Prioritisation of chemical substances for national monitoring

Applied to antibiotics, antiparasitics, carbamates and NSAIDs in bovine, porcine and poultry products

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Summary

Regulation (EU) 2017/625 will apply from December 14, 2019. This Regulation prescribes that EU Member States should have a risk based national monitoring program for verifying compliance with food safety regulations. However, the Regulation does not indicate how such a control program should be established. Therefore, the Office for Risk Assessment & Research of the Netherlands Food and Consumer Product Safety Authority (NVWA-BuRO) asked RIKILT in 2017 to develop an approach for setting up an action plan to establish a more risk-based implementation of the National Plan (NP) for Residues. 'Risk' in this respect is defined as a combination of the probability that a hazard will occur and its possible human health effects (i.e. the severity of the hazard). In this previous study, decision trees were drafted for I. Prohibited substances; II. Natural substances, contaminants and residues of pesticides and III. Authorised active ingredients of veterinary medicines and feed additives. Depending on the substance, the relevant decision tree should be chosen for prioritization.

In the current research, the decision trees were used to prioritise four groups of substances: antibiotics, antiparasitics, carbamates and NSAIDs in bovine, porcine, poultry and eggs. For each of these four groups, a list of substances was drafted that could potentially be present in the specified animal products. These lists were a compilation of substances included in Regulation (EU) 37/2010, additional substances currently present in the national monitoring programs, substances approved for non-food producing species (companion animals) or approved outside the EU. For carbamates, the list of substances was based on the Compendium of Pesticide Common Names. The final lists were then evaluated for each substance separately using legislative status (existence of an MRL), occurrence of non-compliances based on national and EU monitoring data, information on availability of veterinary medicinal products and the use of the substances, information on withdrawal periods and the possible effects of the substances on human health. All information available was used to answer the questions in the decision trees resulting in a low, medium or high classification for inclusion in the national monitoring program.

In total, 68 antibiotics were prioritised for the specified animal products using decision tree III, resulting in 18 substances with a high priority for all animal products. For bovine, 29 substances ended up as medium priority, for porcine this was 20 and for poultry and eggs 15. For the antiparasitics, 33 authorised substances were prioritised using decision tree III and 19 unauthorised substances using decision tree I. None of the authorised antiparasitics was classified as high priority because they are not considered critically important for human medicine. For bovine, 14 substances were classified as medium importance, for porcine, poultry and egg this number was 10, 2 and 1, respectively. With respect to the unauthorised antiparasitics, evaluation was complicated by a lack of data. Classification was done regardless of the animal product. Four substances received a low priority, either because they had no registration for companion animals or available residue information indicated the substance was not used in animals. Only 1 substance (pyriproxyfen) received a medium priority and the other 14 substances a high priority, primarily due to a lack of information on human health effects. The carbamates were also classified regardless of the animal product, since no non-compliant data for the carbamates were found for either of the animal products studied. Four carbamates are authorized and were prioritised using decision tree II, all of which were classified as low priority. The remaining 50 unauthorised carbamates were prioritised using decision tree I. Of these, only 1 substance was classified as medium priority and 6 as high priority. Three of the latter substances were classified as high priority due to a lack of data (none of the questions in the decision tree could be answered with yes or no). The other three received a high classification because there were indications for use. For NSAIDs, 18 unauthorised substances were prioritised using decision tree I. Phenylbutazone was classified as high priority for bovine and porcine products, and 2 other substances (grapiprant and nimesulide) obtained a high priority classification for all species due to a lack of data. For bovine and porcine, three substances obtained a medium priority classification, all other substances were classified as low priority. In total, 13 authorised NSAIDs were prioritised using decision tree III. None of the authorised NSAIDs was classified as high priority because they are not

considered critically important for human medicine. For eggs, there was a lack of data and a survey was recommended for all 13 substances. For poultry, porcine and bovine, respectively 4, 5 and 8 substances received a medium classification. All other substances were classified as low priority.

The research performed in this study showed that the decision trees, with some small adjustments, work well to prioritise veterinary medicinal substances in animal products. It is recommended to include the medium and high priority substances in the national monitoring program. For substances for which appropriate data are lacking, it is recommended to first perform a survey on the possible presence of the substances in animal products. The outcome of the risk-based monitoring program should be evaluated regularly and updated using the latest information on monitoring results, veterinary drug use etc. It would be worthwhile to exchange information on the national monitoring program and on the use of veterinary medicinal substances with other EU MS, in order to further optimise monitoring. Furthermore, it is recommended to perform part of the monitoring randomly in order to ensure that (emerging) hazards are not overlooked.

1 Introduction

Currently, veterinary medicines are regulated in the EU under Regulation (EC) 726/2004 (last amended by Regulation (EU) 2019/5), which establishes authorization procedures for (human and) veterinary medicinal products, and Directive 2001/82/EC, which establishes regulatory requirements for veterinary medicines. Directive 2001/82/EC will be repealed and replaced by Regulation (EU) 2019/6 which will enter into force January 28, 2022.

Regulation (EU) 2017/625 prescribes that member states (MS) need to establish and regularly revise a multi-annual national monitoring program. This Regulation will apply from December 14, 2019 and repeals (amongst others) Directive 96/23/EC, the current Directive aimed at harmonising the control by member states of veterinary drug and banned substances residues in animal products. The current annexes of Directive 96/23/EC, which prescribe the substance groups to be included in the monitoring however, will stay in force until they are replaced by a delegated act (before December 14, 2022). A more risk-based approach is needed focusing on monitoring of the most relevant substances in the most relevant animal species.

In anticipation of this new act, the Office for Risk Assessment & Research of the Netherlands Food and Consumer Product Safety Authority (NVWA-BuRO) started a project in 2017 to establish an action plan that can be used to set up a risk-based national monitoring program on residues in animal products (National Plan Residues; NPR). For this purpose, RIKILT drafted decision trees that can be used to prioritise substances for monitoring (van Asselt et al., 2018a; van Asselt et al., 2018c). The decision trees prioritise substances into low, medium and high priority for monitoring based on the possible presence of substances in animal products and the severity of the substances. Three separate decision trees were established for the evaluation of: I. Prohibited substances (Figure 1); II. Natural substances, contaminants and residues of pesticides (Figure 2) and III. Authorised active ingredients of veterinary medicines and feed additives (Figure 3). If the question on non-compliant residue data (Q1 in DT I, Q2 in DT II and Q3 in DT III) is answered negatively, this could originate from the fact that the substance is not included in monitoring programs. Therefore, additional questions were answered to further differentiate the priority of these substances based on possible use of the substance in the animal species.

Substances are classified in the decision trees as follows (van Asselt et al., 2018a; van Asselt et al., 2018c):

- High priority: this substance/group of substances has high priority for inclusion in a risk-based monitoring plan for animal matrices because of potential risks to human health.
- Medium priority: this substance/group of substances has medium priority for inclusion in a risk-based monitoring plan for animal matrices because of occasional potential risks to human health.
- Low priority: this substance/group of substances has low priority for inclusion in a risk-based monitoring plan for animal matrices because of the very low or negligible risk it poses to human health. However, if this substance/group of substances is already included in a chemical- analytical multi-method for substances/groups of substances with high or medium priority, there is no reason for it to be removed unless precisely that substance has a negative effect on the sensitivity of the method.

The aim of the current research was to prioritise a comprehensive list of substances to be included in the NPR, using the previously established decision trees. As a start, NVWA-BuRO requested to start with evaluating the following four groups of substances: antibiotics, antiparasitic agents, carbamates and non-steroidal anti-inflammatory drugs (NSAIDs). These four groups were based on the classification of group B substances in the draft annex of Regulation (EU) 2017/625 at the time the research started (SANTE 11987-2017Rev1). The substances were prioritised for the following four groups of animal products: bovine products, porcine products, poultry meat and eggs.

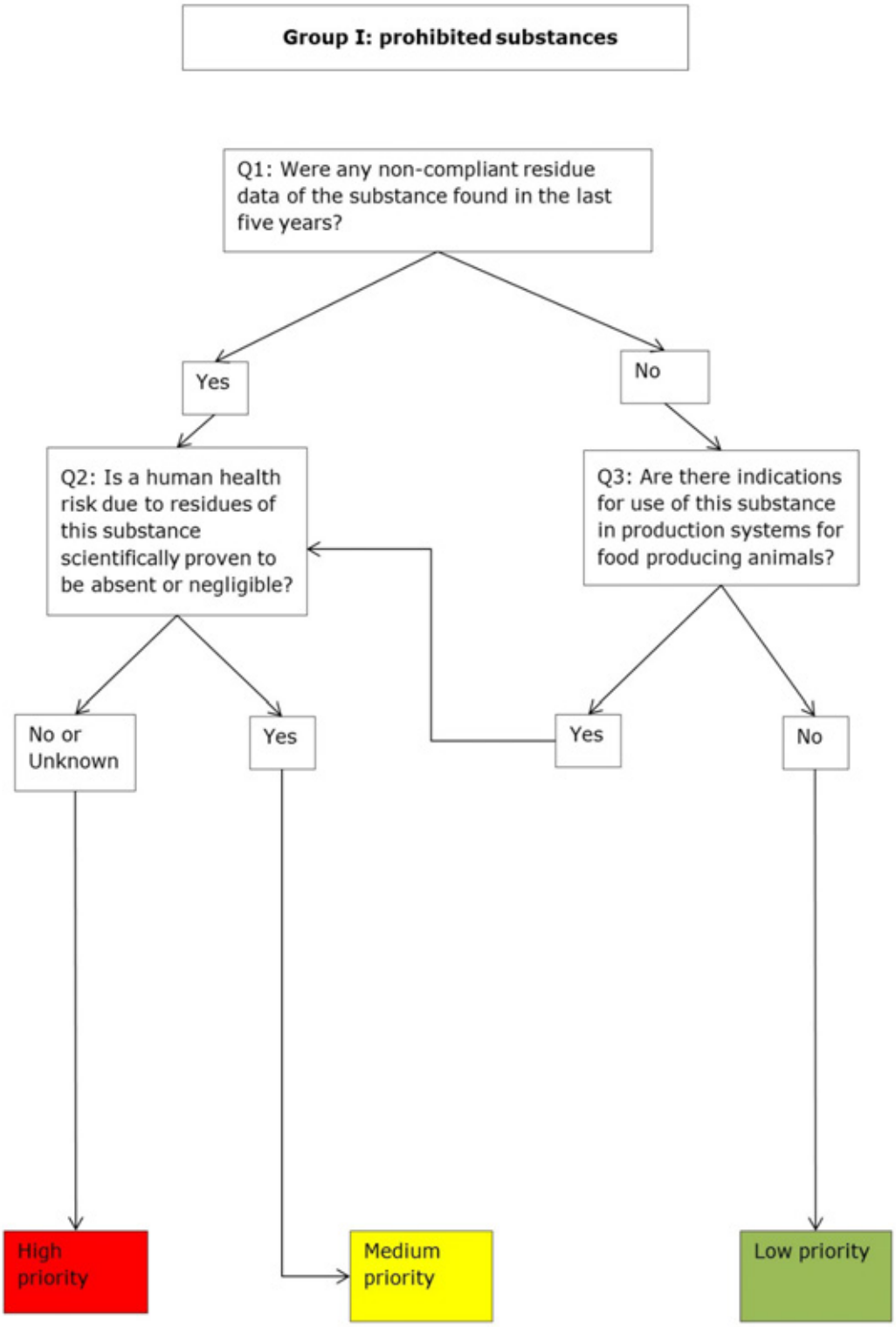

Figure 1 *Decision tree for forbidden substances (group I) (van Asselt et al., 2018b).*

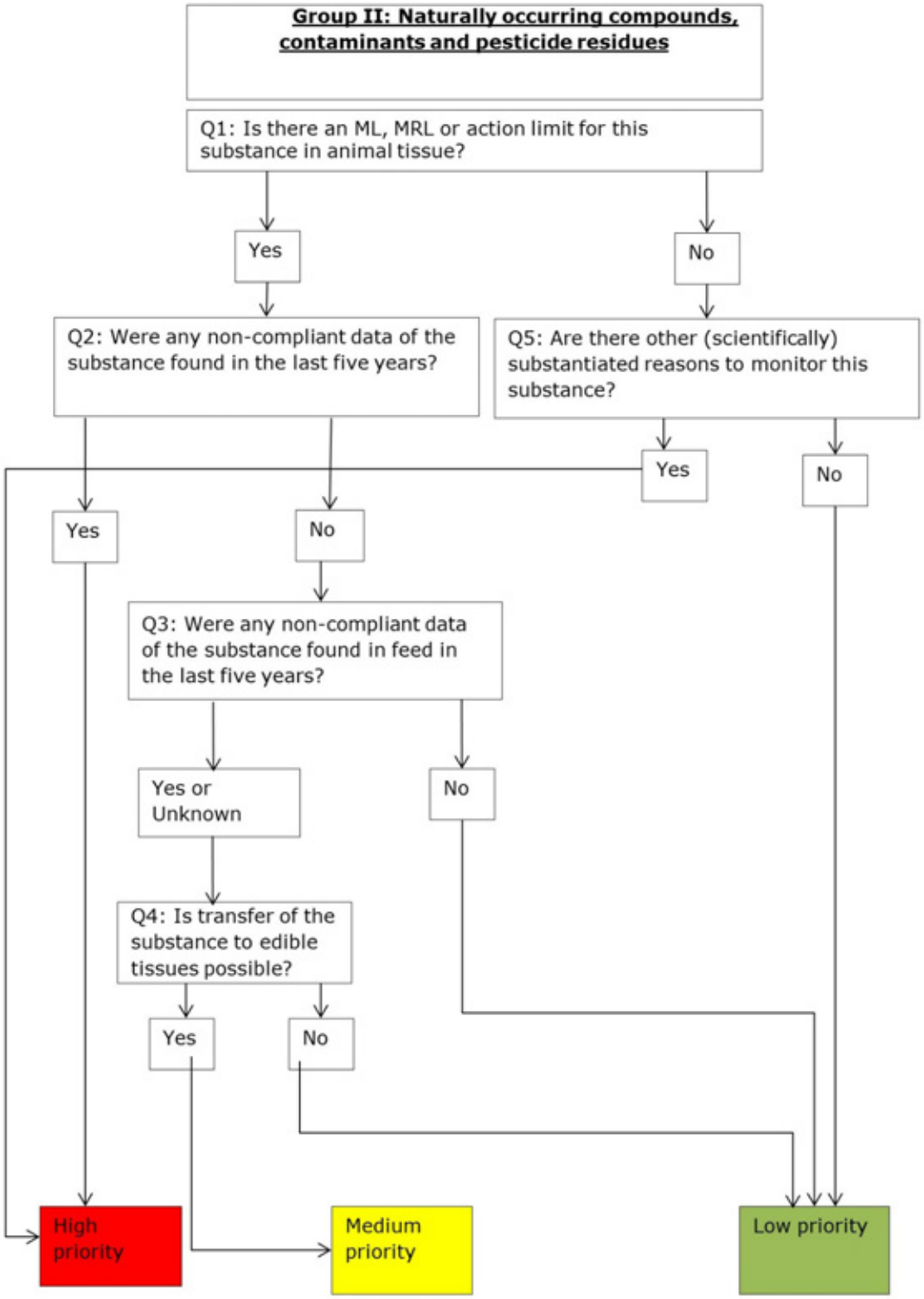

Figure 2 *Decision tree for naturally occurring substances, contaminants and pesticide residues (Group II) (van Asselt et al., 2018b).*

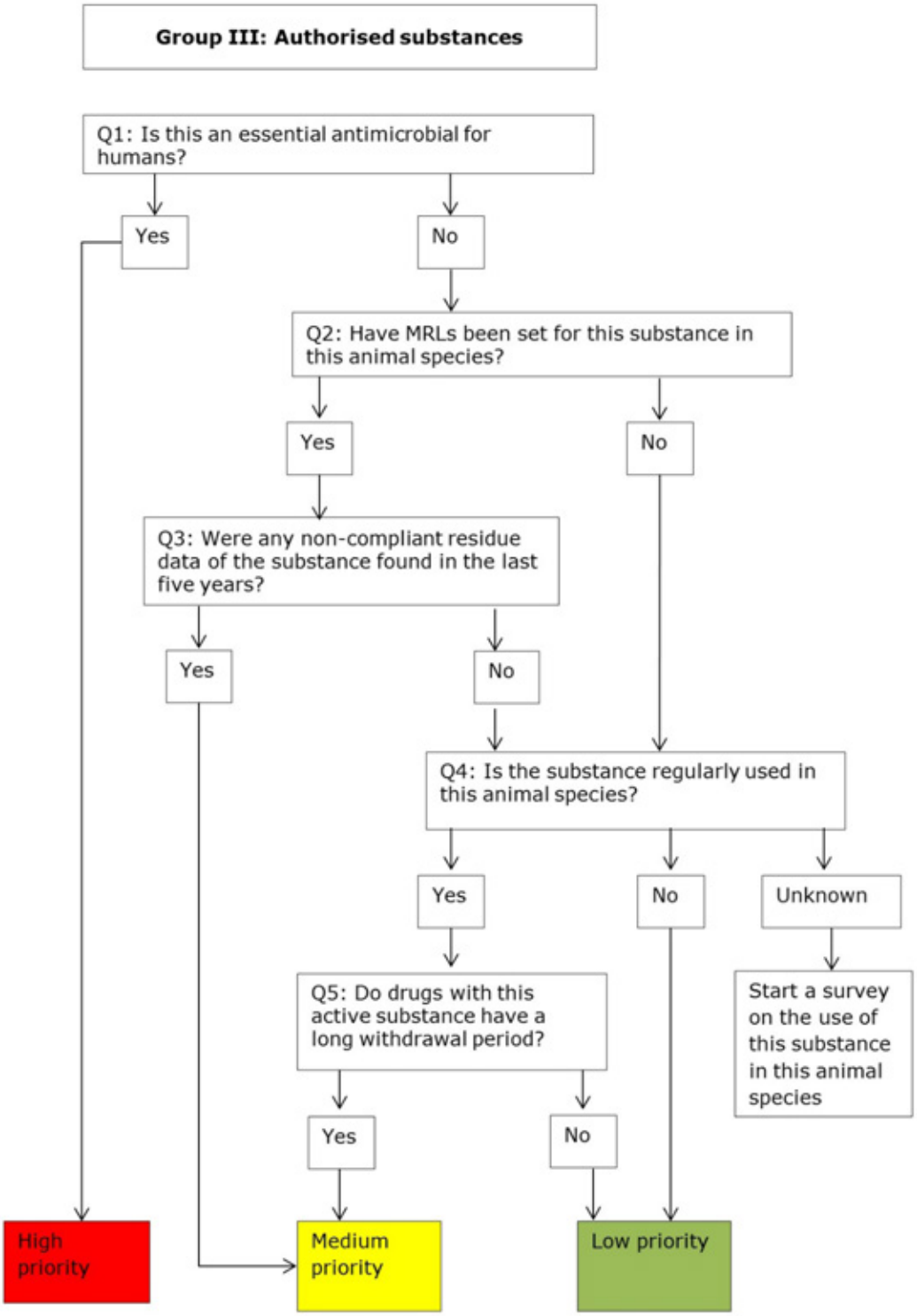

Figure 3 *Decision tree for authorised substances (Group III) (van Asselt et al., 2018b).*

2 Materials and Methods

2.1 Approach

For each of the four groups of substances, a list of substances to be prioritised was established. Substances within each group were selected based on the current Dutch monitoring programs, legislation (listed in Regulation (EU) 37/2010), non-compliances reported in EU MS and other (scientific) information. The details of the established lists are indicated per group of substances below. The selected substances were subsequently run through the decision trees per animal species in order to classify their individual priority for monitoring. For this purpose, the results of Dutch and EU monitoring programs were used as well as information on the use of the substances from (e.g. SDa data on antibiotics use, and data for other substances from FIDIN) and their possible human health effects using EFSA reports. The specific data sources used are indicated below for each group of substances.

2.2 Prioritising antibiotics

2.2.1 List of substances

In principle, all substances in Regulation (EU) 37/2010 with the therapeutic classification 'Anti-infectious agents/Antibiotics' were included. From this primary list, a number of substances was removed, for various reasons. Clavulanic acid was excluded, since it is exclusively used as a beta-lactamase inhibitor in combination with amoxicillin, but by itself exhibits no significant antimicrobial activity. Lasalocid and monensin were excluded, since their main application is as coccidiostats, which positions them as a separate compound group in a draft annex to a delegated act supplementing Regulation (EU) 2017/625 (group B3 of draft annex SANTE 11987-2017 Rev1 and group B2 in draft annex SANTE 11987-2017 Rev5). Oxalic acid was excluded since it is only applied in bees and no maximum residue limit (MRL) is required.

Subsequently, a number of substances was added to the primary list. Josamycin was included because up until 2002 this substance was registered with provisional MRLs and despite the current absence in Regulation (EU) 37/2010, a non-compliant result was reported in 2013 (bovine, DE). For sulfonamides, Regulation (EU) 37/2010 defines a generic MRL, without specifying individual pharmacologically active substances. To build a list with relevant sulfonamides, all sulfonamides for which non-compliances were reported in EU MS were included. Additionally, the Dutch Medicinal Products Agency (CBG-MEB) database for veterinary pharmaceutical products (www.diergeneesmiddeleninformatiebank.nl), as well as similar databases from Belgium (www.vetcompendium.be), Germany (www.vetidata.de), UK (www.vmd.defra.gov.uk/ ProductInformationDatabase), France (www.ircp.anmv.anses.fr) and Italy (https://gestionale.tuttomed.it) were explored for additional sulfonamidess. This yielded the following sulfonamides: sulfachlorpyridazin, sulfaclozin, sulfadiazin, sulfadimethoxin, sulfadoxin, sulfamethazin (=sulfadimidin), sulfamethoxazole, sulfapyridin, sulfaquanidine and sulfaquinoxaline, which were added to the list. This combination of data sources resulted in the final list of substances that were prioritised using the decision trees. The final list is indicated in Table 1 and Annex 2.

2.2.2 Decision tree

The established list of substances was evaluated using decision tree III for authorised substances. Each question was answered using the following information:

1. Is this an essential antimicrobial for humans?
   For this question, the 2017 WHO report was used to identify the highest priority critically important (HPCI) antimicrobials for human medicine. These antimicrobials included quinolones,

3rd and higher generation cephalosporins, macrolides and ketolides, glycopeptides and polymyxins (WHO, 2017).

2. Have MRLs been set for this substance in this animal species?
   This question is answered using Table 1 in the Annex of Regulation (EU) 37/2010 (latest consolidated version 29/09/2018). The extrapolation of MRLs (except for milk and egg) in species with MRLs to species without MRLs as outlined in Regulation (EU) 2017/880 was not taken into account.
3. Were any non-compliant residue data of the substance found in the last five years?
   In order to answer this question, monitoring data on residues of the substances was used. EFSA reports on the results from the monitoring of veterinary medicinal product residues and other substances in live animals and animal products were used for the years 2012-2016 to identify non-compliances in EU MS (EFSA, 2014b, 2015b, 2016b, 2017b, 2018b) as well as RASFF notifications (2012 – 2016, https://webgate.ec.europa.eu/rasff-window/portal). Furthermore, national monitoring data was extracted from the Dutch Quality Program for Agricultural Products (KAP), which is an extensive cooperation between the Dutch government and Dutch agribusiness (www.chemkap.rivm.nl). Data originated from RIKILT- Wageningen UR and the NVWA and were available for the years 2012, 2013 and 2017.
4. Is the substance regularly used in this animal species?
   This question was answered by using data on use of antibiotics as registered by the Netherlands Veterinary Medicines Institute (SDa, https://www.autoriteitdiergeneesmiddelen.nl) for 2017. As a cut-off value, a DDDA ('Defined Daily Dose Animal', the defined average dose of a specified medicine per kg of a specified animal per day, applied for its main indication (Postma et al., 2014; EMA, 2015)) of 50,000 was set. This threshold was set such that at least 95% of the total antibiotics use in each of the animal species would be included in the analyses. Since the SDa data only indicated antibiotics use in poultry, no distinction could be made between use for broilers and use for laying hens. As a result, it was assumed that antibiotics use for poultry meat and eggs was the same (worst case assumption).
5. Do drugs with this active substance have a long withdrawal period?
   Withdrawal periods were obtained from the product specifications retrieved from the CBG-MEB veterinary medicines database. In case the longest withdrawal time was longer than 10 days for beef, pork and poultry meat and longer than 5 days for milk and eggs (Danaher et al., 2016), this question was answered with a 'yes'.

2.3 Prioritising antiparasitics

2.3.1 List of substances

In principle, all substances in Regulation (EU) 37/2010 with the therapeutic classification 'Antiparasitic agents/Agents acting against endo- and/or ectoparasites' were included. This includes the avermectins and benzimidazoles, the chemical groups traditionally analysed in the monitoring program. Substances belonging to the pyrethroids were excluded since they formed (together with carbamates) a separate class in regulation (EU) 2017/625 (group B4 in draft Annex SANTE 11987-2017 Rev1). This group of substances will be evaluated separately in a follow up report. Phoxim and diazinon were excluded since they are organophosphorus pesticides (group B7 in draft Annex SANTE 11987-2017 Rev1 to regulation (EU) 2017/625), which were also out of scope for this study. Coumafos was excluded since it is only used in beekeeping. The final list of authorised antiparasitics can be found in Table 3 and Annex 4. The scope of the current RIKILT method includes several additional substances that are not mentioned in Regulation (EU) 37/2010. These substances were evaluated for possible application as antiparasitics (either non-EU or human), which yielded additional inclusion of bithionol, niclosamide and oxantel. Furthermore, milbemectin was included since it is an EU approved avermectin pesticide. Finally, the following substances were included since they occur in Dutch registered veterinary products approved for companion animals: afoxolaner, emodepside, fipronil, imidacloprid, indoxacarb, lotilaner, lufenuron, methopreen, milbemycine oxime, nitroscanate, pyriprole, pyriproxyfen, sarolaner, selamectin and spinosad. The final list of these non-authorized antiparasitics can be found in Table 2 and Annex 3.

2.3.2 Decision tree

The list of substances mentioned in Regulation (EU) 37/2010 was evaluated using decision tree III for authorised substances. Each question was answered using the following information:

1. Is this an essential antimicrobial for humans? This question is not relevant for antiparasitics. The answer to this question is therefore 'No' for all substances
2. Have MRLs been set for this substance in this animal species?
   This question is answered using Table 1 in the Annex of Regulation (EU) 37/2010 (latest consolidated version 29/09/2018). The extrapolation of MRLs (except for milk and egg) in species with MRLs to species without MRLs as outlined in Regulation (EU) 2017/880 was not taken into account.
3. Were any non-compliant residue data of the substance found in the last five years?
   In order to answer this question, monitoring data on residues of the substances was used. EFSA reports on the results from the monitoring of veterinary medicinal product residues and other substances in live animals and animal products were used for the years 2012-2016 to identify non-compliances in EU MS (EFSA, 2014b, 2015b, 2016b, 2017b, 2018b) as well as RASFF notifications (2012 – 2016, https://webgate.ec.europa.eu/rasff-window/portal). Furthermore, national monitoring data was extracted from the Dutch Quality Program for Agricultural Products (KAP), which is an extensive cooperation between the Dutch government and Dutch agribusiness (www.chemkap.rivm.nl). Data originated from RIKILT- Wageningen UR and the NVWA and was available for the years 2012, 2013 and 2017.
4. Is the substance regularly used in this animal species?
   This question was answered by determining whether registered veterinary medicinal products were available for the substances (listed in the database of CBG-MEB). Furthermore, the most recent sales data (2012-2017) from the Association of Netherlands Manufacturers and Importers of Veterinary Drugs (FIDIN) were used to identify which substances were regularly used. As a cut-off value, an amount of 100 kg was used, since this was the median value of the total antiparasitics sales data. In case more than 100 kg of a substance was sold in a year, the question was answered with 'yes'.
5. Do drugs with this active substance have a long withdrawal period?
   Withdrawal periods were obtained from product specifications retrieved from the CBG-MEB veterinary medicines database. In case withdrawal times were longer than 10 days for beef, pork and poultry meat and longer than 5 days for milk and eggs (Danaher et al., 2016), this question was answered with 'yes'.

Substances not included in Regulation (EU) 37/2010 and therefore not authorised for use in livestock animals, were run through decision tree I. The following questions were answered:

1. Were any non-compliant residue data of the substance found in the last five years?
   In order to answer this question, monitoring data on residues of the substances was used. EFSA reports on the results from the monitoring of veterinary medicinal product residues and other substances in live animals and animal products were used for the years 2012-2016 to identify non-compliances in EU MS (EFSA, 2014b, 2015b, 2016b, 2017b, 2018b) as well as RASFF notifications (2012 – 2016, https://webgate.ec.europa.eu/rasff-window/portal). Furthermore, national monitoring data was extracted from the Dutch Quality Program for Agricultural Products (KAP), which is an extensive cooperation between the Dutch government and Dutch agribusiness (www.chemkap.rivm.nl). Data originated from RIKILT- Wageningen UR and the NVWA and was available for the years 2012, 2013 and 2017.
2. Is a human health risk due to residues of the substance scientifically proven to be absent or negligible?
   Reports from EFSA, JECFA and scientific papers were checked for the effect of the substance on human health. In case no severe and/or irreversible adverse effects were reported, this question was answered positively.
3. Are there indications for use of this substance in production systems for food producing animals?
   Use in livestock outside EU, availability of products for companion animals and use as a pesticide were evaluated to answer this question.

2.4 Prioritising carbamates

2.4.1 List of substances

A list of substances was established based on carbamates mentioned by Alan Wood (http://www.alanwood.net/pesticides). All carbamates listed as insecticides and as acaricides were included. The final list can be found in Annex 5.

2.4.2 Decision tree

Animals may be exposed to carbamates through residues in feed. These substances have an MRL according to Regulation (EC) 396/2005. This was the case for methiocarb, oxamyl, pirimicarb and methomyl. For these substances, decision tree II was used for prioritisation. Since these carbamates are not used for a crop specifically cultured for a certain animal type, the decision tree was answered in general (not separately for poultry, cows and pigs). The following questions were answered:

1. Is there an ML, MRL or action limit for this substance in this animal tissue?
   This question is answered using Regulation (EC) 396/2005.
2. Were any non-compliant residue data of the substance found in the last five years?
   In order to answer this question, monitoring data on residues of the substances was used. European monitoring data of veterinary medicinal product residues and other substances in animal products (EFSA, 2014b, 2015b, 2016b, 2017b, 2018b) and in the European monitoring of pesticide residues in food (EFSA, 2014a, 2015a, 2016a, 2017a, 2018a) were used to identify non-compliances in EU MS. RASFF data (2012-2016) were also used for this purpose Furthermore, national monitoring data was extracted from the Dutch Quality Program for Agricultural Products (KAP), which is an extensive cooperation between the Dutch government and Dutch agribusiness (www.chemkap.rivm.nl). Data originated from RIKILT- Wageningen UR and the NVWA and was available for the years 2012, 2013 and 2017. (https://webgate.ec.europa.eu/rasff-window/portal).
3. Were any non-compliant residue data of the substance found in feed in the last five years?
   This question was also answered using RASFF data (2013-2018) and the KAP database (2012-2016).
4. Is transfer of the substance to edible tissues possible?
   Reports from EFSA and FAO/WHO were checked for information on metabolism and feeding studies in livestock animals.
5. Are there other (scientifically) substantiated reasons to monitor this substance?
   There was no need to answer this question for the four carbamates run through decision tree II.

Apart from the four carbamates mentioned above, the established list of carbamates contained unauthorised substances, which were run through decision tree I. The following questions were answered for these substances:

1. Were any non-compliant residue data of the substance found in the last five years?
   In order to answer this question, monitoring data on residues of the substances was used. European monitoring data of veterinary medicinal product residues and other substances in animal products (EFSA, 2014b, 2015b, 2016b, 2017b, 2018b), the European monitoring of pesticide residues in food (EFSA, 2014a, 2015a, 2016a, 2017a, 2018a) and RASFF notifications (2012-2016) (https://webgate.ec.europa.eu/rasff-window/portal) were used to identify non-compliances in EU MS. Furthermore, national monitoring data was extracted from the Dutch Quality Program for Agricultural Products (KAP), which is an extensive cooperation between the Dutch government and Dutch agribusiness (www.chemkap.rivm.nl). Data originated from RIKILT- Wageningen UR and the NVWA and was available for the years 2012, 2013 and 2017.
2. Is a human health risk due to residues of the substance scientifically proven to be absent or negligible?
   Reports from EFSA, JECFA and scientific papers were checked for the effect of the substance on human health. In case no severe and/or irreversible adverse effects were reported, this question was answered with 'yes'.
3. Are there indications for use of this substance in production systems for food producing animals?
   In case laboratory results or data from other EU MS showed that residues were found, this question was answered positively (EFSA, 2014a, 2015a, 2016a, 2017a, 2018a). In case the

carbamates were listed in the pesticide manual (Turner, 2015) or in the pesticide properties database (PPDB, https://sitem.herts.ac.uk/aeru/ppdb/en/atoz.htm) as obsolete, this question was answered negatively. Furthermore the PPDB, PAN pesticide database (http://www.pesticideinfo.org/), Codex, Australian registrations (https://apvma.gov.au/), and FAO report on hazardous pesticides in Asia (FAO, 2015) were used to check for indications of use in countries outside Europe. The CBG-MEB database was checked as well as the internet (alibaba.com) for available products containing the substance.
Some carbamates will break down into other carbamates; then monitoring data of the break down products were used to answer the question if there are indications for use of this substance.

2.5 Prioritising NSAIDs

2.5.1 List of substances

All NSAIDs listed in Regulation (EU) 37/2010 were included for the prioritisation. Furthermore, NSAIDs that were recommended by the CRL guidance paper were included (BVL-CRL et al., 2007). Additionally, the NSAIDs that are currently included in the national monitoring plan were included. And finally, NSAIDs for companion animals which were found in the CBG-MEB database were included. The final list can be found in Annex 1.

2.5.2 Decision tree

NSAIDs that are listed in Regulation (EU) 37/2010 and are thus authorised for use in animals were run through decision tree III. For these substances, the following questions were answered:

1. Is this an essential antimicrobial for humans?
   This question is not relevant for NSAIDs. The answer to this question is therefore 'No' for all substances
2. Have MRLs been set for this substance in this animal species?
   This question is answered using Table 1 in the Annex of Regulation (EU) 37/2010 (latest consolidated version 29/09/2018). The extrapolation of MRLs (except for milk and egg) in species with MRLs to species without MRLs as outlined in Regulation (EU) 2017/880 was not taken into account.
3. Were any non-compliant residue data of the substance found in the last five years?
   In order to answer this question, monitoring data on residues of the substances was used. EFSA reports on the results from the monitoring of veterinary medicinal product residues and other substances in live animals and animal products were used for the years 2012-2016 to identify non-compliances in EU MS (EFSA, 2014b, 2015b, 2016b, 2017b, 2018b) as well as RASFF notifications (2012 – 2016, https://webgate.ec.europa.eu/rasff-window/portal). Furthermore, national monitoring data was extracted from the Dutch Quality Program for Agricultural Products (KAP), which is an extensive cooperation between the Dutch government and Dutch agribusiness (www.chemkap.rivm.nl). Data originated from RIKILT- Wageningen UR and the NVWA and was available for the years 2012, 2013 and 2017.
4. Is the substance regularly used in this animal species?
   To answer this question, firstly non-compliances were checked based on RASFF, KAP data and EFSA data. In case a monitored substance is found non-compliant, regular use is indicated, answering the question positively. In case no non-compliances were found, this question was answered by determining whether registered veterinary medicinal products were available for the substances. Furthermore, products were searched on websites like alibaba.com and ebay.com to check the availability in case no registration was found. Lastly, sales data from FIDIN for 2017 were used to identify which substances were regularly used. As a cut-off value, an amount of 100 kg was used analogous to the approach for antiparasitics (see section 2.3.2).
5. Do drugs with this active substance have a long withdrawal period?
   Withdrawal periods were obtained from the CBG-MEB site. In case products are registered for an animal species, the longest withdrawal period found was considered. In case no products are registered, the standard cascade withdrawal period was used. In case withdrawal times were

longer than 10 days for beef, pork and poultry meat and longer than 5 days for milk and eggs (Danaher et al., 2016).

NSAIDs not listed in Table 1 of the Annex of Regulation (EU) 37/2010 and therefore not authorised for use in livestock animals, were run through decision tree I for which the following questions were answered:

1. Were any non-compliant residue data of the substance found in the last five years?
   In order to answer this question, monitoring data on residues of the substances was used. EFSA reports on the results from the monitoring of veterinary medicinal product residues and other substances in live animals and animal products were used for the years 2012-2016 to identify non-compliances in EU MS (EFSA, 2014b, 2015b, 2016b, 2017b, 2018b). Also RASFF notifications (2012 – 2016) were used. Furthermore, national monitoring data was extracted from the Dutch Quality Program for Agricultural Products (KAP), which is an extensive cooperation between the Dutch government and Dutch agribusiness (www.chemkap.rivm.nl). Data originated from RIKILT- Wageningen UR and the NVWA and was available for the years 2012, 2013 and 2017.
2. Is a human health risk due to residues of the substance scientifically proven to be absent or negligible?
   Reports from EFSA, JECFA and scientific papers were checked for the effect of the substance on human health. In case no severe and/or irreversible adverse effects were reported, this question was answered with 'yes'.
3. Are there indications for use of this substance in production systems for food producing animals?
   In case national monitoring results or data from other EU MS showed that residues were found in other animals (mammals for bovine and porcine, poultry meat for eggs), this question was answered positively. For substances that are currently not monitored, the possible availability on the market was checked. For this purpose, the CBG-MEB database was checked to determine whether products are authorised for other animal species, such as companion animals as well as the internet (ebay.com and alibaba.com).

3 Results

3.1 Antibiotics

In total, 68 antibiotics were evaluated using the decision trees. All substances were evaluated according to decision tree III for authorised substances. An overview of the prioritization is given in Table 1, and a more detailed overview of the results is provided in Annex 2. Irrespective of the animal product, a total of 18 antibiotics were classified as high priority after answering Q1 – is the substance an essential antimicrobial for human (classified as highest priority critically important antimicrobials for human medicine (WHO, 2017)). These antimicrobials comprised the veterinary approved quinolones, 3rd and 4th generation cephalosporins, macrolides and colistine. Remarkably, the WVAB (Werkgroep Veterinair Antibioticabeleid, part of the Koninklijke Nederlandse Maatschappij voor Diergeneeskunde KNMvD) who is responsible for the development of prescription guidelines (so called 'formularia') for veterinary antibiotic use, does not classify macrolides as critically important (3rd choice) substances. It only discourages the use of macrolides in poultry and the use of long-acting macrolides (e.g. tulathromycin, gamithromycin) by classifying them as 2nd choice antimicrobials (WVAB, 2015).

Most of the remaining substances have MRLs (Q2) for products of the three species of animals included in the analysis. For eggs, however, only a very limited number of MRLs have been established. This implies that the availability of veterinary medicinal products (VMPs) for use with laying hens is limited. VMPs, however, may be prescribed under the Cascade. The Cascade is a risk based decision tree that allows the prescribing of veterinary medicines for a use other than that described in the product information, enabling the treatment of an animal when there is no authorised veterinary medicine available. The prescribing cascade is established under EU legislation to address the lack of authorised VMPs 'to avoid causing unacceptable suffering'. Because of the limited availability of pharmaceutical substances for laying hens, cascade prescription is expected to occur relatively frequent. Since Q2 is answered on animal level, the outcome of Q2 for poultry was extrapolated to eggs. Cascade prescription explains the relative frequent occurrence of non-compliances for substances without an MRL in egg (Q3). It is also the reason why a medium priority was assigned to substances that are regularly used in poultry (Q4), even though no non-compliances in egg were reported. The data on usage did not allow for differentiation between broilers and hens (hence a positive answer for Q4 in eggs) and cascade use requires a 7 days withdrawal period for eggs resulting in a positive answer for Q5 and thus a medium classification.

A few of the substances remaining after Q1 only have an MRL established for milk because their use is limited to intramammary application. In this case, Q2 was positively answered for bovine with an additional remark 'MRL in milk only' (Annex 2). It is generally assumed that the risk for residues in tissue is limited. However, a non-compliant result for cefalonium in bovine (EFSA 2013) shows that it is not negligible. Also the fact that these intramammary products do have withdrawal times for the meat indicates they can potentially be present in bovine products.

In case an MRL has been established (Q2) and non-compliances were reported (Q3), this directly results in classifying the substance as medium priority. Q3 was evaluated according to RASFF notifications and EFSA annual reports on national monitoring results. For the bovine evaluation non-compliances in milk were also taken into account, because of the reasoning outlined above. For three of the substances in Table 1 with a medium priority classification for bovine, this was based on non-compliances exclusively in milk (indicated in Table 1 with *arising from non-compliant results in bovine milk). With respect to Q3 it should be taken into account that some substances may not be generally included in the scope of the analytical methods used in the monitoring, so the possibility exists that lack of non-compliances is due to the fact that the substance was not included in the monitoring program. In that case, Q3 was answered as U (unknown) in Annex 2 and additional questions were answered on the use (Q4) and withdrawal time (Q5) of the substance.

Besides the aforementioned situation with respect to eggs, the evaluation yielded two species-substance combinations for which non-compliances were reported while no MRL has been set in the mentioned species: tiamulin in bovine and dihydrostreptomycin in poultry. Although the occurrence of non-compliances could be an argument for overruling Q2, resulting in a classification as medium priority, these two substances were classified as low priority for monitoring based on the SDa usage data.

Table 1 *Prioritization of antibiotics per animal product using decision tree III.*

Substance	Bovine	Porcine	Poultry	Egg
Amoxicillin	Medium	Medium	Medium	Medium
Ampicillin	Medium	Medium	Medium	Medium
Apramycin	Low	Low	Low	Medium
Avilamycin	Low	Low	Low	Low
Bacitracin	Low	Low	Low	Low
Baquiloprim	Low	Low	Low	Low
Benzylpenicillin/penethamate	Medium	Medium	Low	Low
Cefacetrile	Low	Low	Low	Low
Cefalexin	Medium*	Low	Low	Low
Cefalonium	Medium	Low	Low	Low
Cefapirin	Medium	Low	Low	Low
Cefazolin	Medium*	Low	Low	Low
Cefoperazone	High	High	High	High
Cefquinome	High	High	High	High
Ceftiofur	High	High	High	High
Chlortetracycline	Medium	Medium	Medium	Low
Cloxacillin	Medium*	Low	Low	Low
Colistin	High	High	High	High
Danofloxacin	High	High	High	High
Dicloxacillin	Low	Low	Low	Low
Difloxacin	High	High	High	High
Dihydrostreptomycin	Medium	Medium	Low	Low
Doxycycline	Medium	Medium	Medium	Medium
Enrofloxacin	High	High	High	High
Erythromycin	High	High	High	High
Florfenicol	Medium	Medium	Low	Low
Flumequine	High	High	High	High
Gamitromycin	High	High	High	High
Gentamicin	Medium	Medium	Low	Low
Josamycin	Low	Low	Low	Low
Kanamycin	Medium	Low	Low	Low
Lincomycin	Medium	Medium	Medium	Medium
Marbofloxacin	High	High	High	High
Nafcillin	Low	Low	Low	Low
Neomycin	Medium	Medium	Medium	Medium
Novobiocin	Low	Low	Low	Low
Oxacillin	Low	Low	Low	Low
Oxolinic acid	Low	Low	Low	Low
Oxytetracycline	Medium	Medium	Medium	Medium
Paromomycin	Medium	Low	Low	Low
Phenoxymethylpenicillin	Low	Low	Low	Low
Pirlimycin	Low	Low	Low	Low
Rifaximin	Low	Low	Low	Low
Sarafloxacin	High	High	High	High
Spectinomycin	Medium	Medium	Medium	Medium
Spiramycin	High	High	High	High
Streptomycin	Medium	Medium	Low	Low
Sulfachlorpyridazin	Low	Low	Low	Medium
Sulfaclozin	Low	Low	Low	Low

Substance	Bovine	Porcine	Poultry	Egg
Sulfadiazin	Medium	Medium	Medium	Medium
Sulfadimethoxin	Medium	Medium	Medium	Medium
Sulfadoxin	Medium	Medium	Low	Low
Sulfamethazin (=sulfadimidin)	Medium	Medium	Medium	Medium
Sulfamethoxazole	Medium	Medium	Medium	Medium
Sulfapyridin	Medium	Low	Low	Low
Sulfaquanidine	Low	Low	Low	Low
Sulfaquinoxaline	Low	Low	Medium	Medium
Tetracycline	Medium	Medium	Medium	Low
Thiamphenicol	Medium	Low	Low	Low
Tiamulin	Low	Low	Low	Low
Tildipirosin	High	High	High	High
Tilmicosin	High	High	High	High
Trimethoprim	Medium	Medium	Medium	Medium
Tulathromycin	High	High	High	High
Tylosin	High	High	High	High
Tylvalosin	High	High	High	High
Valnemulin	Low	Low	Low	Low
Virginiamycin	Low	Low	Low	Low

* arising from non-compliant results in bovine milk

3.2 Antiparasitic agents

In total, 52 antiparasitic agents were evaluated. These comprise agents acting against endoparasites (anthelmintics) and ectoparasites (insecticides, acaracides). Parasiticides belonging to chemical classes of the carbamates are evaluated separately within this report. Parasiticides belonging to the chemical class pyrethroids will be evaluated separately in another report. The list does not include anticoccidials (antiprotozoals), since these form a separate category. Also organophosphorus substances were excluded, as these are traditionally classified as 'other substances and contaminants'. These groups of substances were out of scope for this study.

The substances were subdivided in four groups: the two major chemical groups of avermectins and benzimidizoles, a chemically diverse group of 'other substances' that do have an MRL in one or more food producing species, and a (chemically diverse) group of substances that do not have an MRL (and are not included in Regulation (EU) 37/2010). The first three subgroups were evaluated according to decision tree III for authorised substances. The fourth subgroup was evaluated according to decision tree I for prohibited substances.

3.2.1 Prioritization using decision tree I

For the unauthorised antiparasitics no non-compliances were reported during the period 2012-2016 (Q1). These substances, however, are not generally included in monitoring programs, which may be the reason for the absence of non-compliances. Several of the substances are used as pesticide and/or are available for, and extensively used on, companion animals, in particular in treatments to prevent flea and mite infestations. These products often contain multiple active substances. Among the substances in this list is fipronil, which use in laying hen facilities caused a major incident with residues in eggs in 2017 (outside the timeframe set for the current evaluation), underscoring the possible relevance of this category. Since there is no additional animal specific information available, the questions for this decision tree were answered in general for the livestock species evaluated in this study (cows, pigs and poultry). The results of the prioritization are indicated in Table 2 and Annex 3.

For all substances, Q3 was answered on the indications for use. Prioritization for bithionol and milbemectin was considered low, since they are not available as pharmaceutical products for companion animals, and milbemectin pesticide use is only against plant pests. All other substances are available for companion animals, and several of them are also registered as pesticide. For indoxacarb,

EFSA reports of pesticide monitoring data of last five years showed no residues of indoxacarb in animal samples (such as butter, eggs, milk and swine fat) (EFSA, 2014a, 2015a, 2016a, 2017a, 2018a). Therefore, there are no indications for use (Q3 is answered negatively) and indoxacarb is classified as a low priority substance. The same accounts for spinosad for which monitoring results show that there are no indications for use: 398 liver and chicken meat samples showed no residues in 2014 (EFSA, 2016a). This substance is thus also classified as low priority.

For the remaining substances, Q3 is answered with Yes and Q2 on human health risks needed to be answered. For afoxalaner, emodepside, lotilaner, milbemycine oxime, niclosamide, nitroscanate, oxantel, pyriprole, sarolaner and selamectin there are no relevant reports available from trustworthy organisations such as EFSA or JECFA to answer Q2. Therefore, for these substances it is not scientifically proven that human health risk due to residues are absent or negligible. Consequently, Q2 was answered with unknown, which resulted in high priority of these substances. An asterisk was added to indicate that information was lacking.

Imidacloprid, lufenuron and methoprene are substances that are authorised for the use as pesticides and are therefore evaluated by EFSA and/or JECFA. These reports indicated that residues can be found in milk, fat, eggs or meat. No risk assessment has been performed on the use as antiparasitics. As a result, these substances are classified as high priority.

Pyriproxyfen is authorised for use as pesticide. EFSA concluded that for representative uses pyriproxyfen is not likely to occur in animal products. Only 0.1-0.3% retained in tissues, without evidence for accumulation. Pyriproxyfen is extensively metabolised and the excretion of pyriproxyfen is fast. Furthermore, pyriproxyfen has a low acute toxicity, and it is not carcinogenic or genotoxic (EFSA, 2009). Therefore, health risks were considered to be absent or negligible for pyriproxyfen and the priority is classified as medium.

Due to the incident with fipronil residues in eggs in 2017, an extensive evaluation was performed by the NVWA. These risk assessments indicated that human health risks are very low with normal consumption of eggs, chicken meat or chicken fat by Dutch consumers (NVWA, 2017b, 2017a). However, children may exceed the ADI. As a result, human health risks are not absent or negligible and fipronil is classified as a high priority substance.

Table 2 *Prioritization of antiparasitic agents for bovine and porcine products, poultry meat and eggs using decision tree I.*

Substance	Prioritization
Afoxolaner	High*
Bithionol	Low
Emodepside	High*
Fipronil	High
Imidacloprid	High
Indoxacarb	Low
Lotilaner	High*
Lufenuron	High
Methoprene	High
Milbemectin	Low
Milbemycine oxime	High*
Niclosamide	High*
Nitroscanate	High*
Oxantel	High*
Pyriprole	High*
Pyriproxyfen	Medium
Sarolaner	High*
Selamectin	High*
Spinosad	Low

* these substances only have the classification of high priority because there is limited data or information available to answer the questions

3.2.2 Prioritization using decision tree III

The results of the prioritization of avermectins, benzimidazoles and other authorised antiparasitics is indicated in Table 3. More detailed information on the evaluations can be found in Annex 4. Some of the substances (albendazole(oxide)/netobimine and fenbendazole/ oxfendazole/fenbantel) are metabolized *in vivo* to the same marker residue(s). In the evaluation, these substances were combined since the analytical method used in the monitoring targets the metabolite(s).

The medium priority classifications in Table 3 essentially all originate from non-compliant monitoring results. Table 3 shows that the majority of the antiparasitics is classified as low priority for poultry meat and egg. Absence of non-compliances for these matrices, however, needs to be considered with caution, because of the virtual absence of monitoring of these substances, particularly in egg.

For some of the substances non-compliant results were found, despite the fact that they do not have an MRL established (Q2 is No). Several of the substances, however, are also registered and applied as pesticide. In particular when applied as insecticide or acaracide in animal housing facilities, this runs a risk of contamination through environmental exposure, which might explain why for some of the substances without an MRL non-compliant results were found. Following decision tree III, when Q2 is answered with No, Q3 is bypassed, and if Q4 on the use of antiparasitics is subsequently answered No, this results in a low classification of the substance. As this decision tree did not foresee in the possible exposure of animals through the environment, it was decided to always include Q3 (on non-compliant results) in the evaluation of antiparasitics.

Table 3 *Prioritization of antiparasitic agents per animal product in decision tree III.*

Substance	Bovine	Porcine	Poultry	Egg
Ivermectin	Medium	Medium	Low	Low
Doramectin	Medium	Medium	Low	Low
Abamectin	Medium	Low	Low	Low
Moxidectin	Medium	Low	Low	Low
Emamectin	Low	Low	Low	Low
Eprinomectin	Low	Medium	Low	Low
Albendazole (oxide), Netobimine	Medium	Medium	Low	Low
Fenbendazole/febantel/ Oxfendazole	Medium	Medium	Medium	Low
Oxibendazole	Low	Low	Low	Low
Mebendazole	Medium	Low	Low	Low
Flubendazole	Medium	Medium	Low	Low
Thiabendazole	Low	Medium	Low	Low
Levamisole	Medium	Medium	Low	Low
Triclabendazol	Medium	Low	Low	Low
Amitraz	Low	Low	Low	Low
Clorsulon	Medium	Low	Low	Low
Closantel	Medium	Medium	Low	Low
Cyromazine	Low	Low	Medium	Medium
Derquantel	Low	Low	Low	Low
Dicyclanil	Low	Low	Low	Low
Diflubenzuron	Low	Low	Low	Low
Fluazuron	Low	Low	Low	Low
Fluralaner	Low	Low	Low	Low
Monepantel	Low	Low	Low	Low
Morantel	Low	Low	Low	Low
Niclosamide	Low	Low	Low	Low
Nitroxinil	Medium	Low	Low	Low
Oxyclozanide	Medium	Medium	Low	Low
Piperazine	Low	Low	Low	Low
Praziquantel	Low	Low	Low	Low
Pyrantel	Low	Low	Low	Low
Rafoxanide	Low	Low	Low	Low
Sisapronil	Low	Low	Low	Low

3.3 Carbamates

In total, 54 carbamates were included in the prioritization. Four carbamates are approved in the EU: methyocarb, oxamyl, pirimicarb and methomyl. These substances were evaluated using decision tree II. The other carbamates are not approved in the EU and therefore evaluated with decision tree I. The prioritization of the carbamates did not differ between the individual animal species. Therefore, the prioritization of the carbamates as shown in tables 4 and 5 is relevant for bovine, porcine and poultry products.

3.3.1 Prioritization using decision tree I

An overview of the evaluation of carbamates in decision tree I can be found in Table 4. A more detailed table can be found in Annex 5. For all non-authorised carbamates, no non-compliant residue data were found in the last 5 years in the KAP database, RASFF notifications and European monitoring data of veterinary medicinal product residues and other substances in animal products (EFSA, 2014b, 2015b, 2016b, 2017b, 2018b) and in the European monitoring of pesticide residues in food (EFSA, 2014a, 2015a, 2016a, 2017a, 2018a). Therefore, the first question, if there are non-compliant residue data found, is negatively answered and Q3 needs to be answered first for all substances. This question relates to indications for use in production systems for food producing animals.

Eleven carbamates were included in the Dutch monitoring. These carbamates were reported not to be detected in meat and egg products. Therefore, there are no indications for use and this resulted in a 'low priority' for these substances. Furthermore, 24 other carbamates are listed as obsolete, which means no longer manufactured or marketed for crop protections use, in the Pesticide Manual (Turner, 2015) or in the Pesticide Properties Database (https://sitem.herts.ac.uk/aeru/ppdb/en/atoz.htm). This is also a clear indication that these carbamates are not expected to be used and therefore Q3 was negatively answered, which resulted in a 'low priority' for these substances.

Some carbamates will break down into other carbamates. For these carbamates, monitoring data of the break down products were used to answer the question if there are indications for use of this substance. Furathiocarb, benfuracarb and carbosulfan all break down into carbofuran. Thiodicarb breaks down into methomyl. These breakdown products were all monitored and not found in the Dutch monitoring data of meat and egg products. Therefore, these four carbamates were also classified as 'low priority'.

Dimethacarb, dimetan were not listed in the Pesticide Properties Database, no product use was found for the US and other countries. These products were also not available on alibaba.com. Therefore, it was concluded that there are no indications for use in production systems for food producing animals, resulting in a 'low priority' for these substances.

For butoxycarboxim, burocarboxim and alanycarb, no US products were found and only limited use in Asia. These substances are available as insecticide on alibaba.com. However, they were not found in the European pesticide monitoring data of 2012-2016 (EFSA, 2014a, 2015a, 2016a, 2017a, 2018a), where between 5,000 and 50,000 measurements were performed per substance. Therefore, it was concluded that there are no indications for use, which resulted in a 'low priority' for these substances.

Pyrolan, dicresyl and CPMC were not listed in the different pesticide databases, no current uses were found, no registrations were found in US, Asia and Australia. Literature in Scopus resulted in only few hits (7-19 hits) of mainly old data from the 1970s. These papers suggest that the substance was used previously. It is not clear whether they are currently used, but since they are available on alibaba.com, Q3 was answered positively. The literature found did not describe human health risks. Therefore, Q2 was answered with unknown, which resulted in a 'high priority' of these three substances. An asterisk is added to highlight that these substances only have the classification 'high priority' because there is no data or information available to answer the questions.

Benomyl is available in the US and Asia and on alibaba.com; therefore it could be used and Q3 is answered positively. In order to answer Q2, EFSA reports and FAO/WHO reports were used. It has

been demonstrated that benomyl and its metabolites do not accumulate in animal tissues (JMPR, 1975) and that no risk for consumers was identified (EFSA, 2010). A human health risk due to residues of benomyl is scientifically proven to be negligible, which resulted in 'medium priority' for this substance.

Bendiocarb, isoprocarb and fenobucarb are registered in Asia, bendiocarb also in US and Australia, and they are available as insecticide on alibaba.com. Pesticide residue data in Europe showed a few measurements above LOQ out of 5,000-50.,00 measurements. Searches on Scopus showed data on among others residues in crops and drinking water. Therefore, indications for possible use of these substances in production systems for food producing animals cannot be neglected (Q3 is answered positively). Then Q2, is a human health risk due to residues of this substance scientifically proven to be absent or negligible, needs to be answered. No robust assessments from trustworthy organizations such as EFS, JECFA or WHO were available. Therefore, Q2 was answered with unknown, which resulted in a 'high priority' for these substances.

Table 4 *Evaluation of carbamates in decision tree I.*

	Q1: Where any non-compliant residue data of the substance found in the last 5 years?	Q3: Are there indications for use of this substance in production systems for food producing animals?	Q2: Is a human health risk due to residues of this substance scientifically proven to be absent or negligible?	General conclusion
3-Hydroxy carbofuran	N	N, not found in monitoring	→	low
Aldicarb	N	N, not found in monitoring	→	low
Aldicarb-sulfone	N	N, not found in monitoring	→	low
Aldoxycarb (aldicarb-sulfoxide)	N	N, not found in monitoring	→	low
Carbaryl	N	N, not found in monitoring	→	low
Carbofuran	N	N, not found in monitoring	→	low
Ethiofencarb	N	N, not found in monitoring	→	low
Ethiofencarb-sulfone	N	N, not found in monitoring	→	low
Ethiofencarb-sulfoxide	N	N, not found in monitoring	→	low
Propoxur	N	N, not found in monitoring	→	low
Allyxycarb	U	N, obsolete	→	low
Aminocarb	U	N, obsolete	→	low
Bufencarb	U	N, obsolete	→	low
Butacarb	U	N, obsolete	→	low
Carbanolate	U	N, obsolete	→	low
Cloethocarb	U	N, obsolete	→	low
Decarbofuran	U	N, obsolete	→	low
Dioxacarb	U	N, obsolete	→	low
EMPC	U	N, obsolete	→	low
Fenethacarb	U	N, obsolete	→	low
Hyquincarb	U	N, obsolete	→	low
Isolan	U	N, obsolete	→	low
Metolcarb	U	N, obsolete	→	low
Mexacarbate	U	N, obsolete	→	low
Nitrilacarb	U	N, obsolete	→	low
Promacyl	U	N, obsolete	→	low
Promecarb	U	N, obsolete	→	low
Pyramat	U	N, obsolete	→	low
Tazimcarb	U	N, obsolete	→	low
Thiocarboxime	U	N, obsolete	→	low
Thiofanox	U	N, obsolete	→	low
Trimethacarb	U	N, obsolete	→	low
XMC	U	N, obsolete	→	low
Xylylcarb	U	N, obsolete	→	low

	Q1: Where any non-compliant residue data of the substance found in the last 5 years?	Q3: Are there indications for use of this substance in production systems for food producing animals?	Q2: Is a human health risk due to residues of this substance scientifically proven to be absent or negligible?	General conclusion
Benfuracarb	U	N, breakdown product monitored and not found	→	low
Carbosulfan	U	N, breakdown product monitored and not found	→	low
Furathiocarb	U	N, breakdown product monitored and not found	→	low
Thiodicarb	U	N, breakdown product monitored and not found	→	low
Alanycarb	U	N, no indications for use	→	low
Butocarboxim	U	N, no indications for use	→	low
Butoxycarboxim	U	N, no indications for use	→	low
Dimetan	U	N, no indications for use	→	low
Dimethacarb	U	N, no indications for use	→	low
CPMC	U	U	U	high*
Dicresyl	U	U	U	high*
Pyrolan	U	U	U	high*
Benomyl	U	Y, could be used	Y, by EFSA and FAO/WHO	Medium
Bendiocarb	U	Y, could be used	U	High
Fenobucarb	U	Y, could be used	U	High
Isoprocarb	U	Y, could be used	U	High

Y; yes, N; no, U; unknown

* these substances only have the classification of high priority because there is no data or information available to answer the questions

3.3.2 Prioritization using decision tree II

An overview of the evaluation of carbamates in decision tree II can be found in Table 5. Of the four carbamates approved in the EU, only methomyl is not approved in the Netherlands. All four carbamates have an MRL for products of animal origin (Q1).

Methomyl is included in the Dutch monitoring, but there were no non-compliant data reported for methomyl (Q2). Furthermore, there were also no non-compliant data found for methomyl in feed (Q3). Therefore, it can be concluded that this substance has a 'low priority'.

Methiocarb, oxamyl and pirimicarb were not found in RASFF notifications and European monitoring data of veterinary medicinal product residues and other substances in animal products (EFSA, 2014b, 2015b, 2016b, 2017b, 2018b) and in the European monitoring of pesticide residues in food (EFSA, 2014a, 2015a, 2016a, 2017a, 2018a). These substances are not included in the Dutch monitoring program. Therefore, it was unknown if there were any non-compliant data, since it is not clear whether these substances are included in the monitoring programs of other EU MS (Q2).

Oxamyl, pirimicarb and methiocarb are not included in the Dutch monitoring on feed and RASFF showed no non-compliances in feed. Therefore, it was concluded that non-compliant data is unknown for these substances in feed (Q3). Next, EFSA and FAO/WHO reports were used to answer Q4, if transfer of the substance to edible tissues is possible. For methiocarb, old metabolism studies in livestock were considered not reliable by EFSA. Based on residue trials in currently available feed items, which showed all undetectable levels, it was concluded that representative use does not give rise to significant residues in animal products (EFSA, 2006). Metabolism and feeding studies in livestock animals indicated that total methiocarb residues in ruminant commodities will be below the LOD (JMPR, 1999). For oxamyl, EFSA concluded that oxamyl and/or its metabolites will not

accumulate in animal tissue (EFSA, 2005a). For pirimicarb, EFSA concluded that monitoring of animal products is not needed regarding consumer safety, because in metabolism studies no carbamate residues were found in edible tissues (EFSA, 2005b).

Therefore, no transfer to edible tissues is to be expected for these substances and Q4 can be answered negatively. As a result, methiocarb, oxamyl and pirimicarb have a 'low priority'.

Table 5 *Evaluation of carbamates in decision tree II.*

Carbamates	**Q1. Is there an ML, MRL or action limit for this substance in animal tissue?**	**Q2. Were any non-compliant data of the substance found in the last five years?**				**Q3. Were any non-compliant data of the substance found in feed in the last five years?**			**Q4. Is transfer of the substance to edible tissues possible?**	**General conclusion**
	(EC) 396/2005	*EFSA reports*[1]	*RASFF*[2]	*KAP data*[3]	*Conclusion*	*RASFF feed*[4]	*KAP data*[5]	*Conclusion*		*Priority*
Methiocarb	Y	N	N	U	U	N	U	U	N[6]	low
Oxamyl	Y	N	N	U	U	N	U	U	N[7]	low
Pirimicarb	Y	N	N	U	U	N	U	U	N[8]	low
Methomyl	Y	N	N	N	N	N	N	N	→	low

[1] EFSA reports for 2012-2016 on the results from the monitoring of veterinary medicinal product residues and other substances in live animals and animal products (EFSA, 2014b, 2015b, 2016b, 2017b, 2018b)

[2] RASFF data, 2012-2016 (https://webgate.ec.europa.eu/rasff-window/portal/)

[3] KAP data, 2012-2017 (www.chemkap.rivm.nl)

[4] RASFF data. 2012-2018 ((https://webgate.ec.europa.eu/rasff-window/portal/)

[5] KAP data, 2012-2017, (www.chemkap.rivm.nl)

[6] (JMPR, 1999; EFSA, 2006)

[7] (EFSA, 2005a)

[8] (EFSA, 2005b)

3.4 NSAIDs

In total, 31 NSAIDs were included in the prioritization. The NSAIDs that are registered for use and as such included in Regulation (EU) 37/2010 were prioritised using decision tree III (n=13). The NSAIDs that are not mentioned in Regulation (EU) 37/2010 and therefore not allowed for use in food producing animals, were prioritized using decision tree I (n=18). The total list of NSAIDS evaluated and the reason for inclusion in the evaluation can be found in Annex 1.

3.4.1 Prioritization using decision tree I

This decision tree was used on four different animal products: bovine and porcine products, poultry meat and eggs. In Table 6, the priority for each animal product is listed. The rationale for these conclusions can be found in Annex 6.

Table 6 *Prioritization of NSAIDs per animal product using decision tree I.*

Substance	Bovine	Porcine	Poultry	Egg
Cimicoxib	Low	Low	Low	Low
Eltenac	Low	Low	Low	Low
Fenbufen	Low	Low	Low	Low
Flufenamic acid	Low	Low	Low	Low
Grapiprant	High*	High*	High*	High*
Ibuprofen	Medium	Medium	Low	Low
Indoprofen	Low	Low	Low	Low
Mavacoxib	Low	Low	Low	Low
Meclofenamic acid	Low	Low	Low	Low
Mefenamic acid	Medium	Medium	Low	Low
Naproxen	Medium	Medium	Low	Low
Niflumic acid	Low	Low	Low	Low
Nimesulide	High*	High*	High*	High*
Phenylbutazone (FBZ)/Oxy-FBZ	High	High	Low	Low
Piroxicam	Low	Low	Low	Low
Propyphenazone	Low	Low	Low	Low
Robenacoxib	Low	Low	Low	Low
Tolmetin	Low	Low	Low	Low

High*: Not much known about the substance in food producing animals, therefore a risk because of use cannot be ruled out. However, use is less likely compared to substances with medium priority.

Q1 selects the substances for which non-compliant results were reported. Of the 18 listed substances, 12 are monitored in the national monitoring plan. The remaining 6 are eltenac, nimesulide, cimicoxib, grapiprant, robenacoxib and mavacoxib. For the 12 monitored substances, several non-compliant results were found in beef and pork based on the European monitoring data of veterinary medicinal product residues and other substances in animal products for the period 2012-2016 (EFSA, 2014b, 2015b, 2016b, 2017b, 2018b). Based on the KAP database using data of 2012, 2013 and 2017, naproxen was found in imported red meat (1 sample in 2017). Over the period of 2012 – 2016, there was 1 RASFF notification for naproxen in horse meat from Brazil and multiple notifications for phenylbutazone in different horse meat products.

For bovine products, non-compliances were found for the substances phenylbutazone, ibuprofen, mefenamic acid and naproxen (Q1 was answered positively). Interestingly, these are the substances that are recommended by the CRL to include in the national plan analysis (BVL-CRL et al., 2007). In pork, only ibuprofen was reported as non-compliant. For these substances, Q2, regarding the possible human health effects due to residues, needed to be answered. This question was evaluated using EFSA opinions. For phenylbutazone, human health effects cannot be excluded (EFSA, 2013). Therefore, Q2 was answered negatively and this substance was seen as a 'high priority' substance. Since the other substances (ibuprofen, mefenamic acid and naproxen) are openly available to humans in supermarkets and drugstores and are often taken in on a daily basis, a human health risk due to consumption of animal products containing residues of these substances was considered negligible and Q2 is answered positively. These substances thus were a 'medium priority'.

The other 8 monitored substances had no non-compliant results in any of the animal products evaluated and Q1 was answered negatively. For these substances, Q3 regarding the indications of use in production systems for food producing animals, needed to be answered. As no non-compliances were found for these substances in beef, pork or poultry meat, even though they were monitored between 2012 and 2016, it can be concluded that these substances are not likely to be used. Therefore, Q3 is answered negatively for these substances in beef, pork and poultry, resulting in a low priority. An exception is made for phenylbutazone, mefanamic acid and naproxen in pork, since there are indications of use in food producing animals (non-compliances in bovine and horse). This results in a 'medium priority' for these substances in pork. Since it is less likely that products for cows, horses and pigs, all mammals, are used on poultry, non-compliances in these animal products are not seen as an indication of use in poultry. This results in 'low priority' for these substances in poultry.

Egg is not monitored in the national monitoring plan for NSAIDs, therefore no data on non-compliances is available and Q1 is answered with 'unknown' for all substances. Since there were no non-compliances found in poultry, Q3 is answered negatively for egg as well, resulting in 'low priority' in egg for the 12 monitored substances.

The remaining 6 substances are not monitored in any of the products, therefore Q1 is answered as 'unknown' and Q3 needed to be answered. All these substances have registrations (CBG-MEB) for companion animals, but still need to be prescribed by a vet. Indications of use were evaluated based on their availability online (ebay, alibaba).

Of these 6 substances, only nimesulide and grapiprant are found to be available online. The other 4 do not seem to be available besides as registered veterinary medical products for companion animals, resulting in a 'low priority'. Three of these 4 substances are part of the coxib class, just like firoxocib, which has an MRL in food producing animals. It is less likely that other coxib drugs, only prescribed for companion animals, are used if an MRL substance is available, supporting the 'low priority' conclusion.

For nimesulide and grapiprant, Q2 needed to be answered. In Europe, the use of human nimesulide products has been restricted because of side effects affecting the liver (EMA, 2012) and Q2 is answered negatively resulting in a high priority classification. A human health risk due to residues of grapipant in animal products is however unknown. The fact not much is known about these substances in food producing animals results in 'high priority'. The probability that nimesulide and grapipant are used is not very high, because they are only registered for companion animals. Therefore, these substances are given a 'high* priority', to indicate the difference. (EMA, 2012).

3.4.2 Prioritization using decision tree III

As mentioned in section 2.5.2, question 1 of this tree is not applicable to NSAIDs. Therefore, none of the authorised NSAIDs will have a high priority. This decision tree was used on 13 NSAIDs in four different animal products: bovine products, porcine products, poultry meat and eggs. In Table 7, the priority for each matrix is listed. The rationale for these conclusions can be found in Annex 7.

Table 7 *Prioritization of NSAIDs per animal product using decision tree III.*

Substance	Bovine	Porcine	Poultry	Egg
Acetylsalicylic acid	Low	Low	Low	Start survey
(Na) Salicylaat (salicylic acid)	Low	Low	Low	Start survey
(Al) Salicylaat (salicylic acid)	Medium	Low	Low	Start survey
Carprofen	Medium	Low	Low	Start survey
Diclofenac	Medium	Medium	Medium	Start survey**
Firocoxib	Low	Low	Low	Start survey
Flunixin / OH-flunixin	Medium	Medium	Medium	Start survey**
Ketoprofen	Low	Low	Low	Start survey
Meloxicam	Medium	Medium	Low	Start survey
Metamizol (MAA)	Medium	Medium	Medium	Start survey**
Paracetamol	Medium*	Low	Low	Start survey
Tolfenamic acid	Medium	Medium	Medium	Start survey**
Vedaprofen	Low	Low	Low	Start survey

* Based on non-compliant result in milk

** Non-compliances found in poultry meat

Q2 was evaluated based on the presence or absence of an MRL for the animal species studied. Of the substances in Table 7, acetylsalicylic acid, ketoprofen and paracetamol are included in Regulation (EU) 37/2010, but are listed as 'no MRL necessary', while at the same time this classification is limited to specific animal species. For these substances, Q2 was answered negatively for all animal products; however the substances do fit in this tree since they are included in Regulation (EU) 37/2010.

For the substances with an MRL in Table 1 of the Annex of Regulation (EU) 37/2010, Q3 was answered regarding whether non-compliances were found in the animal product. For sodium (Na) salicylate and aluminium (Al) salicylate, the same marker is used (salicylic acid). Since no difference can be made, monitoring results (non-compliances) for salicylic acid were used for both substances. Al-salicylate does have an MRL, while Na-salicylate doesn't. As a result, the questions in the decision tree were answered differently resulting in a different classification for both substances in bovine. Of the substances that have an MRL for bovine and porcine products, all were found non-compliant, resulting in a medium priority for all these substances in that animal product.

For all substances with no MRL in the animal product (Q2 is No), subsequent questions on possible use and withdrawal times were answered. For bovine, this resulted in a medium priority for bovine (milk) and for poultry all four substances were classified as medium priority. For paracetamol, regular use was established in pigs. However, since the withdrawal time for this substance is 0 days, the substance was classified as a low priority.

NSAIDs in egg are not analysed in the current national plan, therefore it is unknown whether non-compliances are to be expected. Q4 was answered based on EU registrations for laying hens and FIDIN sales data. Since all substances are available using cascade, the conclusion is 'unknown', resulting in the need to start a survey on the use of these substances in laying hens. The non-compliant results in poultry give an indication of the most likely substances that could be found in egg, which are indicated with an asterisk in Table 7.

4 Discussion

In this study, four groups of substances were prioritised using predefined decision trees: antibiotics, antiparasitics, carbamates and NSAIDS. The decision trees were tested previously with some substances (van Asselt et al., 2018b). In the current study, a more comprehensive set of substances was prioritised into low, medium and high priority for inclusion in the national monitoring programs. It should be kept in mind that apart from risk-based monitoring, some of the monitoring will need to be done on a random basis in order to ensure that hazards are not overlooked.

Traditionally, the absence of an MRL has been a reason not to include certain substance/matrix combinations in the monitoring program. However, substances might be used under cascade, for example in laying hens due to the limited availability of veterinary drugs for this animal species. The groups of substances previously included in the national monitoring program were based on requirements defined in Directive 96/23/EC annex II. In particular for egg, the EU demands were very limited as there was no requirement to monitor anthelmintics, carbamates and NSAIDs in this matrix. A recent report on occurrence of flubendazole (<MRL) in egg from a private monitoring program, prompted the extension of the monitoring program with anthelmintics in eggs. This indicates that it is important to start with a broad list of substances and prioritise these with the established decision trees. The results in this study indicate that the decision trees in general worked well to prioritise substances. In some cases, however, the decision trees were not strictly followed. For example, for antiparasitics, decision tree III did not foresee in the possible exposure of animals through the environment. Therefore, it was decided that if there are no MRLs for the animal species (Q2), Q3 on non-compliant results was answered nevertheless.

Furthermore, in contrast to the established decision trees in which questions could only be answered with yes and no, the current study showed that in some instances it was more informative to add 'unknown' as a possible answer to the questions. This was particularly the case for substances not included in monitoring. Absence of non-compliances for such substances is actually the result of lack of data and should be interpreted differently from absence of non-compliances of substances that are included in routine monitoring. So, in case a substance is not included in monitoring, this was indicated with 'unknown' instead of 'no' in order to distinguish between substances that were monitored but not found and substances for which there was a lack of data. For the latter group, substances sometimes ended in the high priority group due to a lack of data in the monitoring results and/or a lack of information on possible human health effects. This was indicated with an asterisk to distinguish this classification from substances that were classified as medium or high priority based on available data. Decision tree III does provide the possibility to answer 'unknown' when answering the question on usage, resulting in a recommendation for a survey on possible use. This led to the recommendation to investigate the occurrence of the authorised NSAIDs in eggs. Such a survey could focus on investigating the possible use of the specified NSAIDs, or could focus on the occurrence of drug residues in eggs.

In order to answer the questions of the decision trees, many data were needed, such as monitoring data, data on use of veterinary medicines and data on withdrawal periods. These data were not always freely available. The new Regulation (EU) 2019/6 indicates that an EU-wide database containing veterinary medicinal products authorized within the Union should be established. This will likely facilitate the product availability evaluation, which within this study was still executed by accessing individual national databases. Additionally, Summary of Product Characteristics (SPCs) will be harmonised, which may impact withdrawal times. Hitherto, withdrawal times for the same product could differ between countries.

4.1 Discussion on antibiotics

Only the antibiotics classified by WHO as HPCI antimicrobials will end up as high priority substances according to the currently applied methodology. It should be noted this is not reflecting the probability of residues occurring in animal products. More likely the opposite is true, since increasing awareness on the associated resistance risks and restrictive policies with respect to the veterinary use of these antibiotics resulted in strong reduction in use. However, the decision trees were drafted based on the definition of risk as a combination of probability and severity. Therefore, although the probability of occurrence may be low, the severity of the presence of these antibiotics is high and these substances thus are classified as high priority.

The non-HPCI antibiotics will either be classified as medium or low. Intuitively, this may feel like an underestimation of the situation for substances that are regularly encountered in monitoring programs (and subsequently classified as medium priority), but since MRLs have been established for these substances, their human health risks have been assessed as negligible.

Some substances are not comprehensively included in monitoring programs, which complicated the evaluation, since the absence of non-compliances could be due to a lack of monitoring data. For antibiotics, this concerns substances like avilamycin, bacitracin, novobiocin, rifaximin, virginiamycin, florfenicol and spectinomycin. Partially this occurs from the fact that the analysis is traditionally performed with microbial screening methods, simply lacking sufficient sensitivity for several miscellaneous antibiotics (not belonging to the main classes tetracyclines, macrolides, beta-lactams, sulfonamides, quinolones or aminoglycosides). For most of these antibiotics, their use is very limited, and they are not expected to cause (currently overlooked) residue issues. Florfenicol and spectinomycin, however, are classified as medium priority for multiple matrices in our evaluation. These are currently not covered by the Dutch national monitoring program, but considering the classification as medium priority, it is recommended to include these in the NPR.

4.2 Discussion on antiparasitics

With respect to the antiparasitics evaluated according to decision tree I, fipronil should be mentioned. This substance caused a major incident in 2017 (outside the timeframe set for the current evaluation) when it was found to be illegally applied for treatment of red mite in laying hens (facilities). This affair underscores the necessity to look beyond the veterinary drugs approved for animal production and prompted us to include drugs commonly applied on companion animals as well. Several of these are used as agricultural pesticides as well, complicating matters in terms of exposure (use as animal treatment or environmental exposure) and responsibility (animal drugs and pesticide are traditionally/analytically separate worlds). Our approach resulted in a list of 19 antiparasitics (including fipronil) not included in Regulation (EU) 37/2010 that could potentially be used in livestock animals. Only four of these antiparasitics were classified as low priority. Additional monitoring of the other antiparasitics should yield more insight into the possible presence of these substances in bovine, porcine, poultry and eggs.

With respect to the antiparasitics evaluated according to decision tree III, besides some of the traditional benzimidazoles and avermectins, only a limited number of substances were classified as medium priority. It should be noted however that in particular for poultry and eggs, the monitoring of these substances has been almost non-existent. Nematode and cestode infections do occur in poultry; in particular poultry in free-range production systems may be affected. Only a very limited number of the anthelmintics have an MRL in poultry and/or egg, and flubendazole and fenbendazole are currently the only registered options for treatment. Both have a withdrawal time of 0 days, suggesting residue levels will not exceed the MRL, but substantiation with monitoring data is recommended to confirm the low priority classification. Also the risk of environmental contamination through pesticide use deserves particular attention, especially if substances are persistent. The possible exposure of animals through the environment was not included in decision tree III. As a consequence, if environmental exposure

was deemed possible, Q3 (on non-compliant results) was always included in the evaluation even though Q2 was answered negatively.

Finally, the recent establishment of MRLs for sisapronil (bovine and caprine species) and fluralaner (poultry) should be taken into account. Sisapronil is a new phenylpyrazole (as is fipronil) intended for use as a long-acting injectable ectoparasiticide. So far, no pharmaceutical product has been registered, but it is recommended to include this substance in the analytical scope and monitoring. Fluralaner is an isoxazoline recently introduced in 2017 for the treatment of red mite in poultry. The MRL in egg is exceptionally high (1500 µg/kg) to justify a 0 days withdrawal time for eggs. Based on residue depletion data, MRL exceedance is unlikely to occur, but substantiation with monitoring data is recommended as fluralaner is persistent in the environment and accumulation in laying hens might occur.

4.3 Discussion on carbamates

For prioritizing carbamates, no non-compliant residue data were found in the monitoring data of the last 5 years. However, only 11 out of 54 carbamates were included in the Dutch monitoring. Most carbamates (50) are not approved in Europe and were therefore evaluated using decision tree 1. Several sources were needed to identify possible use of these substances in production systems for food producing animals. Apart from the monitoring data in animal products, other information was used to prioritise the substances: whether the substance was listed as obsolete, the substance's availability and registration in other countries, the online availability (e.g. alibaba.com) and whether residues were found in other food products (fruits and vegetables). For some carbamates, the sources mentioned above did not give information on possible use. Furthermore, no robust assessments from trustworthy organizations were available to conclude on the possible human health risks. This resulted in high priority of these substances. An asterisk was added to distinguish this classification (based on a lack of data) from substances that were prioritised based on available data.

Carbamates are insecticides or acaricides and can also be used as antiparasitic agents, because of their inhibiting activity on cholinesterases. Benomyl was listed as a carbamate and therefore included in the prioritization. This resulted in a medium priority, because the use of benomyl is unknown and a human health risk is negligible based on official reports of EFSA and FAO/WHO. However, benomyl is a benzimidazole with a carbamate group, which has no cholinesterase inhibitor activity. As such, its use as antiparasitic agent is less likely, but since it belongs to the carbamates a possible use cannot be excluded.

4.4 Discussion on NSAIDs

For prioritizing authorised NSAIDs, no monitoring data for eggs were available and indications for use were unknown. This resulted in a recommendation to start a survey for all the NSAIDs evaluated using decision tree III. According to this decision tree, the survey should focus on indications for use of NSAIDs in laying hens. Alternatively, a survey could be organised on the presence of these substances in eggs. For some of these NSAIDs (diclofenac, flunixin, metamizol and tolfenamic acid), non-conformities were found in poultry meat, which may give them a higher priority for inclusion in a survey program.

Within the group of NSAIDs, Na-salicylate and Al-salicylate have the same marker residue (salicylic acid). However, legislation for these two substances is different (Regulation (EU) 37/2010). For prioritization, the substance itself and legislation thereof was used to evaluate the different products. However, in case a non-compliance is found for salicylic acid, both Al-salicylate and Na-salicylate need to be taken into account. Therefore the results should be considered with care. For Na-salicylate no MRL is required in bovine and porcine (only in turkey), in the end resulting in a low priority for these products based on withdrawal time. Al-salicylate does have an MRL for bovine and since non-compliances were found in milk, Q3 was answered positively resulting in a medium priority.

Since both Na- and Al-salicylate have the same marker residue, a worst case approach can be used setting the highest found priority for both substances. This would mean a medium priority in bovine both for Na-salicylate as Al-salicylate.

Beside the NSAIDs included in this study, other NSAIDs can also have a potential risk of illegal use. These are the NSAIDs which are either commercially available for humans, effective but withdrawn or are combined with other NSAIDs. A few examples are the NSAIDs ramifenazon, refecoxib, celecoxib and flurbiprofen. However, in our study, we limited our research to the NSAIDs that are available for animals (both livestock and companion animals).

5 Conclusions and recommendations

Since the new Regulation (EU) 2017/625 will apply from December 14, 2019, MS need to establish risk based monitoring plans and underpin these plans. In this study, previously established decision trees were used to prioritise substances to be included in the Dutch national Plan for Residues (NPR). In the current study, four groups of substances were evaluated for this: antibiotics, antiparasitics, carbamates and NSAIDs. These groups were based on the draft Annex of Regulation (EU) 2017/625 (11987-2017 Rev1). The classification of these groups changed over time. In order to draft a risk based monitoring program for this regulation, it is thus recommended to check the Annex to see if all substances required for monitoring are covered.

The research performed in this study showed that the decision trees, with some small adjustments, as indicated in the discussion session, work well to prioritise residues of veterinary drugs in animal products. For each of the four groups evaluated (antibiotics (n=68), antiparasitics (n=52), carbamates (n=54) and NSAIDs (n=31)), several substances were classified as medium or high priority. For antibiotics, 18 substances received a high priority. A medium priority was obtained for 29 substances in bovine products, 20 substances in porcine products and 15 substances in poultry and eggs. For the authorised antiparasitics, 14 substances were classified as medium priority for bovine, 11 for porcine, 2 for poultry and 1 for eggs. For the unauthorised antiparasitics, 14 substances were classified as high priority for all animal products, primarily due to a lack of data and 1 substance was classified as medium priority. The authorised carbamates (4 in total) were classified as low priority. For the unauthorised carbamates (n=50), 6 substances were classified as high priority (half of which due to a lack of data) and 1 substance as medium priority. For poultry meat, porcine and bovine products, 4, 5 and 8 authorised NSAIDs received a medium classification. For eggs, there was a lack of data and a survey was recommended for all 13 substances. For bovine and porcine products, three unauthorised NSAIDs were classified as high priority and three as medium priority. For poultry and eggs, only two unauthorised NSAIDS were classified as high priority, no substances were classified as medium priority.

The following recommendations are given based on the results of this study:

- Include the substances with a medium and high priority in the national monitoring program. In case existing screening methods are used, it is not necessary to remove the low priority substances from the analytical scope as long as the medium and high priority substances are included. As indicated previously, substances were sometimes classified as high priority due to a lack of data. In such cases it is recommended to first perform a survey on these substances to obtain more information to substantiate the classification.
- Regularly evaluate the prioritisation of the substances using updated information from the results of monitoring programs, figures on veterinary drug use, and registrations of new substances. Besides this, part of the monitoring program should concern broad and non-targeted screening, in order to identify potential additional emerging hazards. Output of such broad screening can provide additional information for updating the routine monitoring programs.
- Prioritise the currently evaluated groups of substances not only for bovine, porcine and poultry products, but for all animal products indicated in Regulation (EU) 2017/625. The other substances included in this regulation can be prioritised analogous to the approach used for the four groups of substances prioritised in this report. Once the high priority substances are known for the various animal products, the action plan as proposed previously (van Asselt et al., 2018c) can be used to come to a risk-based monitoring program.
- Exchange experiences with risk-based monitoring programs with other EU MS. This will improve the national monitoring programs and finally may harmonise these programs at EU level.
- Incorporate regular ‘random’ surveys to prevent bias from entering the prioritisation scheme (higher probability of finding high risk chemicals if that is what the monitoring programme focuses on) and prevent overlooking (emerging) hazards.
- Keep an eye on new developments relevant for prioritising hazards, such as new veterinary drugs used or new methodologies to obtain input data.

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Annex 1 List of NSAIDs for prioritisation

NSAIDs	Included based on
Na-Salicylate (salicylic acid)	37/2010 substance
Al-Salicylate (salicylic acid)	37/2010 substance
Acetylsalicylic acid	37/2010 substance
Carprofen	37/2010 substance
Diclofenac	37/2010 substance
Fenbufen	currently in NP
Phenylbutazone	CRL recommendation
Firocoxib	37/2010 substance
Flufenamic acid	currently in NP
Flunixin	37/2010 substance
Ibuprofen	CRL recommendation
Indoprofen	currently in NP
Ketoprofen	37/2010 substance
Meclofenamic acid	currently in NP
Mefenamic acid	CRL recommendation
Meloxicam	37/2010 substance
Metamizol (MAA)	37/2010 substance
Naproxen	CRL recommendation
Niflumic acid	currently in NP
Paracetamol	37/2010 substance
Piroxicam	currently in NP
Propyphenazone	currently in NP
Tolfenamic acid	37/2010 substance
Tolmetin	currently in NP
Vedaprofen	37/2010 substance
Eltenac	registered in NL/EU for companion animals
Nimesulide	registered in NL/EU for companion animals
Cimicoxib	registered in NL/EU for companion animals
Grapiprant	registered in NL/EU for companion animals
Robenacoxib	registered in NL/EU for companion animals
Mavacoxib	registered in NL/EU for companion animals

Annex 2 Prioritization of antibiotics using decision tree III

Table A2.1 *Prioritisation of antibiotics in bovine products.*

Itallics: not commonly included in scope	Q1: is this an essential antimicrobial for humans?	Q2: Have MRLs been set for this substance in this animal species?	Q3: were any non-compliant residue data of the substance found in the last five years?				Q4: Is the substance regurlarly used in this animal species?		Q5: Do drugs with this active substance have a long withdrawal period?		Conclusion priority
Substance	**Conclusion Q1**	**Conclusion Q2**	**KAP**	**RASFF**	**EFSA**	**Conclusion Q3**	**Sda (>50000 DDDA)**	**Conclusion Q4**	**Withdrawal time**	**Conclusion Q5**	**Overall conclusion**
Amoxicilline	N	Y			Y	Y	→	→	→	→	medium
Ampicilline	N	Y			Y	Y	→	→	→	→	medium
Apramycin	N	Y				N	N	N	→	→	low
Avilamycine	N	N	→	→	→	→	N	N	→	→	low
Bacitracine	N	Y[#]				U	N	N	→	→	low
Baquiloprim	N	Y				N	N	N	→	→	low
Benzylpenicilline/penethamate	N	Y	Y		Y	Y	→	→	→	→	medium
Cefacetril	N	Y[#]				N	N	N	→	→	low
Cefalexine	N	Y			Y*	Y*	→	→	→	→	medium*
Cefalonium	N	Y[#]			Y	Y	→	→	→	→	medium
Cefapirin	N	Y				N	Y	Y		Y	medium
Cefazolin	N	Y[#]			Y*	Y*	→	→	→	→	medium*
Cefoperazon	Y	→	→	→	→	→	→	→	→	→	high
Cefquinome	Y	→	→	→	→	→	→	→	→	→	high
Ceftiofur	Y	→	→	→	→	→	→	→	→	→	high
Chloortetracycline	N	Y		Y	Y	Y	→	→	→	→	medium
Cloxacilline	N	Y			Y*	Y*	→	→	→	→	medium*
Colistine	Y	→	→	→	→	→	→	→	→	→	high
Danofloxacine	Y	→	→	→	→	→	→	→	→	→	high
Dicloxacilline	N	Y				N	N	N	→	→	low
Difloxacin	Y	→	→	→	→	→	→	→	→	→	high

Itallics: not commonly included in scope	Q1: is this an essential antimicrobial for humans?	Q2: Have MRLs been set for this substance in this animal species?	Q3: were any non-compliant residue data of the substance found in the last five years?				Q4: Is the substance regurlarly used in this animal species?		Q5: Do drugs with this active substance have a long withdrawal period?		Conclusion priority
Substance	Conclusion Q1	Conclusion Q2	KAP	RASFF	EFSA	Conclusion Q3	Sda (>50000 DDDA)	Conclusion Q4	Withdrawal time	Conclusion Q5	Overall conclusion
Dihydrostreptomycine	N	Y			Y	Y	→	→	→	→	medium
Doxycycline	N	Y	Y		Y	Y	→	→	→	→	medium
Enrofloxacin	Y	→	→	→	→	→	→	→	→	→	high
Erytromycine	Y	→	→	→	→	→	→	→	→	→	high
Fenoxymethylpenicilline	N	N	→	→	→	→	N	N	→	→	low
Florfenicol	N	Y			Y	Y	→	→	→	→	medium
Flumequine	Y	→	→	→	→	→	→	→	→	→	high
Gamitromycine	Y	→	→	→	→	→	→	→	→	→	high
Gentamicine	N	Y	Y		Y	Y	→	→	→	→	medium
Josamycine	N	N	→	→	→	→	N	N	→	→	low
Kanamycine	N	Y			Y	Y	→	→	→	→	medium
Lincomycine	N	Y			Y	Y	→	→	→	→	medium
Marbofloxacine	Y	→	→	→	→	→	→	→	→	→	high
Nafcillin	N	Y				N	N	N	→	→	low
Neomycine	N	Y	Y		Y	Y	→	→	→	→	medium
Novobiocine	N	Y[#]				U	N	N	→	→	low
Oxacilline	N	Y				N	N	N	→	→	low
Oxolinic acid	N	Y				N	N	N	→	→	low
Oxytetracycline	N	Y		Y	Y	Y	→	→	→	→	medium
Paromomycine	N	Y				N	Y	Y	20 days	Y	medium
Pirlimycine	N	Y				N	N	N	→	→	low
Rifaximine	N	Y[#]				U	N	N	→	→	low
Sarafloxacin	Y	→	→	→	→	→	→	→	→	→	high
Spectinomycine	N	Y			Y	Y	→	→	→	→	medium
Spiramycine	Y	→	→	→	→	→	→	→	→	→	high
Streptomycine	N	Y			Y	Y	→	→	→	→	medium
Sulfadiazine	N	Y			Y	Y	→	→	→	→	medium
Sulfachloorpyridazine	N	Y				N	N	N	→	→	low
Sulfaclozine	N	Y				N	N	N	→	→	low

Italics: not commonly included in scope	Q1: is this an essential antimicrobial for humans?	Q2: Have MRLs been set for this substance in this animal species?	Q3: were any non-compliant residue data of the substance found in the last five years?				Q4: Is the substance regurlarly used in this animal species?		Q5: Do drugs with this active substance have a long withdrawal period?		Conclusion priority
Substance	**Conclusion Q1**	**Conclusion Q2**	**KAP**	**RASFF**	**EFSA**	**Conclusion Q3**	**Sda (>50000 DDDA)**	**Conclusion Q4**	**Withdrawal time**	**Conclusion Q5**	**Overall conclusion**
Sulfadimethoxine	N	Y			Y	Y	→	→	→	→	medium
Sulfadoxine	N	Y			Y	Y	→	→	→	→	medium
Sulfamethazine (sulfadimidine)	N	Y		Y	Y	Y	→	→	→	→	medium
Sulfamethoxazole	N	Y				N	Y	Y	10-12 days	Y	medium
Sulfapyridine	N	Y			Y	Y	→	→	→	→	medium
Sulfaquanidine	N	Y				N	N	N	→	→	low
Sulfaquinoxaline	N	Y				N	N	N	→	→	low
Tetracycline	N	Y			Y	Y	→	→	→	→	medium
Thiamphenicol	N	Y			Y	Y	→	→	→	→	medium
Tiamulin	N	N	→	→	→	→	N	N			low
Tildipirosine	Y	→	→	→	→	→	→	→	→	→	high
Tilmicosine	Y	→	→	→	→	→	→	→	→	→	high
Trimethoprim	N	Y			Y	Y	→	→	→	→	medium
Tulathromycine	Y	→	→	→	→	→	→	→	→	→	high
Tylosine	Y	→	→	→	→	→	→	→	→	→	high
Tylvalosine	Y	→	→	→	→	→	→	→	→	→	high
Valnemuline	N	N	→	→	→	→	N	N	→	→	low
Virginiamycine	N	N	→	→	→	→	N	N	→	→	low

MRL in milk only

* (arising from) non-compliant result(s) in milk

→ based on the outcome of the previous question, this question can be skipped

Table A2.2 *Prioritisation of antibiotics in porcine products.*

Italics: not commonly included in scope	Q1: is this an essential antimicrobial for humans?	Q2: Have MRLs been set for this substance in this animal species?	Q3: were any non-compliant residue data of the substance found in the last five years?				Q4: Is the substance regularly used in this animal species?		Q5: Do drugs with this active substance have a long withdrawal period?		Conclusion priority
Substance	**Conclusion Q1**	**Conclusion Q2**	**KAP**	**RASFF**	**EFSA**	**Conclusion Q3**	**Sda (>50000 DDDA)**	**Conclusion Q4**	**Withdrawal time**	**Conclusion Q5**	**Overall conclusion**
Amoxicilline	N	Y			Y	Y	→	→	→	→	medium
Ampicilline	N	Y			Y	Y	→	→	→	→	medium
Apramycin	N	N	→	→	→	→	N	N	→	→	low
Avilamycine	N	Y				U	N	N	→	→	low
Bacitracine	N	N	→	→	→	→	N	N	→	→	low
Baquiloprim	N	Y				N	N	N	→	→	low
Benzylpenicilline/ Penethamate	N	Y			Y	Y	→	→	→	→	medium
Cefacetril	N	N	→	→	→	→	N	→	→	→	low
Cefalexine	N	N	→	→	→	→	N	→	→	→	low
Cefalonium	N	N	→	→	→	→	N	→	→	→	low
Cefapirin	N	N	→	→	→	→	N	→	→	→	low
Cefazolin	N	N	→	→	→	→	N	→	→	→	low
Cefoperazon	Y	→	→	→	→	→	→	→	→	→	high
Cefquinome	Y	→	→	→	→	→	→	→	→	→	high
Ceftiofur	Y	→	→	→	→	→	→	→	→	→	high
Chloortetracycline	N	Y			Y	Y	→	→	→	→	medium
Cloxacilline	N	Y				N	N	N	→	→	low
Colistine	Y	→	→	→	→	→	→	→	→	→	high
Danofloxacine	Y	→	→	→	→	→	→	→	→	→	high
Dicloxacilline	N	Y				N	N	N	→	→	low
Difloxacin	Y	→	→	→	→	→	→	→	→	→	high
Dihydrostreptomycine	N	Y			Y	Y	→	→	→	→	medium
Doxycycline	N	Y	Y	Y	Y	Y	→	→	→	→	medium
Enrofloxacin	Y	→	→	→	→	→	→	→	→	→	high
Erytromycine	Y	→	→	→	→	→	→	→	→	→	high
Fenoxymethylpenicilline	N	Y				N	N	N	→	→	low
Florfenicol	N	Y			Y	Y	→	→	→	→	medium

Italics: not commonly included in scope	Q1: is this an essential antimicrobial for humans?	Q2: Have MRLs been set for this substance in this animal species?	Q3: were any non-compliant residue data of the substance found in the last five years?				Q4: Is the substance regularly used in this animal species?		Q5: Do drugs with this active substance have a long withdrawal period?		Conclusion priority
Substance	Conclusion Q1	Conclusion Q2	KAP	RASFF	EFSA	Conclusion Q3	Sda (>50000 DDDA)	Conclusion Q4	Withdrawal time	Conclusion Q5	Overall conclusion
Flumequine	Y	→	→	→	→	→	→	→	→	→	high
Gamitromycine	Y	→	→	→	→	→	→	→	→	→	high
Gentamicine	N	Y			Y	Y	→	→	→	→	medium
Josamycine	N	N	→	→	→	→	N	→	→	→	low
Kanamycine	N	Y				N	N	N	→	→	low
Lincomycine	N	Y			Y	Y	→	→	→	→	medium
Marbofloxacine	Y	→	→	→	→	→	→	→	→	→	high
Nafcillin	N	N	→	→	→	→	N	N	→	→	low
Neomycine	N	Y	Y		Y	Y	→	→	→	→	medium
Novobiocine	N	N	→	→	→	→	N	→	→	→	low
Oxacilline	N	Y				N	N	N	→	→	low
Oxolinic acid	N	Y				N	N	N	→	→	low
Oxytetracycline	N	Y	Y	Y	Y	Y	→	→	→	→	medium
Paromomycine	N	Y				N	N	N	→	→	low
Pirlimycine	N	N	→	→	→	→	N	→	→	→	low
Rifaximine	N	N	→	→	→	→	N	→	→	→	low
Sarafloxacin	Y	→	→	→	→	→	→	→	→	→	high
Spectinomycine	N	Y			Y	Y	→	→	→	→	medium
Spiramycine	Y	→	→	→	→	→	→	→	→	→	high
Streptomycine	N	Y			Y	Y	→	→	→	→	medium
Sulfachloorpyridazine	N	Y				N	N	N	→	→	low
Sulfaclozine	N	Y				N	N	N	→	→	low
Sulfadiazine	N	Y	Y	Y	Y	Y	→	→	→	→	medium
Sulfadimethoxine	N	Y		Y	Y	Y	→	→	→	→	medium
Sulfadoxine	N	Y			Y	Y	→	→	→	→	medium
Sulfamethazine	N	Y			Y	Y	→	→	→	→	medium
Sulfamethoxazole	N	Y	Y		Y	Y	→	→	→	→	medium
Sulfapyridine	N	Y				N	N	N	→	→	low
Sulfaquanidine	N	Y				N	N	N	→	→	low

Itallics: not commonly included in scope	Q1: is this an essential antimicrobial for humans?	Q2: Have MRLs been set for this substance in this animal species?	Q3: were any non-compliant residue data of the substance found in the last five years?				Q4: Is the substance regurlarly used in this animal species?		Q5: Do drugs with this active substance have a long withdrawal period?		Conclusion priority
Substance	Conclusion Q1	Conclusion Q2	KAP	RASFF	EFSA	Conclusion Q3	Sda (>50000 DDDA)	Conclusion Q4	Withdrawal time	Conclusion Q5	Overall conclusion
Sulfaquinoxaline	N	Y				N	N	N	→	→	low
Tetracycline	N	Y			Y	Y	→	→	→	→	medium
Thiamphenicol	N	Y				U	N	N	→	→	low
Tiamulin	N	Y				N	N	N	→	→	low
Tildipirosine	Y	→	→	→	→	→	→	→	→	→	high
Tilmicosine	Y	→	→	→	→	→	→	→	→	→	high
Trimethoprim	N	Y		Y	Y	Y	→	→	→	→	medium
Tulathromycine	Y	→	→	→	→	→	→	→	→	→	high
Tylvalosine	Y	→	→	→	→	→	→	→	→	→	high
Tylosine	Y	→	→	→	→	→	→	→	→	→	high
Valnemuline	N	Y				N	N	N	→	→	low
Virginiamycine	N	N	→	→	→	→	N	→	→	→	low

→ based on the outcome of the previous question, this question can be skipped

Table A2.3 *Prioritisation of antibiotics in poultry meat.*

Italics: not commonly included in scope	Q1: is this an essential antimicrobial for humans?	Q2: Have MRLs been set for this substance in this animal species?	Q3: were any non-compliant residue data of the substance found in the last five years?				Q4: Is the substance regurlarly used in this animal species?		Q5: Do drugs with this active substance have a long withdrawal period?		Conclusion priority
Substance	**Conclusion Q1**	**Conclusion Q2**	**KAP**	**RASFF**	**EFSA**	**Conclusion Q3**	**Sda (> 50000 DDDA)**	**Conclusion Q4**	**Withdrawal time**	**Conclusion Q5**	**Overall conclusion**
Amoxicilline	N	Y			Y	Y	→	→	→	→	medium
Ampicilline	N	Y				N	Y	Y	1-28d	Y	medium
Apramycin	N	N	→	→	→	→	Y	Y	0d	N	low
Avilamycine	N	Y				U	N	N	→	→	low
Bacitracine	N	N	→	→	→	→	N	N	→	→	low
Baquiloprim	N	N	→	→	→	→	N	N	→	→	low
Benzylpenicilline/ penethamate	N	Y				N	N	N	→	→	low
Cefacetril	N	N	→	→	→	→	N	N	→	→	low
Cefalexine	N	N	→	→	→	→	N	N	→	→	low
Cefalonium	N	N	→	→	→	→	N	N	→	→	low
Cefapirin	N	N	→	→	→	→	N	N	→	→	low
Cefazolin	N	N	→	→	→	→	N	N	→	→	low
Cefoperazon	Y	→	→	→	→	→	→	→	→	→	high
Cefquinome	Y	→	→	→	→	→	→	→	→	→	high
Ceftiofur	Y	→	→	→	→	→	→	→	→	→	high
Chloortetracycline	N	Y		Y	Y	Y	→	→	→	→	medium
Cloxacilline	N	Y				N	N	N	→	→	low
Colistine	Y	→	→	→	→	→	→	→	→	→	high
Danofloxacine	Y	→	→	→	→	→	→	→	→	→	high
Dicloxacilline	N	Y				N	N	N	→	→	low
Difloxacin	Y	→	→	→	→	→	→	→	→	→	high
Dihydrostreptomycine	N	N	→	→	→	→	N	N	→	→	low
Doxycycline	N	Y	Y	Y	Y	Y	→	→	→	→	medium
Enrofloxacin	Y	→	→	→	→	→	→	→	→	→	high
Erytromycine	Y	→	→	→	→	→	→	→	→	→	high
Fenoxymethylpenicilline	N	Y				N	Y	Y	2d	N	low

Italics: not commonly included in scope	Q1: is this an essential antimicrobial for humans?	Q2: Have MRLs been set for this substance in this animal species?	Q3: were any non-compliant residue data of the substance found in the last five years?				Q4: Is the substance regularly used in this animal species?		Q5: Do drugs with this active substance have a long withdrawal period?		Conclusion priority
Substance	Conclusion Q1	Conclusion Q2	KAP	RASFF	EFSA	Conclusion Q3	Sda (> 50000 DDDA)	Conclusion Q4	Withdrawal time	Conclusion Q5	Overall conclusion
Florfenicol	N	Y				N	N	N	→	→	low
Flumequine	Y	→	→	→	→	→	→	→	→	→	high
Gamitromycine	Y	→	→	→	→	→	→	→	→	→	high
Gentamicine	N	N	→	→	→	→	N	N	→	→	low
Josamycine	N	N	→	→	→	→	N	N	→	→	low
Kanamycine	N	Y				N	N	N	→	→	low
Lincomycine	N	Y			Y	Y	→	→	→	→	medium
Marbofloxacine	Y	→	→	→	→	→	→	→	→	→	high
Nafcillin	N	N	→	→	→	→	N	N	→	→	low
Neomycine	N	Y				N	Y	Y	7d	Y	medium
Novobiocine	N	N	→	→	→	→	N	N	→	→	low
OTHER sulfonamides	N	Y			Y	Y	→	→	→	→	low
Oxacilline	N	N	→	→	→	→	N	N	→	→	low
Oxolinic acid	N	Y				N	N	N	→	→	low
Oxytetracycline	N	Y			Y	Y	→	→	→	→	medium
Paromomycine	N	Y				N	N	N	→	→	low
Pirlimycine	N	N	→	→	→	→	N	N	→	→	low
Rifaximine	N	N	→	→	→	→	N	N	→		low
Sarafloxacin	Y	→	→	→	→	→	→	→	→	→	high
Spectinomycine	N	Y			Y	Y	→	→	→	→	medium
Spiramycine	Y	→	→	→	→	→	→	→	→	→	high
Streptomycine	N	N	→	→	→	→	N	N	→	→	low
Sufadiazine	N	Y			Y	Y	→	→	→	→	medium
Sulfachloorpyridazine	N	Y				N	Y	Y	3d	N	low
Sulfaclozine	N	Y				N	N	N	→	→	low
Sulfadimethoxine	N	Y			Y	Y	→	→	→	→	medium
sulfadoxine	N	Y				N	N	N	→	→	low
Sulfamethazine	N	Y			Y	Y	→	→	→	→	medium

Italics: not commonly included in scope	Q1: is this an essential antimicrobial for humans?	Q2: Have MRLs been set for this substance in this animal species?	Q3: were any non-compliant residue data of the substance found in the last five years?				Q4: Is the substance regurlarly used in this animal species?		Q5: Do drugs with this active substance have a long withdrawal period?		Conclusion priority
Substance	**Conclusion Q1**	**Conclusion Q2**	**KAP**	**RASFF**	**EFSA**	**Conclusion Q3**	**Sda (> 50000 DDDA)**	**Conclusion Q4**	**Withdrawal time**	**Conclusion Q5**	**Overall conclusion**
Sulfamethoxazole	N	Y				N	Y	Y	5-18d	Y	medium
Sulfapyridine	N	Y				N	N	N	→	→	low
Sulfaquanidine	N	Y				N	N	N	→	→	low
Sulfaquinoxaline	N	Y				N	Y	Y	14d	Y	medium
Tetracycline	N	Y		Y	Y	Y	→	→	→	→	medium
Thiamphenicol	N	Y				U	N	N	→	→	low
Tiamulin	N	Y				N	N	N	→	→	low
Tildipirosine	Y	→	→	→	→	→	→	→	→	→	high
Tilmicosine	Y	→	→	→	→	→	→	→	→	→	high
Trimethoprim	N	Y			Y	Y	→	→	→	→	medium
Tulathromycine	Y	→	→	→	→	→	→	→	→	→	high
Tylosine	Y	→	→	→	→	→	→	→	→	→	high
Tylvalosine	Y	→	→	→	→	→	→	→	→	→	high
Valnemuline	N	N	→	→	→	→	N	N	→	→	low
Virginiamycine	N	Y				U	N	N	→	→	low

→ based on the outcome of the previous question, this question can be skipped

Table A2.4 *Prioritisation of antibiotics in eggs.*

Italics: not commonly included in scope	Q1: is this an essential antimicrobial for humans?	Q2: Have MRLs been set for this substance in this animal species?			Q3: were any non-compliant residue data of the substance found in the last five years?				Q4: Is the substance regurlarly used in this animal species?		Q5: Do drugs with this active substance have a long withdrawal period?		Conclusion priority
Substance	Conclusion Q1	MRLs poultry	MRLs eggs	Conclusion Q2	KAP	RASFF	EFSA	Conclusion Q3	Sda (>50000 DDDA)	Conclusion Q4	Withdrawal time	Conclusion Q5	
Amoxicilline	N	Y	N	Y				N	Y	Y	cascade	Y	medium
Ampicilline	N	Y	N	Y				N	Y	Y	cascade	Y	medium
Apramycin	N	N	N	N	→	→	→	→	Y	Y	cascade	Y	medium
Avilamycine	N	Y	N	Y				U	N	N	→	→	low
Bacitracine	N	N	N	N	→	→	→	→	N	N	→	→	low
Baquiloprim	N	N	N	N	→	→	→	→	N	N	→	→	low
Benzylpenicilline/ penethamate	N	Y	N	Y				N	N	N	→	→	low
Cefacetril	N	N	N	N	→	→	→	→	N	N	→	→	low
Cefalexine	N	N	N	N	→	→	→	→	N	N	→	→	low
Cefalonium	N	N	N	N	→	→	→	→	N	N	→	→	low
Cefapirin	N	N	N	N	→	→	→	→	N	N	→	→	low
Cefazolin	N	N	N	N	→	→	→	→	N	N	→	→	low
Cefoperazon	Y	→	→	→	→	→	→	→	→	→	→	→	high
Cefquinome	Y	→	→	→	→	→	→	→	→	→	→	→	high
Ceftiofur	Y	→	→	→	→	→	→	→	→	→	→	→	high
Chloortetracycline	N	Y	Y	Y				N	N	N	→	→	low
Cloxacilline	N	Y	N	Y				N	N	N	→	→	low
Colistine	Y	→	→	→	→	→	→	→	→	→	→	→	high
Danofloxacine	Y	→	→	→	→	→	→	→	→	→	→	→	high
Dicloxacilline	N	Y	N	Y				N	N	N	→	→	low
Difloxacin	Y	→	→	→	→	→	→	→	→	→	→	→	high
Dihydrostreptomycine	N	N	N	N	→	→	→	→	N	N	→	→	low
Doxycycline	N	Y	N	Y			Y	Y	→	→	→	→	medium
Enrofloxacin	Y	→	→	→	→	→	→	→	→	→	→	→	high
Erytromycine	Y	→	→	→	→	→	→	→	→	→	→	→	high
Fenoxymethylpenicilline	N	Y	Y	Y				N	Y	Y	0d	N	low

Italics: not commonly included in scope	Q1: is this an essential antimicrobial for humans?	Q2: Have MRLs been set for this substance in this animal species?			Q3: were any non-compliant residue data of the substance found in the last five years?				Q4: Is the substance regularly used in this animal species?		Q5: Do drugs with this active substance have a long withdrawal period?		Conclusion priority
Substance	Conclusion Q1	MRLs poultry	MRLs eggs	Conclusion Q2	KAP	RASFF	EFSA	Conclusion Q3	Sda (>50000 DDDA)	Conclusion Q4	Withdrawal time	Conclusion Q5	
Florfenicol	N	Y	N	Y				N	N	N	→	→	low
Flumequine	Y	→	→	→	→	→	→	→	→	→	→	→	high
Gamitromycine	Y	→	→	→	→	→	→	→	→	→	→	→	high
Gentamicine	N	N	N	N	→	→	→	→	N	N	→	→	low
Josamycine	N	N	N	N	→	→	→	→	N	N	→	→	low
Kanamycine	N	Y	N	Y				N	N	N	→	→	low
Lincomycine	N	Y	Y	Y				N	Y	Y	cascade	Y	medium
Marbofloxacine	Y	→	→	→	→	→	→	→	→	→	→	→	high
Nafcillin	N	N	N	N	→	→	→	→	N	N	→	→	low
Neomycine	N	Y	Y	Y				N	Y	Y	cascade	Y	medium
Novobiocine	N	N	N	N	→	→	→	→	N	N	→	→	low
Oxacilline	N	N	N	N	→	→	→	→	N	N	→	→	low
Oxolinic acid	N	Y	N	Y				N	N	N	→	→	low
Oxytetracycline	N	Y	Y	Y			Y	Y	→	→	→	→	medium
Paromomycine	N	Y	N	Y				N	N	N	→	→	low
Pirlimycine	N	N	N	N	→	→	→	→	N	N	→	→	low
Rifaximine	N	N	N	N	→	→	→	→	N	N	→	→	low
Sarafloxacin	Y	→	→	→	→	→	→	→	→	→	→	→	high
Spectinomycine	N	Y	N	Y				N	Y	Y	cascade	Y	medium
Spiramycine	Y	→	→	→	→	→	→	→	→	→	→	→	high
Streptomycine	N	N	N	N	→	→	→	→	N	N	→	→	low
Sufadiazine	N	Y	N	Y			Y	Y	→	→	→	→	medium
Sulfachloorpyridazine	N	Y	N	Y				N	Y	Y	cascade	Y	medium
Sulfaclozine	N	Y	N	Y				N	N	N	→	→	low
Sulfadimethoxine	N	Y	N	Y			Y	Y	→	→	→	→	medium
Sulfadoxine	N	Y	N	Y				N	N	N	→	→	low
Sulfamethazine	N	Y	N	Y			Y	Y	→	→	→	→	medium
Sulfamethoxazole	N	Y	N	Y				N	Y	Y	cascade	Y	medium

Italics: not commonly included in scope	Q1: is this an essential antimicrobial for humans?	Q2: Have MRLs been set for this substance in this animal species?			Q3: were any non-compliant residue data of the substance found in the last five years?				Q4: Is the substance regurlarly used in this animal species?		Q5: Do drugs with this active substance have a long withdrawal period?		Conclusion priority
Substance	Conclusion Q1	MRLs poultry	MRLs eggs	Conclusion Q2	KAP	RASFF	EFSA	Conclusion Q3	Sda (>50000 DDDA)	Conclusion Q4	Withdrawal time	Conclusion Q5	
Sulfapyridine	N	Y	N	Y				N	N	N	→	→	low
Sulfaquanidine	N	Y	N	Y				N	N	N	→	→	low
Sulfaquinoxaline	N	Y	N	Y				N	Y	Y	cascade	Y	medium
Tetracycline	N	Y	Y	Y				N	N	N	→	→	low
Thiamphenicol	N	Y	N	Y				U	N	N	→	→	low
Tiamulin	N	Y	Y	Y				N	N	N	→	→	low
Tildipirosine	Y	→	→	→	→	→	→	→	→	→	→	→	high
Tilmicosine	Y	→	→	→	→	→	→	→	→	→	→	→	high
Trimethoprim	N	Y	N	Y		Y	Y	Y	→	→	→	→	medium
Tulathromycine	Y	→	→	→	→	→	→	→	→	→	→	→	high
Tylosine	Y	→	→	→	→	→	→	→	→	→	→	→	high
Tylvalosine	Y	→	→	→	→	→	→	→	→	→	→	→	high
Valnemuline	N	N	N	N	→	→	→	→	N	N	→	→	low
Virginiamycine	N	Y	N	Y				U	N	N	→	→	low

→ based on the outcome of the previous question, this question can be skipped

Annex 3 Prioritization of antiparasitics using decision tree I for bovine, porcine, poultry meat and eggs

Substance	Q1: Were any non-compliant residue data of the substance found in the last five years?			Q3: Are there indications for use of this substance in production systems for food producing animals?					Q2: Is a human health risk due to residues of this substance scientifically proven to be absent or negligible?		Conclusion priority
	EFSA	RASFF	Conclusion	NL/EU registered for companion animals	Used as pesticide?	Availability-other	Pesticide residues found in animal products?	Conclusion	Source	Conclusion	
Afoxolaner	U	N	U	Y	N			Y	U	U	High*
Bithionol	N[a]	N	N	N	N	bolus (USA)		N	→	→	Low
Emodepside	U	N	U	Y	N			Y	U	U	High*
Fipronil	N[a]	N	N	Y	Y	Pour on (South America)	U	Y	NVWA: human risks are low for poultry meat and eggs	N	High
Imidacloprid	N[a]	N	N	Y	Y		U	Y	EFSA/JECFA: residues were found in animal products	N	High
Indoxacarb	N[a]	N	N	Y	Y		N	N	→	→	Low
Lotilaner	U	N	U	Y	N			Y	U	U	High*
Lufenuron	N[a]	N	N	Y	Y		U	Y	EFSA/JECFA: residues were found in animal products	N	High
Methoprene	N[a]	N	N	Y	Y	Feed additive, salt-lick (US)	U	Y	EFSA/JECFA: residues were found in animal products	N	High
*Milbemectin**	N[a]	N	N	N	Y			N	→	→	Low
Milbemycine oxime	U	N	U	Y	N			Y	U	U	High*

Substance	Q1: Were any non-compliant residue data of the substance found in the last five years?			Q3: Are there indications for use of this substance in production systems for food producing animals?					Q2: Is a human health risk due to residues of this substance scientifically proven to be absent or negligible?		Conclusion priority
	EFSA	RASFF	Conclusion	NL/EU registered for companion animals	Used as pesticide?	Availability-other	Pesticide residues found in animal products?	Conclusion	Source	Conclusion	
Niclosamide	N[a]	N	N	Y	N			Y	U	U	High*
Nitroscanate	U	N	U	Y	N			Y	U	U	High*
Oxantel	N[a]	N	N	Y	N			Y	U	U	High*
Pyriprole	U	N	U	Y	N			Y	U	U	High*
Pyriproxyfen	N[a]	N	N	Y	Y		U	Y	EFSA: residues unlikely	Y	Medium
Sarolaner	U	N	U	Y	N			Y	U	U	High*
Selamectin	U	N	U	Y	N			Y	U	U	High*
Spinosad	N[a]	N	N	Y	Y		N	N	→	→	Low

[a] substance is included in monitoring, but not necessarily in relevant matrix

* high priority because of no data or information to answer all questions

→ based on the outcome of the previous question, this question can be skipped

Annex 4 Prioritization of antiparasitics using decision tree III

Table A4.1 *Prioritisation of antiparasitics in bovine products.*

	Q1: is this an essential antimicrobial for humans?	Q2: Have MRLs been set for this substance in this animal species?	Q3: were any non-compliant residue data of the substance found in the last five years?			Q4: Is the substance regurlarly used in this animal species?		Q5: Do drugs with this active substance have a long withdrawal period?		Conclusion priority
Substance	**Conclusion Q1**	**Conclusion Q2**	**RASFF**	**EFSA**	**Conclusion Q3**	**FIDIN (> 100 kg)**	**Conclusion Q4**	**Withdrawal time**	**Conclusion Q5**	**Overall conclusion**
Ivermectin	N	Y	Y	Y	Y	→	→	→	→	medium
Doramectin	N	Y	Y	Y	Y	→	→	→	→	medium
Abamectin	N	Y	N	Y	Y	→	→	→	→	medium
Moxidectin	N	Y	N	Y	Y	→	→	→	→	medium
Emamectin	N	N	N	N	N	N	N	→	→	low
Eprinomectin	N	Y	N	N	N	N	N	→	→	low
Albendazole (oxide), Netobimine	N	Y	Y	Y	Y	→	→	→	→	medium
Febantel	N	Y	N	N	N[#]	N	N	→	→	low
Fenbendazole	N	Y	N	N	N[#]	N	N	→	→	low
Oxfendazole	N	Y	N	N	N[#]	Y	Y	up to 7 months	Y	medium
Oxibendazole	N	N	N	N	N	N	→	→	→	low
Mebendazole	N	N	N	Y	Y	→	→	→	→	medium
Flubendazole	N	N	N	Y	Y	→	→	→	→	medium
Thiabendazole	N	Y	N	N	N	N	→	→	→	low
Levamisole	N	Y	N	Y	Y	→	→	→	→	medium
Triclabendazol	N	Y	N	Y*	Y	→	→	→	→	medium*
Amitraz	N	Y	N	N	N	Y	Y	4d	N	low
Clorsulon	N	Y	N	Y	Y	→	→	→	→	medium
Closantel	N	Y	N	Y	Y	→	→	→	→	medium

Substance	Q1: is this an essential antimicrobial for humans?	Q2: Have MRLs been set for this substance in this animal species?	Q3: were any non-compliant residue data of the substance found in the last five years?			Q4: Is the substance regurlarly used in this animal species?		Q5: Do drugs with this active substance have a long withdrawal period?		Conclusion priority
	Conclusion Q1	Conclusion Q2	RASFF	EFSA	Conclusion Q3	FIDIN (> 100 kg)	Conclusion Q4	Withdrawal time	Conclusion Q5	Overall conclusion
Cyromazine	N	N	N	N	N	N	N	→	→	low
Derquantel	N	N	N	U	U	N	N	→	→	low
Dicyclanil	N	N	N	U	U	N	N	→	→	low
Diflubenzuron	N	N	N	N	N	N	N	→	→	low
Fluazuron	N	Y	N	U	U	N	N	→	→	low
Fluralaner	N	N	N	U	U	N	N	→	→	low
Monepantel	N	Y	N	U	U	N	N	→	→	low
Morantel	N	Y	N	N	N	N	N	→	→	low
Niclosamide	N	N	N	N	N	N	N	→	→	low
Nitroxinil	N	Y	N	Y	Y	→	→	→	→	medium
Oxyclozanide	N	Y	N	Y	Y	→	→	→	→	medium
Piperazine	N	N	N	U	U	N	N	→	→	low
Praziquantel	N	N	N	N	N	N	N	→	→	low
Pyrantel	N	N	N	N	N	N	N	→	→	low
Rafoxanide	N	Y	N	N	N	N	N	→	→	low
Sisapronil	N	Y	N	U	U	N	N	→	→	low

* Based on non-compliant result(s) in bovine milk

#Analytically these concern the same substance

Table A4.2 *Prioritisation of antiparasitics in porcine products.*

	Q1: is this an essential antimicrobial for humans?	Q2: Have MRLs been set for this substance in this animal species?	Q3: were any non-compliant residue data of the substance found in the last five years?			Q4: Is the substance regurlarly used in this animal species?		Q5: Do drugs with this active substance have a long withdrawal period?		Conclusion priority
Substance	Conclusion Q1	Conclusion Q2	RASFF	EFSA	Conclusion Q3	FIDIN	Conclusion Q4	Withdrawal time	Conclusion Q5	Overall conclusion
Ivermectin	N	Y	N	Y	Y	→	→	→	→	medium
Doramectin	N	Y	N	Y	Y	→	→	→	→	medium
Abamectin	N	N	N	N	N	N	N	→	→	low
Moxidectin	N	N	N	N	N	N	N	→	→	low
Emamectin	N	N	N	N	N	N	N	→	→	low
Eprinomectin	N	N	N	Y	Y	→	→	→	→	medium
Albendazole (oxide), Netobimine	N	N	N	Y	Y	→	→	→	→	medium
Febantel	N	Y	N	N	N[#]	N	N	→	→	low
Fenbendazole	N	Y	N	Y	Y[#]	→	→	→	→	medium
Oxfendazole	N	Y	N	Y	Y[#]	→	→	→	→	medium
Oxibendazole	N	Y	N	N	N	N	N	→	→	low
Mebendazole	N	N	N	N	N	N	N	→	→	low
Flubendazole	N	Y	N	Y	Y	→	→	→	→	medium
Thiabendazole	N	N	N	Y	Y	→	→	→	→	medium
Levamisole	N	Y	Y	Y	Y	→	→	→	→	medium
Triclabendazol	N	N	N	N	N	N	N	→	→	low
Amitraz	N	Y	N	N	N	Y	Y	4d	N	low
Clorsulon	N	N	N	N	N	N	N	→	→	low
Closantel	N	N	N	Y	Y	→	→	→	→	medium
Cyromazine	N	N	N	N	N	N	N	→	→	low
Derquantel	N	N	N	U	U	N	N	→	→	low
Dicyclanil	N	N	N	U	U	N	N	→	→	low
Diflubenzuron	N	N	N	N	N	N	N	→	→	low
Fluazuron	N	N	N	U	U	N	N	→	→	low

	Q1: is this an essential antimicrobial for humans?	Q2: Have MRLs been set for this substance in this animal species?	Q3: were any non-compliant residue data of the substance found in the last five years?			Q4: Is the substance regurlarly used in this animal species?		Q5: Do drugs with this active substance have a long withdrawal period?		Conclusion priority
Substance	Conclusion Q1	Conclusion Q2	RASFF	EFSA	Conclusion Q3	FIDIN	Conclusion Q4	Withdrawal time	Conclusion Q5	Overall conclusion
Fluralaner	N	N	N	U	U	N	N	→	→	low
Monepantel	N	N	N	U	U	N	N	→	→	low
Morantel	N	N	N	N	N	N	N	→	→	low
Niclosamide	N	N	N	N	N	N	N	→	→	low
Nitroxinil	N	N	N	N	N	N	N	→	→	low
Oxyclozanide	N	N	N	Y	Y	→	→	→	→	medium
Piperazine	N	Y	N	U	U	N	N	→	→	low
Praziquantel	N	N	N	N	N	N	N	→	→	low
Pyrantel	N	N	N	N	N	N	N	→	→	low
Rafoxanide	N	N	N	N	N	N	N	→	→	low
Sisapronil	N	N	N	U	U	N	N	→	→	low

→ based on the outcome of the previous question, this question can be skipped

#Analytically these concern the same substance

Table A4.3 *Prioritisation of antiparasitics in poultry meat.*

	Q1: is this an essential antimicrobial for humans?	Q2: Have MRLs been set for this substance in this animal species?	Q3: were any non-compliant residue data of the substance found in the last five years?			Q4: Is the substance regurlarly used in this animal species?		Q5: Do drugs with this active substance have a long withdrawal period?		Conclusion priority
Substance	Conclusion Q1	Conclusion Q2	RASFF	EFSA	Conclusion Q3	FIDIN	Conclusion Q4	Withdrawal time	Conclusion Q5	Overall conclusion
Ivermectin	N	N	N	N	N	N	N	→	→	low
Doramectin	N	N	N	N	N	N	N	→	→	low
Abamectin	N	N	N	N	N	N	N	→	→	low
Moxidectin	N	N	N	N	N	N	N	→	→	low
Emamectin	N	N	N	N	N	N	N	→	→	low
Eprinomectin	N	N	N	N	N	N	N	→	→	low
Albendazole (oxide), Netobimine	N	N	N	N	N	N	N	→	→	low
Febantel	N	N	N	N	N[#]	N	N	→	→	low
Fenbendazole	N	Y	N	N	N[#]	Y	Y	6-9d	N	low
Oxfendazole	N	N	N	Y	Y[#]	→	→	→	→	medium
Oxibendazole	N	N	N	N	N	N	N	→	→	low
Mebendazole	N	N	N	N	N	N	N	→	→	low
Flubendazole	N	Y	N	N	N	Y	Y	2-7d	N	low
Thiabendazole	N	N	N	N	N	N	N	→	→	low
Levamisole	N	Y	N	N	N	N	N	→	→	low
Triclabendazol	N	N	N	N	N	N	N	→	→	low
Amitraz	N	N	N	U	U	N	N	→	→	low
Clorsulon	N	N	N	U	U	N	N	→	→	low
Closantel	N	N	N	U	U	N	N	→	→	low
Cyromazine	N	N	Y	U	Y	→	→	→	→	medium
Derquantel	N	N	N	U	U	N	N	→	→	low
Dicyclanil	N	N	N	U	U	N	N	→	→	low
Diflubenzuron	N	N	N	U	U	N	N	→	→	low
Fluazuron	N	N	N	U	U	N	N	→	→	low
Fluralaner	N	Y	N	U	U	N	N	→	→	low

Substance	Q1: is this an essential antimicrobial for humans?	Q2: Have MRLs been set for this substance in this animal species?	Q3: were any non-compliant residue data of the substance found in the last five years?			Q4: Is the substance regurlarly used in this animal species?		Q5: Do drugs with this active substance have a long withdrawal period?		Conclusion priority
	Conclusion Q1	Conclusion Q2	RASFF	EFSA	Conclusion Q3	FIDIN	Conclusion Q4	Withdrawal time	Conclusion Q5	Overall conclusion
Monepantel	N	N	N	U	U	N	N	→	→	low
Morantel	N	N	N	U	U	N	N	→	→	low
Niclosamide	N	N	N	U	U	N	N	→	→	low
Nitroxinil	N	N	N	U	U	N	N	→	→	low
Oxyclozanide	N	N	N	U	U	N	N	→	→	low
Piperazine	N	N	N	U	U	N	N	→	→	low
Praziquantel	N	N	N	U	U	N	N	→	→	low
Pyrantel	N	N	N	U	U	N	N	→	→	low
Rafoxanide	N	N	N	U	U	N	N	→	→	low
Sisapronil	N	N	N	U	U	N	N	→	→	low

#Analytically these concern the same substance

→ based on the outcome of the previous question, this question can be skipped

Table A4.4 *Prioritisation of antiparasitics in eggs.*

	Q1: is this an essential antimicrobial for humans?	Q2: Have MRLs been set for this substance in this animal species?	Q3: were any non-compliant residue data of the substance found in the last five years?			Q4: Is the substance regurlarly used in this animal species?		Q5: Do drugs with this active substance have a long withdrawal period?		Conclusion priority
Substance	**Conclusion Q1**	**Conclusion Q2**	**RASFF**	**EFSA**	**Conclusion Q3**	**FIDIN**	**Conclusion Q4**	**Withdrawal time**	**Conclusion Q5**	**Overall conclusion**
Ivermectin	N	N	N	U	U	N	N	→	→	low
Doramectin	N	N	N	U	U	N	N	→	→	low
Abamectin	N	N	N	U	U	N	N	→	→	low
Moxidectin	N	N	N	U	U	N	N	→	→	low
Emamectin	N	N	N	U	U	N	N	→	→	low
Eprinomectin	N	N	N	U	U	N	N	→	→	low
Albendazole (oxide), Netobimine	N	N	N	U	U	N	N	→	→	low
Febantel	N	N	N	U	U[#]	N	N	→	→	low
Fenbendazole	N	Y	N	U	U[#]	Y	Y	0d	N	low
Oxfendazole	N	N	N	U	U[#]	N	N	→	→	low
Oxibendazole	N	N	N	U	U	N	N	→	→	low
Mebendazole	N	N	N	U	U	N	N	→	→	low
Flubendazole	N	Y	N	U	U	Y	Y	0d	N	low
Thiabendazole	N	N	N	U	U	N	N	→	→	low
Levamisole	N	N*	N	U	U	N	N	→	→	low
Triclabendazol	N	N	N	U	U	N	N	→	→	low
Amitraz	N	N	N	U	U	N	N	→	→	low
Clorsulon	N	N	N	U	U	N	N	→	→	low
Closantel	N	N	N	U	U	N	N	→	→	low
Cyromazine	N	N	N	Y	Y	→	→	→	→	medium
Derquantel	N	N	N	U	U	N	N	→	→	low
Dicyclanil	N	N	N	U	U	N	N	→	→	low
Diflubenzuron	N	N	N	U	U	N	N	→	→	low
Fluazuron	N	N	N	U	U	N	N	→	→	low

Substance	Q1: is this an essential antimicrobial for humans?	Q2: Have MRLs been set for this substance in this animal species?	Q3: were any non-compliant residue data of the substance found in the last five years?			Q4: Is the substance regurlarly used in this animal species?		Q5: Do drugs with this active substance have a long withdrawal period?		Conclusion priority
	Conclusion Q1	Conclusion Q2	RASFF	EFSA	Conclusion Q3	FIDIN	Conclusion Q4	Withdrawal time	Conclusion Q5	Overall conclusion
Fluralaner	N	Y	N	U	U	N	N	→	→	low
Monepantel	N	N	N	U	U	N	N	→	→	low
Morantel	N	N	N	U	U	N	N	→	→	low
Niclosamide	N	N	N	U	U	N	N	→	→	low
Nitroxinil	N	N	N	U	U	N	N	→	→	low
Oxyclozanide	N	N	N	U	U	N	N	→	→	low
Piperazine	N	Y	N	U	U	N	N	→	→	low
Praziquantel	N	N	N	U	U	N	N	→	→	low
Pyrantel	N	N	N	U	U	N	N	→	→	low
Rafoxanide	N	N	N	U	U	N	N	→	→	low
Sisapronil	N	N	N	U	U	N	N	→	→	low

→ based on the outcome of the previous question, this question can be skipped

#Analytically these concern the same substance

Annex 5 Prioritization of carbamates using decision tree I for bovine, porcine, poultry meat and eggs

	Q1: Where any non-compliant residue data of the substance found in the last 5 years?				Q3: Are there indications for use of this substance in production systems for food producing animals?									Q2: Is a human health risk due to residues of this substance scientifically proven to be absent or negligible?	General conclusion
Carbamates	EFSA	RASFF	KAP > MRL	Concl.	Monitored and not found KAP data	Listed as obsolete (Pesticide Manual)	Listed as obsolete (Pesticide Properties DataBase)	Product available in US? (PAN pesticide database)	Registration in other countries?	Available at alibaba.com ?	Break down product monitored?	Pesticide residues found in animal products	Concl.	Concl.	
3-hydroxy carbofuran	N	N	N	N	Y	nd	N	→	→	→	→	→	N, not found in monitoring	→	low
Aldicarb	N	N	N	N	Y	nd	N	→	→	→	→	→	N, not found in monitoring	→	low
Aldicarb (aldicarb-sulfone)	N	N	N	N	Y	nd	N	→	→	→	→	→	N, not found in monitoring	→	low
Aldoxycarb (aldicarb-sulfoxide)	N	N	N	N	Y	nd	N	→	→	→	→	→	N, not found in monitoring	→	low
Carbaryl	N	N	N	N	Y	nd	N	→	→	→	→	→	N, not found in monitoring	→	low
Carbofuran	N	N	N	N	Y	nd	N	→	→	→	→	→	N, not found in monitoring	→	low
Ethiofencarb	N	N	N	N	Y	nd	U	→	→	→	→	→	N, not found in monitoring	→	low
Ethiofencarb (ethiofencarb-sulfone)	N	N	N	N	Y	nd	U	→	→	→	→	→	N, not found in monitoring	→	low

	Q1: Where any non-compliant residue data of the substance found in the last 5 years?				Q3: Are there indications for use of this substance in production systems for food producing animals?									Q2: Is a human health risk due to residues of this substance scientifically proven to be absent or negligible?	General conclusion
Ethiofencarb (ethiofencarb-sulfoxide)	N	N	N	N	Y	nd	U	→	→	→	→	→	N, not found in monitoring	→	low
Propoxur	N	N	N	N	Y	nd	N	→	→	→	→	→	N, not found in monitoring	→	low
Allyxycarb	N	N	U	U	U	Y	Y	→	→	→	→	→	N, obsolete	→	low
Aminocarb	N	N	U	U	U	Y	Y	→	→	→	→	→	N, obsolete	→	low
Bufencarb	N	N	U	U	U	Y	Y	→	→	→	→	→	N, obsolete	→	low
Butacarb	N	N	U	U	U	Y	nd	→	→	→	→	→	N, obsolete	→	low
Carbanolate	N	N	U	U	U	Y	Y	→	→	→	→	→	N, obsolete	→	low
Cloethocarb	N	N	U	U	U	Y	Y	→	→	→	→	→	N, obsolete	→	low
Decarbofuran	N	N	U	U	U	Y	nd	→	→	→	→	→	N, obsolete	→	low
Dioxacarb	N	N	U	U	U	Y	Y	→	→	→	→	→	N, obsolete	→	low
EMPC	N	N	U	U	U	Y	nd	→	→	→	→	→	N, obsolete	→	low
Fenethacarb	N	N	U	U	U	Y	nd	→	→	→	→	→	N, obsolete	→	low
Hyquincarb	N	N	U	U	U	Y	Y	→	→	→	→	→	N, obsolete	→	low
Isolan	N	N	U	U	U	Y	Y	→	→	→	→	→	N, obsolete	→	low
Metolcarb	N	N	U	U	U	Y	Y	→	→	→	→	→	N, obsolete	→	low
Mexacarbate	N	N	U	U	U	Y	Y	→	→	→	→	→	N, obsolete	→	low
Nitrilacarb	N	N	U	U	U	Y	Y	→	→	→	→	→	N, obsolete	→	low
Promacyl	N	N	U	U	U	Y	Y	→	→	→	→	→	N, obsolete	→	low
Promecarb	N	N	U	U	U	Y	Y	→	→	→	→	→	N, obsolete	→	low
Pyramat	N	N	U	U	U	nd	Y	→	→	→	→	→	N, obsolete	→	low
Tazimcarb	N	N	U	U	U	Y	nd	→	→	→	→	→	N, obsolete	→	low
Thiocarboxime	N	N	U	U	U	Y	Y	→	→	→	→	→	N, obsolete	→	low
Thiofanox	N	N	U	U	U	Y	U	→	→	→	→	→	N, obsolete	→	low
Trimethacarb	N	N	U	U	U	Y	Y	→	→	→	→	→	N, obsolete	→	low
XMC	N	N	U	U	U	Y	U	→	→	→	→	→	N, obsolete	→	low
Xylylcarb	N	N	U	U	U	Y	Y	→	→	→	→	→	N, obsolete	→	low

	Q1: Where any non-compliant residue data of the substance found in the last 5 years?				Q3: Are there indications for use of this substance in production systems for food producing animals?								Q2: Is a human health risk due to residues of this substance scientifically proven to be absent or negligible?	General conclusion
Benfuracarb	N	N	U	U	U	nd	U	N	Asia	Y	Y	nd	N, breakdown product monitored and not found	→	low
Carbosulfan	N	N	U	U	U	nd	N	N	Asia	Y	Y	nd	N, breakdown product monitored and not found	→	low
Furathiocarb	N	N	U	U	U	nd	N	N	Australia	Y	Y	nd	N, breakdown product monitored and not found	→	low
Thiodicarb	N	N	U	U	U	nd	N	Y	Australia, Asia	Y	Y	nd	N, breakdown product monitored and not found	→	low
Alanycarb	N	N	U	U	U	nd	N	N	Japan	Y	nd	N	N, no indications for use	→	low
Butocarboxim	N	N	U	U	U	nd	N	N	restricted use in Combodia	N	nd	N	N, no indications for use	→	low

	Q1: Where any non-compliant residue data of the substance found in the last 5 years?				Q3: Are there indications for use of this substance in production systems for food producing animals?								Q2: Is a human health risk due to residues of this substance scientifically proven to be absent or negligible?	General conclusion
Butoxycarboxim	N	N	U	U	U	nd	N	N	not listed in Asia list	Y	nd	N	N, no indications for use	→	low
Dimetan	N	N	U	U	U	nd	nd	N	not listed in Asia list	N	nd	nd	N, no indications for use	→	low
Dimethacarb	N	N	U	U	U	nd	nd	nd	banned in China	N	nd	nd	N, no indications for use	→	low
CPMC, etrofol, 2-chlorophenyl methylcarbamate, hopcide	N	N	U	U	U	nd	nd	nd	not listed in Asia list	Y	nd	nd	U	U	high*
Dicresyl	N	N	U	U	U	nd	nd	nd	not listed in Asia list	Y	nd	nd	U	U	high*
Pyrolan	N	N	U	U	U	nd	nd	N	not listed in Asia list	Y	nd	nd	U	U	high*
Benomyl	N	N	U	U	U	nd	N	Y	Asia	Y	nd	nd	Y, could be used	Y, by EFSA and FAO/WHO	medium
Bendiocarb	N	N	U	U	U	nd	N	Y	Australia, Asia	Y	nd	Y	Y, could be used	U	high
Fenobucarb	N	N	U	U	U	nd	U	N	Asia	Y	nd	Y	Y, could be used	U	high
Isoprocarb	N	N	U	U	U	nd	U	N	Asia	Y	nd	Y	Y, could be used	U	high

* high priority because of no data or information to answer all questions

Annex 6 Prioritization of NSAIDs using decision tree I

Table A6.1 *Prioritization of NSAIDs in bovine products using decision tree I.*

Substances	Q1: Were any non-compliant residue data of the substance found in the last five years?				Q3: Are there indications for use of this substance in production systems for food producing animals?				Q2: Is a human health risk due to residues of this substance scientifically proven to be absent or negligible?	Conclusion priority
	EFSA	RASFF	KAP data	Conclusion	Non-compliances mammals	Registered product EU for companion animals	Availability (alibaba/ebay)	Conclusion	Conclusion	
Fenbufen	N	N	N	N	N	→	→	N	→	Low
Phenylbutazone/Oxy FBZ	Y	N[a]	N	Y	→	→	→	→	N	High
Flufenamic acid	N	N	N	N	N	→	→	N	→	Low
Ibuprofen	Y	N	N	Y	→	→	→	→	Y	Medium
Indoprofen	N	N	N	N	N	→	→	N	→	Low
Meclofenamic acid	N	N	N	N	N	→	→	N	→	Low
Mefenamic acid	Y	N	N	Y	→	→	→	→	Y	Medium
Naproxen	Y	N[a]	N[a]	Y	→	→	→	→	Y	Medium
Niflumic acid	N	N	N	N	N	→	→	N	→	Low
Piroxicam	N	N	N	N	N	→	→	N	→	Low
Propyphenazone	N	N	N	N	N	→	→	N	→	Low
Tolmetin	N	N	N	N	N	→	→	N	→	Low
Eltenac	U	U	N	U	U	Y	N	N	→	Low
Nimesulide	U	U	N	U	U	Y	Y	Y	N	High*
Cimicoxib	U	U	N	U	U	Y	N	N	→	Low
Grapiprant	U	U	N	U	U	Y	Y	Y	U	High*
Robenacoxib	U	U	N	U	U	Y	N	N	→	Low
Mavacoxib	U	U	N	U	U	Y	N	N	→	Low

[a] Not for this animal, or not specified

* Not much known about the substance in food producing animals; therefore a risk because of use cannot be ruled out. However, use is less likely compared to substances with medium priority.

→ based on the outcome of the previous question, this question can be skipped

Table A6.2 *Prioritization of NSAIDs in porcine products using decision tree I.*

Substances	Q1: Were any non-compliant residue data of the substance found in the last five years?				Q3: Are there indications for use of this substance in production systems for food producing animals?				Q2: Is a human health risk due to residues of this substance scientifically proven to be absent or negligible?	Conclusion priority
	EFSA	RASFF	KAP data	Conclusion	Non-compliances mammals	Registered product EU for companion animals	Availability (alibaba/ebay)	Conclusion	Conclusion	
Fenbufen	N	N	N	N	N	→	→	N	→	Low
Phenylbutazone/Oxy FBZ	N	N[a]	N	N	Y[b]	→	→	Y	N	High
Flufenamic acid	N	N	N	N	N	→	→	N	→	Low
Ibuprofen	Y	N	N	Y	→	→	→	→	Y	Medium
Indoprofen	N	N	N	N	N	→	→	N	→	Low
Meclofenamic acid	N	N	N	N	N	→	→	N	→	Low
Mefenamic acid	N	N	N	N	Y[b]	→	→	Y	Y	Medium
Naproxen	N	N[a]	N[a]	N	Y[c]	→	→	Y	Y	Medium
Niflumic acid	N	N	N	N	N	→	→	N	→	Low
Piroxicam	N	N	N	N	N	→	→	N	→	Low
Propyphenazone	N	N	N	N	N	→	→	N	→	Low
Tolmetin	N	N	N	N	N	→	→	N	→	Low
Eltenac	U	U	U	U	U	Y	N	N	→	Low
Nimesulide	U	U	U	U	U	Y	Y	Y	N	High*
Cimicoxib	U	U	U	U	U	Y	N	N	→	Low
Grapiprant	U	U	U	U	U	Y	Y	Y	U	High*
Robenacoxib	U	U	U	U	U	Y	N	N	→	Low
Mavacoxib	U	U	U	U	U	Y	N	N	→	Low

[a] Not for this animal, or not specified

[b] Bovine meat EFSA 2012-2016

[c] Frozen horse meat RASFF and red meat KAP 2017

* Not much known about the substance in food producing animals; therefore a risk because of use cannot be ruled out. However, use is less likely compared to substances with medium priority.

→ based on the outcome of the previous question, this question can be skipped

Table A6.3 *Prioritization of NSAIDs in poultry meat using decision tree I.*

Substances	Q1: Were any non-compliant residue data of the substance found in the last five years?				Q3: Are there indications for use of this substance in production systems for food producing animals?				Q2: Is a human health risk due to residues of this substance scientifically proven to be absent or negligible?	Conclusion priority
	EFSA 2012-2016	RASFF 2012 - 2016	KAP data 2012, 2013, 2017	Conclusion	Non-compliances poultry	Registered product EU for companion animals	Availability (alibaba/ebay)	Conclusion	Conclusion	
Fenbufen	N	N	N	N	N	→	→	N	→	Low
Phenylbutazone/Oxy FBZ	N	N[a]	N	N	N	→	→	N	→	Low
Flufenamic acid	N	N	N	N	N	→	→	N	→	Low
Ibuprofen	N	N	N	N	N	→	→	N	→	Low
Indoprofen	N	N	N	N	N	→	→	N	→	Low
Meclofenamic acid	N	N	N	N	N	→	→	N	→	Low
Mefenamic acid	N	N	N	N	N	→	→	N	→	Low
Naproxen	N	N[a]	N[a]	N	N	→	→	N	→	Low
Niflumic acid	N	N	N	N	N	→	→	N	→	Low
Piroxicam	N	N	N	N	N	→	→	N	→	Low
Propyphenazone	N	N	N	N	N	→	→	N	→	Low
Tolmetin	N	N	N	N	N	→	→	N	→	Low
Eltenac	U	U	N	U	U	Y	N	N	→	Low
Nimesulide	U	U	N	U	U	Y	Y	Y	N	High*
Cimicoxib	U	U	N	U	U	Y	N	N	→	Low
Grapiprant	U	U	N	U	U	Y	Y	Y	U	High*
Robenacoxib	U	U	N	U	U	Y	N	N	→	Low
Mavacoxib	U	U	N	U	U	Y	N	N	→	Low

[a] Not for this animal, or not specified

* Not much known about the substance in food producing animals; therefore a risk because of use cannot be ruled out. However, use is less likely compared to substances with medium priority.

→ based on the outcome of the previous question, this question can be skipped

Table A6.4 *Prioritization of NSAIDs in eggs using decision tree I.*

	Q1: Were any non-compliant residue data of the substance found in the last five years?				Q3: Are there indications for use of this substance in production systems for food producing animals?			Q2: Is a human health risk due to residues of this substance scientifically proven to be absent or negligible?	Conclusion priority	
Substances	**EFSA**	**RASFF**	**KAP data**	**Conclusion**	**Non-compliances poultry**	**Registered product EU for companion animals**	**Availability (alibaba/ebay)**	**Conclusion**	**Conclusion**	
Fenbufen	U	U	U	U	N	→	→	N	→	Low
Phenylbutazone/Oxy FBZ	U	U	U	U	N	→	→	N	→	Low
Flufenamic acid	U	U	U	U	N	→	→	N	→	Low
Ibuprofen	U	U	U	U	N	→	→	N	Y	Low
Indoprofen	U	U	U	U	N	→	→	N	→	Low
Meclofenamic acid	U	U	U	U	N	→	→	N	→	Low
Mefenamic acid	U	U	U	U	N	→	→	N	Y	Low
Naproxen	U	U	U	U	N	→	→	N	Y	Low
Niflumic acid	U	U	U	U	N	→	→	N	→	Low
Piroxicam	U	U	U	U	N	→	→	N	→	Low
Propyphenazone	U	U	U	U	N	→	→	N	Y	Low
Tolmetin	U	U	U	U	N	→	→	N	→	Low
Eltenac	U	U	U	U	U	Y	N	N	→	Low
Nimesulide	U	U	U	U	U	Y	Y	Y	N	High*
Cimicoxib	U	U	U	U	U	Y	N	N	→	Low
Grapiprant	U	U	U	U	U	Y	Y	Y	U	High*
Robenacoxib	U	U	U	U	U	Y	N	N	→	Low
Mavacoxib	U	U	U	U	U	Y	N	N	→	Low

* Not much known about the substance in food producing animals; therefore a risk because of use cannot be ruled out. However, use is less likely compared to substances with medium priority.

→ based on the outcome of the previous question, this question can be skipped

Annex 7 Prioritization of NSAIDs using decision tree III

Table A7.1 *Prioritization of NSAIDs in bovine products using decision tree III.*

Substances	Q2: Have MRLs been set for this substance in this animal species?	Q3: were any non-compliant residue data of the substance found in the last five years?				Q4: Is the substance regurlarly used in this animal species?				Q5: Do drugs with this active substance have a long withdrawal period?		Priority
		EFSA 2012-2016	RASFF 2012 - 2016	KAP data 2012, 2013, 2017	Concl.	Non-compliant	Registr. EU for bovine	FIDIN >100kg bovine	Concl.	Waiting term	Concl.	Bovine
Acetylsalicylic acid (asperin)	N[a]	→	→	→	→	N	Y	Y	Y	0 days	N	Low
Na-Salicylate	N	→	→	→	→	Y	→	→	Y	0 days	N	Low
Al-Salicylate	Y	Y	N	N	Y	→	→	→	→	→	→	Medium
Carprofen	Y	Y	N	N	Y	→	→	→	→	→	→	Medium
Diclofenac	Y	Y	N	N	Y	→	→	→	→	→	→	Medium
Firocoxib	N	→	→	→	→	N	Y	N[b]	N	→	→	Low
Flunixin / OH-flunixin	Y	Y	N	N	Y	→	→	→	→	→	→	Medium
Ketoprofen	N[a]	→	→	→	→	Y	→	→	Y	1-4 days	N	Low
Meloxicam	Y	Y	N	N	Y	→	→	→	→	→	→	Medium
Metamizol (MAA)	Y	Y	N	N	Y	→	→	→	→	→	→	Medium
Paracetamol	N[a]	→	→	→	→	Y[c]	→	→	Y	Cascade (28 days)	Y	Medium[c]
Tolfenamic acid	Y	Y	N	N	Y	→	→	→	→	→	→	Medium
Vedaprofen	N	→	→	→	→	N	N	N[b]	N	→	→	Low

[a] No MRL necessary based on certain matrices, but present in 37/2010

[b] Not in FIDIN data

[c] Based on milk

→ based on the outcome of the previous question, this question can be skipped

Table A7.2 *Prioritization of NSAIDs in porcine products using decision tree III.*

Substances	Q2: Have MRLs been set for this substance in this animal species?	Q3: were any non-compliant residue data of the substance found in the last five years?				Q4: Is the substance regurlarly used in this animal species?				Q5: Do drugs with this active substance have a long withdrawal period?		Priority
		EFSA 2012-2016	RASFF 2012 - 2016	KAP data 2012, 2013, 2017	Concl.	Non-compliant	Registr. EU for porcine	FIDIN >100kg porcine	Concl.	Waiting term	Concl.	
Acetylsalicylic acid (asperin)	N[a]	→	→	→	→	N	Y	N	N	→	→	Low
Na-Salicylate	N	→	→	→	→	N	Y	Y	Y	0 days	N	Low
Al-Salicylate	N	→	→	→	→	N	N	N[b]	N	→	→	Low
Carprofen	N	→	→	→	→	N	N	N	N	→	→	Low
Diclofenac	Y	Y	N	N	Y	→	→	→	→	→	→	Medium
Firocoxib	N	→	→	→	→	N	N	N[b]	N	→	→	Low
Flunixin / OH-flunixin	Y	Y	N	N	Y	→	→	→	→	→	→	Medium
Ketoprofen	N[a]	→	→	→	→	N	Y	Y	Y	1-5 days	N	Low
Meloxicam	Y	Y	N	N	Y	→	→	→	→	→	→	Medium
Metamizol (MAA)	Y	Y	N	N	Y	→	→	→	→	→	→	Medium
Paracetamol	N[a]	→	→	→	→	N	Y	Y	Y	0 days	N	Low
Tolfenamic acid	Y	Y	N	N	Y	→	→	→	→	→	→	Medium
Vedaprofen	N	→	→	→	→	N	N	N[b]	N	→	→	Low

[a] No MRL necessary based on certain matrices, but present in 37/2010

[b] Not in FIDIN data

→ based on the outcome of the previous question, this question can be skipped

Table A7.3 *Prioritization of NSAIDs in poultry meat using decision tree III.*

Substances	Q2: Have MRLs been set for this substance in this animal species?	Q3: were any non-compliant residue data of the substance found in the last five years?				Q4: Is the substance regurlarly used in this animal species?				Q5: Do drugs with this active substance have a long withdrawal period?		Priority
		EFSA 2012-2016	RASFF 2012 - 2016	KAP data 2012, 2013, 2017	Concl.	Non-compliant	Registr. EU for poultry	FIDIN >100kg poultry	Concl.	Waiting term	Concl.	poultry
Acetylsalicylic acid (asperin)	N[a]	→	→	→	→	N	Y	N	N	→	→	Low
Na-Salicylate	Y (turkey)	N	N	N	N	N	Y	N	N	→	→	Low
Al-Salicylate	N	→	→	→	→	N	N	N[b]	N	→	→	Low
Carprofen	N	→	→	→	→	N	N	N	N	→	→	Low
Diclofenac	N	→	→	→	→	Y	→	→	Y	28 days (cascade)	Y	Medium
Firocoxib	N	→	→	→	→	N	N	N[b]	N	→	→	Low
Flunixin / OH-flunixin	N	→	→	→	→	Y	→	→	Y	28 days (cascade)	Y	Medium
Ketoprofen	N[a]	→	→	→	→	N	N	N	N	→	→	Low
Meloxicam	N	→	→	→	→	N	N	N	N	→	→	Low
Metamizol (MAA)	N	→	→	→	→	Y	→	→	Y	28 days (cascade)	Y	Medium
Paracetamol	N[a]	→	→	→	→	N	N	N	N	→	→	Low
Tolfenamic acid	N	→	→	→	→	Y	→	→	Y	28 days (cascade)	Y	Medium
Vedaprofen	N	→	→	→	→	N	N	N[b]	N	→	→	Low

[a] No MRL necessary based on certain matrices, but present in 37/2010

[b] Not in FIDIN data

→ based on the outcome of the previous question, this question can be skipped

Table A7.4 *Prioritization of NSAIDs in eggs using decision tree III.*

Substances	Q2: Have MRLs been set for this substance in this animal species?	Q3: were any non-compliant residue data of the substance found in the last five years?				Q4: Is the substance regurlarly used in this animal species?				Q5: Do drugs with this active substance have a long withdrawal period?		Priority
		EFSA 2012-2016	RASFF 2012 - 2016	KAP data 2012, 2013, 2017	Concl.	Non-compliant	Registr. EU for egg	FIDIN >100kg egg	Concl.	Waiting term	Concl.	egg
Acetylsalicylic acid (asperin)	N[a]	→	→	→	→	U	N	N	U	→	→	Start survey
Na-Salicylate	N	→	→	→	→	U	N	N	U	→	→	Start survey
Al-Salicylate	N	→	→	→	→	U	N	N[b]	U	→	→	Start survey
Carprofen	N	→	→	→	→	U	N	N	U	→	→	Start survey
Diclofenac	N	→	→	→	→	U	N	N[b]	U	→	→	Start survey[c]
Firocoxib	N	→	→	→	→	U	N	N[b]	U	→	→	Start survey
Flunixin / OH-flunixin	N	→	→	→	→	U	N	N	U	→	→	Start survey[c]
Ketoprofen	N[a]	→	→	→	→	U	N	N	U	→	→	Start survey
Meloxicam	N	→	→	→	→	U	N	N	U	→	→	Start survey
Metamizol (MAA)	N	→	→	→	→	U	N	N	U	→	→	Start survey[c]
Paracetamol	N[a]	→	→	→	→	U	N	N	U	→	→	Start survey
Tolfenamic acid	N	→	→	→	→	U	N	N	U	→	→	Start survey[c]
Vedaprofen	N	→	→	→	→	U	N	N[b]	U	→	→	Start survey

[a] No MRL necessary based on certain matrices, but present in 37/2010

[b] Not in FIDIN data

[c] Substances with non-compliances in poultry meat

→ based on the outcome of the previous question, this question can be skipped

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Report 2019.008

The mission of Wageningen University & Research is "To explore the potential of nature to improve the quality of life". Under the banner Wageningen University & Research, Wageningen University and the specialised research institutes of the Wageningen Research Foundation have joined forces in contributing to finding solutions to important questions in the domain of healthy food and living environment. With its roughly 30 branches, 5,000 employees and 10,000 students, Wageningen University & Research is one of the leading organisations in its domain. The unique Wageningen approach lies in its integrated approach to issues and the collaboration between different disciplines.