldom included in EU testing schemes. Limited knowledge on potential use in 3rd countries.	1
Total	(A+B) x (C+D+E+F)	42

NTP (1989). Toxicology and Carcinogenesis Studies of Nalidixic Acid (CAS No. 389-08-2) in F344/N Rats and B6C3F$_1$ Mice (Feed Studies). Technical Report Series, No. 368. National Toxicology Program. US Department of Health and Human Services, Public Health Service, National Institutes of Health. Available at http://ntp.niehs.nih.gov/ntp/htdocs/LT_rpts/tr368.pdf

Naphthalene

Reviewed 2013 (FSA)

Criterion	Rationale	Score
Hazard (A)	Haemolytic anaemia. (EPA 1998) Classified in IARC as 2B (possible carcinogen in humans) but at high levels, which are not likely to be found in residues.	2
Potency (B)	The US Environmental Protection Agency (EPA) has set a chronic RfD (equivalent to a TDI) of 20 µg/kg bw/day.(EPA 1998)	0
Diet (C)	Only used in honey production – low % in diet	0
Use (D)	When used, 100% of frames are treated	3
High Exposure (E)	No evidence for high exposure groups for honey	0
Detectable residues (F)	Seldom included in EU testing schemes. . Used in UK apiaries for storage of hive frames over winter but should not be used during production season, limited knowledge on potential use in 3rd countries.	1
Total		8

EPA (1998). Toxicological review of naphthalene. In support of summary information on the Integrated Risk Information System (IRIS). US Environmental Protection Agency, Washington DC. Available at http://www.epa.gov/iris/toxreviews/0436tr.pdf

Narasin

Reviewed 2013 (FSA)

	Rationale	Score
Hazard (A)	Neurotoxic effects in dogs – peripheral neuropathy (EFSA 2004)	5
Potency (B)	ADI = 5 µg/kg bw (EFSA 2004)	1
Diet (C)	Only used in broiler chickens in the EU, but also in cattle and pigs in some other countries.	2
Use (D)	Poultry, so entire flock medicated	3
High Exposure (E)	No evidence for high exposure groups for beef, pork or lamb	0
Detectable residues (F)	No RASFFs. Included in many EU countries' surveillance schemes as a "standard". No information from 3rd countries suggests misuse. When co-formulated with nicarbazin for UK poultry, nicarbazin residues were detected in most birds whilst narasin residues never detected, even << MRL.	0
Total	(A+B) x (C+D+E+F)	30

EFSA (2004). Opinion of the Scientific Panel on Additives and Products or Substances used in Animal Feed on a request from the Commission on the re-evaluation of efficacy and safety of the coccidiostat Monteban® G100 in accordance with article 9G of Council Directive 70/524/EEC. European Food Safety Authority. EFSA Journal 90, 1-44. Available at: http://www.efsa.europa.eu/en/efsajournal/doc/90.pdf

Nicarbazin

Reviewed 2013 (FSA)

	Rationale	Score
Hazard (A)	Possible effect on the liver (increased serum ALT in dogs). (EFSA 2010)	2
Potency (B)	ADI for 4,4'-dinitrocarbanilide, the component of nicarbazin that is the main residue in food, is 770 µg/kg bw/day (EFSA 2010)	0
Diet (C)	Poultry and eggs	1
Use (D)	Poultry, so entire flock medicated.	3
High Exposure (E)	No evidence for high exposure groups for poultry.	0
Detectable residues (F)	Residues detected in eggs (no MRLs).	3
Total	(A+B) x (C+D+E+F)	14

EFSA (2010). Scientific Opinion on the safety and efficacy of Koffogran (nicarbazin) as a feed additive for chickens for fattening. EFSA Panel on Additives and Products or Substances use in Animal Feed (FEEDAP). European Food Safety Authority. EFSA Journal 8(3): 1551. Available at http://www.efsa.europa.eu/en/efsajournal/doc/1551.pdf.

Nitrofurans

Reviewed 2013 (FSA)

	Rationale	Score
Hazard (A)	Concern regarding possible genotoxicity and carcinogenicity (EMEA 1996). Furazolidone is genotoxic and carcinogenic (WHO 1993). The furazolidone metabolite AOZ is genotoxic in vivo (EMEA 1997).	6
Potency (B)	Genotoxicity and carcinogenicity may not have a threshold.	3
Diet (C)	Primarily aquaculture and poultry, but nitrofurazone has also been used as mastitis treatment in dairy cattle	3
Use (D)	Weighted categorisation: for fish and poultry, entire flock will be treated, for large animals it may be administered to treat individuals	2
High Exposure (E)	Dairy uses = milk powder, thus infant formula milk.	2
Detectable residues (F)	Multiple RASFFs (even discounting SEM in prawns and stomach/casings, on the assumption that these are natural).	3
Total	(A+B) x (C+D+E+F)	90

EMEA (1996). Nitrofurans: summary report. Committee for Veterinary Medicinal Products, European Medicines Evaluation Agency. Available at http://www.ema.europa.eu/docs/en_GB/document_library/Maximum_Residue_Limits_-_Report/2009/11/WC500015183.pdf

EMEA (1997) Furazolidone: summary report. Committee for Veterinary Medicinal Products, European Medicines Evaluation Agency. Available at http://www.ema.europa.eu/docs/en_GB/document_library/Maximum_Residue_Limits_-_Report/2009/11/WC500014332.pdf

WHO (1993). Furazolidone. In: *Toxicological Evaluation of Certain Veterinary Drug Residues in Food*. Prepared by the fortieth meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA).WHO Food Additives Series: 31. World Health Organization, Geneva. Available at http://www.inchem.org/documents/jecfa/jecmono/v31je06.htm

http://ec.europa.eu/food/fvo/audit_reports/details.cfm?rep_id=2737, accessed 26 October 2015

Nitroxinil

Reviewed 2013 (FSA)

Criterion	Rationale	Score
Hazard (A)	Effects on the thyroid. Thyroid and pituitary tumours in rats, secondary to thyroid effects. (EMEA 1999)	4
Potency (B)	ADI = 5.0 µg/kg bw/day (EMEA 1999).	1
Diet (C)	Cattle and sheep, including (although counter to label instructions) dairy.	3
Use (D)	Trodax is injectabled, so individual animals treated, but on farms where used likely to be given to multiple cattle in the herd	1
High Exposure (E)	Dairy uses = milk powder, thus infant formula milk.	2
Detectable residues (F)	Not so far included in non-statutory surveillance programme. No RASFFs but unclear if looked for by other Member States in imported foods.	3
Total	(A+B) x (C+D+E+F)	45

EMEA (1999). Nitroxinil: summary report. Committee for Veterinary Medicinal Products, European Medicines Evaluation Agency. Available at http://www.ema.europa.eu/docs/en_GB/document_library/Maximum_Residue_Limits_-_Report/2009/11/WC500015185.pdf

Nortestosterone

Reviewed 2013 (FSA)

	Rationale	Score
Hazard (A)	Hazards expected to be similar to testosterone, including developmental toxicity (virilisation of female fetus). May be carcinogenic. (IPCS 1998)	5
Potency (B)	Binds to androgen receptor with similar affinity to testosterone, but may be less potent in some respects because while testosterone is metabolised in certain tissues to the more potent androgen dihydrotestosterone, nortestosterone is metabolised to a less potent androgen (Sundaram et al. 1995). Oral bioavailability is expected to be similarly low as for testosterone due to extensive first pass metabolism (IPCS 1998). ADI for testosterone = 2 µg/kg bw (WHO 2000).	1
Diet (C)	Only beef cattle (aquaculture potential not counted – highly unlikely, as better sex-regulation treatments are available).	1
Use (D)	Administered on an individual basis.	0
High Exposure (E)	No evidence for high exposure groups for beef.	0
Detectable residues (F)	Unable to differentiate natural residues from abuse. Included in most testing programmes, few reported non-compliants. Found in syringes seized on continental Europe, widely detected in racing horses and injectables for horses readily available on-line which could easily be administered to cattle.	2
Total	(A+B) x (C+D+E+F)	18

IPCS (1998). Nandrolone. Poisons Information Monograph 910. International Programme on Chemical Safety. Available at http://www.inchem.org/documents/pims/pharm/pim910.htm

Sundaram K, Kumar N, Monder C, Bardin CW (1995). Different patterns of metabolism determine the relative androgenic activity of 19-norandrogens. J. Steroid Biochem. Mol. Biol. 53, 253-7

WHO (2000). Estradiol-17β, Progesterone, and Testosterone. In: *Toxicological Evaluation of Certain Veterinary Drug Residues in Food.* Prepared by the fifty-second meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA).WHO Food Additives Series: 43. World Health Organization, Geneva. Available at: http://www.inchem.org/documents/jecfa/jecmono/v43jec05.htm

Oxolinic acid

Reviewed 2013 (FSA)

Criterion	Rationale	Score
Hazard (A)	Carcinogenic in rats by a non-genotoxic mechanism (Leydig cell tumours related to chronic stimulation of luteinising hormone release). Disturbance of the ecology of the microflora in the large intestine. (EMEA 2000)	1 for microbiological effects 4 for carcinogenicity
Potency (B)	Microbiological ADI of 2.5 µg/kg bw/day. Toxicological ADI of 42 µg/kg bw/day. (EMEA 2000)	1 0 for toxicological/carcinogenic effects
Diet (C)	For consistency with flumequin.	3
Use (D)	Administered to whole flock for poultry and aquaculture.	3
High Exposure (E)	Some consumers rely on fish for their protein (ethical avoidance of meat).	1
Detectable residues (F)	No RASFFs. Included in many EU countries' surveillance schemes as a "standard" quinolone. No evidence from exporting countries suggesting misuse.	0
Total	(A+B) x (C+D+E+F)	28

EMEA (2000). Oxolinic acid: summary report 2. Committee for Veterinary Medicinal Products, European Medicines Evaluation Agency. Available at http://www.ema.europa.eu/docs/en_GB/document_library/Maximum_Residue_Limits_-_Report/2009/11/WC500015340.pdf

Oxyclozanide

Reviewed 2013 (VMD)

Criterion	Rationale	Score
Hazard (A)	Irreversible brain toxicity (vacuolation of brain cells in the region of the pons)	5
Potency (B)	Toxicological ADI of 0.03 mg/kg	0
Diet (C)	Products unavailable in UK. But imported under SIC scheme and used under cascade (off label use) for use in cattle or sheep. UK products out of stock.	3
Use (D)	If a flukeworm problem, the entire herd would be treated.	3
High Exposure (E)	Dairy uses = milk powder, thus infant formula milk.	2
Detectable residues (F)	Seldom included in EU testing schemes. Limited knowledge on potential use in 3rd countries.	1
Total	(A+B) x (C+D+E+F)	45

Oxyclozanide: Summary report (1) - Committee for Veterinary Medicinal Products (1998)

Phenylbutazone

Reviewed 2013 (FSA)

Criterion	Rationale	Score
Hazard (A)	Idiosyncratic cases of aplastic anaemia (very serious, life-threatening, condition); some evidence of mutagenicity, including in humans; some evidence of carcinogenicity in rats and mice. (Jones 2005)	6
Potency (B)	No identified threshold for inducing aplastic anaemia; there may not be a threshold for mutagenic/carcinogenic effects.	3
Diet (C)	Only cattle or horses.	1
Use (D)	Administered on an individual basis.	0
High Exposure (E)	No evidence for high exposure groups for beef.	0
Detectable residues (F)	Several RASFFs in 2012 and 2013 relating to horsemeat or beef products containing horse meat.	3
Total	(A+B) x (C+D+E+F)	36

Jones PGH (2005). Phenylbutazone and equine research. Veterinary Record 156, 554-555

Note

A joint Statement of the European Food Safety Authority (EFSA) and European Medicines Agency (EMA) on the presence of residues of phenylbutazone in horse meat was published in April 2013. EFSA/EMA confirmed that the main risks for the consumer were idiosyncratic blood dyscrasias and the genotoxic/carcinogenic potential, for which no thresholds could be identified. However, EFSA/EMA considered the reported presence of phenylbutazone in horse meat to be of low concern for consumers, taking into account the low likelihood of exposure and overall low likelihood of adverse effects. EFSA/EMA recommended various measures to further minimise the risk to consumers, including continued monitoring for phenylbutazone residues. The Statement can be found at : http://www.efsa.europa.eu/en/efsajournal/pub/3190.htm.

Ractopamine

Reviewed 2013 (FSA)

Criterion	Rationale	Score
Hazard (A)	Beta-adrenoceptor agonist with pharmacological cardiac effects (EFSA 2009)	1
Potency (B)	EFSA has concluded that an ADI cannot be set based on the data available (EFSA 2009). JECFA ADI = 1 µg/kg bw (WHO 2004).	3[4]
Diet (C)	Pigs and beef cattle.	2
Use (D)	Used in intensive pig production systems, whole herd administration.	3
High Exposure (E)	No evidence for high exposure groups for beef, pork or lamb.	0
Detectable residues (F)	One RASFF in 2012. Used in countries with split domestic-EU production (South Africa, USA, South America), including some countries where medicine controls have been criticised by FVO.	2
Total	(A+B) x (C+D+E+F)	28

EFSA (2009). Safety evaluation of ractopamine. Scientific Opinion of the Panel on Additives and Products or Substances used in Animal Feed. European Food Safety Authority. EFSA Journal 1041, 1-152. Available at http://www.efsa.europa.eu/en/efsajournal/doc/1041.pdf

WHO (2004). Ractopamine (addendum). In: *Toxicological Evaluation of Certain Veterinary Drug Residues in Food*. Prepared by the sixty-second meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA). WHO Food Additives Series: 53. World Health Organization, Geneva. Available at http://www.inchem.org/documents/jecfa/jecmono/v53je08.htm

[4] Scored 3 based on the EFSA conclusion that no ADI can be set at present. The score would be 1 if the JECFA ADI was used.

Salinomycin

Reviewed 2013 (VMD)

	Rationale	Score
Hazard (A)	At doses less than 5-fold higher than the NOAEL used to set the ADI, effects such as moderate neuronal degeneration of spinal ganglia are evident in rats and retinotoxic effects in dogs. Therefore, the hazard score is based on these neurotoxic effects.	5
Potency (B)	ADI = 5 µg/kg (ANADA 200-357 (2003))	1
Diet (C)	Poultry and eggs.	1
Use (D)	Poultry, so entire flock medicated.	3
High Exposure (E)	No evidence for high exposure groups for poultry.	0
Detectable residues (F)	One RASFF in 2013 at <10 times the MRL.	2
Total	(A+B) x (C+D+E+F)	36

ANADA 200-357 (2003)
http://www.fda.gov/downloads/AnimalVeterinary/Products/ApprovedAnimalDrugProducts/FOIADrugSummaries/ucm059266.pdf.

Sarafloxacin

Reviewed 2013 (FSA)

	Rationale	Score
Hazard (A)	Arthropathy in dogs; effects on gut microflora (EMEA 1996)	4
Potency (B)	ADI (toxicological) = 100 µg/kg bw; ADI (microbiological) = 0.4 µg/kg bw (EMEA 1996)	0[5]
Diet (C)	Poultry, eggs and aquaculture.	2
Use (D)	Administered to whole flock for poultry and aquaculture.	3
High Exposure (E)	Some consumers rely on fish for their protein (ethical avoidance of meat).	1
Detectable residues (F)	No RASFFs. Included in many EU countries' surveillance schemes as a "standard" quinolone. No evidence from exporting countries suggesting misuse.	0
Total	(A+B) x (C+D+E+F)	24

EMEA (1996). Sarafloxacin: summary report. Committee for Veterinary Medicinal Products. European Agency for the Evaluation of Medicinal Products. Available at: http://www.ema.europa.eu/docs/en_GB/document_library/Maximum_Residue_Limits_-_Report/2009/11/WC500015842.pdf

[5] The potency score is based on the toxicological ADI as this was set to protect against the arthropathy observed in dogs. On the basis of microbiological effects, the hazard score would be 1 and the potency score would be 1, leading to a lower overall score

Streptomycin

Reviewed 2013 (VMD)

Criterion	Rationale	Score
Hazard (A)	Potential embryo-foetal developmental effects	5
Potency (B)	Toxicological ADI of 25 µg/kg Microbiological ADI of 4800 µg/kg The toxicological ADI is established for consumer risk.	0
Diet (C)	Bovine, ovine and porcine uses. Including animals producing milk for human consumption. Also used in rabbits.	3
Use (D)	Usually administered as an injection or an intra mammary suspension to cattle, horses, pigs or sheep. Because the product may be used to treat respiratory infection it cannot be considered as for treatment of a small number of animals.	1
High Exposure (E)	Dairy uses = milk powder, thus infant formula milk.	2
Detectable residues (F)	RASFFs, including 2011 RASFF for >10 x MRL in beef	3
Total	(A+B) x (C+D+E+F)	45

Streptomycin and dihydrostreptomycin: Summary report (1) - Committee for Veterinary Medicinal Products (1995)

Sulphonamides

Reviewed 2013 (FSA)

	Rationale	Score
Hazard (A)	Effects on the thyroid gland including thyroid tumours in rodents by a non-genotoxic mechanism (WHO 1994, EMEA 1995). May trigger hypersensitivity reactions in people who are allergic to sulphonamides (skin reactions) (WHO 1989, 1994, EMEA 1995).	4 or 3 for allergic reactions
Potency (B)	Toxicological ADI for sulphadimidine = 50 µg/kg bw/day (WHO 1994). There is no evidence from which a threshold dose can be identified for triggering hypersensitivity reactions in people sensitised to sulphonamides. Residue levels should be as low as practicable (WHO 1989, 1994).	1 (based on ADI) or 3 based on no identified threshold for allergic reactions
Diet (C)	EU MRLs for all food-producing species and Codex MRLs for a wide range of species.	3
Use (D)	Administered to poultry flock or pig herd	3
High Exposure (E)	No evidence for high exposure groups for poultry or pork.	0
Detectable residues (F)	RASFFs include in veal, fish and honey.	3
Total	(A+B) x (C+D+E+F)	54

EMEA (1995). Sulphonamides: summary report 2. Committee for Veterinary Medicinal Products, European Medicines Evaluation Agency. Available at http://www.ema.europa.eu/docs/en_GB/document_library/Maximum_Residue_Limits_-_Report/2009/11/WC500015931.pdf

WHO (1989). Effects on sulphonamides on human health. In: *Evaluation of Certain Veterinary Drug Residues in Food*. Thirty-Fourth Report of the Joint FAO/WHO Expert Committee on Food Additives. WHO Technical Report Series, No. 788. World Health Organization, Geneva. Available at http://whqlibdoc.who.int/trs/WHO_TRS_788.pdf

WHO (1994). Sulfadimidine. In: *Toxicological Evaluation of Certain Veterinary Drug Residues in Food*. Prepared by the forty-second meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA).WHO Food Additives Series: 33. World Health Organization, Geneva. Available at http://www.inchem.org/documents/jecfa/jecmono/v33je07.htm

Tetracyclines

Reviewed 2013 (FSA)

	Rationale	Score
Hazard (A)	Disturbance of the ecology of microflora in the large intestine (EMEA 1995, WHO 1998)	1
Potency (B)	ADI of 3 µg/kg bw (EMEA 1995).	1
Diet (C)	EU MRLs for all food-producing species and Codex MRLs for a wide range of species.	3
Use (D)	Administered to poultry flock or pig herd.	3
High Exposure (E)	Some consumers rely on fish for their protein (ethical avoidance of meat).	1
Detectable residues (F)	Residues detected at ≥ 10 X the MRL e.g. calves in UK NRCP samples.	3
Total	(A+B) x (C+D+E+F)	20

EMEA (1995). Oxytetracycline, tetracycline, chlortetracycline: summary report 3. Committee for Veterinary Medicinal Products, European Medicines Evaluation Agency. Available at http://www.ema.europa.eu/docs/en_GB/document_library/Maximum_Residue_Limits_-_Report/2009/11/WC500015378.pdf

WHO (1998). Tetracyclines: oxytetracycline, chlortetracycline and tetracycline (addendum). In: Toxicological Evaluation of Certain Veterinary Drug Residues in Food. Prepared by the fiftieth meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA).WHO Food Additives Series: 41. World Health Organization, Geneva. Available at: http://www.inchem.org/documents/jecfa/jecmono/v041je07.htm

Toltrazuril

Reviewed 2013 (FSA)

	Rationale	Score
Hazard (A)	Evidence of embryotoxicity, teratogenicity (LOEL of 0.3 mg/kg bw/day) and carcinogenicity (1.0 mg/kg bw/day threshold dose for tumour promotion) (EMEA, 1998)	5
Potency (B)	ADI = 2 µg/kg bw/day (EMEA, 2005)	1
Diet (C)	For use in chickens, turkeys, pigs, cattle (EMEA, 2005), also lambs and rabbits (NOAH). EU MRLs for all mammalian species and poultry. Possible use outside the EU, e.g. in piglets.	3
Use (D)	Administered to poultry flock or pig herd.	3
High Exposure (E)	No evidence for high exposure groups for poultry or pork.	0
Detectable residues (F)	Detected in poultry above MRL of 100 µg/kg in muscle (RASFF) in 2012. Infrequently sought in Member State residue control plans.	2
Total	(A+B) x (C+D+E+F)	48

EMEA, 1998 Toltrazuril: Summary Report 1. Committee for Medicinal Products for Veterinary Use (CVMP)
EMEA, 2005 Toltrazuril (Extension to cattle and extrapolation to all mammalian food-producing species and poultry): Summary Report 5. Committee for Medicinal Products for Veterinary Use (CVMP) EMEA/CVMP/278616/2006-final September 2005
NOAH, National Office of Animal Health Website, Compendium of Animal Medicines (www.noah.co.uk). (accessed September 2012).

Trenbolone

Reviewed 2013 (FSA)

	Rationale	Score
Hazard (A)	Hazards expected to be similar to other androgens, e.g. effects on development (virilisation of female fetus) (IPCS 1998). May be carcinogenic. (IPCS 1998, WHO 1988)	5
Potency (B)	ADI of 0.02 µg/kg (WHO 1990)	2
Diet (C)	Beef cattle and veal calf use, but not dairy (natural sources not considered for ranking purposes) (clenbuterol residues sought in poultry, but use is unlikely – other beta-agonists would be preferred).	2
Use (D)	Administered as an implant, so individual animals treated, but on farms where used likely to be given to all young cattle in the herd.	2
High Exposure (E)	No evidence for high exposure groups for beef.	0
Detectable residues (F)	No RASFFs / residues detected (excluding those attributed to natural sources). Used in domestic production in territories which have split domestic/EU-export production systems e.g. USA but including in some e.g. Brazil where medicine controls have been criticised by FVO thus undermining confidence in the effective segregation of the split production	2
Total	(A+B) x (C+D+E+F)	42

IPCS (1998). Anabolic steroids. Poisons Information Monograph (Group Monograph) G007. International Programme on Chemical Safety. Available at http://www.inchem.org/documents/pims/pharm/pimg007.htm

WHO (1988). Trenbolone actetate. In: *Toxicological evaluation of certain veterinary drug residues.* Prepared by the thirty-second meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA). WHO Food Additives Series: 23. World Health Organization, Geneva. Available at: http://www.inchem.org/documents/jecfa/jecmono/v23je03.htm

WHO (1990). Trenbolone actetate. In: Toxicological evaluation of certain veterinary drug residues. Prepared by the thirty-fourth meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA). WHO Food Additives Series: 25. World Health Organization, Geneva. Available at: http://www.inchem.org/documents/jecfa/jecmono/v25je08.htm

Triclabendazole

Reviewed 2013 (FSA)

	Rationale	Score
Hazard (A)	Increased postpartum mortality of the F_2 generation in a two-generation rat reproduction study (NOEL estimated as 0.15 mg/kg bw/day) (EMEA, 1997)	5
Potency (B)	ADI = 1.5 µg/kg bw/day (EMEA, 2006)	1
Diet (C)	Cattle, sheep and dairy.	3
Use (D)	Oral suspension used in cattle and sheep for treatment of GI roundworm, lungworm, tapeworm and adult liver fluke. 100% of the herd is likely to be treated.	3
High Exposure (E)	Dairy uses = milk powder, thus infant formula milk.	2
Detectable residues (F)	Seldom included in EU testing schemes. Limited knowledge on potential use in 3rd countries.	1
Total	(A+B) x (C+D+E+F)	54

EMEA, 1997 Triclabendazole: Summary Report 3. Committee for Medicinal Products for Veterinary Use (CVMP) EMEA/MRL/196/97-final November 1997

EMEA, 2006 Triclabendazole (Modification of Maximum Residue Limits): Summary Report 4. Committee for Medicinal Products for Veterinary Use (CVMP) EMEA/CVMP/320386/2005-final June 2006

Tylosin

Reviewed 2013 (VMD)

	Rationale	Score
Hazard (A)	Reversible microbiological effects	1
Potency (B)	Toxicological ADI 500 µg/kg Microbiological ADI 6.06 µg/kg The micobiological ADI is established for assessing risk to the consumer.	1
Diet (C)	Bovine, porcine and poultry use	2
Use (D)	Can be administered via injection to pigs or via the drinking water for cattle, pigs chickens and turkeys	3
High Exposure (E)	No evidence for high exposure groups for poultry or pork.	0
Detectable residues (F)	Two RASFFs in 2009, including >10x MRL in egg	3
Total	(A+B) x (C+D+E+F)	16

Tylosin: Summary Report (1) – Committee for Veterinary Medicinal Products (1996)

Zeranol

Reviewed 2013 (FSA)

Criterion	Rationale	Score
Hazard (A)	Hormonal effects (VPC 2006). Evidence that the zeranol metabolite zearalenone is genotoxic in vivo (EFSA 2011).	5
Potency (B)	Genotoxicity of zearalenone is partly ameliorated by antioxidants indicating that the mechanism may be oxidative stress; however, it cannot be exluded that catechol metabolites of zearalenone also form depurinating DNA adducts (EFSA 2011). Therefore it is prudent to assume there may be no threshold.	3
Diet (C)	Beef cattle and veal calf use, but not dairy (natural sources not considered for ranking purposes) (clenbuterol residues sought in poultry, but use is unlikely – other beta-agonists would be preferred).	2
Use (D)	Administered on an individual basis.	0
High Exposure (E)	No evidence for high exposure groups for beef	0
Detectable residues (F)	No RASFFs / residues detected (excluding those attributed to natural sources). Used in domestic production in territories which have split domestic/EU-export production systems e.g. USA but including in some e.g. Brazil where medicine controls have been criticised by FVO thus undermining confidence in the effective segregation of the split production	2
Total	(A+B) x (C+D+E+F)	32

EFSA (2011). Scientific Opinion on the risks to public health related to the presence of zearalenone in food. EFSA Panel on Contaminants in the Food Chain. EFSA Journal 9(6): 2197. Available at http://www.efsa.europa.eu/en/efsajournal/doc/2197.pdf

VPC (2006). Risks Associated with the Use of Hormonal Substances in Food-Producing Animals. Report of the Veterinary Products Committee. Available at http://www.vmd.defra.gov.uk/vpc/pdf/WG_Hormones_report.pdf

Summary table of Matrix Ranking assessments

Substance	Nature of the hazard (A)	Potency of the Substance (B)	Diet (C)	Usage (D)	High Exposure groups (E)	Evidence of Detectable Residues (F)	Total (A+B) x (C+D+E+F)	Rank
Nitrofurans	6	3	3	2	2	3	90	1
Chloramphenicol	6	3	3	1	2	3	81	2
Malachite Green	6	3	1	3	1	3	72	3
Crystal Violet	6	3	1	3	1	2	63	4
Albendazole	5	1	3	3	2	2	60	5
Enrofloxacin / Ciprofloxacin	5	1	3	3	1	3	60	5
17ß-oestradiol	6	3	2	2	0	2	54	7
Metronidazole	6	3	2	3	0	1	54	7
Sulphonamides	3	3	3	3	0	3	54	7
Triclabendazole	5	1	3	3	2	1	54	7
Methylene Blue	5	3	1	3	1	1	48	11
Toltrazuril	5	1	3	3	0	2	48	11
Florfenicol	4	1	3	2	1	3	45	13
Nitroxynil	4	1	3	1	2	3	45	13
Oxyclozanide	5	0	3	3	2	1	45	13
Streptomycin	5	0	3	1	2	3	45	13
Dexamethasone	4	2	3	0	2	2	42	17
Dimetridazole	5	1	2	3	0	2	42	17
Naladixic acid	4	3	1	3	1	1	42	17
Trenbolone	5	2	2	2	0	2	42	17
Maduramycin	5	1	2	3	0	1	36	21
Phenylbutazone	6	3	1	0	0	3	36	21
Salinomycin	5	1	1	3	0	2	36	21
Monensin	4	1	3	2	2	0	35	24
Zeranol	5	3	2	0	0	2	32	25
Diazinon	5	1	1	3	0	1	30	26
Difloxacin	4	1	3	2	1	0	30	26
Doramectin	2	1	3	3	2	2	30	26
Narasin	5	1	2	3	0	0	30	26
Clopidol	4	0	1	3	0	3	28	30
Erythromycin	3	1	3	3	0	1	28	30
Flumequine	4	0	3	3	1	0	28	30
Oxolinic acid	4	0	3	3	1	0	28	30
Ractopamine	1	3	2	3	0	2	28	30

Ivermectin	**2**	**1**	**2**	**3**	**1**	**3**	**27**	**35**
1,4, dichlorobenzene	**6**	**0**	**0**	**3**	**0**	**1**	**24**	**36**
Danofloxacin	**4**	**0**	**3**	**2**	**1**	**0**	**24**	**36**
Marbofloxacin	**4**	**0**	**3**	**0**	**2**	**1**	**24**	**36**
Sarafloxacin	**4**	**0**	**2**	**3**	**1**	**0**	**24**	**36**
Levamisole	**3**	**1**	**3**	**0**	**2**	**0**	**20**	**40**
Tetracyclines	**1**	**1**	**3**	**3**	**1**	**3**	**20**	**40**
Cypermethrin	**2**	**0**	**3**	**3**	**1**	**2**	**18**	**42**
Monepantal	**2**	**0**	**3**	**3**	**2**	**1**	**18**	**42**
Nortestosterone	**5**	**1**	**1**	**0**	**0**	**2**	**18**	**42**
Lasalocid	**1**	**1**	**3**	**3**	**0**	**2**	**16**	**45**
Tylosin	**1**	**1**	**2**	**3**	**0**	**3**	**16**	**45**
Fipronil	**2**	**1**	**1**	**3**	**0**	**1**	**15**	**47**
Nicarbazin	**2**	**0**	**1**	**3**	**0**	**3**	**14**	**48**
Diclofenac	**1**	**1**	**3**	**0**	**2**	**1**	**12**	**49**
Bromopropylate	**2**	**0**	**0**	**3**	**0**	**1**	**8**	**50**
Clenbuterol	**1**	**1**	**2**	**0**	**0**	**2**	**8**	**50**
Naphthalene	**2**	**0**	**0**	**3**	**0**	**1**	**8**	**50**