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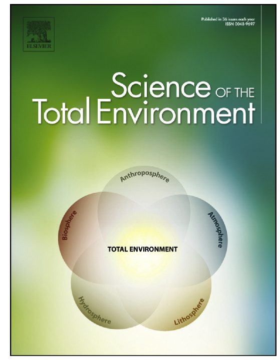

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A review of the occurrence of selected micropollutants and microorganisms in different raw and treated manure – Environmental risk due to antibiotics after application to soil.

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Abstract

This study consists of a review based on 104 papers published between 1980 and 2019, which dealt with the occurrence of pharmaceuticals, hormones and a selection of microorganisms in raw and treated manure from different types of animal farms. The selected pharmaceuticals and hormones are those regularly administered to livestock for treating and preventing diseases. Worldwide, manure is commonly spread on soil as a fertilizer due to its nutrient content. However, this practice also represents a potential pathway for micropollutant release into the environment. In this context, this study evaluates the predicted concentrations of some antibiotics in soil after the application of swine slurry on soil and compares them with corresponding measured concentrations found in the literature. Enrofloxacin, oxytetracycline and chlortetracycline were the antibiotics with the highest concentrations that were found in raw and treated manure and that showed a high risk together with sulfamethazine. Future research should focus on monitoring other pathogens, parent compounds and their main metabolites in raw and treated manure, studying the spread and development of antibiotic resistance genes in the environment due to residues of antibiotics in manure applied to soil, and evaluating predicted no effect concentrations of pharmaceuticals and hormones commonly administered to livestock with regard to terrestrial organisms.

Keywords: antibiotics, environmental risk assessment, hormones, livestock, manure-amended soil, predicted concentration in soil, raw manure, treated manure.

1 Introduction

Livestock is one of the main economic activities in many countries worldwide and farm management can differ from country to country, as well as the management of the waste produced by the activities themselves, in particular zootechnical effluent (Verlicchi et al., 2019).

The distribution maps of various livestock provided by FAO (Gilbert et al., 2018) show that the most common types of animal are cattle, followed by sheep and goats, swine, poultry and finally horses. The highest densities of cattle (number of heads/km^2) are in America (mainly South America), India, and some European countries; sheep are distributed as leopard spots across Europe, Asia and Africa; poultry farming takes place in many European and Asian countries; pig farms are common in Europe and China; and horse farms are present at a very lower density in America and other parts of the world. One problem related to livestock farms is the management of the manure and other types of zootechnical effluents generated at the farms.

In China, the production of livestock manure was up to 3.26 billion tons in 2009 (Zhang et al., 2009), while in the US and Canada, the annual estimated quantities of livestock manure were 132 million tons and 178 million tons, respectively (Dolliver and Gupta, 2008; Hofmann and Beaulieu, 2006). More specifically, the ranges of amounts of manure produced by the 1,000 heads registered for the different animals are 17,400–

26,100 kg/d for cattle, 21,000–25,000 kg/d for swine, 1,200–1,800 kg/d for sheep, 1,000–1,600 kg/d for goats, and 45–58 kg/d for poultry (MLA, 2003; Sims and Manguire, 2005). These figures underline the consistent daily amount of animal waste, even in small-medium livestock, which requires proper management (accumulation and/or treatment) and disposal (recovery, cotreatment with other wastewater and with the organic fraction of solid wastes, etc.).

Due to their nutrient contents, raw and treated zootechnical effluents may be considered as amendments (Combalbert et al., 2012) and applied to the soil for agricultural needs. This practice was and still is commonly followed in many countries, but there is an ongoing debate on the potential risks caused by the emission of the residues of contaminants that have not been properly retained or that cannot be removed during the treatment process. Over the last few years, increasing attention has been paid to the occurrence of (unregulated) contaminants of emerging interest (the so called micropollutants, in particular pharmaceuticals and personal care products) in any environmental compartment and to the main pathways which allow their introduction/release in the environment (Verlicchi et al., 2012; Ghirardini and Verlicchi, 2019; Al Aukidy and Verlicchi, 2017; Kuppusamy et al., 2018; Tasho and Cho, 2016).

With regard to the zootechnical sector, based on the technical literature, it was found that different classes of pharmaceuticals are (regularly or as needed) administered to farm animals for the treatment and prevention of bacteria, parasite diseases, and fungal and yeast infections; the control of gastrointestinal worms, liver flukes and lung worms; the control of hormonal activities and growth promotion (Boxall et al., 2004; Sarmah et al., 2006a; Pan et al., 2011).

The main groups of veterinary medicines administered in the UK and in the Netherlands, as reported in a study by Boxall et al. (2003), include: antimicrobials, endectocides, coccidiostats and antiprotozoals, antifungals, aquaculture treatment drugs, hormones, growth promoters, anaesthetics, euthanasia products, tranquillizers, nonsteroidal anti-inflammatories agents, and enteric bloat preparations. A more detailed list of the classes and main agents is compiled in the European Commission report (Tavazzi et al., 2018).

About 11 million kg of antibiotics are sold for disease control (therapeutic), prevention and growth promotion (sub-therapeutic) purposes in the US alone (USFDA, 2018) and more than 90 % of the cattle in the US receives steroid hormone treatments for growth promotion through implants behind the ears or as feed additives (USDA, 2013). Sweden banned the use of antibiotics as livestock growth promoters in 1986, Switzerland in 1999 (Haller et al., 2002) and the European Commission has banned the marketing and use of antibiotics as growth promoters in animal feed since January 2006 (EC 2003). This practice is still commonly adopted in many other parts of the world (Pikkemaat et al., 2016).

In addition to pharmaceuticals and hormones, other groups of micropollutants may be found in the different manures. This is the case of the plasticizer bisphenol A (released from the food containers or manure storage tanks) and the parabens methylparaben and propylparaben (Aznar et al., 2018; Zhang et al., 2014). Another category among contaminants to consider in order to better characterize manure includes microorganisms, both indicator microorganisms as well as pathogen microorganisms.

Being this said, the disposal of manure in soil for agricultural needs represents an opportunity but at the same time a threat. This review intends to provide a snapshot of the concentrations of the main contaminants of emerging interest and of selected microorganisms in different types of raw and treated manure produced by different animals. In addition, it presents and discusses a method for the prediction of the manure-amended soil concentrations for a selection of compounds and compares predicted concentrations with measured concentrations (found in the literature). The review ends with a focus on an environmental risk assessment in swine manure-amended soil, by means of the risk quotient approach, for a selection of antibiotics commonly administered to pigs. The collection of data presented and discussed herein aims to represent the baseline for further studies in order to evaluate the impact of the spreading of manure on soil and its contribution to the immission of residues of micropollutants in the environment via soil and the subsequent percolation/runoff. In addition, the adopted approach for an environmental risk assessment may also be applied to other types of manure if applied to land.

2 Definition and types of manure included in this review

Manure characteristics are strongly related to the animal producing it (namely animal type, weight, growing stage, sex, age), to the environment and conditions in which the livestock live, to the farm (in terms of type, size and management). Table 1 reports the principal groups of raw manure, based on manure constituents and phases, the types considered in this study, the corresponding percentage content of nutrients and dry matter, and the main types of treated manure used in land amending with their main chemical characteristics.

We will call manure in which concentrations of selected pollutants are generally expressed in terms of ng/L "liquid manure": this will refer to urine, flushing materials, lagoon effluent, lagooning sludge and anaerobically digested manure. We will refer to "semiliquid manure" in case of slurry or liquid fraction of manure. In a few cases, the authors have provided concentrations in lagooning sludge and anaerobically digested manure in ng/g dry matter (dm)). It is thus useful to note that manure bulk density may be assumed equal to 500–780 kg/m^3 for bedding manure, and around 1,000 kg/m^3 for raw liquid manure and slurry (BUR Regolamento Regionale ER 2017; EC-TGD, 2003).

Collected values of concentrations of micropollutants and microorganisms will be reported according to this classification. We tried to relate micropolluatnt concentrations to other types of classification, such as stall type and size or stall management. Due to an incomplete description of the farms and of their management in the reviewed papers, these attempts did not lead to consistent results and we preferred to maintain the classification reported in Table 1. The only further analysis we carried out referred to a comparison between micropollutant concentrations in dairy and beef cattle raw manure.

Table 1

3 Framework of the study

The study is based on 104 published papers on peer reviewed journals between 1980 and 2019. They were selected from Scopus, assuming the following keywords "Pollutants AND manure", "Microorganisms AND manure", "Pharmaceuticals AND manure", "Antibiotics AND manure", "Hormones AND manure".

A paper was included in the review if it referred to *real* concentrations of veterinary pharmaceuticals, hormones and microorganisms, and clearly stated the animal producing the manure and the type of raw or treated manure.

The studies were carried out in 20 countries all over the world (mainly in the US, China, Canada, Spain and Germany) and refer to manure produced (in descending order) by pigs, cattle, poultry and, to a lesser extent, sheep and horses. Figure S1 reports the types of manure investigated in the different countries and gives the corresponding references.

Some studies included more than one investigation (different manure, different treatment before application, etc.), therefore, based on the 104 papers that were included in the review, 241 investigations were identified.

Table S1 reports the details of the 241 experimental campaigns carried out in the 104 papers, as well as the principal features addressed in each of them (e.g. seasonal variation of micropollutant content in manure, environmental risk assessment after spreading, measured or predicted concentration of micropollutants in manure-amended soil, study of the fate of micropollutants once spread on rural land, factors influencing pollutant mobility in soil, etc.).

The pollutants monitored in the reviewed studies were: 145 chemical compounds (including parent compounds, some metabolites and transformation products) belonging to 11 therapeutic classes and 16 microorganisms. Table 2 summarises the compounds according to their classes, whereas Table S2 includes the main properties of the compounds and the references for the occurrence data included in this review.

First of all, the study briefly addresses manure management (stockpiling or onsite treatment) and common practices applied in different countries across the world. It gives a quick overview of the main characteristics of legislation in force and then presents the ranges of concentrations found in both raw and treated manure.
Concentrations in raw manure are generally expressed in terms of ng/g of dry matter (dm) for all the types described in Table 1. For manures with a dry matter content of less than 10 %, micropollutant concentrations may also be reported in ng/L (this is the case for investigations referring to slurry, liquid fractions of manure due to percolation, flushing materials, and urine). With regard to treated manure, data referring to lagoon effluent are only given in ng/L while data regarding lagooning sludge and anaerobically digested manure are expressed in terms of both ng/L and ng/g dm. Finally, data referring to composting and alum treated manure are given in ng/g dm. Tables S3–S5 provide information about the observed excretion factors of pharmaceuticals and hormones administered to the different animals as well as their half-life in manure and manure-amended soil.
Collected concentrations of microcontaminants in raw manure and treated manure produced by different animals are reported in Figures 1–10 and Figures 11–16, respectively. A comparison of the concentrations in raw and treated manure is reported in Figures S2-S9. Concentration values and the highest ranges of variability of the selected micropollutants are discussed (Table 3 and 4) and an attempt to correlate them with the main factors characterizing the farm type, activity and management operations was carried out. In particular the influence of the type of cattle farm (dairy or beef cattle farm) on the concentrations of the selected micropollutants in raw manure is presented in Figures S10 and S11.
Concentrations of microorganisms in raw manure are shown in Figure 17 and concentrations in treated manure in Figure 18. Tables S6–S16 report the descriptive statistical analysis for each type of manure in terms of number of data, minimum, maximum, average values, standard deviation and the 75th percentile. Then an estimation of the soil concentration (predicted environmental concentration [PEC]) for a selection of 10 antibiotics in cases of swine slurry-amended soil was carried out following the model described in the European Technical Guidance Document on risk assessment (EC-TGD 2003) (Tab. 5). These values are compared with the measured concentrations found in the literature (Tab. 5 and also Tab. S18 with many details). Based on the PECs, an environmental risk assessment was carried out by means of the risk quotient approach (Fig. 19). The study is completed with a discussion of the most critical compounds which can enter into the environment via manure disposal and the main risks for the environment due to manure spreading on the soil.

Table 2.

3.1 Quality assurance of literature data

As reported by the EC Technical Guidance Document on risk assessment (EC TGD, 2003) and as stated by many Authors (among them Liebig et al., 2006; Ternes and Joss, 2006, Verlicchi et al., 2012), it is vital that the quality of literature data is assured. In this context, to be included in the current review, studies had to provide an in-depth description of the animal producing the manure, the type of manure to be sampled and analysed, its treatment (if present), a description of the analytical methodology used for the assessment of measured concentrations of microcontaminants and microorganisms, and the quality assurance programme adopted for sampling, analysis and processing. In particular, with regard to microcontaminants, the following information had to be provided: list of analytes, solvents and chemicals used; details of sampling, transport and storage in addition to sample volume; analytical methods adopted, including pH adjustment, filtration and filter material; extraction and solvent evaporation techniques; derivatization and detection method; surrogate and/or instrumental standards used; methods and limits of quantification, recovery measurements, procedural and instrumental blanks used; sampling conditions,

location, sampling frequency and mode (in particular spatial distribution of sampling to produce a representative manure sample.
If reported values of concentrations referred to spiked concentrations, or the type of manure was not well described, the paper was rejected.
In a few cases, studies were included even if the sampling procedure was not exhaustively reported but the analytical methods were clearly reported and the data collected allowed us to complete the chemical and bacteriological characterisation of the wide spectrum of manure types reviewed (see Table 1) in terms of micropollutants and microorganisms.
It was found that studies published more recently were more accurate than older ones in the description of Materials and Methods. Those published before 2000 provide fewer details. These studies were included because they reported the concentrations of microorganisms and selected micropollutants in different manures, but their main aims were to analyse the land runoff once the manure was distributed on the soil (Busheé et al., 1998; Nichols et al., 1997, 1998) or the effects on nutrient mineralisation on soil and plant growth (Patten et al., 1980). In Table S1, the level of accuracy of each study is highlighted as well as the main issues addressed in the reviewed papers.
The collected data reported in the graphs and tables in the manuscript and supplementary material come not only from tables, but also from graphs. In this case, the uncertainties associated with the values add to the sampling and analysis uncertainties (as discussed in Verlicchi and Zambello, 2016 and, following the same approach, reported in Ghirardini and Verlicchi, 2019), even in cases where the data reading was quite accurate. If a literature value was reported below its limit of detection (LOD), in this review it was assumed equal to the corresponding LOD and if it was reported below its limit of quantification (LOQ), it was assumed to be half its LOQ value.

4 Manure generation, management, treatment, disposal and available legal requirements

Pharmaceuticals may be administered to animals for different periods of time, sometimes for prevention, other times for specific treatments. For instance, in swine livestock, the antibiotics chlortetracycline and tylosin are regularly administered for treatment, prevention and growth promotion with treatment lengths ranging from 27 days (respiratory diseases), 41 days (enteric diseases) and 62 days for promoting growth and weight gain (APHIS, 2012). Further details of the administration of specific pharmaceuticals are reported in Table S1 lines 15 and 16, see for instance Ray et al., (2017), Sura et al. (2015) and van Donke et al. (2013).
Once administrated, the compound is only partially assimilated, and the remaining fraction is excreted via animal urine and faeces. Available values of excretion factors are reported in Table S3 for a group of the selected compounds. Management operations of the farms vary depending on the animal type, the size and the country. Unfortunately, they are not always reported. On the basis of the description provided by Arikan et al. (2007), Chen et al. (2018), Derby et al (2001), Hoise et al. (2009), Joy et al., 2014) Ray et al. (2017), Sarmah et al (2006b), Watanabe et al. (2010), Zhang et al. (2013), Zhou et al (2013a, 2013b) it is possible to have an idea of how different they may be.
When excreted, manure is generally stored in pits and lagoons if it is semiliquid or liquid (Combalbert et al., 2012; Ben et al. 2013, Gadd et al., 2010) or in heaps in the case of bedding or solid manure (Derby et al.,2011, Kelley et al., 1994). As reported in Raman et al. (2004), manure storage pits and holding ponds are designed to store the volume of a given time period (6-12 months), after which the stored manure can be land applied. In dairy cattle farms, different units may be present: calf hutches, hospital pens, milking barns, heifer freestall. These units are characterized by specific management operations leading to the generation of different manure types which may be mixed or destinated to different ways of disposal (Watanabe et al., 2010). During storage, organic matter may be subjected to degradation processes the

kinetics of which is strictly related to environmental conditions (namely oxygen concentration, temperature and rainfall) (Tavazzi et al., 2018). At the same time, there could also be a reduction in the content of the different microorganisms due to unfavourable conditions. Sometimes, as is the case for dairy manure collected by flushing freestalls, it is first necessary to separate the liquid fraction from the solid fraction by using different techniques (settling basin sedimentation or mechanical screening) (Hafner et l., 2017). If the manure is subjected to composting, degradation of the different compounds may occur. This is strictly related to the adopted temperature, pH, microbial enzymes present and microorganisms developed in the system (Ramaswamy et al., 2010, Ezzariai et al., 2018; Spielmeyer, 2018).

To have an idea of the degradation kinetics of the compounds in the stockpiled manure under investigation, Table S4 reports the half-life times and corresponding kinetic model for a group of pharmaceuticals according to the different animals. Most of these data refer to batch tests and not to real and prolonged investigations. The interesting investigations carried out by Berendsen et al. (2018) state that degradation of antibiotics is mainly due to abiotic processes and varies considerably mainly depending on the manure type and, to a lesser extent, the type of animal producing it. Of all the antibiotic classes, sulphonamides dissipate quickly in all manure types, presenting a half-life between 0.2 and 30 days, whereas, tetracyclines, quinolones, macrolides and lincomicides are more persistent (much higher than 30 days). The fate and transport of microcontaminants are correlated with the manure type in soil, for instance if it is spread as a solid phase or a liquid phase (Wallace and Aga, 2016, Tasho and Cho, 2016, Gros et al., 2019).

According to Zhang et al. (2013), lagoon effluent is often pumped for irrigation at least once a year, lagooning sludge instead is removed every 5–20 years and then spread on soil.

Once disposed on soil, the behaviour of the residues of micropollutants depends on their nature (Chen et al., 2018) and different biotic and abiotic processes may occur (Tasho and Cho, 2016). An interesting analysis is carried out by Solliec et al. (2016) and Gros et al. (2019), who tried to explain the attenuation of antibiotics in soil amended with (swine) manure over a prolonged period, correlating it with the properties of the compound and the soil characteristics. According to Hutchison et al. (2005), once manure is spread on soil, commonly microorganisms (*E. coli*, *Salmonella*, *Listeria*) decline rapidly: 1 log unit reduction was observed within 1.5–2.5 days for all these species. *E. coli* was detected up to 32 days, Salmonella up to 63 days and Listeria up to 128 days.

Land disposal of manure has to fulfil the legal limits set in the various countries regarding maximum quantity of manure of different origins as well as specific periods and weather conditions (rainy periods must be avoided) in which manure can be applied. An in depth analysis of the legal requirements set in the different countries is beyond the aims of this review. In general, a common parameter is organic nitrogen content, which defines the maximum quantity of manure, which can be spread (Aga et al., 2005). The limit has been established to avoid the risk of contaminating aquifers due to percolation. At EU level, Directive 91/676/EEC (EU, 1991), establishes the value at 170 kg organic N/(ha year) in areas at risk of nitrate contamination (vulnerable zones). In the Po Valley in Northern Italy, according to a regional regulation (Regione Emilia-Romagna, 2017), there is another limit in addition to the above limit for areas that are not at risk of eutrophication which corresponds to 340 kg organic N/(ha year). Other maximum values may also be adopted. For instance, the annual application rate in Australia corresponds to 240 kg N/ha year (Eldridge et al. (2009)).

To have an idea of the required area where the produced manure may be applied, we can consider a farm with 100 dairy cows. Assuming that the manure produced corresponds to 1,700 kg/d (MLA, 2003) and a percentage of nitrogen varying between 0.6 %–4.6%, the daily amount of nitrogen produced results equal to 10 and 78 kg N/d and on an annual basis to 3,700 and 28,500 kg N/year. This quantity would require an arable area between 21 and 168 ha to respect the limit of 170 kg N/ha year set down by some of the regulations mentioned above.

5 Results

As reported above, the investigations included in this review refer to cattle, poultry, swine and, to a lesser extent, horses, sheep and goats. They were carried out in different countries worldwide, mainly in Canada and the US, Europe and (East) China. The map in Figure S1 shows the various locations and corresponding references. It emerges that most of the investigations in North America dealt with three main types of manure (cattle, swine and poultry), swine and cattle manure in Europe, and swine and poultry manure in China. Horse manure was investigated by Busheé et al. (1998) in North America; manure produced by sheep and goats was investigated by Sarmah et al. (2006b) in New Zealand; and by Hutchison et al. (2004) in the United Kingdom.

As a whole, with regard to the 241 investigations (see Table S1), 37 % referred to cattle manure, 34 % to swine manure, 27 % to poultry manure and 1 % (each) to sheep/goat and horse manure.

As mentioned above, although the use of antibiotics as growth promoters in animal feed has been banned in some countries, this practice is still followed worldwide. Data presented in the graphs may also include investigations in countries where antibiotics are still used as feed additives. The snapshot provided by this overview aims to show the observed ranges of variability for the different pharmaceuticals investigated.

5.1 Occurrence of selected micropollutants in different raw manures

Figures 1–10 below report the concentrations of selected micropollutants grouped according to their class in the different types of raw manure under review (see Table 1).

In Figures 1–6, concentrations are given in ng/g dm, whereas in Figures 7–10 they are given in ng/L as they refer to manure with a content of solids less than 10 % (known as liquid or semiliquid manure), namely: slurry, liquid (fraction) manure, flushing material and urine. In some cases, as mentioned in Table 1, the concentrations referring to these kinds of manure are in both units (ng/g dm and ng/L).

With regard to raw cattle manure (Figures 1 and 2), the collected data refer to 98 compounds belonging to 6 different groups: analgesics/antinflammatories, anticonvulsants, antihelmintics, antimicrobials, hormones and plasticizers, as well as four types of raw manure: bedding manure, liquid fraction manure, slurry and solid manure. As a whole, the concentrations varied between 0.02 ng/g dm (the hormone trendione in slurry) and 225,000 ng/g dm (the antibiotic oxytetracycline in bedding manure).

It emerges that there was highest number of collected data for sulfamethazine and tylosin (69), chlortetracycline (68), oxytetracycline (62), tetracycline (56), sulfadimethoxine (42) and epi-tetracycline (35). The remaining compounds present a lower number of values. Moreover, the widest variability range was found for oxytetracycline (6 orders of magnitude: from $1\ 10^{-1}$ to $2.25\ 10^{5}$ ng/g dm), followed by chlortetracycline, enrofloxacin and sulfamethazine (5 orders of magnitude each). 11 compounds have a variability range between 1,000 and 6,000 ng/g dm. When limiting the attention to compounds exhibiting more than 5 collected values, it emerges that the highest average values (± standard deviation) were found for oxytetracycline (5,815 ± 29,452 ng/g dm), monensin (2,434 ± 2,272 ng/g dm) and enrofloxacin (2,318 ± 10,176 ng/g dm). It is interesting to note that as reported in detail in Table S6, the 75th percentile is lower than the corresponding average value for 27 out of the 98 compounds considered. The highest differences were found for oxytetracycline and enrofloxacin: the 75th percentile values were 166 ng/g dm for the first and 33 ng/g dm for the second compound. This is due to the extraordinarily high maximum value of each of compound. In some investigations, the analysis of antibiotics in manure where carried out soon after 5 days of administration to the animals in order to focus on the most critical scenario (Arikan et al., 2007).

With regard to the different raw cattle manure, it emerges that most collected data refer to solid manure (571 values), followed by bedding manure (296) and slurry (116), whereas the liquid fraction was rarely sampled and analysed: only 6 data were collected and all refer to antibiotics.

A rapid glance at Figures 1 and 2 shows that the maximum values mainly occurred in solid manure (57 %) followed by slurry (20 %) and then bedding manure (22 %).

Figure 1

Figure 2.

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With regard to poultry manure (Figures 3 and 4), concentrations are available for 92 compounds belonging to 10 different groups: analgesics/antinflammatories (7 compounds), anticonvulsants (1), antimicrobials (53), antiseptics (3), beta-blockers (1), hormones (20), inhibitors (1), lipid regulators (3), parabens (2) and plasticizers (1) and two types of raw manure.

A quick look at the graphs shows that the concentrations varied between 0.03 ng/g dm (the hormone testosterone in poultry litter) and 1.4 10^6 ng/g dm (the antibiotic enrofloxacin in poultry litter produced in a poultry feedlot in China, according to Zhao et al., 2010).

It emerges that the highest numbers of collected data occurred for sulfadiazine (54 values), doxycycline (47), enrofloxacin (44), progesterone (40), chlortetracycline (34), oxytetracycline (33), sulfachlorpyridazine and 17β-estradiol (32), norfloxacin and trimethoprim (31). The remaining compounds present a lower number of collected values. Moreover, the widest variability ranges were found for enrofloxacin (7 orders of magnitude), followed by fleroxacin and oxytetracycline (6 orders of magnitude) and tylosin, sulfadiazine, salinomycin, trimethoprim, erythromycin and difloxacin (5 orders of magnitude). 13 compounds have 4 orders of magnitude variability range and for 8 substances the width of the variability range varied between 1,500 and 8,500 ng/g dm.

Limiting the attention to compounds exhibiting more than 5 collected values, it emerges that the highest average values (± standard deviation) were found for enrofloxacin (35,774 ± 213,817 ng/g dm), oxytetracycline (13,769 ± 72,375 ng/g dm), flumequine (11,833 ± 19,581 ng/g dm) and doxycycline (10,935 ± 22,260 ng/g dm). A descriptive statistical analysis of the collected data referring to poultry is reported in Table S7. Based on this, it is interesting to note that for 27 out of the 92 compounds considered, the 75^{th} percentile was less than the corresponding average value. The highest differences were found for enrofloxacin and oxytetracycline (of which the 75^{th} percentiles were 939 ng/g dm and 1,600 ng/g dm, respectively) due to the extraordinarily high maximum value of each of them (for details see: Zhao et al., 2010 and Zhang et al., 2015).

With regard to poultry manure, it emerges that only two types of manure are present: poultry manure (exhibiting 699 values) and poultry litter (with 349 values). Details about the definition and characteristics of the two types of manure are reported in Table 1.

A rapid glance at Figures 3 and 4 shows that maximum values mainly occurred in solid manure (61 %) followed by poultry litter (39 %).

Figure 3

Figure 4

With regard to swine manure (Figures 5 and 6 and Table S8), the collected data refer to 77 compounds belonging to 5 different classes: analgesics/antinflammatories (2), antimicrobials (62), antihelmintics (1), hormones (11) and plasticizers (1) and 5 types of raw manure.

As a whole, the micropollutant concentrations varied between 0.05 ng/g dm (the antibiotic trimethoprim in pig slurry) and to 879,600 ng/g dm (this is due to the antibiotic chlortetracycline in solid (fraction) manure, according to Bao et al., 2009). It emerges that the highest number of collected data occurred for antibiotics: doxycycline (100 values), sulfadiazine (93), oxytetracycline (72), chlortetracycline (65), tetracycline and sulfamethazine (59), tylosin (44) and ciprofloxacin (41). Five further antibiotics present a number of values between 30 and 40, another six compounds between 20 and 29, fifteen compounds between 10 and 19. The remaining forty-three substances have 1–9 values.

Moreover, the widest variability ranges were found for oxytetracycline and chlortetracycline (6 orders of magnitude), followed by bacitracin A, doxycycline, tetracycline, lomefloxacin, enrofloxacin, tylosin, sulfamethazine, sulfamonomethoxine, lincomycin and sulfathiazole (5 orders of magnitude). For 19 compounds the variability range width varied between 1,000 and 7,500 ng/g dm.

Limiting the attention to the 51 compounds exhibiting more than 5 collected values, it emerges that the highest average values (± standard deviation) were found for chlortetracycline (76,667 ± 176,264 ng/g dm), bacitracin A (28,133 ± 85,165 ng/g dm), chloramphenicol (11,693 ± 28,761 ng/g dm) and oxytetracycline (11,180 ± 43,662 ng/g dm). It is interesting to note that, as reported in detail in Table S8, and similar to the results found in the previous analysis of cattle and poultry manure, for 36 out of 77 compounds the 75th percentile is lower than the corresponding average. The highest differences (75th percentile – average value) were found for bacitracin A, lomefloxacin and oxytetracycline. This is explained with the extraordinarily high maximum value for the corresponding compound (for details see: Joy et al., 2013; Zhao et al., 2010; Chen et al., 2012).

With regard to the different types of swine manure, it emerges that most of the collected data refers to solid (fraction) manure (780), followed by slurry (327) and the other types presenting less than 100 data (70 for flushing material, 46 for liquid fraction manure and 15 for bedding manure).

A rapid glance at Figures 5 and 6 shows that the maximum values mainly occurred in solid (fraction) manure (62 %) followed by slurry (32 %) and flushing material (6 %).

Figure 5.

Figure 6.

A comparison of the collected data for cattle, poultry and swine manure shows that the maximum values of concentration always occurred in the solid fraction of manure; the antibiotics chlortetracycline and oxytetracycline are the most investigated compounds and they are always the compounds with the highest average values; finally swine manure is the object of the highest number of studies. As to monensin, it was found that it is commonly investigated in cattle manure rather than the other types and it also presented very high concentrations only in cattle manure. According to Łowicki and Huczyński (2013), this can be explained by the fact that it is largely administered for cattle as it may improve food metabolism in the ruminants and it leads to faster growth in cattle. In poultry, it is mainly used for the prevention of Coccidiosis and thus its use is rarer.

With regard to the liquid/semiliquid cattle manure analysis (Figures 7 and 8, Table S9), it emerges that the collected concentrations refer to 80 compounds belonging to 5 different classes (1 analgesic/antinflammatory, 1 anticonvulsant, 62 antimicrobials, 15 hormones and 1 plasticizer) and to 4 different types of manures: flushing material, liquid manure, slurry and urine. Their concentrations varied between 0.5 ng/L (some sulphonamides in flushing material investigated by Zhang et al., 2013) and 5.86 10^6 ng/L (chlortetracycline, in slurry, according to Arikan, 2008).

The most analysed compounds were the hormones 17β-estradiol and estrone (34 values) followed by the antibiotics oxytetracycline, sulfamethazine and tetracycline and the hormone 17 α- estradiol (32 values). The widest variability ranges were found for chlortetracycline and epi-chlortetracycline (6 orders of magnitude), followed by iso-chlortetracycline, sulfamethoxazole and sulfamethazine (5 orders of magnitude). 5 compounds have 4 orders of magnitude variability and two compounds variability range of 3 orders of magnitude. The highest values were reported by Arikan (2008) in a dedicated investigation on characteristics of calf manure soon after administration of the antibiotics at the permitted dose of 22 mg/kg body mass per day for 5 days (a standard dose in agricultural practice).

With regard to compounds with at least 5 collected values of concentrations, the highest average concentrations were found for epi-chlortetracycline (766,691 ± 1,649,564 ng/L), followed by chlortetracycline (281,281 ± 1,247,918 ng/L) and iso-chlortetracycline (280,274 ± 687,556 ng/L).

In this case, 25 out of 80 compounds had a 75th percentile lower than the corresponding average value (see Table S9), being the highest differences (75th percentile – average value) for epi-chlortetracycline chlortetracycline and iso-chlortetracycline. Most of the collected data refer to flushing material (473 values of concentrations) followed by urine (103 values). As for liquid manure, only 36 data are available and refer to antibiotics. Most of the maximum values refer to flushing material

Figure 7.

Figure 8.

With regard to raw liquid and semiliquid swine manure (Figures 9 and 10 and Table S10), the collected data are available for 72 compounds from 5 classes (2 analgesics/antinflammatories, 57 antimicrobials, 1 antihelmintic, 11 hormones and 1 plasticizer) and for 4 types of manures (flushing material, liquid manure, slurry and urine). The collected concentrations vary between 0.1 ng/L (sulfamonomethoxine in flushing material found by Li et al., 2018) and 1.1 10^8 ng/L (chlortetracycline in slurry found by Hoese et al., 2009). A reduced number of papers report concentration data in ng/L, with respect to concentration in ng/g dm. The highest number of values is only 19 for chlortetracycline, 18 for oxytetracycline and sulfamethazine, and 15 for ciprofloxacin and tylosin.

As for the observed variability range, it was found that in some cases it is wider than the previous analysis, referring to ng/g dm, where it was 6 orders of magnitude as a maximum: for chlortetracycline it is 9 orders of magnitude, for sulfamethazine it is 8 orders of magnitude and for sulfamonomethoxine and oxytetracycline it is 7 orders of magnitude. There are 4 compounds with range of 6 orders of magnitude and two with 5 orders of magnitude and the remaining compounds with ranges of 4 orders of magnitude or less.

The highest average concentrations (± standard deviation) was found for chlortetracycline (5.78 10^6 ± 2.5 10^7 ng/L), followed by lincomycin (2.9 10^6 ± 7.7 10^6 ng/L). In Table S10, further details are reported, together with a descriptive statistical analysis of the collected data. An analysis of the 75th percentile values shows that for 11 antimicrobials the 75th percentile is lower than the corresponding average value. The highest differences were found for chlortetracycline, lincomycin, sulfamethazine, sulfamonomethoxine and tylosin.

Extraordinary high concentrations were found for chlortetracycline and tylosin reported by Hoese et al. (2009). The authors noted that they were higher than those found in other investigations (such as Kumar et al., 2004 and Martinez Carballo et al., 2007) and were due to the fact that they refer to *fresh* swine manure and not to manure collected in a pit or a lagoon, and that they then sampled and analysed it like in the other investigations.

With regard to the number of values collected per manure type, it emerges that for flushing material there are 188 concentrations, 38 for liquid manure, 53 for slurry, and 31 for urine. The maximum values occurred mainly for slurry (45 %), flushing material (34 %), urine (11 %) and liquid manure (10 %).

Figure 9.

Figure 10.

With regard to poultry house flushing material, data are available only for 8 antibiotics: chlortetracycline, cyromazine, doxycycline, oxytetracycline, sulfadiazine, sulfamethazine, sulfaquinoxaline and tetracycline (Wei et al., 2011). Their highest concentrations vary between 550 ng/L (cyromazine) and 20,700 ng/L (oxytetracycline) and their average concentrations between 90 ng/L (sulfamethazine) and 950 ng/L (doxycycline).

Seasonal variations in antibiotic concentrations may be expected. According to the study carried out by Ben et al. (2013) on the quality of swine wastewater collected in sinks and lagoons in 21 types of livestock in China in winter and summer, it emerges that average concentrations of the monitored antibiotics (5 sulfonamides, 3 tetracycline and 1 macrolide) and their detection frequency are higher in winter than in summer. They explain these seasonal fluctuations by the fact that, in summer, an enhanced dilution is due to more frequent washing operations and the intensified precipitation events, which are characteristic of the monsoon climate of the area being studied. In addition, they state that, in winter, a higher amount of tetracyclines is administered to animals to prevent flu and other respiratory illnesses which are more frequent in the cold weather. The same conclusions are confirmed by the investigations by Wang et al. (2019) referring to pig flushing material generated by two swine farms in China. In a previous study (Pan et al., 2011) carried out in the same study area by Ben et al., (2013), it was found that sulphonamides occurred at a higher detection frequency and higher concentrations in summer than in winter (except for sulfamethoxazole) as these antibiotics are generally used to treat a variety of bacterial and protozoal infections which occur more frequently in the hot season. Raman et al., 2004, note that differences between the concentrations referred to in winter and summer could also be due to environmental effects, namely the temperature of the environment which may affect the degradation processes in the case of stored manure.

Wallace et al., 2018, investigated seasonal variations of antibiotics belonging to the class of tetracyclines in solid raw manure from cattle and found that the concentrations of all the investigated compounds (oxytetracycline, chlortetracycline, tetracycline, epi-tetracycline, epi-chlortetracycline and anhydrochlortetracycline) were higher in spring than in winter.

5.2 Occurrence of selected micropollutants in treated manure

In many cases, manure is stocked and treated before being spread on soil. Common treatments include lagooning, composting, anaerobic digestion, pelletization and alum treatment (Wallace et al., 1018; Cessna et al., 2011, Combalbert et al., 2012). Their main aim is to promote nutrient degradation, liquid-solid separation, dewatering and coagulation.

At the same time, micropollutants may undergo different degradation processes and parent compounds may generate transformation products. The collected data reported in Figures 11–16 (in Figures 11 and 12 they are given in ng/g dm, and in Figures 13–16 in ng/L) refer to different types of manure undergoing different treatments. The observed variability ranges of occurrence of selected compounds, average concentrations and the number of data available are discussed here and compared with the corresponding type of raw manure.

Figure 11 (and Table S11) reports data from treated cattle manure for 41 compounds (1 analgesic/antinflammatory, 1 anticonvulsant, 22 antimicrobials and 17 hormones). 58 % of them refers to hormones and 41 % to antimicrobials. The most common manure treatment was composting, followed by lagooning and finally anaerobic digestion.

The observed range of concentrations varies between 0.06 ng/g dm (pirlimycin in composted solid manure, Chen et al., 2018) and 4,000 ng/g dm (iso-chlortetracycline in composted bedding manure, Arikan et al. (2009)). The most investigated compounds were chlortetracycline (10), followed by progesterone, α-zearalanol and estrone (9). The widest variability range was found for 17α-estradiol (3 orders of magnitude). As to compounds with at least 5 values in the graph, the highest average concentrations were found for chlortetracycline (179 ± 114 ng/g dm) and tetracycline (134 ± 148 ng/g dm). 4 compounds out of 41 present the 75th percentile value lower than the corresponding average value: this the case for hormones, 17β-estradiol, estrone, α-zearalanol and β-zearalanol.

Figure 11

Swine manure is commonly subjected to lagooning, composting and anaerobic digestion (Combalbert et al., 2012). Studies investigating occurrence of micropollutants in swine treated manure are summarized in Figure 12 and Table S12. From these it emerges that 59 compounds were analysed (56 antimicrobials and 3 hormones); the most applied treatment is lagooning (427 values of concentrations included in the review), followed by anaerobic digestion (44 values) and composting (12 values). The observed range of occurrence varies between 0.45 ng/g dm (danofloxacin in lagooning sludge, reported by Zhou et al. 2013b) and 87,900 ng/g dm for chlortetracycline in lagooning sludge (by Zhou et al., 2013b). The most studied compounds were chlortetracycline, doxycycline, oxytetracycline, sulfadiazine and tetracycline with there being 21 values collected for each of them. The highest variability range covers 4 orders of magnitude and refers to oxytetracycline, tylosin, norfloxacin and sulfamethazine. 13 compounds have a range of 3 orders of magnitude. The highest average concentrations were due to iso-chlortetracycline (28,200 ± 6,930 ng/g dm), epi-chlortetracycline (22,850 ± 3,323 ng/g dm) and chlortetracycline (8,985 ± 21,417 ng/g dm).

16 out of 60 compounds present a 75th percentile lower than the corresponding average value. Most of the maximum values were found in lagooning sludge (68 %), followed by anaerobically digested flushing material (28 %).

Figure 12.

Regarding hormones, it was found that: aerobic treatments (aerated lagoons and composting) generally promote the reduction of the hormone concentrations, but their effect on reducing the endocrine-disrupting activity is very modest (Combalbert et al., 2012, Derby et al., 2011). Zhang et al. (2014) stated that oxygen and composting time are the main factors affecting the removal efficiency of hormones.

Figures 13 and 14 refer to concentrations collected for 63 micropollutants in treated liquid-semiliquid cattle manure (further details are also reported in Table S13). The compounds belong to 4 classes: 1 analgesic/anti-inflammatory, 1 anticonvulsant, 36 antimicrobials and 25 hormones. The adopted treatments were lagooning (493 concentrations value), followed by anaerobic digestion (13 values). The observed variability range varies between 0.01 ng/L for estriol (E3) in lagoon effluent (according to

Kolodziej et al., 2004), and 6.8 10^6 ng/L for oxytetracycline in anaerobic digested bedding manure (Arikan et al., 2006). The most investigated compounds were hormones (42 values for estrone, 40 for 17β-estradiol and 37 for 17α-estradiol). The widest variability range was of 5 orders of magnitude and were found for 5 antibiotics: oxytetracycline, epi-oxytetracycline, chlortetracycline, and epi- and iso-chlortetracycline.
The highest average values were found for epi-chlortetracycline (1.1 10^6 ± 1.3 10^6 ng/L), iso--chlortetracycline (7.3 10^5 ± 1.6 10^6 ng/L), epi-oxytetracycline (6.7 10^5 ± 5.4 10^5 ng/L) and oxytetracycline (5.4 10^5 ± 1.7 10^6 ng/L). On the basis of the statistical analysis reported in Table S13, it emerges that for 14 compounds, the 75th percentile is lower than the corresponding average value. The highest differences were found for iso-chlortetracycline (7.2 10^5 ng/L), oxytetracycline (5.4 10^5 ng/L) and chlortetracycline (1.1 10^5 ng/L). The maximum values occurred in lagoon effluent (88 %) and anaerobic digested manure (12 %).
With regard to treated poultry manure a limited number of data are available and refer to the antibiotic salinomycin (3 values) and the hormones 17β-estradiol (2 values) and testosterone (3 values) (Nichols et al., 1997, Ramaswamy et al., 2010, Hakk et al., 2005 and Shore et al., 1993). Limiting the attention to the investigations providing concentrations before and after a specific poultry treatment, it emerges that salinomycin reduces from 22,000 ng/g dm to 76 ng/g dm in the case of composting (Ramaswamy et al., 2010), 17β-estradiol reduces from the initial concentration of 83 ng/g dm to 13 ng/g dm after a composting step (Hakk et al., 2005) and from 133 ng/g dm to 101 ng/g dm if treated with alum (Nichols et al., 1997).
The behaviour of testosterone in the case of composting is different: according to Hakk et al. (2005) it reduces from 115 ng/g dm to 11 ng/g dm, whereas according to Shore et al. (1993), it increases from 298 ng/g dm to 525 ng/g dm.

Figure 13.

Figure 14.

With regard to treated liquid/semiliquid swine manure, Figures 15 and 16 (and Table S14) report concentration values for 74 compounds (56 antimicrobials and 18 hormones) in lagoon effluent (503 values) and lagooning sludge (25 values). The observed range of variability varies between 0.11 ng/L (17β-estradiol in lagoon effluent, by Gall et al., 2014) and 4.9 10^6 ng/L (tylosin in lagooning sludge by Dolliver and Gupta, 2008).
The most investigated compounds were chlortetracycline (29 values), lincomycin (27 values) and tetracycline (26 values). The widest variability ranges cover 6 orders of magnitude and occurred for sulfamethazine, tylosin and lincomycin. 5 orders of magnitude intervals were found for estrone, sulfadimethoxine. 9 compounds present a range of 4 orders of magnitude.
With regard to compounds with more than 5 values, the highest average concentrations were found for tylosin (3.9 10^5 ± 1.2 10^6 ng/L), chlortetracycline (1.2 10^5 ± 2.5 10^5 ng/L) and lincomycin (5.4 10^4 ± 7.9 10^4 ng/L).
Based on the data reported in Table S14, 15 compounds present the 75th percentile lower than the corresponding average value. The highest differences were for tylosin (3.8 10^5 ng/L), sulfamethazine (3.9 10^4 ng/L) and tetracycline (3.7 10^4 ng/L). As for the maximum values, they were mainly found in lagoon effluent (88 %).

Figure 15.

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Figure 16.

Concentrations of 17 hormones in the effluent of a lagoon receiving poultry house flushing material were provided by the investigations by Gall et al., (2014) and Hutchins et al., (2007). The most analysed compounds were 17α-estradiol, 17β-estradiol, estriol and estrone being seven measures available for each of them. In Gall et al., (2014), the lagoon treatment consisted of three basins in series. The measured concentrations reported referred to each lagoon effluent (influent data are not available) and highlighted that the concentrations of the selected compounds greatly reduced from the first to the second step and even more from the second to the third. For instance, estrone at the exit of the first basin was 2,970 ng/L, at the exit of the secondary lagoon 1,570 ng/L and after the polishing lagoon 21 ng/L.

Some investigations reported data of concentrations of the same compounds in the raw manure and after its treatment: see for instance Wallace et al., (2018), Arikan et al., (2009) and Ray et al., (2017). Figures S2–S3 (concentration in ng/g dm) and Figures S6–S7 (concentration in ng/L) report and compare the values for raw and treated manure from cattle, Figures S4–S5 (concentration in ng/g dm) and Figures S8–S9 (concentration in ng/L) for raw and treated manure from swine.
It was found that operational conditions may greatly affect the removal of specific compounds. For instance, in composting, temperature has a key role: according to the investigations on pig and poultry solid manure composting by Zhang et al., (2019), swine manure by Liu et al., (2015), and cattle solid manure by Ray et al., (2017), thermophilic conditions allow higher removal efficiency for a wide spectrum of antibiotics. Arikan et al., (2016) found that in the composting of dairy and poultry bedding manure, temperatures in the range 45–65 °C lead to a high removal of salinomycin, whereas ambient temperatures may guarantee a high removal of monensin, lasalocid and amprolium. Bao et al., (2009) and Ho et al., (2013) reported that in the composting of poultry manure, antibiotic removal is strictly correlated not only to temperature, but also to total organic carbon, total nitrogen, C/N ratio and metal content, such as copper as found by Liu et al., (2015).
Aerobic conditions seem to favour the degradation of antibiotics in lagoons (Hafner et al., 2017). Some antibiotics such as chlortetracycline, sulfamethazine and tylosin seem to be degraded better under the anaerobic conditions occurring in stockpiling instead of in composting processes (see for instance: Sura et al., 2014 and Cessna et al., 2011).

5.2.1 Influence of the main parameters on the concentration of selected pharmaceuticals in manure

A rapid look at the graphs of the concentrations of selected micropollutants in the different manures points out that pharmaceuticals and hormones may occur with a wide range of variability. To better understand which could be the main reasons of this variability, Tables 3 and 4 report minimum and maximum values for the compounds exhibiting the highest variability ranges in raw and treated manure respectively, together with (when available) manure type, farm size, animal type, administered dose of pharmaceutical, manure age, and corresponding reference.

Table 3.

Table 4.

It emerges that it is not possible to correlate the maximum values with specific conditions and also to explain the widest ranges of variability. An in depth anaylisis showed that pharmaceutical administration pattern (in terms of pharmaceutical dose and administration time interval), manure sampling time, animals in different growing stages (namely piglets (14-20 kg and 20-35 kg), growing pigs (2-3 months, 35-55 kg), finising pigs (3-7 months, 55-125 kg) and sows (7-50 months)), different manure production area (for instance: milking area and stalls in case of dairy cattle farms), open or closed feedlot, farm management operations (mode and frequency), manure age may strongly influence the occurrence of microcontaminants. Unfortunately an in depth description of all these aspects is not always available. The main lessons learned from this analysis are herein reported.

Farm size. -Chen et al. (2012) reported that there are not great differences in antibiotic concentrations in manure provided by animal farms of different size.

Animal growing stage (swine manure). Antibiotics are generally administrated to prevent disease (higher amounts to young pigs) and to improve feeding efficiency (mainly for to fattening pigs). The highest concentrations in manure were found for young pigs followed by fattening pigs. Very lower values were found in manure generated by sows (Chen et al., 2012, Hou et al., 2015, Zhou et al., 2013b). As to the hormones estrone, 17β-estradiol, 17α-estradiol and estriol, the highest values of concentrations in manure were found for sows with respect to piglets and finishing pigs (Gall et al., 2014).

Dairy and beef cattle farms (cattle manure). Figures S10 and S11 report the same values of concentrations in raw cattle manure of Figures 1 and 2, but grouped according to the two types of cattle farms (diary and beef cattle). A comparison of the distribution of values shows that in beef cattle raw manure the highest concentrations were found for oxytetracycline (225,000 ng/g dm, Arikan et al., 2007) and sulfamethazine (30,250 ng/g dm, Aust et al., 2008). In diary cattle raw manure, the highest values were for oxytetracycline (59,590 ng/g dm, Zhao et al., 2010), enrofloxacin (46,700 ng/g dm Zhao et al., 2010), followed by ciprofloxacin (29,590 ng/g dm, Zhao et al. 2010) and chlortetracycline (27,590 ng/g dm, Zhao et al., 2010). The ranges of variability are still wide for some antibiotics in both graphs. This is the case of oxytetracycline (7 orders of magnitude in both dairy and milk cattle manure), enrofloxacin (6 orders of magnitude in dairy cattle manure), chlortetracycline (5 orders of magnitude in dairy cattle manure and 4 in beef cattle manure), sulfamethazine (5 orders in beef cattle manure and 4 in dairy cattle manure). Finally, dairy cattle raw manure contains hormones up to 1001,000 ng/g dm. In beef cattle manure hormone concentrations were always found in the range 0.1180 ng/g dm and they refer to a higher number of compounds.

Broiler and layer poultry farms.This two types of farms lead to the production of poultry litter and poultry manure. These kinds of manure are exactly what reported in the figures of this study.

Farm management. On the basis of the collected literature data it is not possible to correlate concentrations of antibiotics and hormones in manure with respect to the different farm management operations.

5.3 Occurrence of microorganisms in raw and treated manures

The investigations on microorganisms included in this review referred to different types of manure (bedding manure, liquid manure, slurry and solid manure, according to Table 1) produced by four different animals (cattle, swine, poultry and sheep).

The investigations dealt with the occurrence of indicator bacteria (Heterotrophic bacteria, Total coliforms, Faecal coliforms, *E. coli*, Faecal streptococci) and selected pathogens (mainly *Aeromonas hydrophila, Campylobacter coli, Cryptosporidium parvum, Giardia intestinalis, Listeria, Pseudomonas aeruginosa, Salmonella* and *Yersinia enterocolitica*). Limiting the attention to concentrations provided in cfu/g dm, the collected data are those reported in Figure 17 (referring to 13 microorganisms in different types of raw manure) and Figure 18 (9 microorganisms in three different treated manures). In addition, Tables S15 and

S16 report a descriptive statistical analysis of the literature data under review for raw and treated manures, respectively.
The literature also provides concentrations of microorganisms in manure expressed in other units of measurement: for instance, cells/g dm, MPN/100 g dm and cfu/100 mL. For the sake of completeness, bacteria are listed in Table S2 with the corresponding references, but due to the limited number of values available we chose not to include all of them in this discussion.
As for raw manure, it emerges that poultry manure was the object of 10 studies, cattle manure of 9 and sheep and swine manure of 6 studies each. The highest number of concentrations were found for *E. coli* (54 concentrations), followed by *Campylobacter coli* (32 values) and *Salmonella* (30 values). All of them were observed in manure from the four different animals listed.
The group of heterotrophic bacteria exhibited the highest concentrations (in poultry they were found in the range 10^9–10^{11} cfu/g dm) followed by other indicator bacteria (Total coliform in poultry manure equal to 3.8 10^8 cfu/g dm; *E. coli* in poultry and cattle manure around 2.3–2.6 10^8 cfu/g dm; faecal streptococci in cattle manure 1.7 10^8 cfu/g dm, and faecal coliform equal to 3.7 10^7 cfu/g dm in cattle manure).
As for pathogens, the highest concentrations were found for *Yersinia enterocolitica* (2.1 10^6 in poultry manure), *Listeria* (9.7 10^5 cfu/g dm in swine manure), *Salmonella* (5.8 10^5 cfu/g dm in cattle manure) and also *Giardia intestinalis* (1.6 10^5 cfu/g dm in swine manure), and *Campylobacter coli* (1.5 10^5 cfu/g dm in cattle manure). The highest concentrations were more frequently detected in cattle manure followed by poultry manure. With regard to the type of manure sampled, it emerges that bedding manure more frequently presented the highest values (around 50 % of cases).
A focus on the content of indicator bacteria and pathogens in the different animal manures shows that there are some orders of magnitude difference between the concentrations detected in the two groups. In particular, in cattle manure, average concentrations of the reviewed indicator bacteria range between 2.1 10^7 cfu/g dm and 1.3 10^8 cfu/g dm, whereas average concentrations of pathogens between 1.9 10^3 cfu/g dm and 3.1 10^5 cfu/g dm; in poultry manure, average concentrations of indicator bacteria range between 1.5 10^5 cfu/g dm and 2.7 10^{10} cfu/g dm, those of pathogens vary between 1.1 10^4 cfu/g dm and 3.4 10^5 cfu/g dm. In swine manure, concentrations of indicator bacteria (the only available is *E. coli*) vary between 10^2 cfu/g dm and 7.5 10^5 cfu/g dm, whereas average concentrations of pathogens vary between 9 10^2 cfu/g dm and 5.1 10^5 cfu/g dm. Finally, in sheep manure, the concentration of *E. coli* in raw manure varies from 1.1 10^4 cfu/g dm to 4.9 10^4 cfu/g dm and average concentrations of pathogens between 1.5 10^2 cfu/g dm and 1.5 10^3 cfu/g dm.

Figure 17.

A lower number of values are available for the content of microorganisms in treated manure, as shown in Figure 18. Most of them (50 out of 64 values) refer to concentrations of microorganisms found in the sediments of lagoons (lagooning sludge) receiving swine manure (Hutchison et al., 2004; Frey et al.,2013; Van der Merchee et al., 2019). 8 values refer to different microorganisms in composted bedding sheep manure (Hutchison et al.,2004) and composted solid poultry manure. Unfortunately, it is not possible to make a comparison of the different treatments for the same type of manure.
As with the raw manure, the most studied microorganisms are the indicator *E. coli* (20 values), followed by the pathogen *Campylobacter coli* (13 values). With regard to the maximum observed values, it emerges that *Salmonella* occurred up to 7.2 10^6 cfu/g dm (Hutchison et al., 2004) and *Listeria* up to 9.8 10^5 cfu/g dm, and all the other microorganisms generally presented less than 2 10^5 cfu/g dm.
The average concentrations of indicator bacteria in treated manure vary between 2.3 10^3 cfu/g dm (*E. coli* in swine lagooning sludge) and 1.6 10^5 cfu/g dm (total coliform in swine lagooning sludge) and for pathogens between 1.2 10 cfu/g dm (*Giardia intestinalis* in swine lagooning sludge) and 3.7 10^6 cfu/g dm (Salmonella in cattle lagooning sludge).

The highest average concentrations were 3.7 10^6 cfu/g dm (*Salmonella* in cattle lagooning sludge), 5.0 10^5 cfu/g dm for *Listeria* in cattle lagooning sludge), 1.6 10^5 cfu/g dm for total coliform in swine lagooning sludge. All the other values of average concentrations referred to the reviewed microorganisms, the different animals and treatment may be found in Table S16. A comparison with the above reported range of variability in the case of raw manure shows that the treatment is generally able to reduce the content of indicator bacteria.

Figure 18.

6 Manure land application and predicted concentration of micropollutants in soil – Comparison with measured concentrations

Predicted concentrations in manure-amended soil (PEC) for a selection of antibiotics under review was carried out under the following assumptions:

- swine slurry (with PhC concentrations in ng/g dm) was applied to soil;
- two application rates of this slurry 2,200 kg dm/(ha year) (scenario 1) and 9,500 kg dm/(ha year) (scenario 2), were applied to soil. These application rates would be able to respect the limit of 170 kg N/ha year discussed above (the first defined by Pappas et al. (2008) should be able to guarantee the respect of 168 kg N/ha year and the second rate, according to Joy et al. (2013) should respect 151 kg N/ha year;
- the estimation of the concentration in soil was made for compounds for which predicted no effect concentrations in soil ($PNEC_{soil}$) are known from the literature, namely the antibiotics: chlortetracycline, ciprofloxacin, doxycycline, enrofloxacin, oxytetracycline, sulfamethazine, sulfamethoxazole tetracycline, tiamulin and tylosin (see Table S17 for details).

PECs were evaluated according to the well-known equation 1, recommended by the European Technical Guidance Document on risk assessment EUR 20418 EN/2 (EC-TGD 2003)

$$PEC_{i,\,soil} = c_{0,soil} + \frac{c_{i,slurry}\ x\ APP_{slurry}}{DEPTH_{soil}\ x\ RHO_{soil}} \qquad \text{(eq. 1)}$$

where $c_{0,soil}$ corresponds to the background concentration in the soil (ng/g dm), before the manure has been spread on it (in this study it was assumed equal to zero); $c_{i,slurry}$ is the measured concentration (MEC) in swine slurry (ng/g dm); APP_{slurry} is the yearly application rate of dry slurry on soil; $DEPTH_{soil}$ is the mixing depth (0.10–0.20 m is generally the depth of the mixing during application (Dutta et al., 2012; Ghirardini and Verlicchi, 2019). Here the value of 0.20 m is used as well as discussed in Ghirardini and Verlicchi (2019). RHO_{soil} is the bulk density of wet soil (1,700 kg/m^3 for agricultural soils as discussed in Verlicchi and Zambello, 2015 and recommended by EC-TGD, 2003).

The evaluation of the PEC in soil was carried out assuming the measured minimum, maximum and average concentrations of the selected antibiotics in swine slurry for the two scenarios of the manure application rate (the lowest and the highest values of slurry application rates mentioned above).
Table 5 reports $c_{i,slurry}$, APP_{slurry}, the corresponding maximum, minimum and average PEC_{soil} in the two situations. It also compiles ranges of measured concentrations in soil (MEC_{soil}) found in the literature for the same antibiotics in swine slurry-amended soil (Gros et al., 2019; Solliec et al., 2016; Christian et al., 2003) or in the lagoon effluent (receiving pig slurry) applied to arable land (Zhou et al., 2013a,b).
A comparison between PECs and MECs in soil shows that average $PECs_{soil}$ is always in the range of the reported MEC_{soil}. Maximum PEC_{soil} exceed the MEC_{soil} for tetracycline, tiamulin and tylosin at both

application rates and for chlortetracycline, oxytetracycline, sulfamethazine and sulfamethoxazole at the highest allowed application rate (see the underlined values in Table 5).
An in-depth description of the studies from which $MECs_{soil}$ are taken is reported in Table S18, in particular, $MECs_{soil}$ refer to soils amended with pig slurry or effluent from lagoons receiving pig wastewater or slurry.

Table 5

7 Environmental risk assessment in the case of swine slurry-amended soil

The environmental risk assessment was based on the risk quotient evaluation, as discussed in Verlicchi and Zambello (2015), as the ratio between PEC_{soil} and $PNEC_{soil}$.
With regard to $PNEC_{soil}$, different proposals are available in the literature including Eriksen et al., (2009), Munoz et al. (2009), Chen et al. (2018), Thomaidi et al. (2016), Bourdat-Deschampes et al. (2017) and Gros et al. (2019). In this study, $PNEC_{soil}$ were those used in the study by Bourdat-Deschampes et al. (2017) and Gros et al. (2019) obtained from a literature survey targeting relevant endpoints for (micro)-organisms in agrosystems.
The corresponding risk quotient values are reported in Figure 19 grouped according to the slurry rate applied (2,200 kg dm/(ha year) and 9,500 kg dm/(ha year)) and ordered according to the average RQ value (descending order). On the y-axis, the number appearing in brackets after the name of the antibiotic is the adopted $PNEC_{soil}$.
It emerges that average RQ are always less than 1. A medium risk was found for ciprofloxacin, sulfamethazine, chlortetracycline and doxycycline (at an application rate of 9,500 kg dm/(ha year)) and only for ciprofloxacin in the case of the lowest application rate. A high risk was found in the case of maximum concentrations of sulfamethazine, chlortetracycline and doxycycline in swine slurry in the case of 9,500 kg dm/(ha year) of the application rate.

Figure 19.

It is worth noting that the environmental risk assessment carried out in this study refers to a vulnerable area where a maximum application rate is set according to the maximum quantity of nitrogen disposed on soil with the manure. In case of no vulnerable area, the application rate should be higher than the assumed value and also the subsequent soil concentrations of micropollutants resulting in higher RQ values.

8 Discussion and Future perspectives – Conclusions

The overview highlighted that concentrations of antibiotics are higher in swine manure rather than in cattle manure.This could be explained with the fact that antibiotics are administered at higher dosages and with higher frequencies in pig farms than in the other type of farm as comparing the living environments, pigs have much smaller space available with worse air and more pathogenic bacteria which make pigs prone to catch diseases.
Hou et al., 2015 compared concentrations of sulphonamides, tetracyclines, quinolones and macrolidesantibiotics in manure from different types of animal farms and they found them in this order: swin manure > poultry manure > cattle manure.
The antibiotic oxytetracycline was the compound with the highest concentrations in all types of raw manure (concentrations in ng/g dm) and chlortetracycline in the case of semiliquid and liquid raw manure

(concentrations in ng/L). As for treated manure, chlortetracycline and its main metabolites (iso- and epi-chlortetracycline) presented the highest values (both ng/g dm and ng/L) in cattle and swine treated manure.
Looking at the hormones, they always occurred at lower concentrations: the highest were 17β -estradiol-3-glucuronide in raw swine manure (2.8 10^4 ng/L), and progesterone in raw cattle manure (2.1 10^4 ng/g dm), around 3 orders of magnitude lower than the highest concentrations of the antibiotic in the same type of manure. Only in cattle treated manure, estrone was found at a concentration only one order of magnitude lower than the top antibiotic (8.5 10^2 ng/g dm versus iso-chlortetracycline 4 10^3 ng/g dm).
A summary of the highest concentrations is reported in Table 6 with regard to the different manure (source and untreated/treated).

Table 6.

As remarked in the previous sections, great differences may be found in the occurrence of micropollutants in different tyes of manures. These differences may be attributed to variations in the dosage levels, different metabolic characteristics of the animals, geographical variations due to different prescribing habits in different regions. These were confirmed by Zhao et al. (2010) who statistically analyzed samples taken from different farms in different regions in China.

With regard to the potential environmental risk posed by residues in manure-amended soil, the analysis referred to the application of swine manure (Figure 19) noted that sulfamethazine, chlortetracycline and doxycycline presented the maximum values in the case of an application rate of 9,500 kg dm/(ha year). Interesting results are provided by Zhang et al. (2015), who compared the environmental risk posed by residues of veterinary antibiotics in raw and treated manures from different animal farms (chickens, ducks, pigs and cattle) if applied to soil as a fertilizer. It emerged that the risk is higher (in terms of risk quotient) for raw manures than in the composted mixture of the different manures, for all the investigated antibiotics. In more detail: in raw manure RQ was found greater than 1 for tetracycline (pigs, chickens and cattle), oxytetracycline (pigs, chickens and cattle), chlortetracycline (pigs), sulfadiazine (chickens and pigs), ciprofloxacin (chickens and cattle), and after composting the mixture of the different types of manure RQ > 1 for tetracycline, oxytetracycline, sulfadiazine and ciprofloxacin. The study by Gros et al. (2019) showed that RQ > 1 in the case of swine slurry application on soil for enrofloxacin.
If a liquid or semiliquid manure is spread on the land it may percolate through the soil more easily than manures with a higher content of suspended solid and, in particular, if there is rain soon after it has been applied to the land, it is more likely to reach the groundwater.
Zheng et al. (2008) found that the use of sequencing lagoons (that is a multi-stage lagooning system) and increasing manure-piling time promotes degradation processes of pharmaceuticals and hormones (in particular) and thus represents feasible, efficient and promising practices to reduce the risk of environmental contamination due to pharmaceuticals and hormones commonly administered to animals.
Once disposed on soil, the behaviour of the residues of micropollutants depends on their nature. For instance, oxytetracycline demonstrates a high persistence in pig slurry-amended soil: Aga et al. (2005) reported that it has a strong potential to absorb on solid matter which makes it unavailable for microbial attack, but at the same time it remains in the soil without being mobilized in the aqueous phase (this means that it is not present in the runoff or tile drainage induced by rain). However, the subsequent application of the same type of manure on the same soil over the years will cause it to accumulated (Blackwell et al., 2007). Other investigations pointed out that the persistence of antibiotics in soil is higher in the case of composted-amended soil instead of raw manure-amended soil. The advantage to spread composted manure is due to the (expected and observed) lower concentrations of antibiotics, but sometimes these compounds could resist biodegradation in the soil.

To sum up, based on the collected results, it emerges that future researches should focus on:

- the detection in raw and treated manure not only of the parent compounds, but also of their main metabolites, as they may retransform into their parent compounds during piling or treatments as noted by Lamshöft et al., (2010);
- the dispersion in the environment not only of antibiotics, but also of antibiotic-resistant genes and different types of microorganisms, especially if a high rate of manure is applied on arable land and on the subsequent risks for the environment as noted by Van der Meersche et al. (2019) and Gros et al. (2019). In fact, exceptional quantities of rain may lead to the unexpected release (through drainage and surface runoff) of very higher amounts of residues (and microorganisms) that have accumulated over the years on and in the soil, due to recurrent manure application and (Gall et al., 2014);
- the mobility mechanisms which may take place within the soil over time, after manure application;
- an investigation on the relationship between occurrence of micropollutants in manure-amended soil and soils and manure characteristics;
- a prediction of the fate and dissipation of selected micropollutants, based on their chemical and physical properties.

Lessons learned from municipal sludge application on rural land could be useful, keeping in mind the differences between their compositions in terms of macro- and microcontaminants which may affect their behaviour once they have entered the environment.

As for microorganisms, it was found that in the top 10 cm of soil (where manure was not added), the concentration of *E. coli* was in the range 10^2–10^5 cfu/g dm (Stocker et al., 2015) and faecal coliform around 2.58 10^4 CFU/g dm (Gondim-Porto et al., 2016). If manure is spread, the concentration increases up to 2 log units and the environmental conditions define its survival/decay: a removal of 1 log unit may be reached from a few days (Hutchinson et al., 2005) to 19 weeks (Lau and Ingham, 2001). Rainfall intensity occurring soon after manure amendment results in an immediate reduction of deposited bacteria within the first cm of soil (Stocker et al., 2015).

It is worth noting that the contribution to microorganism release in surface water in the case of heavy rainfall on manure-amended soil may be critical especially in the case of a catchment area discharging in a bathing area or close to water that is used for drinking.

Supplementary data

The Supplementary Data includes tables referring to (i) the main issues addressed in the papers included in the review; (ii) the main characteristics of the selected contaminants: chemical and physical properties, excretion factors with regard to the different types of animals, half-life time in manure and in manure-amended soil; (iii) the descriptive statistical analysis of the selected compounds and microorganisms in the different types of raw and treated manure; (iv) predicted no effect concentrations for a selection of compounds with regard to terrestrial organisms; (v) measured environmental concentrations in soil for a selection of antibiotics. The Supplementary data also includes figures providing the worldwide distribution of the investigations included in the review, the comparisons between concentrations of selected contaminants in raw and treated manures for the different types of animal farms and the comparison among concentrations of micropollutants in manure produced in dairy and beef cattle farms.

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FIGURES

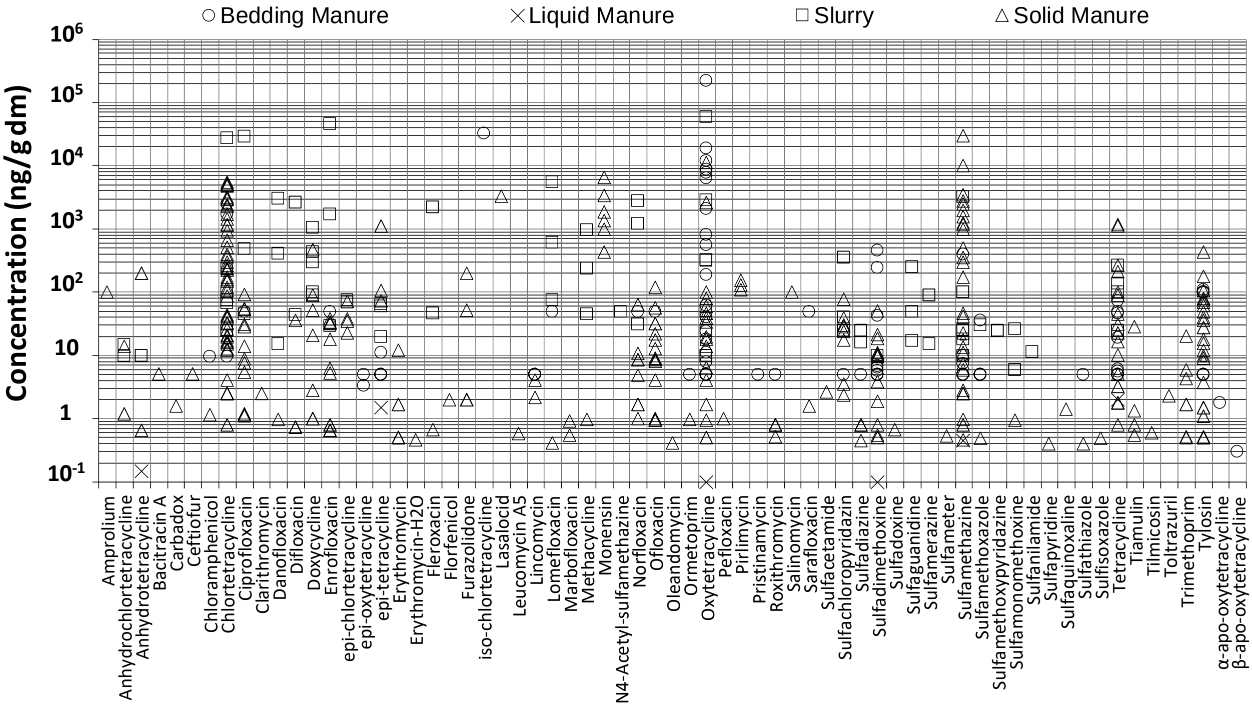


Figure 1. Occurrence of antibiotics in different types of raw cattle manure.

Data from: Aga et al., 2005; Amarakoon et al., 2014; Arikan et al., 2006; 2007; 2009; 2016; Aust et al., 2008; Cessna et al., 2011; Chen et al., 2018; Christian et al., 2003; Conde-Cid et al., 2018; De Liguoro et al., 2003; Dolliver and Gupta, 2008; Gros et al., 2019; Hafner et al., 2017; Haller et al., 2002; Hou et al., 2015; Karci and Balcioğlu, 2009; Patten et al., 1980; Ray et al., 2017; Sura et al., 2014; Sura et al., 2015; Wallace and Aga, 2016; Wallace et al., 2018; Watanabe et al., 2010; Zhang et al., 2015; Zhao et al., 2010; Zhou et al., 2013a.

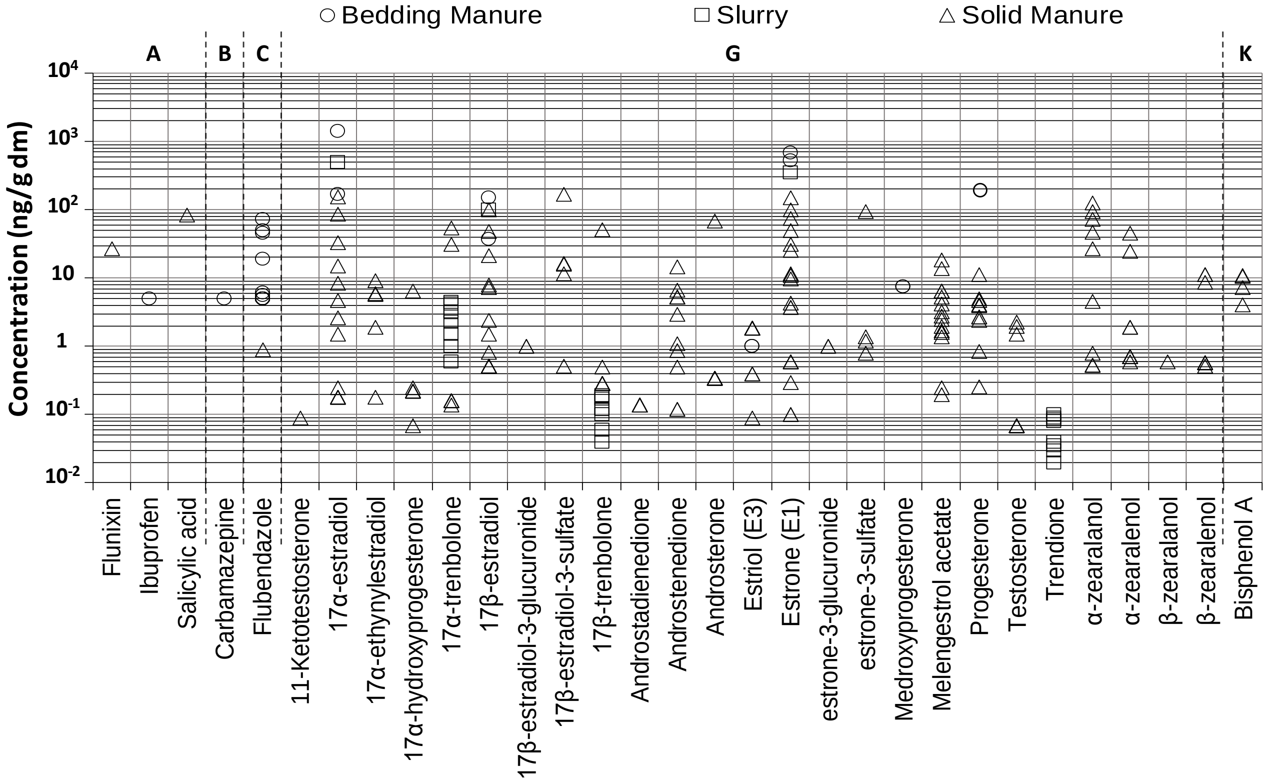


Figure 2. Occurrence of other micropollutants, belonging to classes A (Analgesics and anti-inflammatories), B (Anticonvulsants), C (Antihelmintics), G (Hormones) and K (Plasticizer) in raw cattle manure.

Data from: Bartelt-Hunt et al., 2012; 2013; Biswas et al., 2017; Gall et al., 2014; Gros et al., 2019; Mansell et al., 2011; Raman et al., 2004; Schiffer et al., 2001; van Donk et al., 2013; Watanabe et al., 2010; Zhang et al., 2014; Zheng et al., 2008.

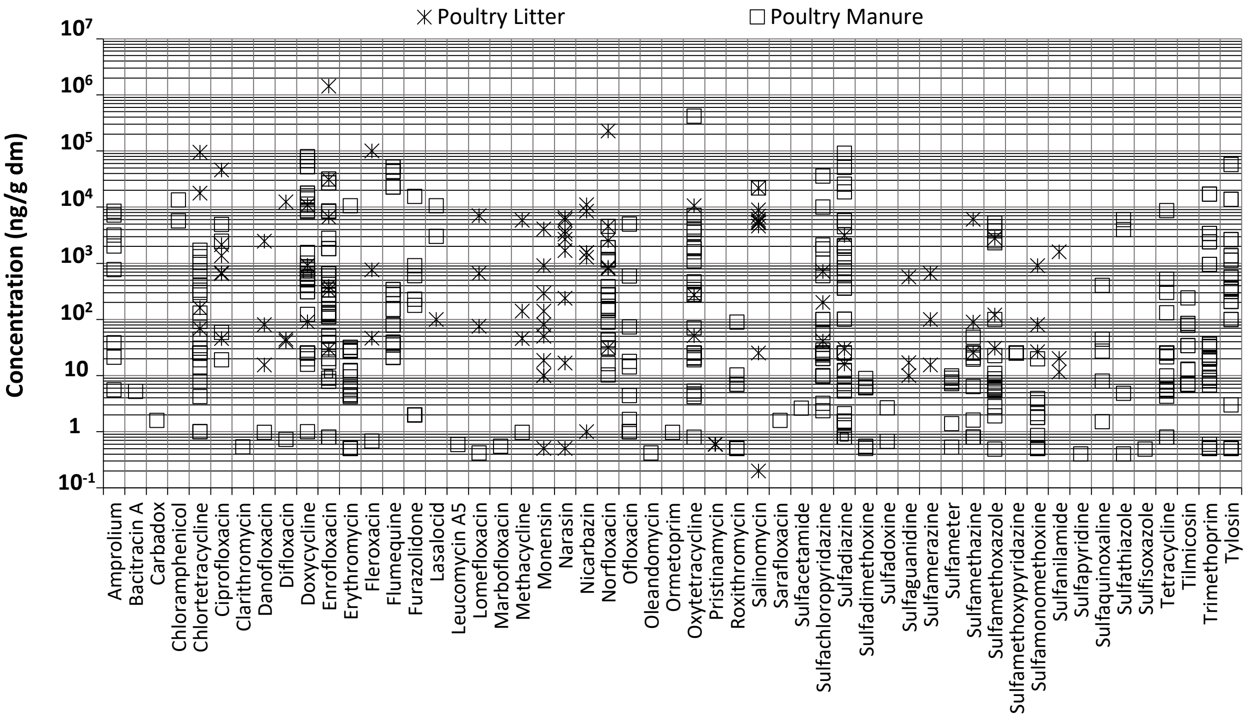


Figure 3. Occurrence of antibiotics in different types of raw poultry manure.

Data from: Arikan et al., 2016; Bao et al., 2009; Conde-Cid et al., 2018; Furtula et al., 2009; Ho et al., 2012; 2013; 2014; Hou et al. 2015; Hu et al., 2008; Karci and Balcioğlu, 2009; Leal et al., 2012; Martínez-Carballo et al., 2007; Ramaswamy et al., 2010; Sun et al., 2013; Zhang et al., 2015; Zhang et al., 2019; Zhao et al., 2010; Žižek et al., 2015

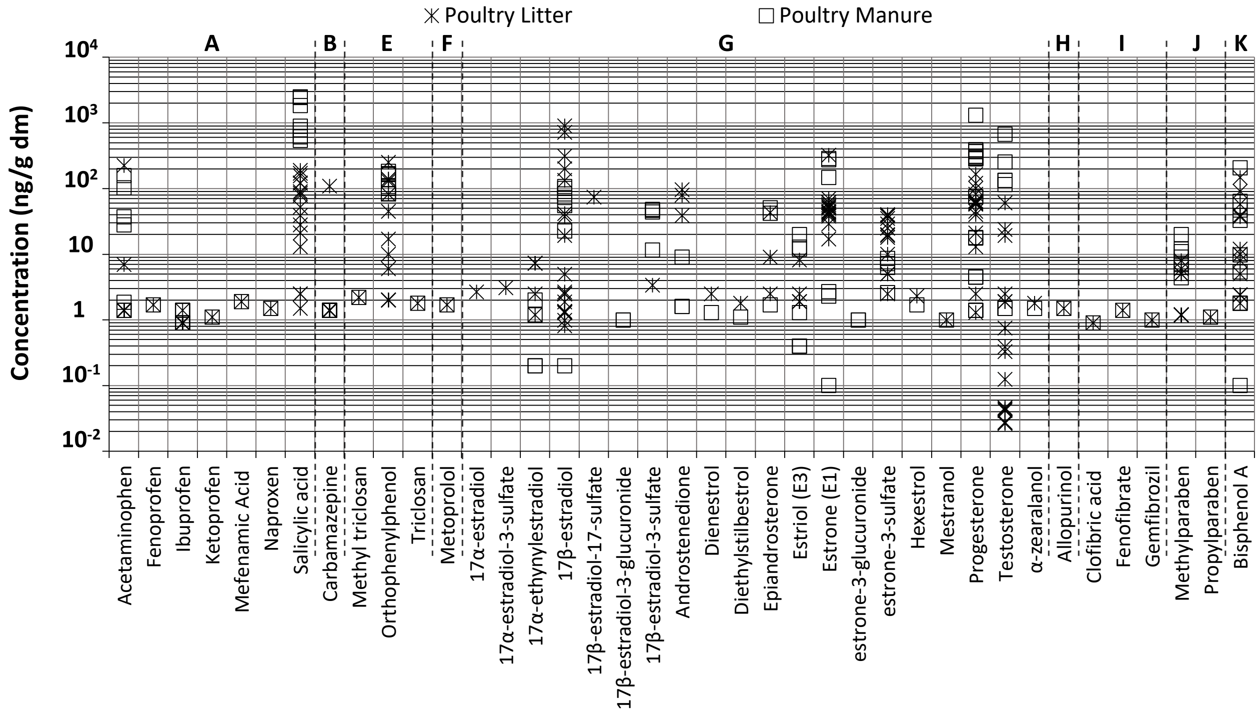


Figure 4. Occurrence of micropollutants belonging to classes A (Analgesics and anti-inflammatories), B (Anticonvulsants), E (Antiseptics), F (Beta-blockers), G (Hormones), H (Inhibitors), I (Lipid Regulators), J (Parabens) and K (Plasticizer) in raw poultry manure.

Data from: Albero et al., 2014; Aznar et al., 2018; Bevacqua et al., 2011; Dutta et al., 2012; Finlay-Moore et al., 2000; Hakk et al., 2005; Ho et al., 2012; 2013; 2014; Jenkins et al., 2006; 2008; 2009; Lu et al., 2014; Nichols et al., 1997, 1998; Shore et al., 1993; Zhang et al., 2014

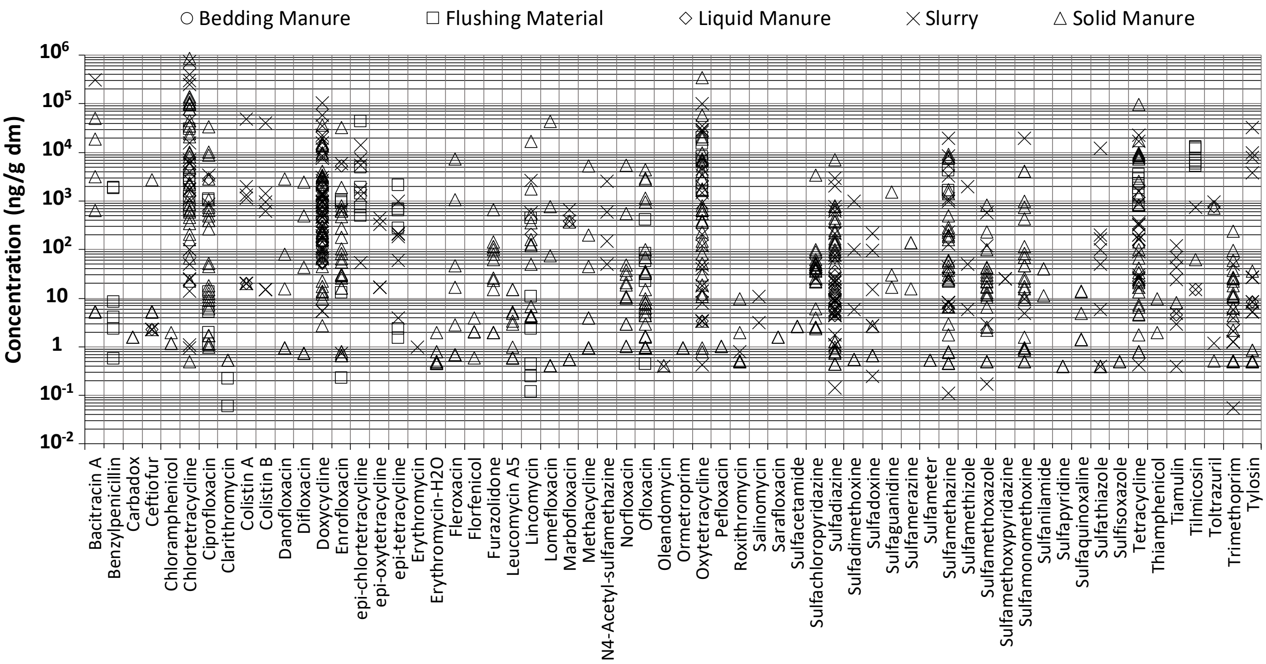


Figure 5. Occurrence of antibiotics in different types of raw swine manure.

Data from: Bao et al., 2009; Chen et al., 2012; Christian et al., 2003; Conde-Cid et al., 2018; Gros et al., 2019; Haller et al., 2002; Hou et al., 2015; Hu et al., 2008; Jacobsen and Halling-Sørensen, 2006; Joy et al., 2013; 2014; Martínez-Carballo et al., 2007; Pan et al., 2011; Schlüsener et al., 2003; Tylová et al., 2010; Van den Meersche et al., 2016; 2019; Wang et al., 2019; Zhang et al., 2019; Zhao et al., 2010; Zhou et al., 2012; 2013a; 2013b.

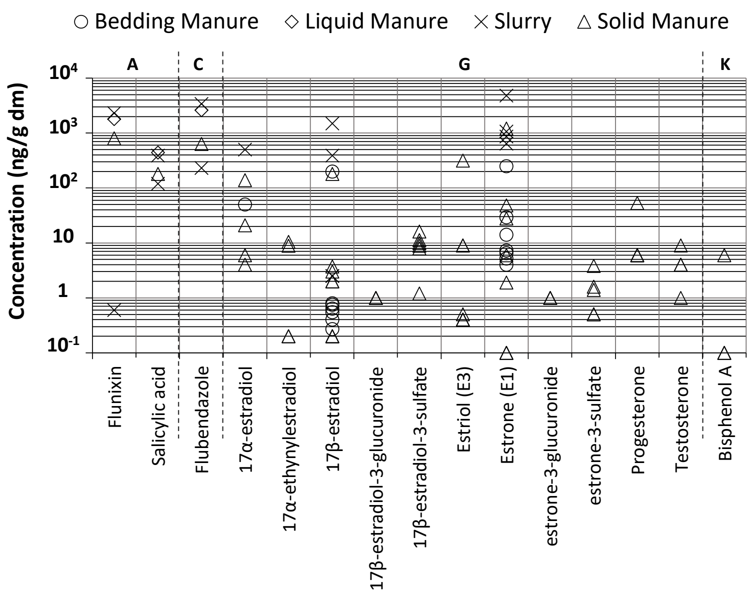


Figure 6. Occurrence of micropollutants belonging to classes A (Analgesics and anti-inflammatories), C (Antihelmintics), G (Hormones) and K (Plasticizer) in raw swine manure.
Data from: Combalbert et al., 2010; Derby et al., 2011; Gros et al., 2019; Kjær et al., 2007; Raman et al.,2004; Zhang et al., 2014.

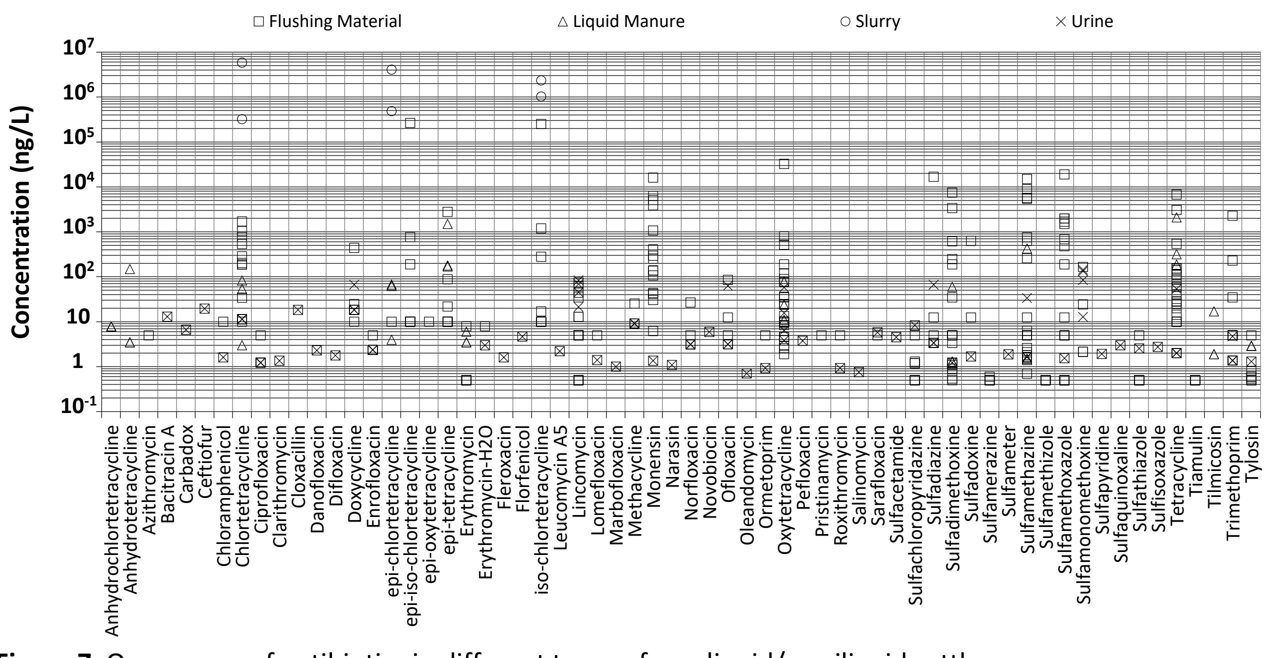


Figure 7. Occurrence of antibiotics in different types of raw liquid/semiliquid cattle manure.
Data from: Arikan, 2008; Hafner et al., 2017; Wallace and Aga, 2016; Watanabe et al., 2010; Wei et al., 2011; Zhang et al., 2013; Zhou et al., 2013a.

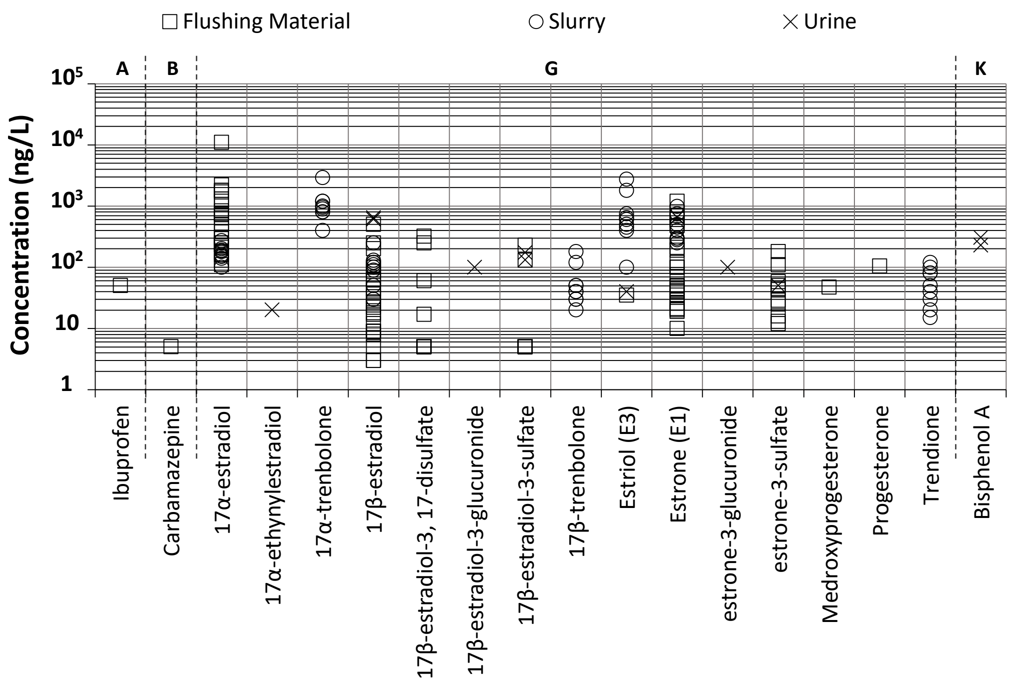


Figure 8. Occurrence of micropollutants belonging to classes A (Analgesics/anti-inflammatories), B (Anticonvulsants), G (Hormones), and K (Plasticizers) in different types of raw liquid/semiliquid cattle manure.

Data from: Gadd et al., 2010; Khan and Lee, 2012; Watanabe et al., 2010; Zhang et al., 2014; Zheng et al., 2008.

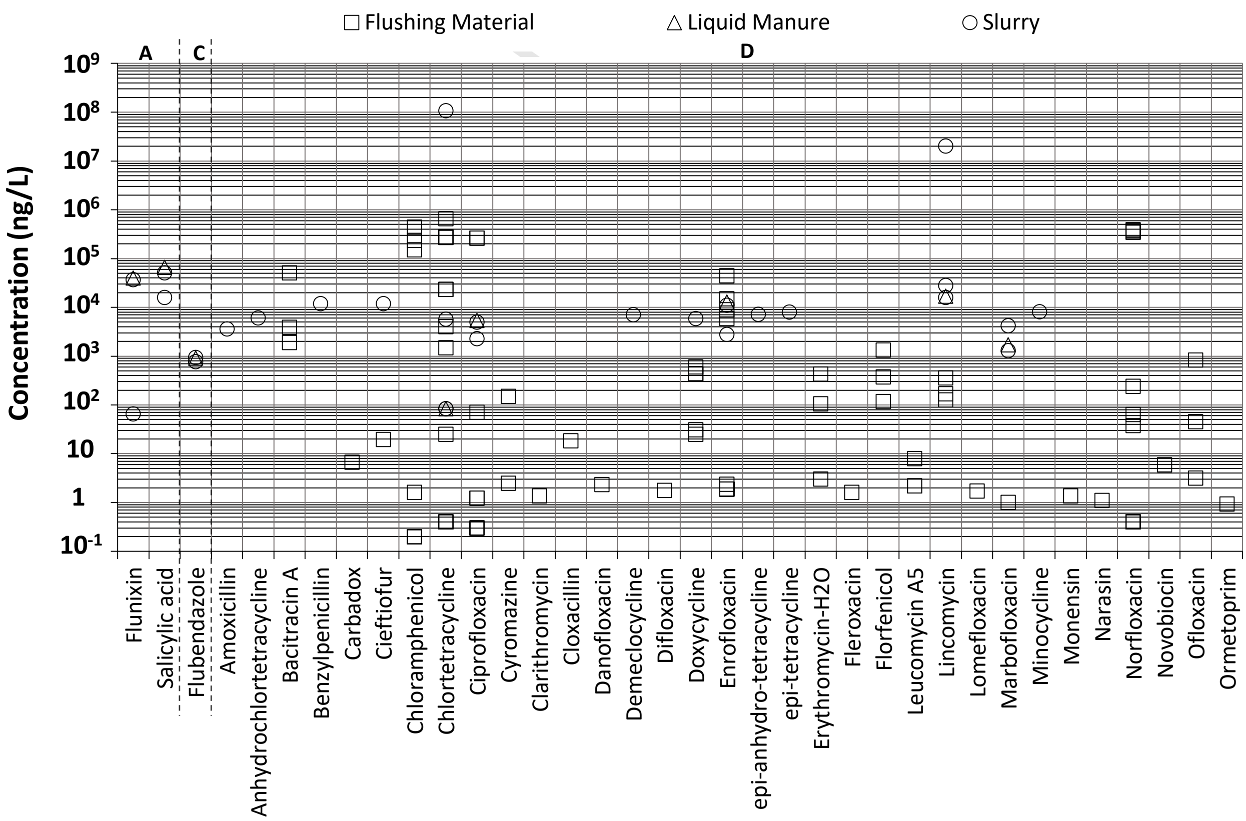


Figure 9. Occurrence of analgesics/antinflammatories (A), antihelmintics (C) some antibiotics (D) in different types of raw liquid/semiliquid swine manure.

Data from: Gros et al., 2019; Hoese et al., 2009; Li et al., 2018; Solliec et al., 2016; Wei et al., 2011; Zhou et al., 2013b.

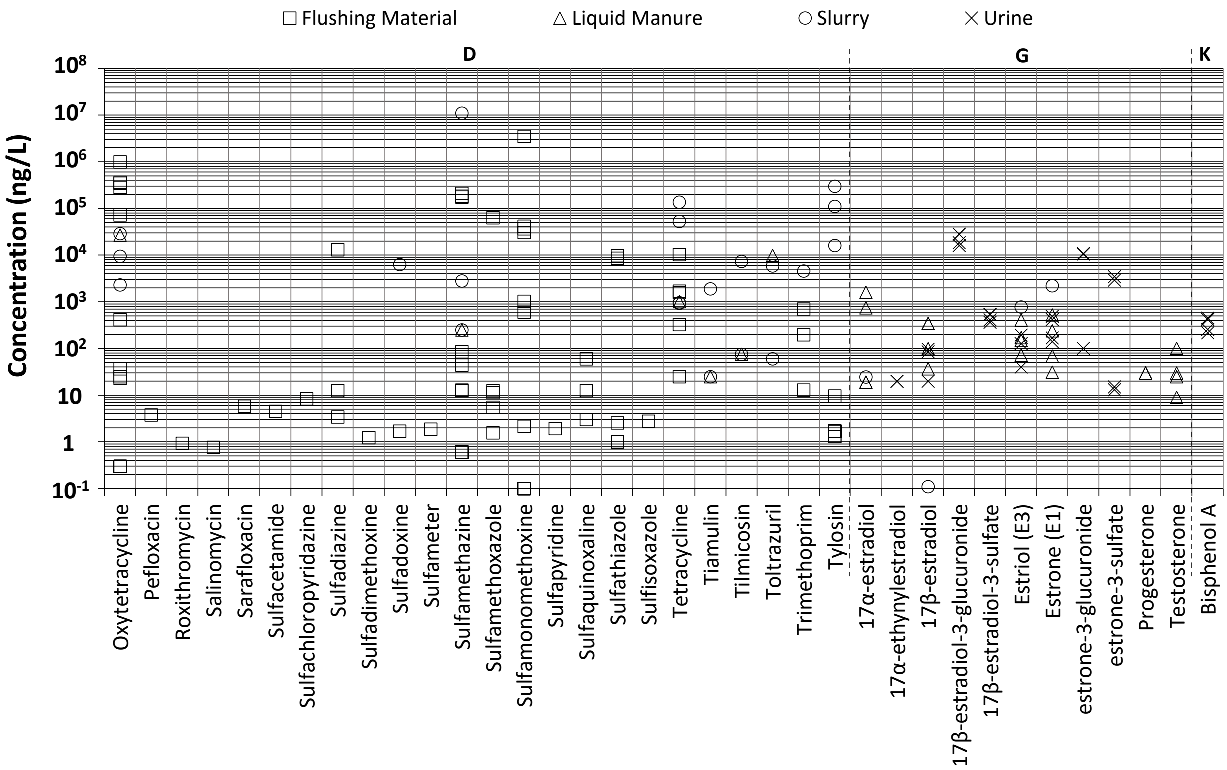


Figure 10. Occurrence of other antibiotics (D), hormones (G), and plasticizers (K) in different types of raw liquid/semiliquid swine manure.

Data from: Burkhardt et al., 2005; Combalbert et al., 2010; Gall et al., 2014; Gros et al., 2019; Hoese et al., 2009; Li et al., 2018; Solliec et al., 2016; Wei et al., 2011; Zhang et al., 2014; Zhou et al., 2013b.

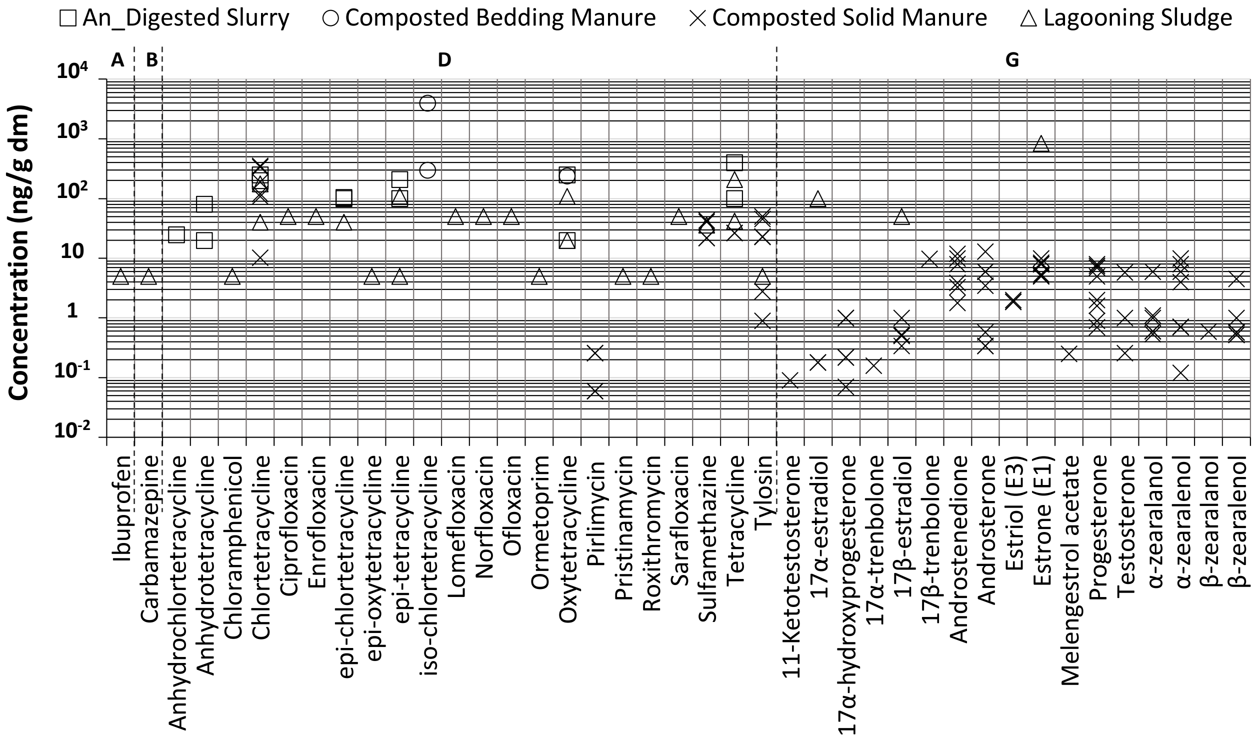


Figure 11. Occurrence of micropollutants belonging to classes A (Analgesics and anti-inflammatories), B (Anticonvulsants), D (Antimicrobials) and G (Hormones) in treated cattle manure.
Data from: Arikan 2007; 2009; Bartelt-Hunt et al., 2013; Biswas et al., 2017; Cessna et al., 2011; Chen et al., 2018; Ray et al., 2017; Raman et al., 2004; van Donk et al., 2013; Wallace et al., 2018; Watanabe et al., 2010.

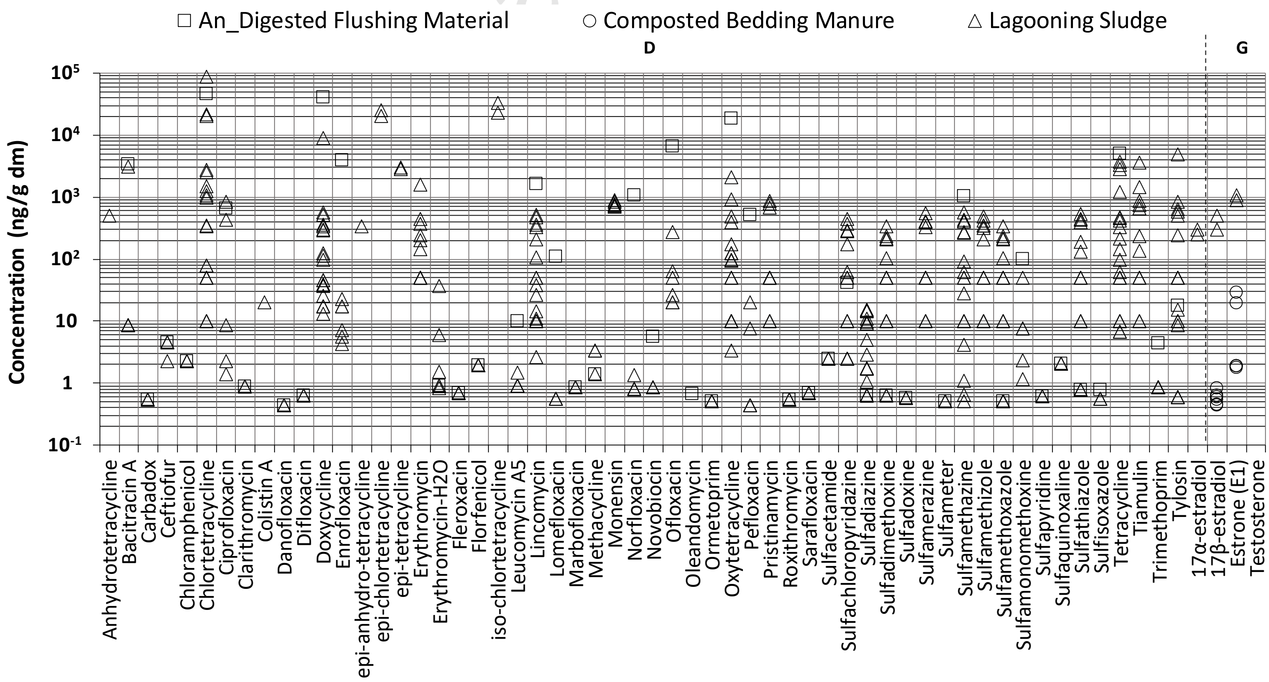


Figure 12. Occurrence of micropollutants belonging to classes D (Antimicrobials) and G (Hormones) in treated swine manure.
Data from: Derby et al., 2011; Frey et al., 2015; Raman et al., 2004; Van den Meersche et al., 2019; Zhang et al., 2013; Zhou et al., 2012; 2013a; 2013b.

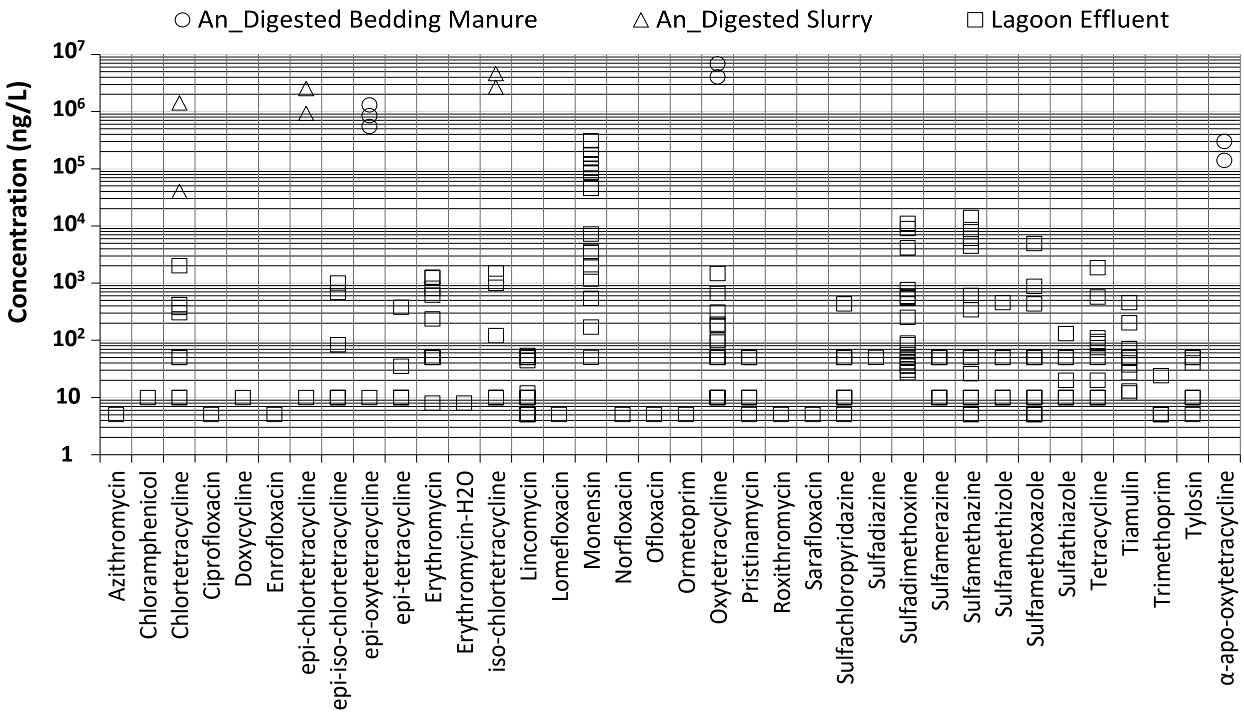


Figure 13. Occurrence of antibiotics in different types of treated liquid/semiliquid cattle manure.
Data from: Arikan, 2008; Arikan et al., 2006; Hafner et al., 2017; Watanabe et al., 2010; Zhang et al., 2013.

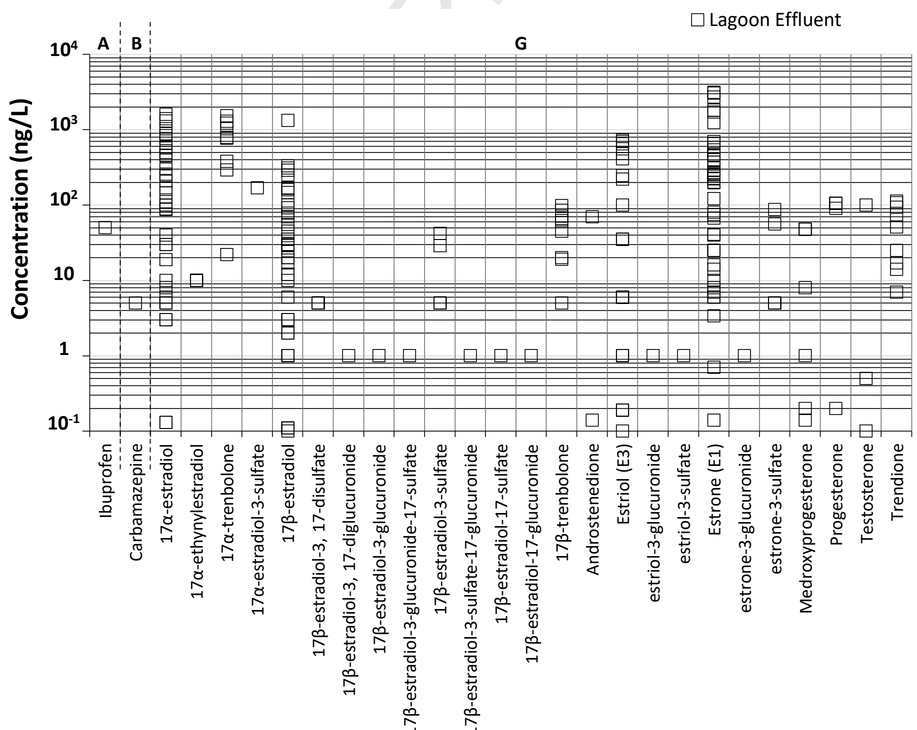


Figure 14. Occurrence of other micropollutants belonging to classes A (Analgesics and anti-inflammatories), B (Anticonvulsants), and G (Hormones) in different types of treated liquid/semiliquid cattle manure.
Data from: Gadd et al., 2010; Gall et al., 2014; Hutchins et al., 2007; Khan and Lee, 2012; Kolodziej et al., 2004; Sarmah et al., 2006b; Watanabe et al., 2010; Zhang et al., 2014; Zheng et al., 2008

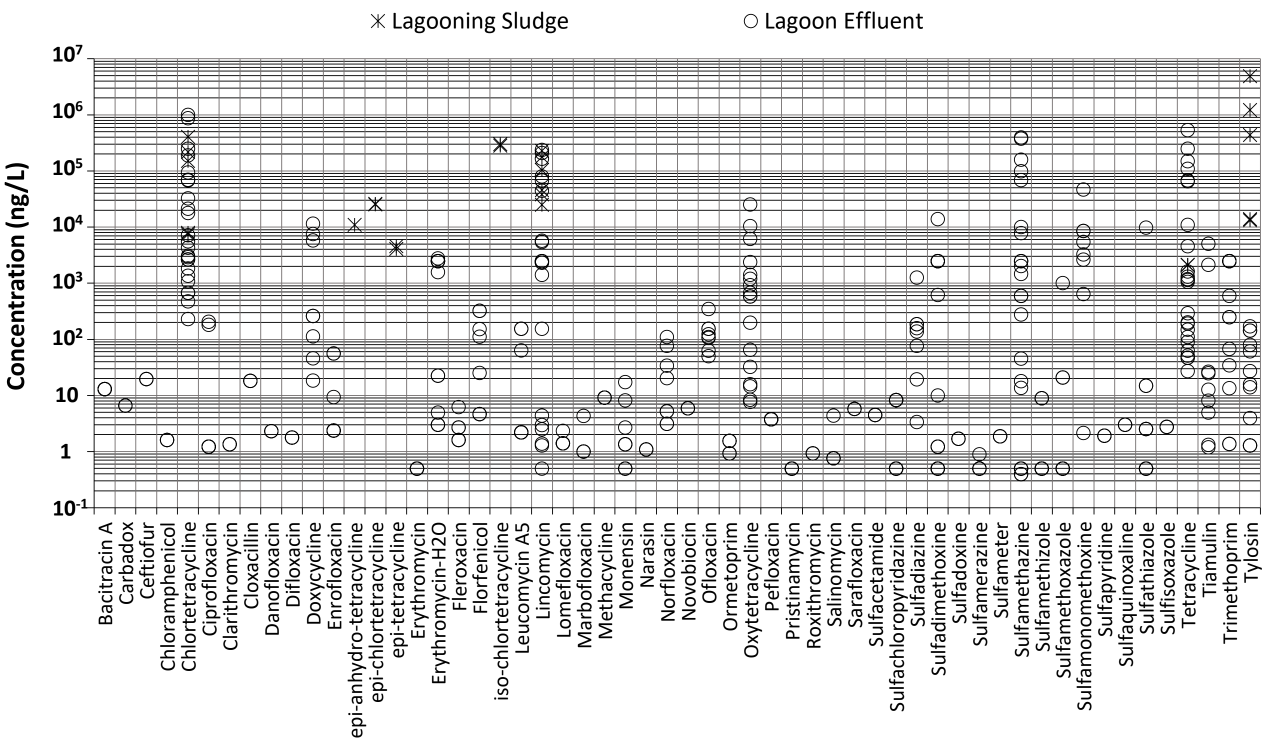


Figure 15. Occurrence of selected antibiotics in different types of treated liquid/semiliquid swine manure.
Data from: Ben et al., 2008; Campagnolo et al., 2002; Dolliver and Gupta, 2008; Frey et al., 2015; Kuchta and Cessna, 2009; Kuctha et al., 2009; Zhang et al., 2013; Zhou et al., 2012; 2013a; 2013b.

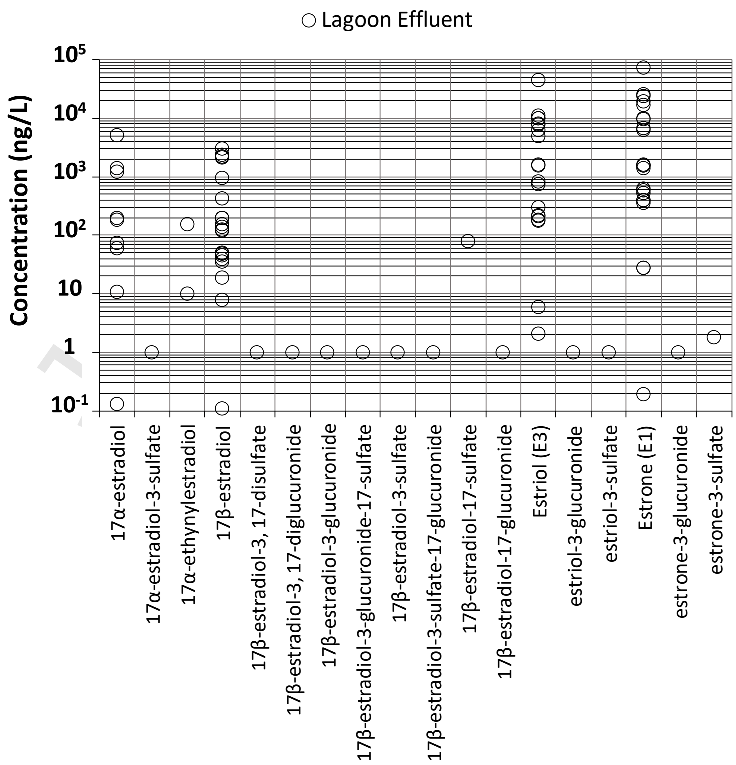


Figure 16. Occurrence of selected hormones in the effluent of a lagoon receiving swine manure.
Data from: Fine et al., 2003; Gall et al., 2014; Hutchins et al., 2007; Sarmah et al., 2006b; Zhang et al., 2014.

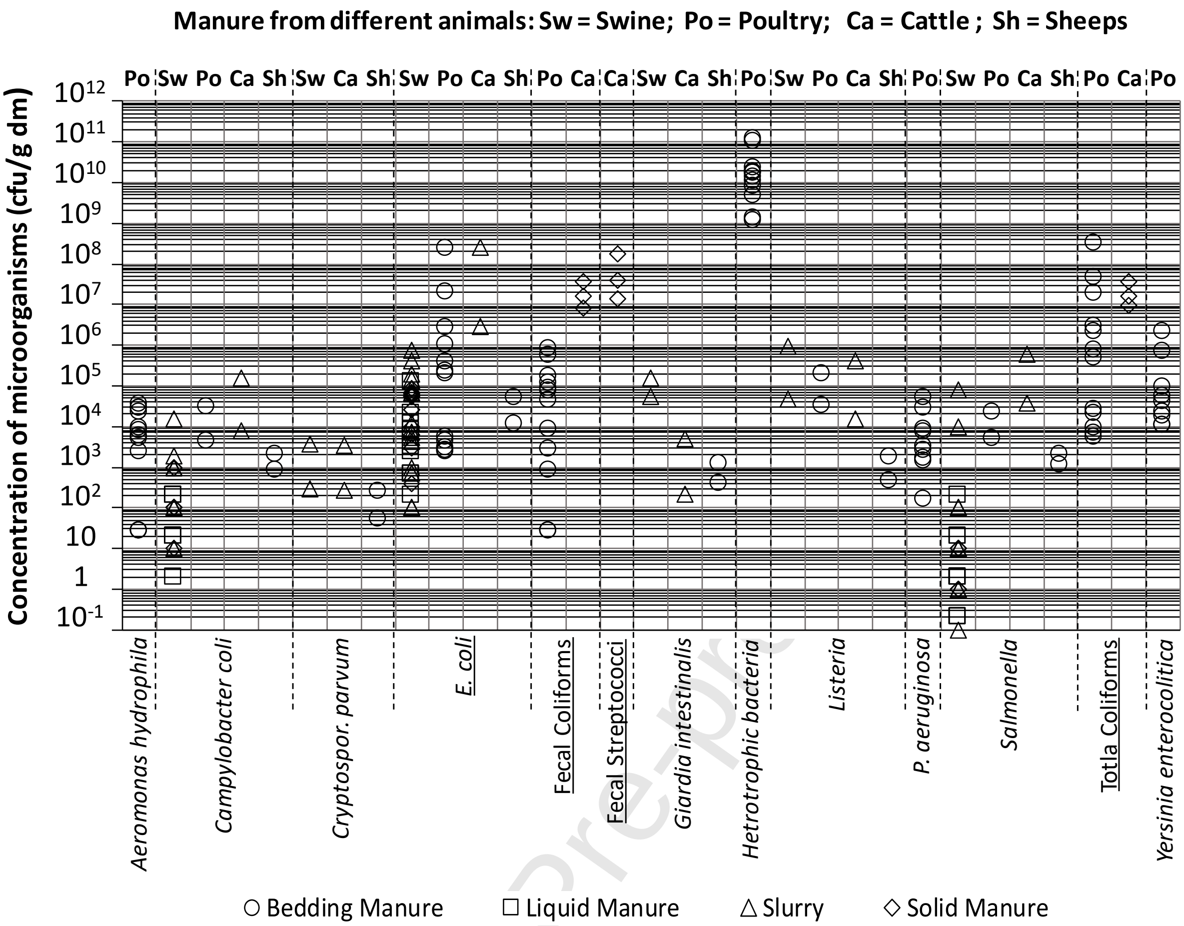


Figure 17. Observed concentrations of microorganisms in different types of raw manure generated by different animals (swine, poultry, cattle and sheep). (On the X axis, the underlined names correspond to indicator organisms, those not underlined to pathogens).

Data from: Hutchinson et al., 2004; Kelley et al., 1994; Patten et al., 1980; Van den Meersche et al., 2019.

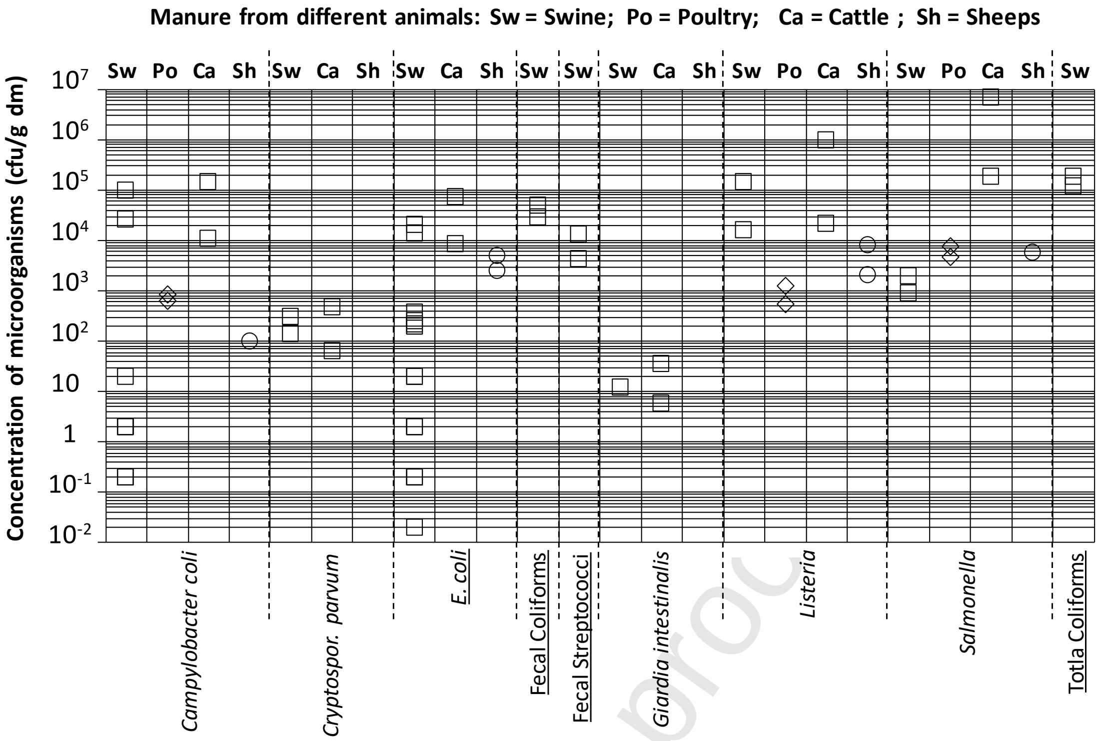


Figure 18. Observed concentrations of microorganisms in treated manures from different animals.
Data from: Frey et al., 2013; Hutchison et al., 2004; Van den Meersche et al., 2019.

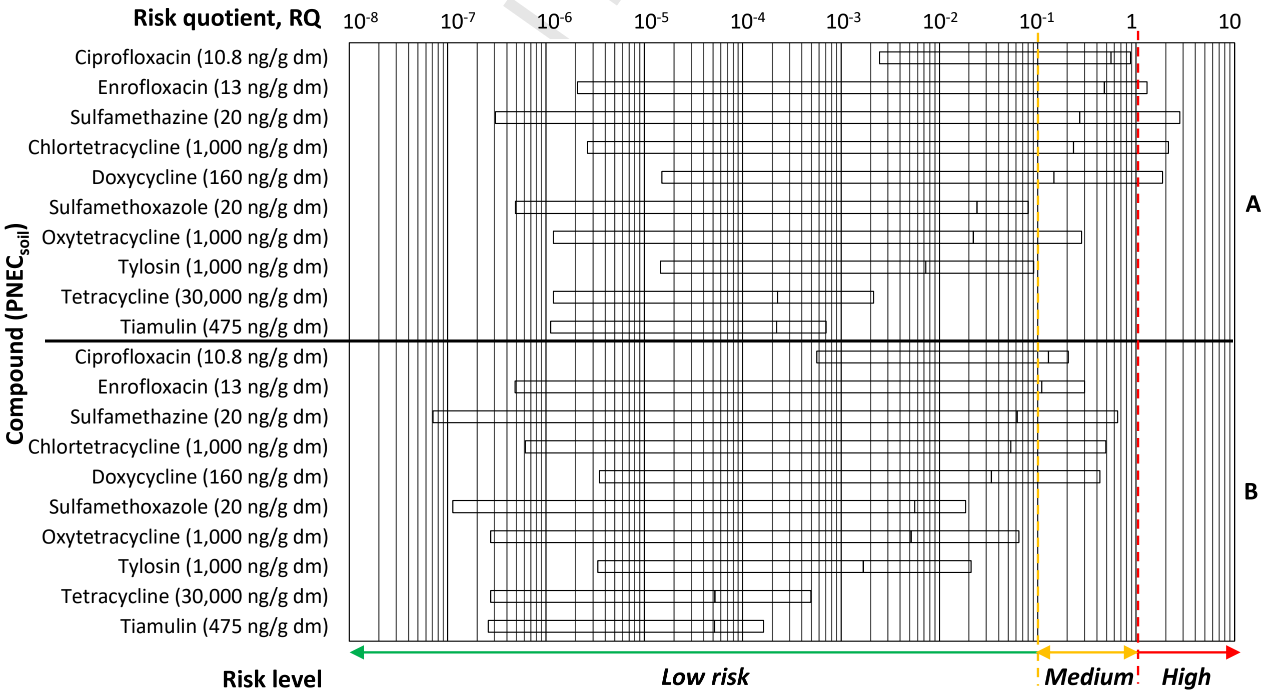


Figure 19. RQ for a selection of antibiotics under review in the case of the different application rate of swine slurry. The number in brackets after the name of the antibiotic corresponds to the adopted $PNEC_{soil}$. Application rate of: A) 9,500 kg dm/(ha year); B) 2,200 kg dm/(ha year).

TABLES

Table 1. Definition of the different types of raw and treated manure considered in this review, their content of macronutrients and the corresponding references.

Manure categories	Manure types	Description [unit of measurement for micropollutant concentrations]	Dry matter [%]	C_{tot} [%] N_{tot} [%] P_{tot} [%] K_{tot} [%]	References
Raw manure					
Bedding manure	Cattle, horse, sheep or pig bedding manure	Mixture of faeces, urine and bedding material (including straw, wood shavings and sawdust) and other dry adsorbents, low-cost material. [ng/g dm]	20.9–69.9	11.8–12.9 0.4–2.2 0.2–4.0 0.9–4.0	Arikan et al., 2009; Derby et al., 2011; Hutchison et al., 2004; Patten et al., 1980
	Poultry litter	Mixture of faeces, urine, spilled feed, animal waste (feathers, blood, etc.) and bedding material. Generally deriving from indoor ground breeding of broiler chickens. [ng/g dm]	33.3–78.5	12.6–50.4 1.1–5.9 1.1–3.2 2.0–3.3	Aznar et al., 2018; Arikan et al., 2016; Dutta et al., 2010; Jenkins et al., 2006; Leal et al., 2012; Nichols et al., 1997
Solid manure	Cattle and horse solid manure	Manure with medium-high dry matter content that could be scraped from stalls (mostly faeces, but may contain urine), or solid fraction of slurry obtained with separation processes. [ng/g dm]	24.4–65.0	10.4–48.1 0.6–4.6 0.1–2.5 0.1–3.2	Amarakoon et al., 2014; Arikan et al., 2016; Aust et al., 2008; Karci and Balcioğlu, 2009; Ray et al., 2017; Wallace and Aga, 2016; Wallace et al., 2018
	Pig solid manure		28.0–29.0	35.3–41.0 1.3–2.7 1.5–3.2 0.7	Bao et al., 2009; Gros et al., 2019; Zhang et al., 2019
	Poultry manure	Mixture of faeces, urine and, to a lesser extent, animal waste (feathers, blood, etc.). Bedding material is absent. Generally obtained from shallow scrape of alley in egg production facility (e.g. from laying hens in battery cages). [micropollutants in ng/g dm]	33.0–79.4	24.9–46.2 1.7–7.1 0.7–6.7 1.9–5.0	Bao et al., 2009; Conde-Cid et al., 2018; Delgado et al., 2018; Dutta et al., 2010; Ho et al., 2014; Karci and Balcioğlu, 2009
Semi-liquid manure	Cattle slurry	Faeces and urine (often accumulated from slatted floor) accumulated in slurry pit. [ng/g dm and also ng/L]	0.5–8.3	17.5–36.5 0.2–2.8 0.04–0.1 0.4–0.5	Conde-Cid et al., 2018; Khan and Lee, 2012; Peyton et al., 2016; Wallace et al., 2018
	Pig slurry		0.3–8.3	16.3–41.4 0.1–3.4 0.01–3.1 0.1–2.5	Blackwell et al., 2009; Conde-Cid et al., 2018; Gros et al., 2019; Hutchison et al., 2004; Jacobsen and Halling-Sørensen, 2006; Joy et al., 2014; Kjær et al., 2007; Lamshöft et al., 2010
	Cattle and horse liquid (fraction) manure	Liquid fraction of manure, obtained through percolation, centrifugation or other separation practices. [micropollutants in ng/g dm and also ng/L]	4.9	NA NA 0.05 0.2	Wallace and Aga, 2016; Wallace et al., 2018
	Pig liquid (fraction) manure		<1–1.6	NA 0.1 1.0 NA	Combalbert et al., 2012; Gros et al., 2019
Liquid manure	Cattle, horse and	Liquid waste generated by any animal species.	NA	NA 0.1–1.7	Hoogendoorn et al., 2010

Manure categories	Manure types	Description [unit of measurement for micropollutant concentrations]	Dry matter [%]	C_{tot} [%] N_{tot} [%] P_{tot} [%] K_{tot} [%]	References
	pig urine	[ng/L]		NA NA	
	Cattle shed flushing material	Dirty water composed of faeces, urine, wash water from stalls and, if collecting tank is outdoors, rainwater. [ng/g dm and also ng/L]	<2	NA NA NA NA	Hutchison et al., 2004
	Pig house flushing material		<2	NA 0.6* 0.1* 0.4*	Edwards and Daniel, 1994; Hutchison et al., 2004
	Poultry house flushing material		<2	NA NA NA NA	Hutchison et al., 2004
Types of treated manure and brief description of treatment:					
Lagooning sludge		Sludge accumulated in 1–5 m deep open air or covered ponds. Generally removed from 5–20 years and applied on soil as amendment (Hamilton et al.,2006). [ng/g dm and also ng/L]	3.2[33]–25[34]	NA 0.5 0.06 0.4	Frey et al., 2013; Kuchta and Cessna, 2009; Wallace et al., 2018
Lagoon effluent		Water collected from upper part of lagoon receiving manure (water phase). Residence time generally varies from 2–6 months. Often used for irrigation purposes (Bodman 1996). [ng/L]		NA 0.04–0.15 0.03–0.14 0.02–0.04	Khan and Lee, 2012
Compost		Mixture of manure and organic material (e.g. hay, straw or decomposed leaves) that results from aerobic composting process favoured by regular turning and controlling of moisture and temperature. [micropollutants in ng/L]	33.5–79.0	10.1–48.8 0.8–3.6 0.2–3.7 1.4–3.2	Aznar et al., 2018; Biswas et al., 2017; Cessna et al., 2011; Derby et al., 2011; Larney et al., 2003; Liu et al., 2015; Ray et al., 2017
Digested manure		Mixture of manure and organic material (e.g. hay, straw or decomposed leaves) that results from anaerobic digestion process generally occurring at least at 40 °C for up to 6 months. [ng/g dm and also ng/L]	4.3	NA 0.3 0.02 0.1	Wallace et al., 2018
Pellet manure		Extremely dense and low moisture content manure granules made by compression of dung at high temperature (at last 100 °C). [ng/g dm]	78–94	NA 2–4.5 1.6–1.8 NA	Dutta et al., 2010; Haggard et al., 2005; McMullen et al., 2005
Alum treated manure		Manure in which $Al_2(SO_4)_3$ is added to reduce water extractable constituents between flocks. [ng/g dm]	75.0–78.5	NA 5.2 1.3 NA	Haggard et al., 2005; Nichols et al., 1997

*Estimated assuming a bulk density of 1000 kg m^{-3}.

Table 2. Micropollutants and microorganisms included in the review. Micropollutants are grouped according to their therapeutic class. The number in brackets corresponds to the number of compounds or microorganisms included in the group.

Class	Compounds included

Analgesics and anti-inflammatories (8)	Acetaminophen; fenoprofen; flunixin; ibuprofen; ketoprofen; mefenamic acid; naproxen and salicylic acid
Anticonvulsants (1)	Carbamazepine
Antihelminthics (1)	Flubendazole
Antimicrobials (85)	Amoxicillin; amprolium; anhydrochlortetracycline; anhydrotetracycline; atrazine; azithromycin; bacitracin A; benzylpenicillin (or Penicillin G); carbadox; ceftiofur; chloramphenicol; chlortetracycline; ciprofloxacin; clarithromycin; cloxacillin; colistin A; colistin B; cyromazine; danofloxacin; demeclocycline; difloxacin; doxycycline; enrofloxacin; epi-anhydro-tetracycline; epi-chlortetracycline; epi-iso-chlortetracycline; epi-oxytetracycline; epi-tetracycline; erythromycin; erythromycin H_2O; fleroxacin; florfenicol; flumequine; furazolidone; iso-chlortetracycline; lasalocid; leucomycin A5; lincomycin; lomefloxacin; marbofloxacin; metacycline; minocycline; monensin; n^4-acetyl-sulfamethazine; narasin; nicarbazin; norfloxacin; novobiocin; ofloxacin; oleandomycin; ormetoprim; oxytetracycline; pefloxacin; pirlimycin; pristinamycin (or virginiamycin); roxithromycin; salinomycin; sarafloxacin; sulfacetamide; sulfachlorpyridazine; sulfadiazine; sulfadimethoxine; sulfadoxine; sulfaguanidine; sulfamerazine; sulfameter; sulfamethazine; sulfamethizole; sulfamethoxazole; sulfamethoxypyridazine; sulfamonomethoxine; sulfanilamide; sulfapyridine; sulfaquinoxaline; sulfathiazole; sulfisoxazole; tetracycline; thiamphenicol; tiamulin; tilmicosin; toltrazuril; trimethoprim; tylosin; α-apo-oxytetracycline; β-apo-oxytetracycline
Antiseptics (3)	Methyl triclosan; ortho-phenylphenol; triclosan
Beta-blockers (1)	Metoprolol
Hormones (39)	11-ketotestosterone; 17α-estradiol (E2α or alfatradiol); 17α-estradiol-3-sulfate; 17α-ethynylestradiol (EE2 or ethinyl estradiol); 17α-hydroxyprogesterone; 17α-trenbolone; 17β-estradiol (E2β or estradiol); 17β-estradiol-3, 17-diglucuronide; 17β-estradiol-3, 17-disulfate; 17β-estradiol-3-glucuronide; 17β-estradiol-3-glucuronide-17-sulfate; 17β-estradiol-3-sulfate; 17β-estradiol-3-sulfate-17-glucuronide; 17β-estradiol-17-sulfate; 17β-estradiol-17-glucuronide; 17β-trenbolone; androstadienedione; androstenedione; androsterone; dienestrol; diethylstilbestrol; epiandrosterone (or trans-androsterone); estriol (E3); estriol-3-glucuronide; estriol-3-sulfate; estrone (E1); estrone-3-glucuronide; estrone-3-sulfate; hexestrol; medroxyprogesterone; melengestrol acetate; mestranol; progesterone; testosterone; trendione; α-zearalanol; α-zearalanol; β-zearalanol; β-zearalanol
Inhibitors (xanthine oxidase) (1)	Allopurinol
Lipid regulators (3)	Clofibric acid; fenofibrate; gemfibrozil
Parabens (2)	Methylparaben; propylparaben
Plasticizer (1)	Bisphenol A
Microorganisms (16)	Indicators: *E. coli*; Faecal coliforms; Faecal enterococci; Faecal streptococci; Heterotrophic bacteria; Total coliforms Pathogens: *Aeromonas hydrophila; Campylobacter coli*; *Campylobacter jejuni*; *Clostridium perfringens*; *Cryptosporidium parvum*; *Enterococci*; *Giardia intestinalis*; *Listeria*; *Pseudomonas aeruginosa*; *Salmonella*

Table 3. Analysis of the main characteristics of the raw manure containing the micropollutants with the highest variability range.

Figure number-Animal type	Compound	Manure type	Range	Order of magnit.	Farm size[1]	Animal details	Dose[2]	Manure age; other notes	Reference
1 Cattle (ng/g dm)	*Oxytetracycline*	Liquid	0.1 ng/g dm	6	L		n.a.		Wallace et al., 2018
		Bedding	225,000 ng/g dm		VS		D		Arikan et al., 2007
	Chlortetracycline	Solid	0.8 ng/g dm	5	n.a.	Beef	n.a.	Fresh manure	Hou et al., 2015
		Slurry	27,590 ng/g dm		L		n.a.		Zhao et al., 2010
	Enrofloxacin	Solid	0.66 ng/g dm	5	L		R		Zhou et al., 2013a
		Slurry	46,700 ng/g dm		L		n.a.		Zhao et al., 2010
	Sulfamethazine	Liquid	0.45 ng/g dm	5	L		n.a.		Wallace et al., 2018
		Solid	30,250 ng/g dm		S		R		Aust et al., 2008
2. Cattle (ng/g dm)	*17α-estradiol*	Solid	0.18 ng/g dm	4	S		D		Bartelt-Hunt et al., 2012
		Bedding	1416 ng/g dm		L	Dairy	n.a.		Zheng et al., 2008
	Estrone	Solid	0.1 ng/g dm	3	L		n.a.		Zhang et al., 2014
		Bedding	697 ng/g dm		L	Dairy	n.a.	Piled manure 2 weeks	Zheng et al., 2008
	Progesterone	Solid	0.26 ng/g dm	3	S		D		Bartelt-Hunt et al., 2012
		Solid	196 ng/g dm		L	Dairy	n.a.	Piled manure 2 weeks	Zheng et al., 2008
3. Poultry (ng/g dm)	*Enrofloxacin*	Poultry manure	0.8 ng/g dm	7	n.a.		n.a.	Fresh manure	Hou et al., 2015
		Poultry litter	1,420,760 ng/g dm		L		n.a.		Zhao et al., 2010
	Fleroxacin	Poultry manure	0.68 ng/g dm	6	n.a.		n.a.		Zhang et al., 2019
		Poultry litter	99,430 ng/g dm		L		n.a.		Zhao et al., 2010
	Oxytetracycline	Poultry manure	0.8 ng/g dm	6	n.a.		n.a.	Fresh manure	Hou et al., 2015
		Poultry manure	416,750 ng/g dm		n.a.		n.a.		Zhang et al., 2015
	Erythromycin	Poultry manure	0.5 ng/g dm	5	n.a.		n.a.	Fresh manure	Hou et al., 2015
		Poultry manure	12,380 ng/g dm		L		n.a.		Ho et al., 2013
	Difloxacin	Poultry manure	0.73 ng/g dm	5	n.a.		n.a.		Zhang et al., 2019
		Poultry litter	10,910 ng/g dm		L		n.a.		Zhao et al., 2010
	Sulfadiazine	Poultry manure	0.8 ng/g dm	5	n.a.		n.a.	Fresh manure	Hou et al., 2015
		Poultry manure	91,000 ng/g dm		M		n.a.		Martinez-Carballo et al., 2007
	Salinomycin	Poultry litter	0.2 ng/g dm	5	n.a.		n.a.		Furtula et al., 2009
		Poultry manure	22,000 ng/g dm		n.a.		n.a.		Ramasmamy et al., 2010
	Trimethoprim	Poultry manure	0.5 ng/g dm	5	n.a.		n.a.	Fresh manure	Hou et al., 2015
		Poultry manure	17,000 ng/g dm		M		n.a.		Martinez-Carballo et al., 2007
	Tylosin	Poultry manure	0.5 ng/g dm	5	n.a.		n.a.	Fresh manure	Hou et al., 2015
		Poultry manure	57,570 ng/g dm		L		n.a.		Ho et al., 2013
4. Poultry (ng/g dm)	*Testosterone*	Poultry litter	0.03 ng/g dm	4	n.a.		n.a.		Jenkins et al., 2006
		Poultry manure	670 ng/g dm		n.a.	Rooster	n.a.		Shore et al., 1993
	17β-estradiol	Poultry manure	0.2 ng/g dm	3	L	Brood hen			Zhang et al., 2014

Figure number-Animal type	Compound	Manure type	Range	Order of magnit.	Farm size[1]	Animal details	Dose[2]	Manure age; other notes	Reference
		Poultry litter	904 ng/g dm		n.a.		n.a.		Nichols et al., 1998
	Bisphenol A	Poultry manure	0.1 ng/g dm	3	L	Brood hen	n.a.		Zhang et al., 2014
		Poultry manure	207 ng/g dm		n.a.	Indoor broiler	n.a.		Aznar et al., 2018
	Estrone	Poultry manure	0.1 ng/g dm	3	L	Brood hen			Zhang et al., 2014
		Poultry litter	321 ng/g dm		n.a.		n.a.		Albero et al., 2014
	Progesterone	Poultry litter	1.3 ng/g dm	3	n.a.		n.a.		Albero et al., 2014
		Poultry manure	1,310 ng/g dm		L		n.a.		Ho et al., 2013
	Salicylic acid	Poultry litter	1.5 ng/g dm	3	n.a.	Indoor broiler	n.a.		Aznar et al., 2018
		Poultry manure	2,501 ng/g dm		n.a.	Battery cage	n.a.		Aznar et al., 2018
5. Swine (ng/g dm)	*Oxytetracycline*	Slurry	0.43 ng/g dm	6	M		n.a.		Martinez-Carballo et al., 2007
		Solid	354,000 ng/g dm		n.a.	Piglets	n.a.		Chen et al., 2012
	Chlortetracycline	Solid	0.5 ng/g dm (LOD)	6	n.a.		n.a.	Fresh manure	Hou et al., 2015
		Solid	879,600 ng/g dm		n.a.	Hog	n.a.		Bao et al., 2009
	Bacitracin A	Solid	5.22 ng/g dm	5	L	Finishing pigs and sows	n.a.	Collected every day. Feces	Zhou et al., 2013b
		Slurry	320,000 ng/g dm		n.a.		D	Fresh manure	Joy et al., 2013
	Doxycycline	Solid	2.79 ng/g dm	5	L	Finishing pigs	n.a.	Collected every day. Feces	Zhou et al., 2013b
		Slurry	106,000 ng/g dm		n.a.		n.a.		Conde-cid et al., 2018
6. Swine (ng/g dm)	*17β-estradiol*	Solid	0.2 ng/g dm	4	L	Piglets, sow, barrow	n.a.		Zhang et al., 2014
		Slurry	1,500 ng/g dm		n.a.		n.a.		Raman et al., 2004
	Estrone	Solid	0.1 ng/g dm	4	L	Piglets, sow, barrow	n.a.		Zhang et al., 2014
		Slurry	4,800 ng/g dm		n.a.		n.a.		Raman et al., 2004
	Flunixin	Slurry	0.6 ng/g dm	4	n.a.		n.a.		Gros et al., 2019
		Slurry	2,300 ng/g dm		n.a.		n.a.		Gros et al., 2019
	Estriol	Solid	0.4 ng/g dm	3	L		n.a.		Zhang et al., 2014
		Solid	315 ng/g dm		n.a.		n.a.	6 months	Combalbert et al., 2010
7. Cattle (ng/L)	*Chlortetracycline*	Liquid	3 ng/L	6	n.a.		n.a.		Wallace and Aga, 2013
		Slurry	5,860,000 ng/L		VS	Beef calves	D	After 5 days of medication	Arikan, 2008
	epi-chlortetracycline	Liquid	4 ng/L	6	n.a.		n.a.		Wallace and Aga, 2013
		Slurry	4,110,000 ng/L		VS	Beef calves	D	After 5 days of medication	Arikan, 2008
	iso-chlortetracycline	Flushing material	10 ng/L	5	L	Calf hutches	n.a.		Watanabe et al., 2010
		Slurry	2,360,000 ng/L		VS	Beef calves	D	After 5 days of medication	Arikan, 2008
	Sulfamethazine	Flushing material	0.7 ng/L	5	n.a.	Beef cattle	n.a.		Zhang et al., 2013
		Flushing material	15,000 ng/L		L	Calf hutches	n.a.		Watanabe et al., 2010

Figure number-Animal type	Compound	Manure type	Range	Order of magnit.	Farm size[1]	Animal details	Dose[2]	Manure age; other notes	Reference
	Sulfamethoxazole	Flushing material	0.5 ng/L	5	n.a.	Beef cattle	n.a.		Zhang et al., 2013
		Flushing material	19,000 ng/L		L	Calf hutches	n.a.		Watanabe et al., 2010
9. Swine (ng/L)	*Chlortetracycline*	Flushing material	0.4 ng/L	9	n.a.		n.a.		Li et al., 2018
		Slurry	108,000,000 ng/L		VS		D	After 5 days of medication	Hoese et al., 2009
	Chloramphenicol	Flushing material	0.2 ng/L	6	n.a.		n.a.		Li et al., 2018
		Flushing material	441,900 ng/L		n.a.		n.a.		Li et al., 2018
	Ciprofloxacin	Flushing material	0.3 ng/L	6	n.a.		n.a.		Li et al., 2018
		Flushing material	263,100 ng/L		n.a.		n.a.		Li et al., 2018
	Norfloxacin	Flushing material	0.4 ng/L	6	n.a.		n.a.		Li et al., 2018
		Flushing material	389,200 ng/L		n.a.		n.a.		Li et al., 2018
	Lincomycin	Flushing material	126 ng/L	5	L	Piglets	n.a.	Collected every day	Zhou et al., 2013b
		Slurry	20,400,000 ng/L		n.a.		n.a.		Gros et al., 2019
10. Swine (ng/L)	*Sulfamethazine*	Flushing material	0.6 ng/L	8	n.a.		n.a.		Li et al., 2018
		Slurry	11,000,000 ng/L		n.a.		n.a.		Burkhardt et al., 2005
	Sulfamonomethoxine	Flushing material	0.1 ng/L	7	n.a.		n.a.		Li et al., 2018
		Flushing material	3,494,100 ng/L		n.a.		n.a.		Li et al., 2018
	Oxytetracycline	Flushing material	0.3 ng/L	6	n.a.		n.a.		Li et al., 2018
		Slurry	993,800 ng/L		n.a.		n.a.		Li et al., 2018
	Tylosin	Flushing material	1.3 ng/L	5	L	Piglets and sows	n.a.	Collected every day	Zhou et al., 2013b
		Slurry	300,000 ng/L		VS		D	After 5 days of medication	Hoese et al., 2009

[1] Farm size: L= large, M= Medium, S= Small, VS= Very small. See Table S1 for further details

[2] Dose: R= Rough description in the reference study; D= Detailed description in the reference study

n.a.= not available

Table 4. Analysis of the main characteristics of the treated manure containing the micropollutants with the highest variability range.

Figure number-Treatment type	Compound	Treated manure	Range	Order of magnit	Farm size[1]	Animal details	Dose[2]	Manure age; other note	Reference
11. Treated cattle manure (ng/g dm)	*17α-estradiol*	Composted solid	0.18 ng/g dm	3	S		D		van Donk et al., 2013
		Lagooning sludge	100 ng/g dm		n.a.		n.a.		Raman et al., 2004
12. Treated swine manure (ng/g dm)	*Norfloxacin*	Lagooning sludge	0.81 ng/g dm	4	L		R	Lagoon feeding= mixture of manure from animals in different stages	Zhou et al., 2013a
		An-digested flushing material	1,080 ng/g dm		L		R	Flushing material from farms housing animals in different stages	Zhou et al., 2013a
	Oxytetracycline	Lagooning sludge	3.4 ng/g dm	4	n.a.		R		Van den Meersche et al., 2019
		An-digested flushing material	19,000 ng/g dm		L		R	Flushing material from farms housing animals in different stages	Zhou et al., 2013a
	Sulfamethazine	Lagooning sludge	0.52 ng/g dm	4	L		n.a.		Zhou et al., 2012
		An-digested flushing material	1060 ng/g dm		L		R	Flushing material from farms housing animals in different stages	Zhou et al., 2013a
	Tylosin	Lagooning sludge	0.61 ng/g dm	4	L		n.a.	Collected every day Lagoon feeding= mixture of manure from animals in different stages	Zhou et al., 2013b
		Lagooning sludge	4,913 ng/g dm		n.a.	Beef cattle	n.a.		Zhang et al., 2013
13. Treated cattle manure (ng/L)	*Chlortetracycline*	Lagoon effluent	10 ng/L	5	L		n.a.		Watanabe et al., 2010
		An-digested slurry	1,400,000 ng/L		VS	Beef calves	D	After 5 days of medication	Arikan, 2008
	epi-chlortetracycline	Lagoon effluent	10 ng/L	5	L		n.a.		Watanabe et al., 2010
		An-digested slurry	2,500,000 ng/L		VS	Beef calves	D	After 5 days of medication	Arikan, 2008
	epi-oxytetracycline	Lagoon effluent	10 ng/L	5	L		n.a.		Watanabe et al., 2010
		An-digested bedding	1,300,000 ng/L		VS	Beef calves	D	After 5 days of medication	Arikan et al., 2006
	iso-chlortetracycline	Lagoon effluent	10 ng/L	5	L		n.a.		Watanabe et al., 2010
		An-digested slurry	4,600,000 ng/L		VS	Beef calves	D	After 5 days of medication	Arikan, 2008
	Oxytetracycline	Lagoon effluent	10 ng/L	5	L		n.a.		Watanabe et al., 2010
		An-digested	6,800,000 ng/L		VS	Beef calves	D	After 5 days of medication	Arikan et al., 2006

		bedding							
14. Treated cattle manure (ng/L)	*17α-estradiol*	Lagoon Effluent	0.13 ng/L	4	n.a.	Dairy and beef cattle	n.a.		Gall et al., 2014
		Lagoon Effluent	1,600 ng/L		n.a.	Dairy cattle	n.a.		Gadd et al., 2010
	17β-estradiol	Lagoon Effluent	0.1 ng/L	4	n.a.	Dairy cattle	n.a.		Kolodziej et al., 2004
		Lagoon Effluent	1,326 ng/L		L		n.a.		Zhang et al., 2014
	Estrone	Lagoon Effluent	0.14 ng/L	4	n.a.	Dairy cattle	n.a.		Kolodziej et al., 2004
		Lagoon Effluent	3,123 ng/L		n.a.		n.a.		Sarmah et al., 2006b
	Estriol	Lagoon Effluent	0.1 ng/L	3	n.a.	Dairy cattle	n.a.		Kolodziej et al., 2004
		Lagoon Effluent	725 ng/L		n.a.		n.a.	Implanted cows	Khan and Lee, 2012
15. Treated swine manure (ng/L)	*Lincomycin*	Lagoon Effluent	0.5 ng/L	6	n.a.		n.a.		Zhang et al., 2013
		Lagoon Effluent	240,000 ng/L		n.a.		n.a.		Campagnolo et al., 2002
	Sulfamethazine	Lagoon Effluent	0.4 ng/L	6	n.a.		n.a.		Zhang et al., 2013
		Lagoon Effluent	400,000 ng/L		n.a.		n.a.		Campagnolo et al., 2002
	Tylosin	Lagoon Effluent	1.3 ng/L	6	L		R	Lagoon feeding= mixture of manure from animals in different stages	Zhou et al., 2013a
		Lagooning sludge	4,924,867 ng/L		n.a.		n.a.		Dolliver and Gupta, 2008
	Sulfadimethoxine	Lagoon Effluent	0.5 ng/L	5	n.a.		n.a.		Zhang et al., 2013
		Lagoon Effluent	14,050 ng/L		n.a.		n.a.		Ben et al., 2008
16. Treated swine manure (ng/L)	*Estrone*	Lagoon Effluent	0.19 ng/L	5	n.a.		n.a.		Gall et al., 2014
		Lagoon Effluent	74,700 ng/L		n.a.		n.a.		Fine et al., 2003
	17α-estradiol	Lagoon Effluent	0.13 ng/L	4	n.a.		n.a.		Gall et al., 2014
		Lagoon Effluent	5,189 ng/L		n.a.		n.a.		Gall et al., 2014
	17β-estradiol	Lagoon Effluent	0.11 ng/L	4	n.a.		n.a.		Gall et al., 2014
		Lagoon Effluent	3000 ng/L		n.a.		n.a.		Fine et al., 2003
	Estriol	Lagoon Effluent	2.1 ng/L	4	n.a.		n.a.		Gall et al., 2014
		Lagoon Effluent	45,379 ng/L		n.a.		n.a.		Gall et al., 2014

[1] Farm size: L= large, M= Medium, S= Small, VS= Very small. See Table S1 for further details

[2] Dose: R= Rough description in the reference study; D= Detailed description in the reference study

n.a.= not available

Table 5. PEC soils by assuming the two application rates discussed in the manuscript (2,200 kg dm/ha year; 9,500 kg dm/ha year) and ranges of measured concentrations found in the literature.

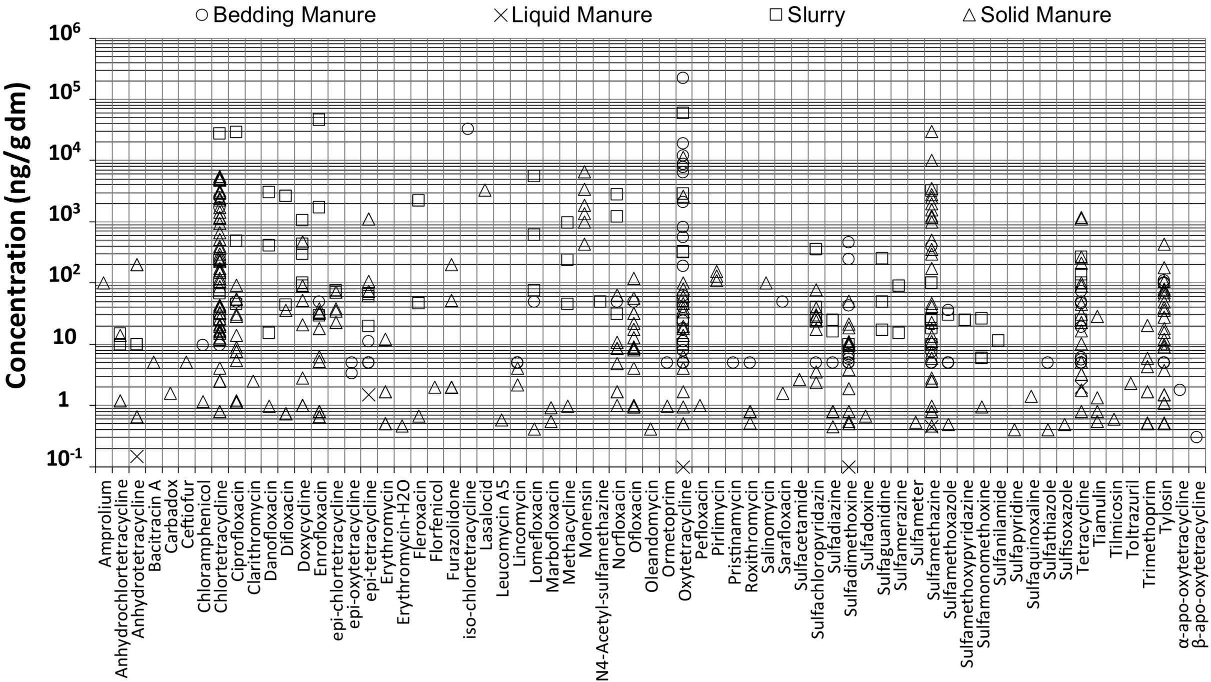
Compound	***Swine slurry c_i [ng/g dm]***			***PEC_{soil} [ng/g dm]– 2,200 kg dm/(ha year)***			***PEC_{soil} [ng/g dm]– 9,500 kg dm/(ha year)***			***MEC_{soil} [ng/g dm]***	***References for MEC***
	min	max	average	min	max	average	min	max	average	(literature)	
Chlortetracycline	0.95	764,400	82,313	6.15E-04	495	53.26	2.65E-03	2136	230	N.D--1430	Gros et al., 2019; Zhou et al., 2013a
Ciprofloxacin	880	3400	2140	5.69E-01	2.20	1.38	2.46E+00	9.50	5.98	N.D.-32.8	Gros et al., 2019; Zhou et al., 2013a
Doxycycline	5.4	106,000	8,383	3.49E-03	68.6	5.42	1.51E-02	296	23.4	ND-499	Zhou et al., 2013a
Enrofloxacin	0.75	6010	2,216	4.85E-04	3.89	1.43	2.10E-03	16.8	6.19	2.3-151	Gros et al., 2019
Oxytetracycline	0.425	100,000	7,950	2.75E-04	64.7	5.14	1.19E-03	279	22.2	1-75	Gros et al., 2019
Sulfamethazine	0.11	20,000	1912	7.12E-05	12.9	1.24	3.07E-04	55.9	5.34	ND-15	Christian et al., 2003
Sulfamethoxazole	0.175	570	173	1.13E-04	0.37	0.11	4.89E-04	1.59	0.48	ND	Gros et al., 2019
Tetracycline	0.425	23,000	2424	2.75E-04	14.9	1.57	1.19E-03	64.3	6.77	0.22-10.25	Gros et al., 2019
Tiamulin	0.4	120	37.9	2.59E-04	7.76E-03	2.45E-02	1.12E-03	0.34	0.11	ND	Gros et al., 2019
Tylosin	5.2	32,500	2,597	3.36E-03	21.0	1.68	1.45E-02	90.81	7.26	ND	Gros et al., 2019; Zhou et al., 2013b

Table 6. Top pharmaceuticals in the three types of manures most investigated (raw and treated).

Source	Untreated [ng/g dm]	Untreated [ng/L]	Treated [ng/g dm]	Treated [ng/L]
Cattle	Oxytetracycline, 2.3 10^5 Enrofloxacin 4.7 10^4 Sulfamethazine 3.0 10^4	Chlortetracycline 5.9 10^6 epi-chlortetracycline 4.1 10^6 iso- chlortetracycline 2.4 10^6	iso-chlortetracycline 4 10^3 Estrone, 8.5 10^2	Oxytetracycline, 6.8 10^6 iso-chlortetracycline 4.6 10^6
Poultry	Enrofloxacin, 1.4 10^6 Oxytetracycline, 4.2 10^5 Norfloxacin, 2.3 10^5	Oxytetracycline 2.1 10^4		
Swine	Chlortetracycline, 8.8 10^5 Bacitracin A, 3.2 10^5 Oxytetracycline, 3.5 10^5	Chlortetracycline, 1.1 10^8 Sulfamethazine 1.1 10^7 Lincomycin, 2.0 10^5	Chlortetracycline, 8.8 10^5 iso-chlortetracycline 3.3 10^5 epi-chlortetracycline, 2.5 10^5	Tylosin, 4.9 10^6 Chlortetracycline, 1 10^6

HIGHLIGHTS

Cattle, swine, poultry and horse manures were included in the current study
Concentrations of antibiotics and hormones in different manures were reviewed
Concentrations of antibiotics in swine manure-amended soil were predicted
Environmental risk assessment was carried out in case of swine manure application
Sulfamethazine, chlortetracycline and doxycycline are the most critical compounds



○ Bedding Manure
× Liquid Manure
□ Slurry
△ Solid Manure
Concentration (ng/g dm)
10^6
10^5
10^4
10^3
10^2
10
1
10^-1
Amprolium
Anhydrochlortetracycline
Anhydrotetracycline
Bacitracin A
Carbadox
Ceftiofur
Chloramphenicol
Chlortetracycline
Ciprofloxacin
Clarithromycin
Danofloxacin
Difloxacin
Doxycycline
Enrofloxacin
epi-chlortetracycline
epi-oxytetracycline
epi-tetracycline
Erythromycin
Erythromycin-H2O
Fleroxacin
Florfenicol
Furazolidone
iso-chlortetracycline
Lasalocid
Leucomycin A5
Lincomycin
Lomefloxacin
Marbofloxacin
Methacycline
Monensin
N4-Acetyl-sulfamethazine
Norfloxacin
Ofloxacin
Oleandomycin
Ormetoprim
Oxytetracycline
Pefloxacin
Pirlimycin
Pristinamycin
Roxithromycin
Salinomycin
Sarafloxacin
Sulfacetamide
Sulfachloropyridazin
Sulfadiazine
Sulfadimethoxine
Sulfadoxine
Sulfaguanidine
Sulfamerazine
Sulfameter
Sulfamethazine
Sulfamethoxazole
Sulfamethoxypyridazine
Sulfamonomethoxine
Sulfanilamide
Sulfapyridine
Sulfaquinoxaline
Sulfathiazole
Sulfisoxazole
Tetracycline
Tiamulin
Tilmicosin
Toltrazuril
Trimethoprim
Tylosin
α-apo-oxytetracycline
β-apo-oxytetracycline

Figure 1

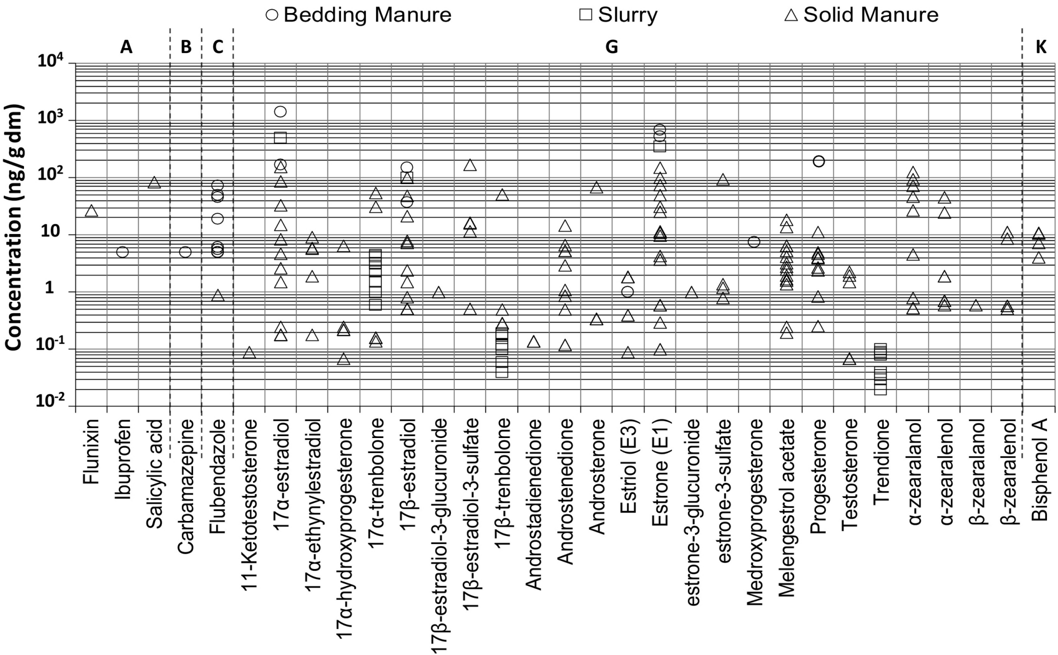
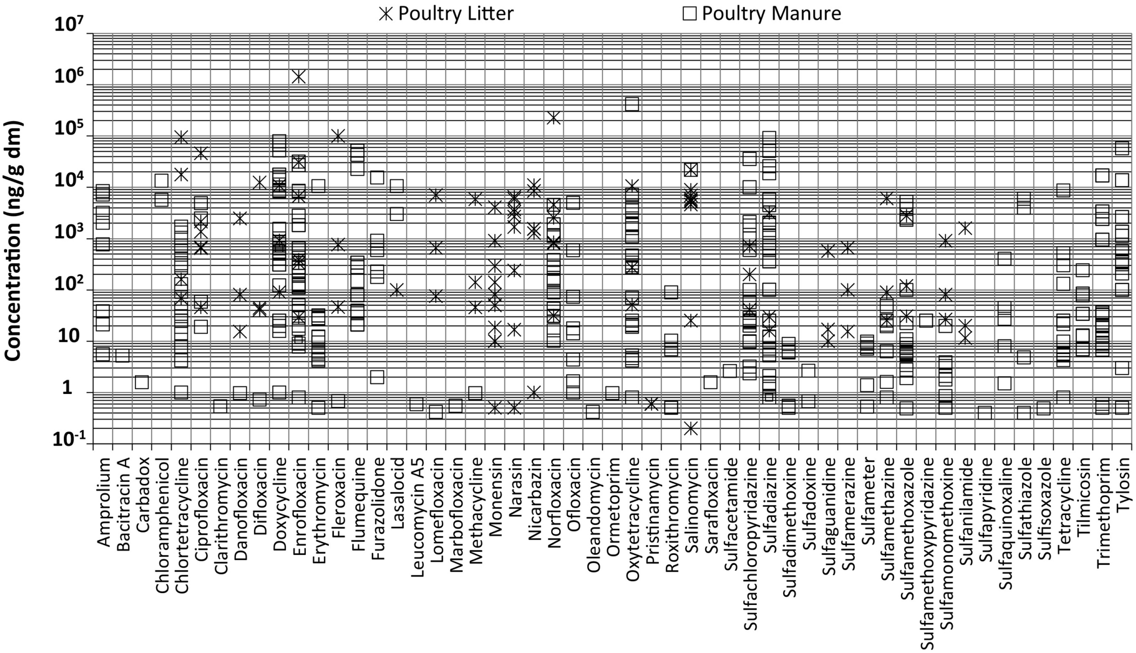

○ Bedding Manure
□ Slurry
△ Solid Manure
A
B
C
G
K
Concentration (ng/g dm)
10^4
10^3
10^2
10
1
10^-1
10^-2
Flunixin
Ibuprofen
Salicylic acid
Carbamazepine
Flubendazole
11-Ketotestosterone
17α-estradiol
17α-ethynylestradiol
17α-hydroxyprogesterone
17α-trenbolone
17β-estradiol
17β-estradiol-3-glucuronide
17β-estradiol-3-sulfate
17β-trenbolone
Androstadienedione
Androstenedione
Androsterone
Estriol (E3)
Estrone (E1)
estrone-3-glucuronide
estrone-3-sulfate
Medroxyprogesterone
Melengestrol acetate
Progesterone
Testosterone
Trendione
α-zearalanol
α-zearalenol
β-zearalanol
β-zearalenol
Bisphenol A

Figure 2



Poultry Litter
Poultry Manure
Concentration (ng/g dm)
10^7
10^6
10^5
10^4
10^3
10^2
10
1
10^-1
Amprolium
Bacitracin A
Carbadox
Chloramphenicol
Chlortetracycline
Ciprofloxacin
Clarithromycin
Danofloxacin
Difloxacin
Doxycycline
Enrofloxacin
Erythromycin
Fleroxacin
Flumequine
Furazolidone
Lasalocid
Leucomycin A5
Lomefloxacin
Marbofloxacin
Methacycline
Monensin
Narasin
Nicarbazin
Norfloxacin
Ofloxacin
Oleandomycin
Ormetoprim
Oxytetracycline
Pristinamycin
Roxithromycin
Salinomycin
Sarafloxacin
Sulfacetamide
Sulfachloropyridazine
Sulfadiazine
Sulfadimethoxine
Sulfadoxine
Sulfaguanidine
Sulfamerazine
Sulfameter
Sulfamethazine
Sulfamethoxazole
Sulfamethoxypyridazine
Sulfamonomethoxine
Sulfanilamide
Sulfapyridine
Sulfaquinoxaline
Sulfathiazole
Sulfisoxazole
Tetracycline
Tilmicosin
Trimethoprim
Tylosin

Figure 3

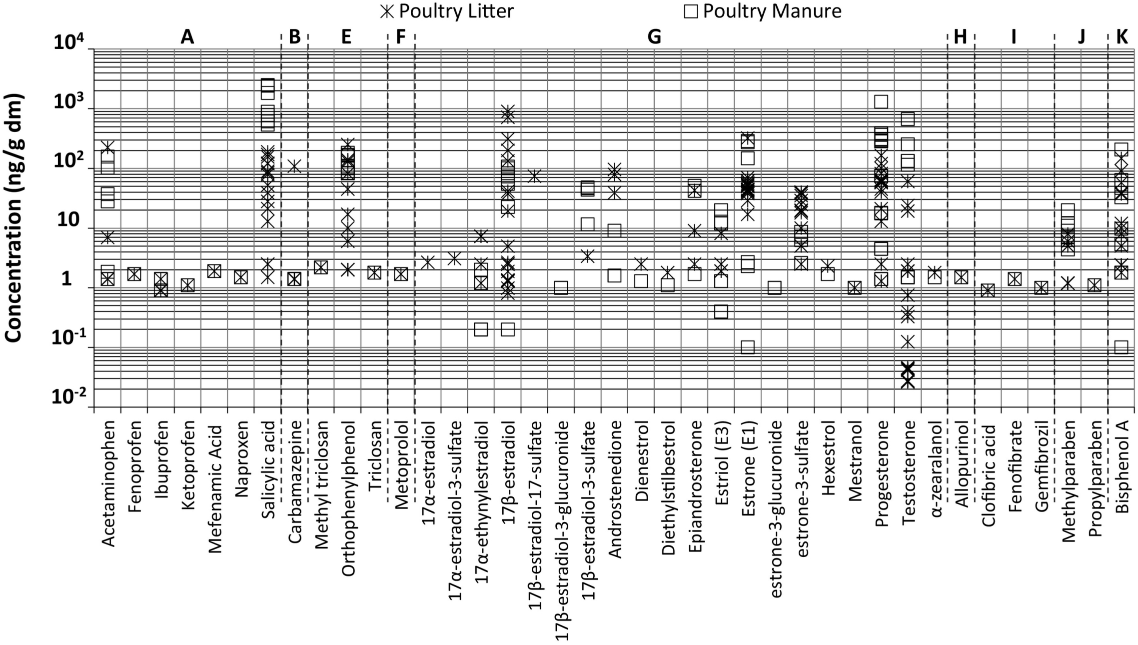

Poultry Litter
Poultry Manure
A
B
E
F
G
H
I
J
K
Concentration (ng/g dm)
10^4
10^3
10^2
10
1
10^-1
10^-2
Acetaminophen
Fenoprofen
Ibuprofen
Ketoprofen
Mefenamic Acid
Naproxen
Salicylic acid
Carbamazepine
Methyl triclosan
Orthophenylphenol
Triclosan
Metoprolol
17α-estradiol
17α-estradiol-3-sulfate
17α-ethynylestradiol
17β-estradiol
17β-estradiol-17-sulfate
17β-estradiol-3-glucuronide
17β-estradiol-3-sulfate
Androstenedione
Dienestrol
Diethylstilbestrol
Epiandrosterone
Estriol (E3)
Estrone (E1)
estrone-3-glucuronide
estrone-3-sulfate
Hexestrol
Mestranol
Progesterone
Testosterone
α-zearalanol
Allopurinol
Clofibric acid
Fenofibrate
Gemfibrozil
Methylparaben
Propylparaben
Bisphenol A

Figure 4

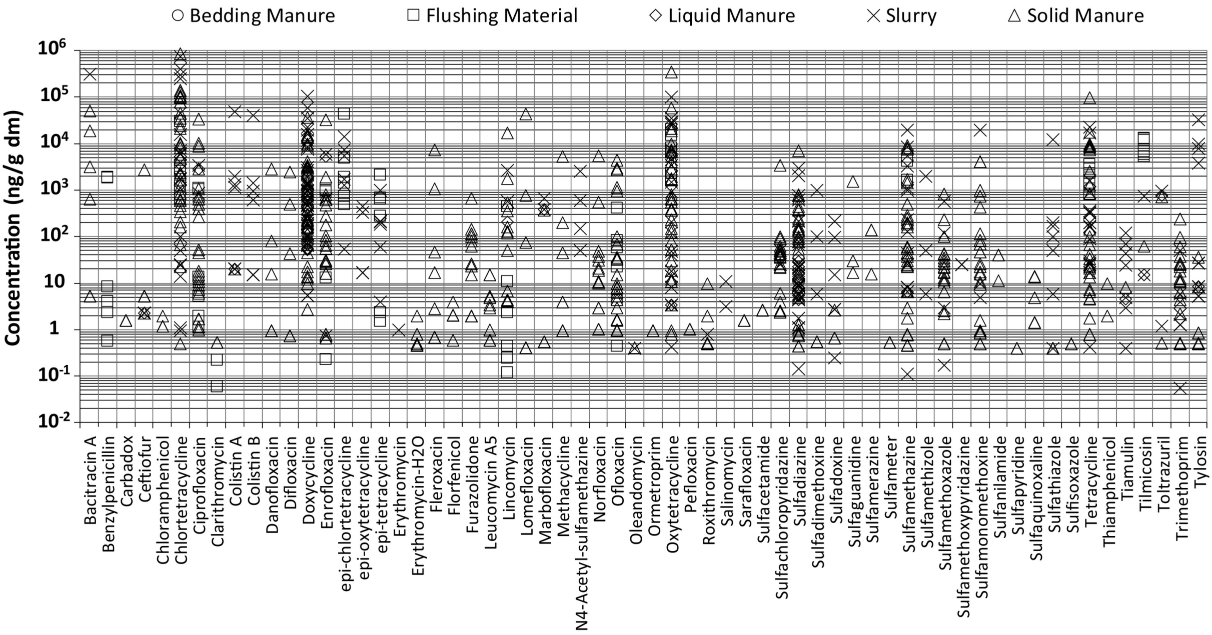

○ Bedding Manure
□ Flushing Material
◇ Liquid Manure
× Slurry
△ Solid Manure
Concentration (ng/g dm)
10^6
10^5
10^4
10^3
10^2
10
1
10^-1
10^-2
Bacitracin A
Benzylpenicillin
Carbadox
Ceftiofur
Chloramphenicol
Chlortetracycline
Ciprofloxacin
Clarithromycin
Colistin A
Colistin B
Danofloxacin
Difloxacin
Doxycycline
Enrofloxacin
epi-chlortetracycline
epi-oxytetracycline
epi-tetracycline
Erythromycin
Erythromycin-H2O
Fleroxacin
Florfenicol
Furazolidone
Leucomycin A5
Lincomycin
Lomefloxacin
Marbofloxacin
Methacycline
N4-Acetyl-sulfamethazine
Norfloxacin
Ofloxacin
Oleandomycin
Ormetoprim
Oxytetracycline
Pefloxacin
Roxithromycin
Salinomycin
Sarafloxacin
Sulfacetamide
Sulfachloropyridazine
Sulfadiazine
Sulfadimethoxine
Sulfadoxine
Sulfaguanidine
Sulfamerazine
Sulfameter
Sulfamethazine
Sulfamethizole
Sulfamethoxazole
Sulfamethoxypyridazine
Sulfamonomethoxine
Sulfanilamide
Sulfapyridine
Sulfaquinoxaline
Sulfathiazole
Sulfisoxazole
Tetracycline
Thiamphenicol
Tiamulin
Tilmicosin
Toltrazuril
Trimethoprim
Tylosin

Figure 5

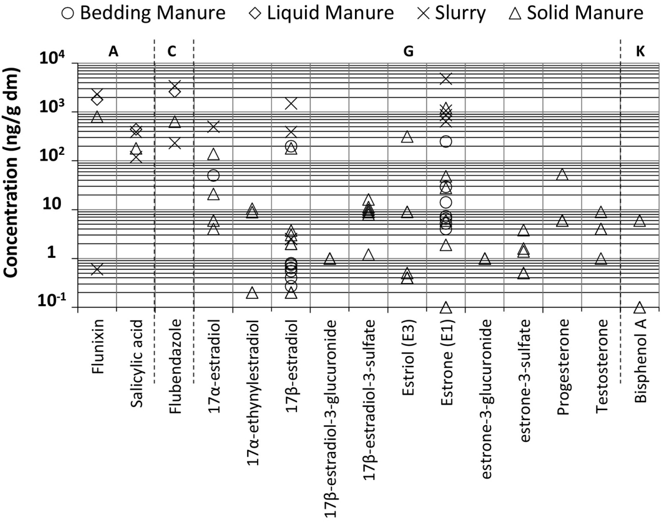

○ Bedding Manure
◇ Liquid Manure
× Slurry
△ Solid Manure
A
C
G
K
Concentration (ng/g dm)
10^4
10^3
10^2
10
1
10^-1
Flunixin
Salicylic acid
Flubendazole
17α-estradiol
17α-ethynylestradiol
17β-estradiol
17β-estradiol-3-glucuronide
17β-estradiol-3-sulfate
Estriol (E3)
Estrone (E1)
estrone-3-glucuronide
estrone-3-sulfate
Progesterone
Testosterone
Bisphenol A

Figure 6

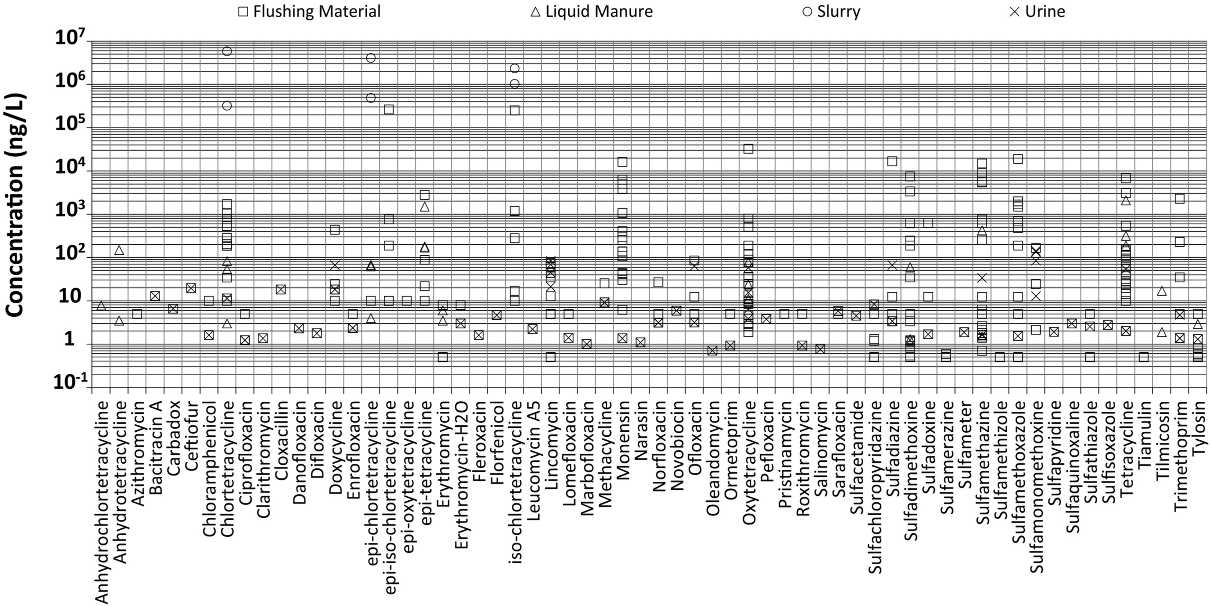

□ Flushing Material
△ Liquid Manure
○ Slurry
× Urine
Concentration (ng/L)
10^7
10^6
10^5
10^4
10^3
10^2
10
1
10^-1
Anhydrochlortetracycline
Anhydrotetracycline
Azithromycin
Bacitracin A
Carbadox
Ceftiofur
Chloramphenicol
Chlortetracycline
Ciprofloxacin
Clarithromycin
Cloxacillin
Danofloxacin
Difloxacin
Doxycycline
Enrofloxacin
epi-chlortetracycline
epi-iso-chlortetracycline
epi-oxytetracycline
epi-tetracycline
Erythromycin
Erythromycin-H2O
Fleroxacin
Florfenicol
iso-chlortetracycline
Leucomycin A5
Lincomycin
Lomefloxacin
Marbofloxacin
Methacycline
Monensin
Narasin
Norfloxacin
Novobiocin
Ofloxacin
Oleandomycin
Ormetoprim
Oxytetracycline
Pefloxacin
Pristinamycin
Roxithromycin
Salinomycin
Sarafloxacin
Sulfacetamide
Sulfachloropyridazine
Sulfadiazine
Sulfadimethoxine
Sulfadoxine
Sulfamerazine
Sulfameter
Sulfamethazine
Sulfamethizole
Sulfamethoxazole
Sulfamonomethoxine
Sulfapyridine
Sulfaquinoxaline
Sulfathiazole
Sulfisoxazole
Tetracycline
Tiamulin
Tilmicosin
Trimethoprim
Tylosin

Figure 7

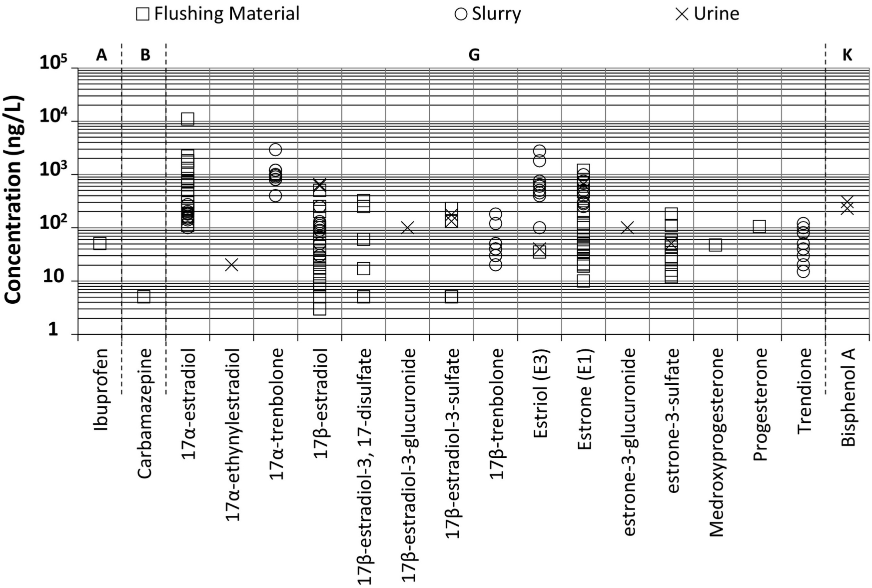

□ Flushing Material
○ Slurry
× Urine
A
B
G
K
Concentration (ng/L)
10^5
10^4
10^3
10^2
10
1
Ibuprofen
Carbamazepine
17α-estradiol
17α-ethynylestradiol
17α-trenbolone
17β-estradiol
17β-estradiol-3, 17-disulfate
17β-estradiol-3-glucuronide
17β-estradiol-3-sulfate
17β-trenbolone
Estriol (E3)
Estrone (E1)
estrone-3-glucuronide
estrone-3-sulfate
Medroxyprogesterone
Progesterone
Trendione
Bisphenol A

Figure 8

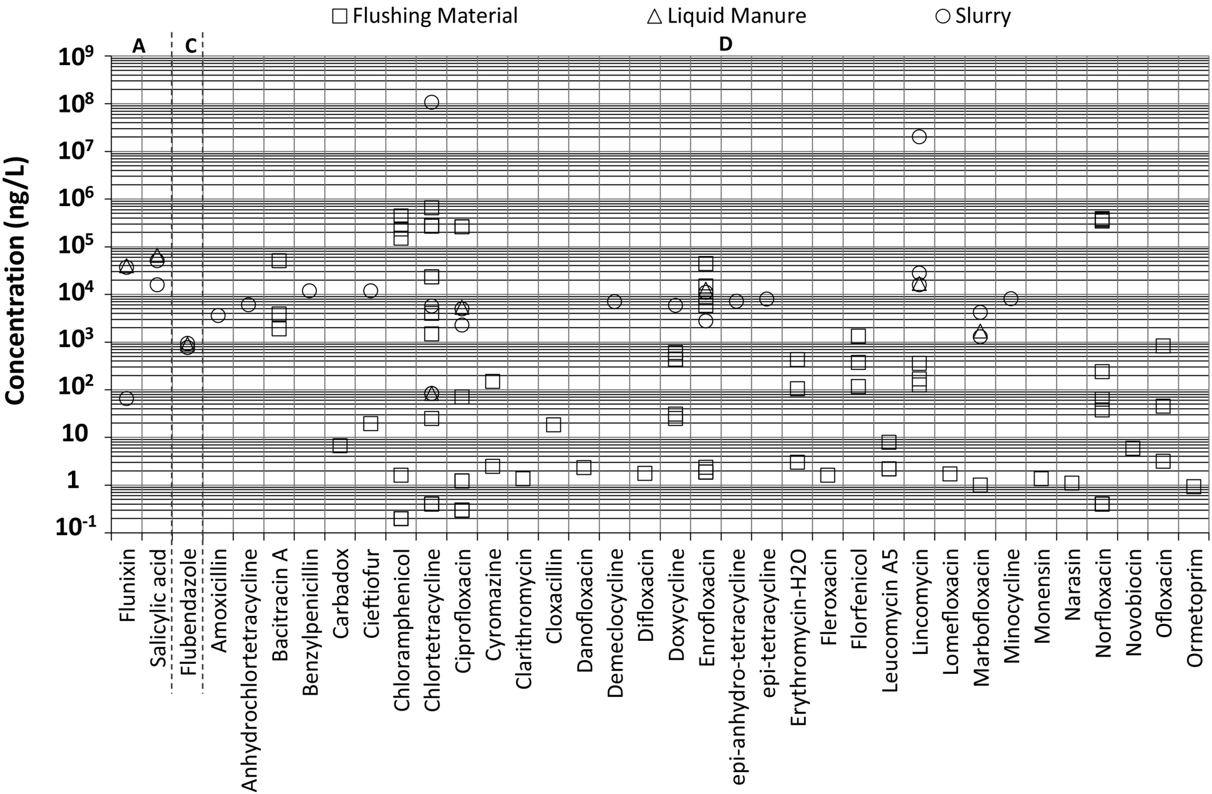
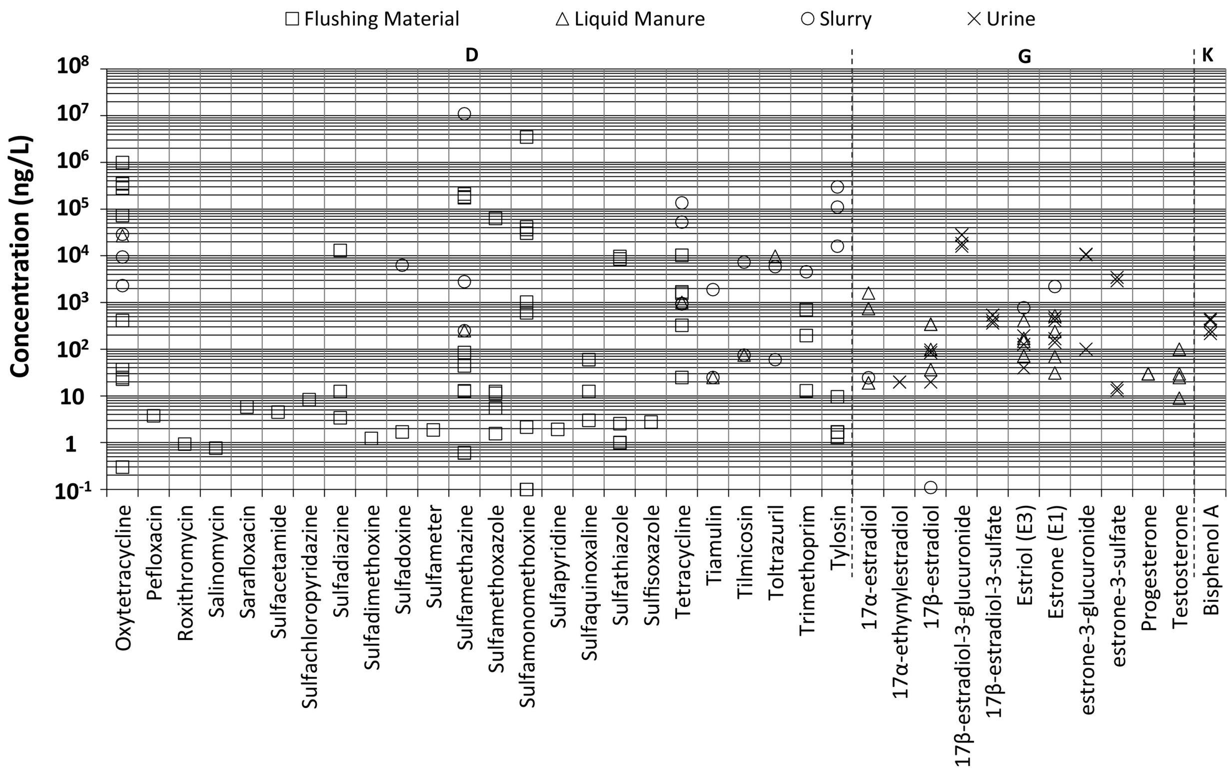
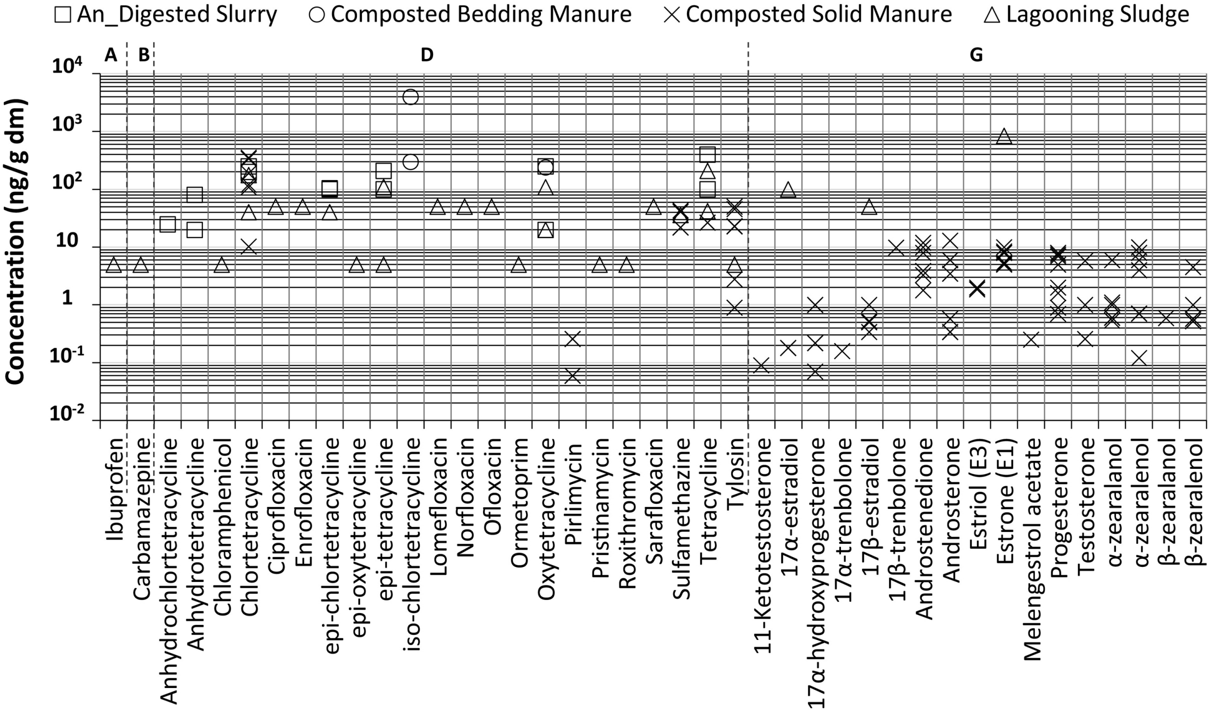

□ Flushing Material
△ Liquid Manure
○ Slurry
A
C
D
Concentration (ng/L)
10^9
10^8
10^7
10^6
10^5
10^4
10^3
10^2
10
1
10^-1
Flunixin
Salicylic acid
Flubendazole
Amoxicillin
Anhydrochlortetracycline
Bacitracin A
Benzylpenicillin
Carbadox
Cieftiofur
Chloramphenicol
Chlortetracycline
Ciprofloxacin
Cyromazine
Clarithromycin
Cloxacillin
Danofloxacin
Demeclocycline
Difloxacin
Doxycycline
Enrofloxacin
epi-anhydro-tetracycline
epi-tetracycline
Erythromycin-H2O
Fleroxacin
Florfenicol
Leucomycin A5
Lincomycin
Lomefloxacin
Marbofloxacin
Minocycline
Monensin
Narasin
Norfloxacin
Novobiocin
Ofloxacin
Ormetoprim

Figure 9



□ Flushing Material
△ Liquid Manure
○ Slurry
× Urine
D
G
K
Concentration (ng/L)
10^8
10^7
10^6
10^5
10^4
10^3
10^2
10
1
10^{-1}
Oxytetracycline
Pefloxacin
Roxithromycin
Salinomycin
Sarafloxacin
Sulfacetamide
Sulfachloropyridazine
Sulfadiazine
Sulfadimethoxine
Sulfadoxine
Sulfameter
Sulfamethazine
Sulfamethoxazole
Sulfamonomethoxine
Sulfapyridine
Sulfaquinoxaline
Sulfathiazole
Sulfisoxazole
Tetracycline
Tiamulin
Tilmicosin
Toltrazuril
Trimethoprim
Tylosin
17α-estradiol
17α-ethynylestradiol
17β-estradiol
17β-estradiol-3-glucuronide
17β-estradiol-3-sulfate
Estriol (E3)
Estrone (E1)
estrone-3-glucuronide
estrone-3-sulfate
Progesterone
Testosterone
Bisphenol A

Figure 10



□ An_Digested Slurry
○ Composted Bedding Manure
× Composted Solid Manure
△ Lagooning Sludge
A
B
D
G
Concentration (ng/g dm)
10^4
10^3
10^2
10
1
10^-1
10^-2
Ibuprofen
Carbamazepine
Anhydrochlortetracycline
Anhydrotetracycline
Chloramphenicol
Chlortetracycline
Ciprofloxacin
Enrofloxacin
epi-chlortetracycline
epi-oxytetracycline
epi-tetracycline
iso-chlortetracycline
Lomefloxacin
Norfloxacin
Ofloxacin
Ormetoprim
Oxytetracycline
Pirlimycin
Pristinamycin
Roxithromycin
Sarafloxacin
Sulfamethazine
Tetracycline
Tylosin
11-Ketotestosterone
17α-estradiol
17α-hydroxyprogesterone
17α-trenbolone
17β-estradiol
17β-trenbolone
Androstenedione
Androsterone
Estriol (E3)
Estrone (E1)
Melengestrol acetate
Progesterone
Testosterone
α-zearalanol
α-zearalenol
β-zearalanol
β-zearalenol

Figure 11

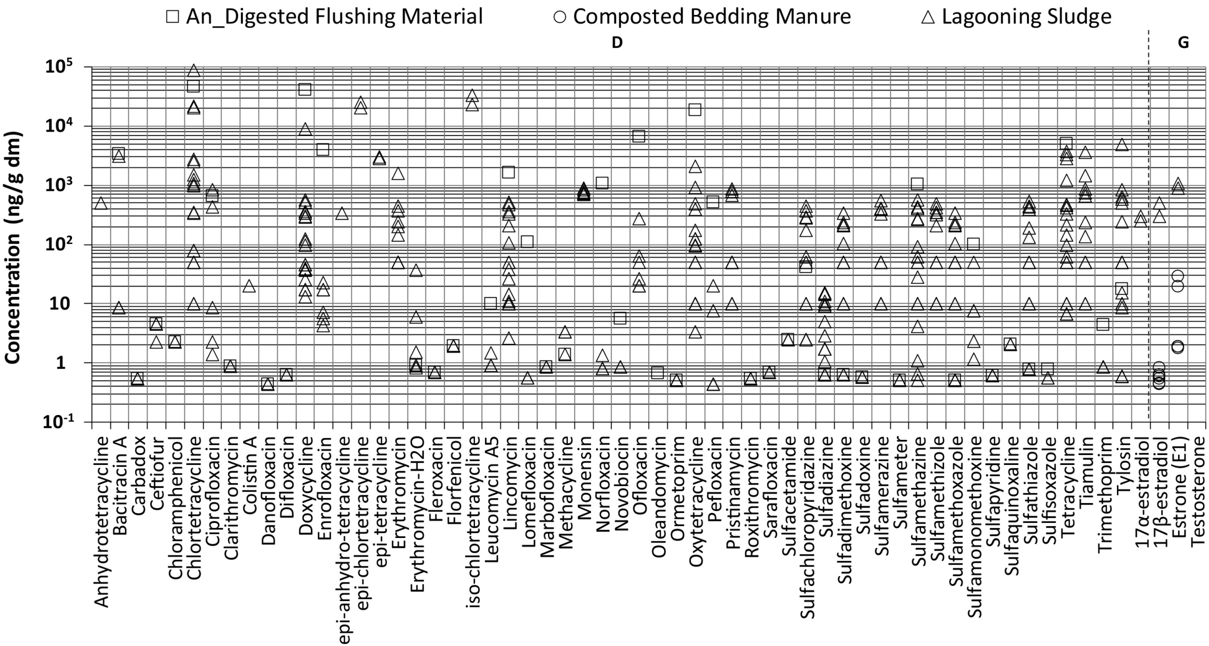

□ An_Digested Flushing Material
○ Composted Bedding Manure
△ Lagooning Sludge
D
G
Concentration (ng/g dm)
10^5
10^4
10^3
10^2
10
1
10^{-1}
Anhydrotetracycline
Bacitracin A
Carbadox
Ceftiofur
Chloramphenicol
Chlortetracycline
Ciprofloxacin
Clarithromycin
Colistin A
Danofloxacin
Difloxacin
Doxycycline
Enrofloxacin
epi-anhydro-tetracycline
epi-chlortetracycline
epi-tetracycline
Erythromycin
Erythromycin-H2O
Fleroxacin
Florfenicol
iso-chlortetracycline
Leucomycin A5
Lincomycin
Lomefloxacin
Marbofloxacin
Methacycline
Monensin
Norfloxacin
Novobiocin
Ofloxacin
Oleandomycin
Ormetoprim
Oxytetracycline
Pefloxacin
Pristinamycin
Roxithromycin
Sarafloxacin
Sulfacetamide
Sulfachloropyridazine
Sulfadiazine
Sulfadimethoxine
Sulfadoxine
Sulfamerazine
Sulfameter
Sulfamethazine
Sulfamethizole
Sulfamethoxazole
Sulfamonomethoxine
Sulfapyridine
Sulfaquinoxaline
Sulfathiazole
Sulfisoxazole
Tetracycline
Tiamulin
Trimethoprim
Tylosin
17α-estradiol
17β-estradiol
Estrone (E1)
Testosterone

Figure 12


○ An_Digested Bedding Manure
△ An_Digested Slurry
□ Lagoon Effluent
Concentration (ng/L)
10⁷
10⁶
10⁵
10⁴
10³
10²
10
1
Azithromycin
Chloramphenicol
Chlortetracycline
Ciprofloxacin
Doxycycline
Enrofloxacin
epi-chlortetracycline
epi-iso-chlortetracycline
epi-oxytetracycline
epi-tetracycline
Erythromycin
Erythromycin-H2O
iso-chlortetracycline
Lincomycin
Lomefloxacin
Monensin
Norfloxacin
Ofloxacin
Ormetoprim
Oxytetracycline
Pristinamycin
Roxithromycin
Sarafloxacin
Sulfachloropyridazine
Sulfadiazine
Sulfadimethoxine
Sulfamerazine
Sulfamethazine
Sulfamethizole
Sulfamethoxazole
Sulfathiazole
Tetracycline
Tiamulin
Trimethoprim
Tylosin
α-apo-oxytetracycline

Figure 13

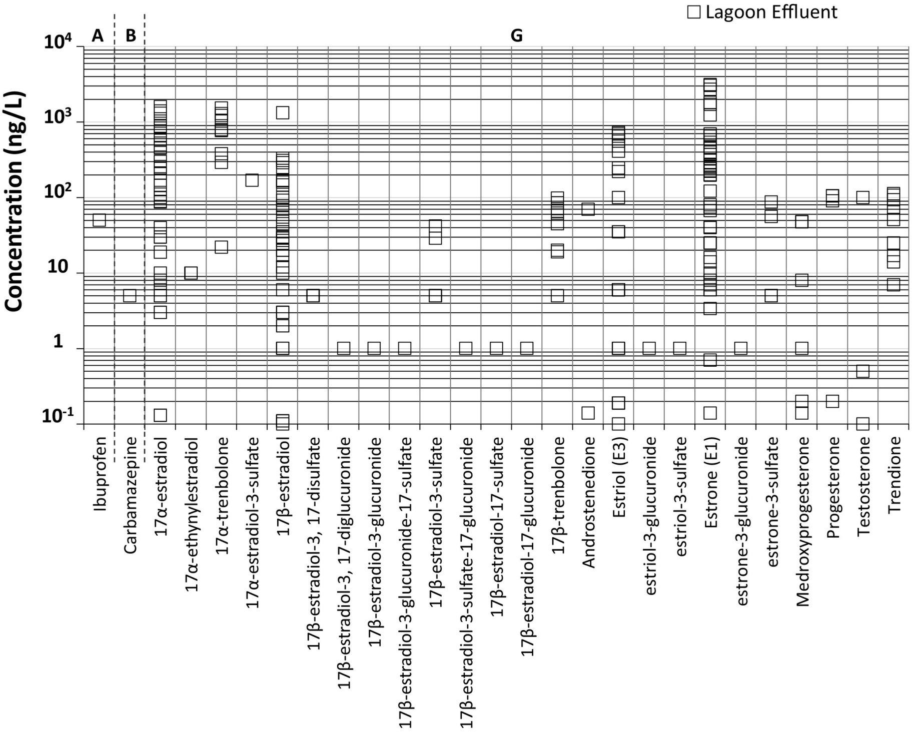
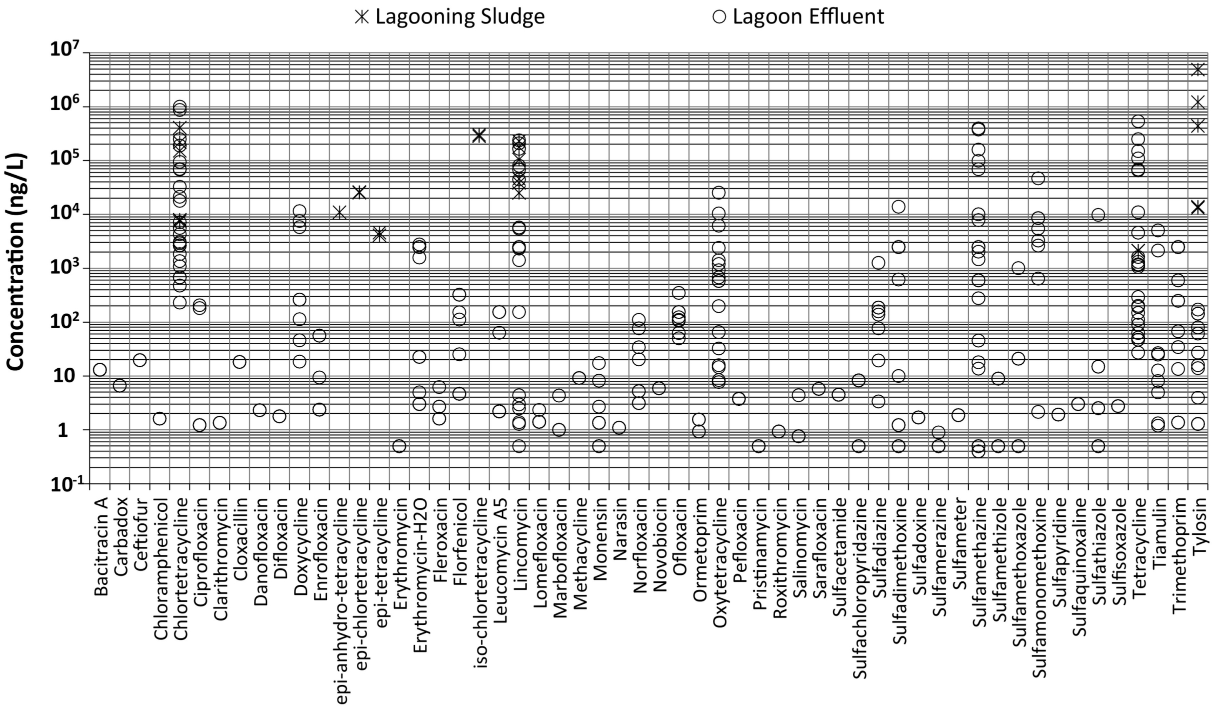

□ Lagoon Effluent
A
B
G
Concentration (ng/L)
10^4
10^3
10^2
10
1
10^-1
Ibuprofen
Carbamazepine
17α-estradiol
17α-ethynylestradiol
17α-trenbolone
17α-estradiol-3-sulfate
17β-estradiol
17β-estradiol-3, 17-disulfate
17β-estradiol-3, 17-diglucuronide
17β-estradiol-3-glucuronide
17β-estradiol-3-glucuronide-17-sulfate
17β-estradiol-3-sulfate
17β-estradiol-3-sulfate-17-glucuronide
17β-estradiol-17-sulfate
17β-estradiol-17-glucuronide
17β-trenbolone
Androstenedione
Estriol (E3)
estriol-3-glucuronide
estriol-3-sulfate
Estrone (E1)
estrone-3-glucuronide
estrone-3-sulfate
Medroxyprogesterone
Progesterone
Testosterone
Trendione

Figure 14



Lagooning Sludge
Lagoon Effluent
Concentration (ng/L)
10^7
10^6
10^5
10^4
10^3
10^2
10
1
10^{-1}
Bacitracin A
Carbadox
Ceftiofur
Chloramphenicol
Chlortetracycline
Ciprofloxacin
Clarithromycin
Cloxacillin
Danofloxacin
Difloxacin
Doxycycline
Enrofloxacin
epi-anhydro-tetracycline
epi-chlortetracycline
epi-tetracycline
Erythromycin
Erythromycin-H2O
Fleroxacin
Florfenicol
iso-chlortetracycline
Leucomycin A5
Lincomycin
Lomefloxacin
Marbofloxacin
Methacycline
Monensin
Narasin
Norfloxacin
Novobiocin
Ofloxacin
Ormetoprim
Oxytetracycline
Pefloxacin
Pristinamycin
Roxithromycin
Salinomycin
Sarafloxacin
Sulfacetamide
Sulfachloropyridazine
Sulfadiazine
Sulfadimethoxine
Sulfadoxine
Sulfamerazine
Sulfameter
Sulfamethazine
Sulfamethizole
Sulfamethoxazole
Sulfamonomethoxine
Sulfapyridine
Sulfaquinoxaline
Sulfathiazole
Sulfisoxazole
Tetracycline
Tiamulin
Trimethoprim
Tylosin

Figure 15

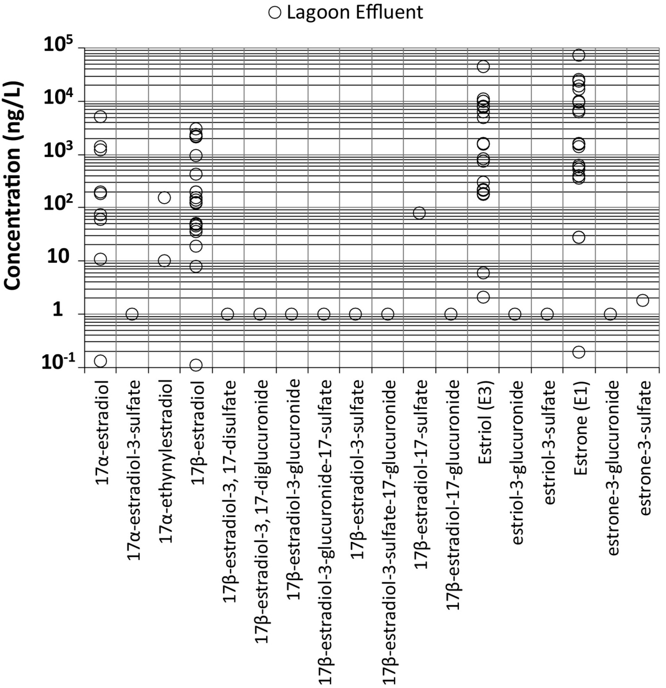

Lagoon Effluent
Concentration (ng/L)
10^5
10^4
10^3
10^2
10
1
10^-1
17α-estradiol
17α-estradiol-3-sulfate
17α-ethynylestradiol
17β-estradiol
17β-estradiol-3, 17-disulfate
17β-estradiol-3, 17-diglucuronide
17β-estradiol-3-glucuronide
17β-estradiol-3-glucuronide-17-sulfate
17β-estradiol-3-sulfate
17β-estradiol-3-sulfate-17-glucuronide
17β-estradiol-17-sulfate
17β-estradiol-17-glucuronide
Estriol (E3)
estriol-3-glucuronide
estriol-3-sulfate
Estrone (E1)
estrone-3-glucuronide
estrone-3-sulfate

Figure 16

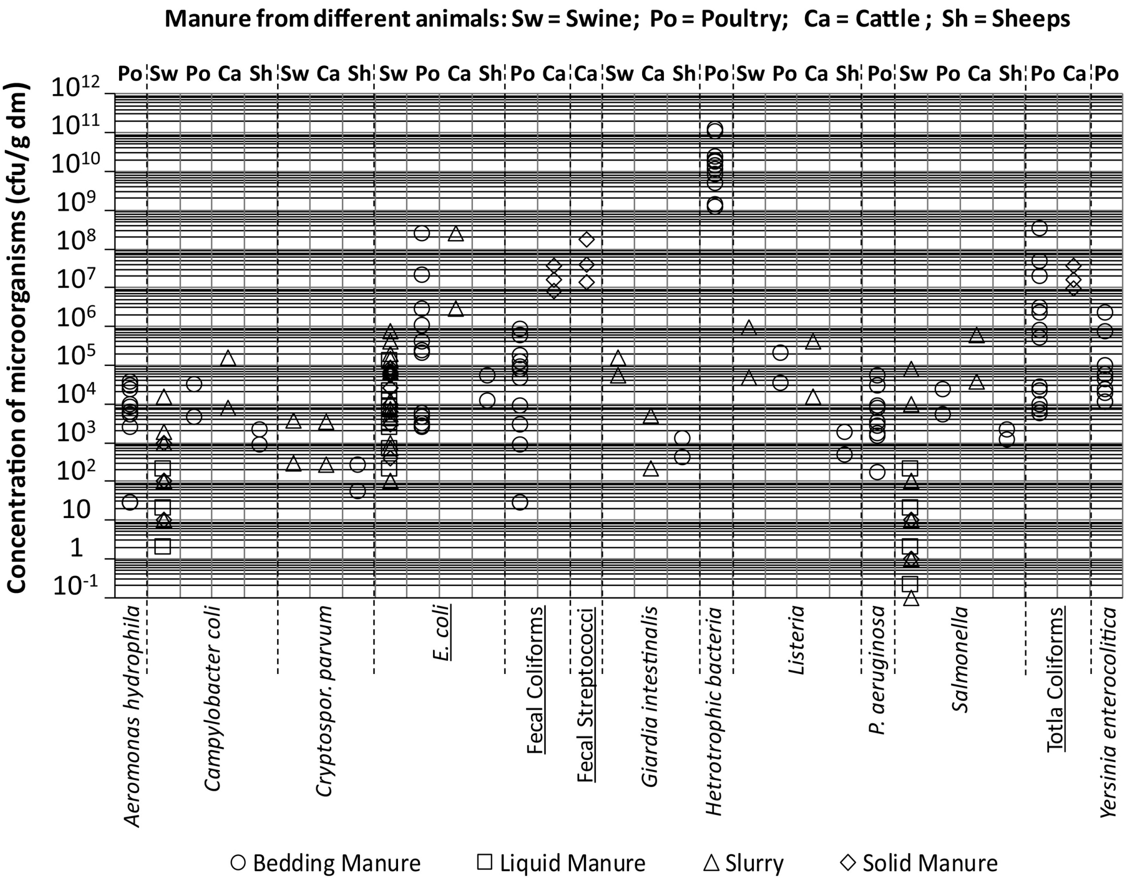

Manure from different animals: Sw = Swine; Po = Poultry; Ca = Cattle ; Sh = Sheeps
Po Sw Po Ca Sh Sw Ca Sh Sw Po Ca Sh Po Ca Ca Sw Ca Sh Po Sw Po Ca Sh Po Sw Po Ca Sh Po Ca Po
Concentration of microorganisms (cfu/g dm)
10^{12}
10^{11}
10^{10}
10^{9}
10^{8}
10^{7}
10^{6}
10^{5}
10^{4}
10^{3}
10^{2}
10
1
10^{-1}
Aeromonas hydrophila
Campylobacter coli
Cryptospor. parvum
E. coli
Fecal Coliforms
Fecal Streptococci
Giardia intestinalis
Hetrotrophic bacteria
Listeria
P. aeruginosa
Salmonella
Totla Coliforms
Yersinia enterocolitica
Bedding Manure
Liquid Manure
Slurry
Solid Manure

Figure 17

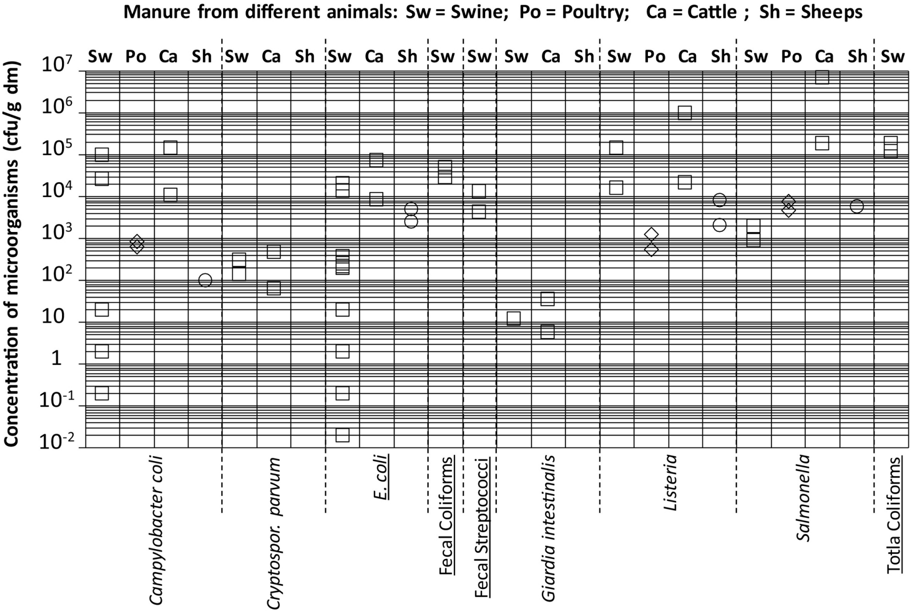

Manure from different animals: Sw = Swine; Po = Poultry; Ca = Cattle ; Sh = Sheeps
Sw Po Ca Sh Sw Ca Sh Sw Ca Sh Sw Sw Sw Ca Sh Sw Po Ca Sh Sw Po Ca Sh Sw
Concentration of microorganisms (cfu/g dm)
10^7
10^6
10^5
10^4
10^3
10^2
10
1
10^{-1}
10^{-2}
Campylobacter coli
Cryptospor. parvum
E. coli
Fecal Coliforms
Fecal Streptococci
Giardia intestinalis
Listeria
Salmonella
Totla Coliforms

Figure 18

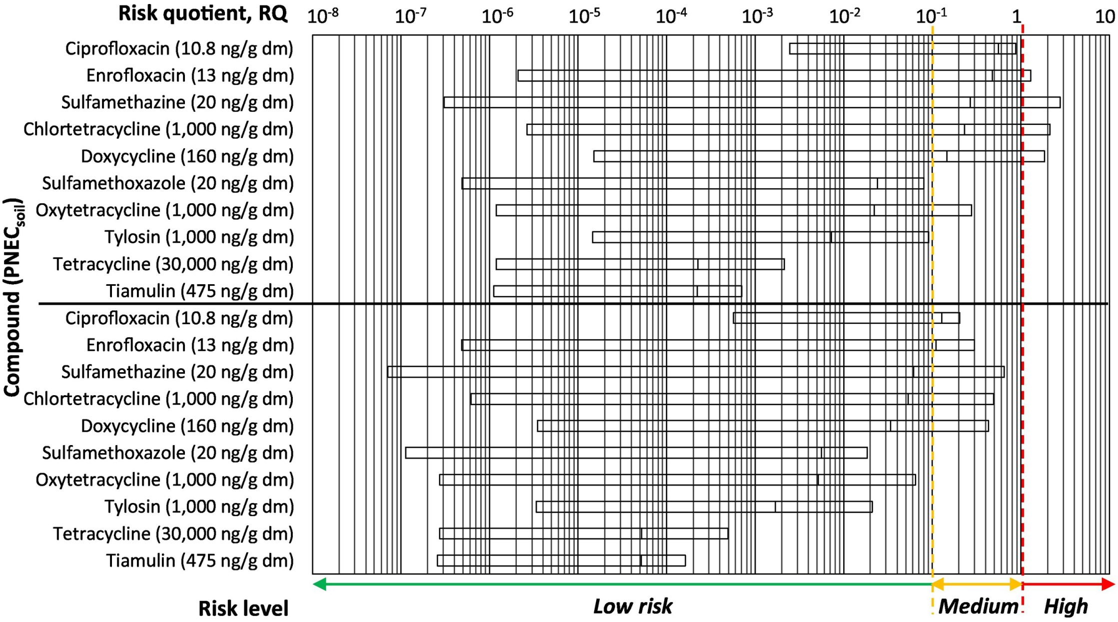

Risk quotient, RQ
10-8
10-7
10-6
10-5
10-4
10-3
10-2
10-1
1
10
Compound (PNECsoil)
Ciprofloxacin (10.8 ng/g dm)
Enrofloxacin (13 ng/g dm)
Sulfamethazine (20 ng/g dm)
Chlortetracycline (1,000 ng/g dm)
Doxycycline (160 ng/g dm)
Sulfamethoxazole (20 ng/g dm)
Oxytetracycline (1,000 ng/g dm)
Tylosin (1,000 ng/g dm)
Tetracycline (30,000 ng/g dm)
Tiamulin (475 ng/g dm)
Ciprofloxacin (10.8 ng/g dm)
Enrofloxacin (13 ng/g dm)
Sulfamethazine (20 ng/g dm)
Chlortetracycline (1,000 ng/g dm)
Doxycycline (160 ng/g dm)
Sulfamethoxazole (20 ng/g dm)
Oxytetracycline (1,000 ng/g dm)
Tylosin (1,000 ng/g dm)
Tetracycline (30,000 ng/g dm)
Tiamulin (475 ng/g dm)
A
B
Risk level
Low risk
Medium
High

Figure 19