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Antimicrobial use, resistance and economic benefits and costs to livestock producers in Brazil

Marisa Cardoso

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ANTIMICROBIAL USE, RESISTANCE AND ECONOMIC BENEFITS AND COSTS TO LIVESTOCK PRODUCERS IN BRAZIL

Marisa Cardoso
Universidade Federal do Rio Grande do Sul, Brazil

Brazil is one of the world's largest producers and exporters of meat and animal products. This report compiles information and data on antimicrobial use and antimicrobial resistance in food-producing animals in Brazil. Antimicrobials are used in food producing animals, mainly as a growth promoter. While the use of antibiotics is estimated to be falling, there is concern amongst livestock producers as to the possible rise in production costs resulting from the withdrawal of these antibiotics, and they are currently exploring alternative interventions and their likely economic impact on their incomes. Recent regulatory and policy changes, including the implementation of the National Action Plan on Antimicrobial Resistance in Agriculture, are aimed at limiting the use of antibiotics in livestock production and containing the rise in antimicrobial resistance.

Key words: Antibiotics

JEL code: Q1

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Abbreviations

ABCS	Brazilian Association of Swine Producers
ABIEC	Brazilian Beef Exporters Association
ABPA	Brazilian Association of Animal Protein
AGP	Antimicrobial Growth Promoter
ANVISA	Health Surveillance Agency
BRL	Brazilian reals
CCRC	Coordination for the Control of Residues and Contaminants
CEPEA	National Centre for Advanced Research in Applied Economics
CIA	Critically Important Antimicrobials
CNA	Confederation of Agriculture and Livestock
HPCIA	Highest Priority Critically Important Antimicrobials
IBGE	Brazilian Institute of Geography and Statistics
ICU	Intensive Care Unit
IN	Normative Instruction
GDP	Gross Domestic Production
MAPA	Ministry for Agriculture, Livestock and Supply
OIE	World Organisation for Animal Health
PAN-BR Agro	Plan of Action for the Prevention and Control of Antimicrobial Resistance in Livestock
PNCRC	National Plan for the Control of Residues and Contaminants
SIF	Federal Inspection Services
SINDAN	National Union of Animal Health Products Industries
SINDIRAÇÕES	National Union of Animal Feed Industries
WHO	World Health Organisation

1. Introduction

This paper aims to compile all relevant and current information on antimicrobial use and antimicrobial resistance in food-producing animals in Brazil. It was requested by the Organisation for Economic Co-operation and Development (OECD) to feed into the larger OECD report “Evaluating the Economic Benefits and Costs of Antimicrobial Use in Food Producing Animals”. The work specifically encompasses the following:

- Estimates of the level of antibiotic use in livestock production and its usage. Subject to the availability of data, a breakdown of the usage figures by the main food animal species: pigs, broilers and cattle.
- Recent information on antimicrobial resistance in Brazil (humans and animals) and indications of overall trends.
- A synthesis of recent farm level studies on the cost/benefits of antibiotic use in livestock production.
- A summary of the overall policy on antimicrobial use and antimicrobial resistance in Brazil, as well as recent regulatory changes, including the key components of Brazil’s National Action Plan on Combating Antimicrobial Resistance.

Before starting the work, all parties were aware of the difficulty of gathering information on these topics, especially concerning the level of antimicrobial use and its costs/benefits. The approach adopted was to search all possible scientific publications, official documents, reports published by organisations or associations involved in the food production sector, and key notes presented in conferences on swine, poultry or cattle production. For this purpose, search strategies were constructed and applied on databases such as Google, Scielo, Scopus, Medline, Ovid, Web of Science and others. Only information from credible sources, such as academic researchers, government departments and agencies, and associations representing the production sector, were taken into account. The author compiled and organized the available information in text, tables and figures. When there were insufficient data, the author did not fill the gap by expressing her own opinion or estimates.

2. Profile of livestock production in Brazil

Brazilian economic performance, which peaked in 2013, has declined since then and in 2017 was lower than in 2010. After two years of negative performance, the Brazilian Gross Domestic Product (GDP) grew by 1% in 2017 to reach BRL 6.5 trillion. Agricultural and mineral extractive activities showed the highest growth in 2017 (12.8% and 4.5%, respectively) (FGV, 2018). Agriculture accounts for 5.3% of GDP, and contributed 0.7% of the total value added to GDP in the last year (CNA, 2018).

In 2017, Brazilian agribusiness exports totalled USD 96.01 billion, representing growth of 13% over the previous year. Moreover, agribusiness accounted for 44.1% of Brazil’s total foreign sales in this period. The meat industry recorded growth of 8.9% in foreign sales, and reached a total value of USD 15.47 billion for exported meat. Chicken meat, which is the main product of this sector, accounted for almost half (46.1%) of the total value. Around USD 7.14 billion came from chicken meat exports, a value 5.5% higher than the previous year. The second most important product was beef, which reached USD 6.07 billion in exports. In comparison to the previous year, sales increased by a further 13.7%. This increase was a result of both the expansion of the quantity shipped (an increase of 9.5%; from 1.35 Mt to 1.48 Mt) and the average price (an increase of 3.8%; from USD 3,958 to USD 4 109 per tonne). Also in 2017, pork exports reached a new record, totalling USD 1.61 billion, even with the decrease in the amount shipped (-5.0%) (MAPA, 2018a).

According to the last census on Agriculture (IBGE, 2006), Brazil had 1 143 458 thousand poultry (roosters, hens and broilers), 176 147 501 cattle and 31 189,351 pigs. A total of 12 710 701 cows were milked in 2006. In addition, data from the Municipal Livestock Survey conducted by the Brazilian Institute of Geography and Statistics (IBGE) are published every year. Data collected in 2015 recorded a population

of 218 255 177 cattle; 39 950 310 pigs and 1 330 thousand poultry (IBGE/PPM, 2015). The distribution of the livestock population among the Brazilian regions is presented in Figures 1 to 3.

Figure 1. Distribution of the bovine population across the Brazilian regions, 2015

Thousand heads

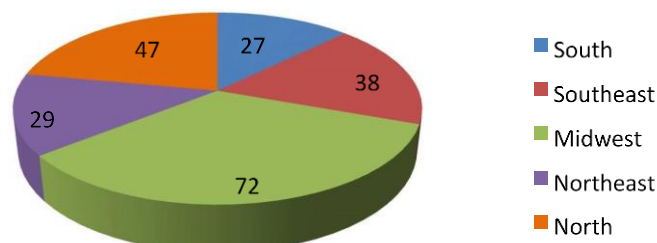


Figure 2. Distribution of the swine population across the Brazilian regions, 2015

Thousand heads

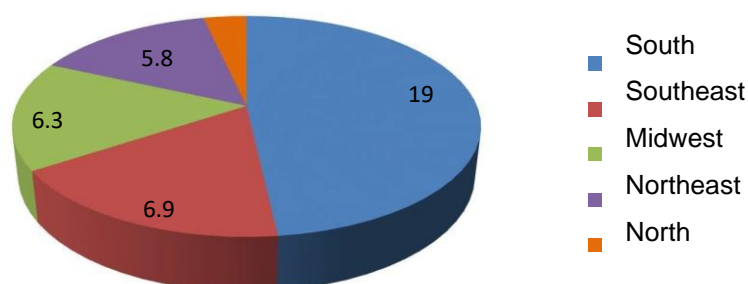
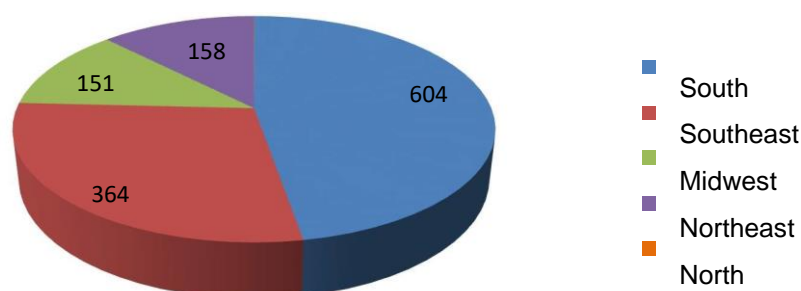


Figure 3. Distribution of the poultry population across the Brazilian regions, 2015

Millions



Source: IBGE/PPM (2015).

In 2017, a total of 3.75 Mt of pork were produced in Brazil, of which 80.4% was destined for the domestic market (ABPA, 2018). According to the Brazilian Association of Swine Producers (ABCS), the profile of pork production in Brazil varies according to the region. In the south, about 60% of breeding farms have up to 500 sows; approximately 81% of these farms are engaged in an integrated or cooperative system. This region represents 96% of the finishing farms, 95% of nursery farms, and 56% of wean to finish farms in Brazil. Similar to the breeding farms, they are mostly engaged in integrated systems with the industry or

cooperatives. In the southeast region there is a high concentration of independent farmers (77% of the production), and the states of São Paulo and Minas Gerais are the main swine producers in this region. The engagement of swine producers in cooperative systems is negligible. Moreover, only 1.7% of fattening farms in Brazil are located in this region. In the midwest, pig production farms are large, with 46% of the breeding farms having more than 1 000 sows. About half the producers are integrated in agroindustry. The midwest region is the location of 2.5% of finishing farms, 2.3% of nursery farming, and 44% of wean-to-finish farms in Brazil. In the north and northeast regions, production is characterized by small-scale farms with approximately 200 sows. These farmers are not engaged in co-operatives or integrated systems, and production is mainly sold at local markets (ABCS, 2017).

Over 90% of Brazil's poultry production is currently produced by the integrated production system. In 2017, 13.05 Mt of chicken meat was produced, of which 66% was destined for the domestic market (ABPA, 2018). Poultry production is concentrated in the southern region, although expansion towards the midwest has been observed. The production of table eggs in Brazil is less concentrated than chicken meat. In 2015, 981 788 chickens were housed, and 39 511 378 639 eggs were produced, of which approximately 99.57% was destined for the domestic market. The states of São Paulo and Minas Gerais accounted for 45% of table egg production in Brazil (ABPA, 2016).

The cattle population is concentrated in the midwest, where 29% of beef cattle are raised (MAPA, 2018). In 2017, beef production reached 9.71 Mt, of which 79.43% was consumed on the domestic market (ABIEC, 2018). Regarding the production system, open grazing predominates. Grazing is frequently characterized by the use of extensive systems, with the low use of technologies. Intensive grazing systems associated with the use of protein and/or energy supplements during the dry season or throughout the year are also found in some regions. The majority of Brazilian farms adopt the extensive system for beef cattle production due to its low cost. In this system, slaughtering is concentrated on animals over three years old. In recent years, the confinement of animals for fattening has been increasing (MILLEN et al., 2011); in spite of that, only 13% of slaughtered animals came from confine production systems in 2015 (ABIEC, 2017). The confinement of cattle is concentrated in medium and large-sized properties, mainly in the states of Goiás, Minas Gerais, São Paulo, Mato Grosso do Sul, Mato Grosso, Bahia, Rio Grande do Sul and Paraná, which account for approximately 91% of the confined beef cattle (ANUALPEC, 2013). Regarding bovine milk, around 33.6 Mt of milk was produced in 2016 (IBGE, 2017). Milk production is mostly commercial and focussed on the domestic market, with less than 0.5 Mt exported in 2016 (ABIEC, 2017). The production of milk is unevenly distributed between big players and small farms based on family labour. The latter are responsible for more than half of total production. Dairy farms are distributed across all regions, but the main producing areas are located in the southeast and south. Brazilian milk production is characterised by a heterogeneous production system, with animal productivity slightly less than 1 400 litres/cow/year, relatively low compared to traditional milk-producing countries (IFCN, 2012).

A pronounced rising trend in chicken meat production has been observed over the last decade, while pork and beef have had stable production (Table 1).

Table 1. Volume of beef, chicken meat and pork produced in Brazil, 2008 to 2017

Production volume per year in millions of tonnes

Year	Beef	Chicken	Pork
2008	9.32	10.94	3.02
2009	9.18	10.93	3.19
2010	9.36	12.23	3.23
2011	9.03	13.06	3.40
2012	9.30	12.65	3.49
2013	9.67	12.31	3.41
2014	9.72	12.69	3.47
2015	9.42	13.15	3.64
2016	9.62	12.90	3.73
2017	9.71	13.06	3.76

Source: ABIEC (2017), ABPA (2018).

3. Use of antimicrobials in animal production, and the costs and benefits of their use

The use of antimicrobials for therapeutic, prophylactic and metaphylactic purposes is not prohibited in Brazil. While some antimicrobials are allowed as growth promoters (AGPs) in defined livestock species (Table 2), other active molecules are banned from use in animal production by the Normative Instructions (IN) published over the last two decades (Table 3).

Table 2. Antimicrobials allowed as growth promoters and the respective animal species

Avilamycin	Poultry; swine
Bacitracin	Poultry, swine, cattle
Enramycin	Poultry, swine
Flavomycin	Poultry, swine, cattle
Halquinol	Poultry, swine
Lasalocid	Cattle
Lincomycin	Poultry, swine
Monensin	Cattle, ovine
Narasin	Swine, cattle
Salinomycin	Swine, cattle
Tiamulin	Swine
Tylosin	Poultry, swine
Virginiamycin	Poultry, swine, cattle

Source: Bresslau (2017).

Table 3. Normative instructions (IN) on antimicrobials for animal use and their scope

Year	Normative instruction	Antimicrobial	Use withdrawn
1998	Circular letter 047/1998	Avoparcin	Additive in animal feed
2003	IN 09 from 27 June 2003	Chloramphenicol and Nitrofurans	Veterinary use
2004	IN 11 from 24 November 2004	Olaquinox	Growth promotion
2005	IN 35 from 14 November 2005	Carbadox	Additive in animal feed
2009	IN 26 from 9 July 2009*	Amphenicol, tetracyclines, beta lactams (benzyl penicillin group, cephalosporins), quinolones, systemic sulphonamides	Growth promotion and feed preservative
2012	IN 14 from 17 May 2012	Spiramycin and Erythromycin	Growth promotion
2016	IN 45 from 22 November 2016	Colistin	Growth promotion

Note: A Decree from the Ministry of Agriculture on 12 May 1998 prohibited the use of chloramphenicol, penicillins, tetracyclines and systemic sulphonamides as growth promoting additives. This Decree was later revoked by the Normative Instruction No. 26 in 2009, which extended the prohibition to amphiphiles, tetraphenones, beta-lactams (benzylpenicillins and cephalosporins), quinolones and systemic sulphonamides. The prohibition dates back to 1998.

*Substitutes the MAPA decision 193 from 12 May 1998, which prohibited the use of chloramphenicol, penicillin, tetracycline and systemic sulphonamide as growth promoters.

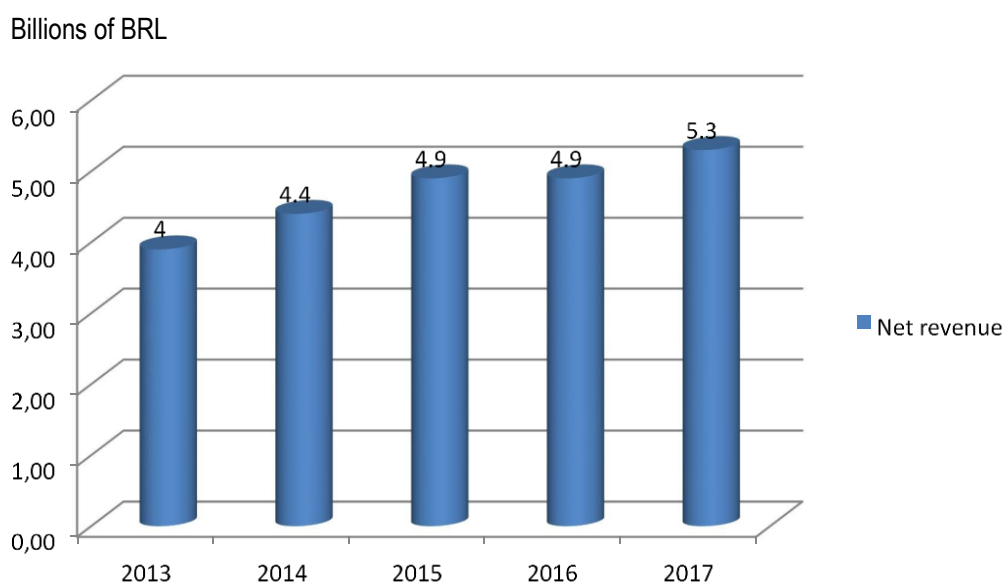
Source: MAPA (2018b).

Official data on the volume of antimicrobials used in animal production is not publicly available in Brazil. In the second Annual Report on the use of antimicrobials in animals of the World Organisation for Animal Health (OIE), all member countries of the Americas provided data. Thus, it can be inferred that Brazil reported data on the use of antimicrobials; however, it is not possible to conclude if quantitative data were reported. Moreover, Brazil is not among the countries listed in this report as having information available on the web concerning antimicrobial use in animals (OIE, 2017).

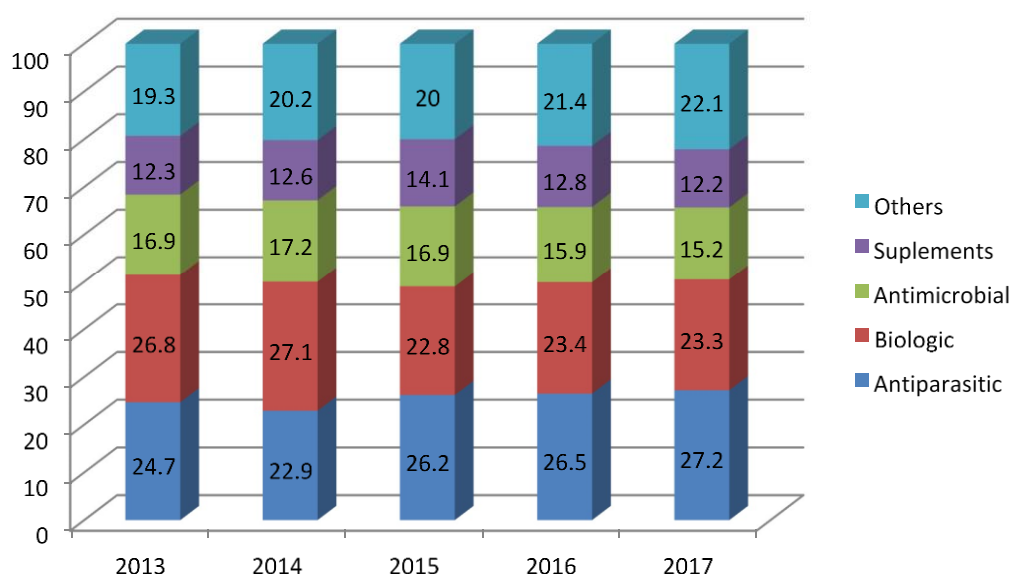
The sales volume published by the National Union of Animal Health Products Industries (SINDAN, 2018) is the only official data source available. According to SINDAN, the animal health products industries earned BRL 5.3 billion in 2017. Of this amount, antimicrobials accounted for 15.2% (about BRL 0.8 billion), and represented the third highest cost item. This total includes the sale of antibiotics for both animal production and small animals. The net sales evolution of this sector and the participation of antimicrobials are presented in Figures 4 and 5.

In the study conducted by Van Boeckel et al. (2015), the volume of antimicrobial usage in food animals was estimated for Brazil. The approach of this study to address the information gap was the adoption of Bayesian statistical models combining maps of livestock densities, economic projections of demand for meat products, and current estimates of antimicrobial consumption in high-income countries for the estimation of antimicrobial consumption in 2010. According to this study, the global consumption of antimicrobials in food animal production was estimated at 63 151 ($\pm 1,560$) tonnes in 2010. About 9% of the total was estimated to be consumed in Brazil (around 5 683 tonnes).

Figure 4. Estimated net sales of animal health products industry in Brazil



Source: SINDAN (2018).

Figure 5. Distribution of revenue among therapeutic classes

Source: SINDAN (2018).

In a report published by the Ministry of Development, Industry and Foreign Trade entitled “Technical and Economic Feasibility Study for the implementation of the National Production Park of Feed Additives for Food Animals”, the consumption (tonnes) of feed additives by different production chains was reported. Information obtained from the National Union of Animal Feed Industries (Sindirações) is cited as the original source of these data (Table 4).

Table 4. Consumption of feed additives, 2011

In tonnes

Additive	Broiler	Laying chicken	Swine	Dairy cattle	Beef cattle	Others	Total
Enzymes	2 132	302	1 041	665	NI	209	4 349
Antimicrobial growth promoters	2 473	422	1 405	NI	NI	350	4 650
Prebiotics and probiotics	284	16	1 106	501	312	165	2 384
Total of additives	4 889	739	3 552	1 166	312	724	11 383
Anticoccidial drugs	27 200	4 800	0	0	0	0	32 000

Note: According to the report published by the Ministry of Development Industry and Foreign Trade, based on information obtained from the Sindirações (2012).

NI= Not informed in this document

Source: Ministério do Desenvolvimento Indústria e Comércio Exterior (2012).

The evolution of growth promoters and anticoccidial drugs imported is depicted in Table A1. An increase in the value of imports and exports was observed in 2011. However, only data from less comprehensive studies of pig production chain are publicly available. For example, Machado (2016) presented partial data on antimicrobial usage from the PhD thesis of Maurício Cabral Dutra (2017). The average amount of antimicrobials consumed was estimated at 367.7 (5.4 – 573.4) mg/kg of pigs produced on 13 pig farms in southern Brazil. The final results were included in a published PhD thesis (Dutra, 2017). Data obtained from 25 swine production systems showed the average antimicrobials consumption to be at 358 mg/kg of pigs produced. The same study estimated that pigs were exposed on average 66.3% (ranging from 2.9 to 90.4%) of their lifespan to antimicrobials in these systems.

The share of antimicrobials in the total cost of production is mentioned in some publications, but there is no comprehensive study published for any production chain.

In 2017, the Brazilian Association of Pork Producers (ABCS) published a report entitled “The Mapping of Pig Production”, where the total financial movement in the pig production chain was estimated at USD 44 892 in 2015. The total value was divided among four stages of the production chain (Table A.A.2). Antimicrobial expenditures are included in the stage “Before the farm” and represented 1.48% of the total financial costs in pig production in Brazil (Table A.A.3).

Data collected by the National Centre for Advanced Research in Applied Economics (CEPEA-ESALQ / USP) for the Confederation of Agriculture and Livestock of Brazil (CNA) indicated that veterinary products represented 3.33% of the Operational Cost of chicken production in 2017 in the state of Mato Grosso do Sul. The anticoccidial drugs accounted for the highest expenditure in feed additives (Table A3) and are included in this percentage. Therefore, antimicrobials may have represented a much lower percentage of operational costs.

Regarding beef cattle originated from the extensive production system, the same institute (CEPEA-ESALQ / USP) estimated that antibiotics represented 0.16% of the total operation costs in 11 Brazilian states, in December 2016 (Table 5). As mentioned above, 87% of Brazil's slaughtered bovine come from the extensive system of production (ABIEC, 2017).

Table 5. Weighted average of the main inputs in the total operational costs for beef cattle production in 11 Brazilian states

December 2016

Item	Total operation cost weighting (%)
Animals	45.63
Mineral supplements	10.38
Feed	3.3
Fertilizer	0.91
Forage seeds	1.59
Agricultural machinery	4.13
Agricultural inputs	1.18
Pesticides	2.14
Medicines - vaccines	1.05
Medicines anti-parasitic drugs	1.01
Medicines - antimicrobials	0.16
Medicines - others	0.25
Consumables for reproductive management	0.23
Labour	12.00
Building	7.96
Others	6.17

Note: The 11 states are Bahia, Goiás, Mato Grosso, Mato Grosso do Sul, Pará, Roraima, Rio Grande do Sul, Minas Gerais, Paraná, Tocantins and São Paulo

Source: CEPEA (2016).

According to CEPEA-ESALQ / USP estimates, medicines used in dairy cattle represented 3.5% of the effective operational cost of milk production in the first bimester of 2017 (Table A4). In Brazilian dairy farming, antimicrobials are mainly used for the treatment of mastitis (VEIGA, 2014); therefore, antimicrobials may not be the most important item in the total amount of veterinary medicines used.

The main concern of Brazilian food animal producers is that the withdrawal of antimicrobials from animal production will lead to an increase in meat production costs and, ultimately, in the final price of food (Zani, 2017). Studies on the impact of an antimicrobial ban in poultry and swine production have been conducted

at the Animal Science Department of the Federal University of Rio Grande do Sul, and partial results have been published in scientific congresses held in Brazil.

In one of these studies, Rampi et al. (2016) conducted a meta-analysis in order to estimate the economic impact of the withdrawal of growth promoters from pig diets. The database consisted of 67 articles, published since 1990, encompassing 90 experiments and totalling 40 592 pigs. The mean initial and final live weight of the animals was 17.8 kg and 29.7 kg, respectively. Nursery pigs were used in 83% of the studies (mean age at weaning, 23 days; minimum, 14 days; maximum, 35 days). The performance of fattening pigs was evaluated in the remaining 17% of the studies. The experiments were conducted for an average of 29 days (maximum 134 days). The most frequent antibiotics in the database were: avilamycin (27% of the AGP treatments), colistin (17%), tiamulin (11%), tylosin (9%), lincomycin (8%) and bacitracin (6%). The results obtained in the meta-analysis were used to compose a model that estimated the effects of withdrawal on production costs. This model was built in spreadsheets and adjusted for specific scenarios considering the expected performance in animal diets with or without AGP (data obtained in the meta-analysis), in addition to the average cost of the AGP and feed (data collected from the industry, Table 6). In most of the experiments, a negative impact of AGPs withdrawal on pig performance was observed. A worsening in feed conversion was observed in 73% of the studies compared to treatments that did not use AGPs. Animal diets without AGPs, from nursery to slaughter, showed an increase of 4.02% in feed conversion (with AGPs: 1.82, without AGP: 1.89, $P < 0.01$) compared to the treatments with AGPs. An increase in consumption of around 9.73 kg of feed was needed to reach the same slaughter weight of AGP-fed animals, thus increasing the cost of feeding per animal by 3.80%. The authors estimated that in this scenario, the withdrawal of AGPs from pig feed resulted in losses estimated at BRL 277.2 million for Brazilian swine producers.

Table 6. Cost of AGPs in pig production (BRL)

Variables	Cost in BRL
Average AGP cost (BRL/kg product)	170.00
AGP cost (BRL/tonne of feed)*	1.70
Average cost of feed without AGP	810
Average cost of feed with AGP	811.70

Note: Considering an average addition of 10 mg of AGP per tonne of feed

Source: Rampi et al. (2016).

A similar study, based on meta-analysis, was conducted by Cardinal et al. (2018) for broiler chicken production. The database was composed of 150 scientific articles, which have been published since 1990, encompassing 155 experiments and totalling 108 882 broilers. The experiments were conducted for an average of 23 days (maximum 49 days). The most frequent antibiotics included in the treatments were: avilamycin (42% of the treatments with AGP), flavomycin (20%), bacitracin (15%) and virginiamycin (15%). Male broilers were most frequently included in the studies (55% of treatments), followed by mixed lots (24%) and females (2%). The broilers belonged to the following breeder brands: Ross (59% of the treatments), Cobb (24%) and Arbor Acres (10%). The results obtained in the meta-analysis were used to compose a model that estimates the effects of withdrawal on production costs. This model was developed in a spreadsheet and adjusted for specific scenarios considering the expected performance in animal diets with or without AGPs, in addition to the average cost of the AGPs and feed (data collected from the industry). Feed consumption did not differ ($P > 0.05$) between treatments with or without AGPs. In addition, animal diets without AGPs presented a 1.91% lower weight gain ($P < 0.05$), and a 3.65% increase in feed conversion ($P < 0.01$) in comparison with treatments with AGPs. The authors estimated that in this scenario, the withdrawal of AGPs from broiler feed resulted in annual losses estimated at BRL 639.2 million for the Brazilian poultry production industry.

There is no robust evidence that Brazilian consumers are well informed, or highly concerned about the use of antimicrobials in animals. Antimicrobial resistance has been addressed in newspapers and the electronic media. For example, on 18 May 2017 the Abril Publishing Group posted information about antimicrobial

resistance. In this posting the resistance mechanism and possible origins were explained in a non-technical language, and the use of antimicrobials in animal production was pointed out as an important driver of resistance (<https://saude.abril.com.br/medicina/como-bacterias-criam-resistencia-a-antibioticos/>). The ban of colistin for growth promotion in Brazil was widely reported in 2016/2017 by the media. The hazard for humans of antimicrobial use in animals was referred to and the importance of colistin as the “last-ditch” drug for resistant bacteria infection treatment was mentioned, for instance in (<https://veja.abril.com.br/saude/por-que-o-abuso-dehttps://veja.abril.com.br/saude/por-que-o-abuso-de-antibioticos-em-animais-e-uma-ameaca-a-saude/>). Activist groups also published information about this topic, but usually the approach is in line with their convictions. One example is the Animal Equality Brazil, an international organization dedicated to defending animals through public education and campaigns. on their website they stated that beef is not an expensive food item due to the massive use of antimicrobials in cattle (<https://medium.com/@animalequality/entenda-as-consequ%C3%A2ncias-do-usomassivo-de-antibi%C3%B3ticos-na-produ%C3%A7%C3%A3o-de-gado1e03e3e73494>).

Information on antimicrobial use in food animals and the emergence of “superbugs” is also mentioned on the site of Korin, a Brazilian company founded in 1994 and on which its corporate vision is based on the concept of Nature Farming (<http://www.korin.com.br/blog/ha-cada-vez-mais-antibiotico-na-carne-que-voce-come/>). The portfolio includes organic beef (no AGPs, antimicrobials only used therapeutically), beef from cattle with no antimicrobial administration, chicken meat from organic production (no AGPs, antimicrobials used only for disease treatment), and chicken meat from production with no antimicrobial use (<http://www.korin.com.br/produtos/>). The production system has been awarded the HFAC Animal Welfare Certification – Humane Farm Animal Care by the Certified Humane Brazil, a non-profit entity with the objective of representing Humane Farm Animal Care in South America and concentrating efforts on the development of the Certified Humane program in the region (<http://certifiedhumanebrasil.org>).

In addition to certification of Korin's beef and chicken meat as produced without antimicrobials, one of the largest food companies in Brazil (JBS) offers the “Seara da Granja” portfolio, which includes whole chickens and tray cuts originating from broilers raised without antimicrobials. Seara DaGranja products have international certification (WQF; <https://wgscert.com/>), which ensures animal welfare and attests that these chickens did not receive any type of antibiotics, hormone and preservative at any stage of breeding (<https://jbs.com.br/imprensa/release/seara-registra-87-de-crescimento-na-producao-e,https://jbs.com.br/imprensa/release/seara-registra-87-de-crescimento-na-producao-e-vendas-de-frango-natural-em-2017/>).

The other large food company in Brazil (BRF) states on its website that there is no prophylactic use of antibiotics in poultry production. They also indicate that the company seeks to continuously improve its processes to allow for the gradual reduction of antimicrobial use throughout the chain. The information available indicates that by the end of 2018 all poultry and pork will be produced free of antibiotic growth promoters (AGP-Free). Moreover, it is indicated that BRF has reduced the use of antibiotics considered by the World Health Organization (WHO) as critical for use in human medicine (<https://www.brfhttps://www.brf-global.com/sustentabilidade/bem-estar-animal/nossas-praticas/>).

A survey conducted in 2016 by Cargill of consumers in the United States and Brazil showed that the majority want to buy beef produced without antibiotics. However, only 35% of the more than 2 000 consumers interviewed are prepared to pay more for this. (<https://revistagloborural.globo.com/Noticias/Criacao/Boi/noticia/2016/08/globohttps://revistagloborural.globo.com/Noticias/Criacao/Boi/noticia/2016/08/globo-rural-carne-bovina-consumidores-querem-produto-sem-antibiotico-apontapesquisa.html>).

4. Antimicrobial resistance in animals and humans

The only monitoring of antimicrobial resistance encompassing all Brazilian regions was conducted between 2004 and 2006 by the Health Surveillance Agency (ANVISA) of the Ministry of Health. With the task of evaluating the public health impact associated with the use of veterinary drugs, a Working Group was officially created by ANVISA. The group was composed of professionals of MAPA and organized civil society sectors, including the pharmaceutical industry, veterinary institutions, universities and research institutes, state health surveillance agencies, and official public health laboratories. One of their recommendations targeted antimicrobial resistance and the need to implement a project for the monitoring and surveillance of bacteria from food of animal origin. In this regard, ANVISA has conducted the “National Program for Monitoring Prevalence and Bacterial Resistance in Chicken (PREBAF)”. The Program conducted a diagnosis with standardized methodologies on the prevalence of antimicrobial resistance of *Enterococcus* sp. and *Salmonella* spp. isolated from frozen chicken carcasses marketed in Brazil (ANVISA, 2010).

The study was conducted in 14 states, and a total of 2 710 sample units of chicken were analysed in the period from 2004 to 2006. Regarding *Salmonella* sp., the mean prevalence found was 3.03%. A total of 250 strains were submitted to antigenic characterization, which identified 18 serovars, with a higher frequency for *S. Enteritidis* (48.8% of the strains), followed by *S. Infantis* (7.6%), *S. Typhimurium* (7.2%), *S. Heidelberg* (6.4%), *S. Mbandaka* (4.8%) and 15 (5.2%) strains characterized as *Salmonella* sp. Regarding *Enterococcus*, 98.7% of the chicken samples were positive for this bacterium and a total of 8 188 isolates was submitted to species identification. *Enterococcus* isolates were distributed in twelve species. However, it was observed that four species predominated: *E. faecalis* (61.4%), *E. gallinarum* (28.7%), *E. casseliflavus* (5.06%) and *E. faecium* (2.2%). A total of 2,136 strains were evaluated for antimicrobial resistance. The level of antimicrobial susceptibility of *Enterococcus* and *Salmonella* was evaluated by means of determining the minimum inhibitory concentration (MIC) by microdilution in broth or agar dilution, based on the methodology recommended by the National Committee for Clinical Laboratory Standards (NCCLS, 2003). The results of antimicrobial resistance frequency are shown in Tables A.B.1, and B.2.

Regarding *Salmonella* sp. isolated from poultry and humans, VossRech et al. (2017) conducted a meta-analysis to assess the profile and temporal evolution of antimicrobial resistance of strains isolated from 1995 to 2014. Twenty-nine scientific articles met the eligibility criteria and were included in the analysis. The authors presented the antimicrobial resistance of non-typhoidal *Salmonella* isolated from poultry and humans in terms of average frequency of resistance in the period (Table 7). Poultry strains showed a quadratic temporal distribution ($p=0.029$, $R^2=33.9\%$) of resistance against streptomycin, with the superior limit in 2004. Human non-typhoid *Salmonella* strains displayed a growing linear temporal evolution of antimicrobial resistance against nalidixic acid ($p=0.0004$, $R^2=80.5\%$). No temporal effect was identified for any of the other antimicrobials.

Another study conducted by Fitch et al. (2016) assessed the antimicrobial resistance profile to the same antimicrobials in a large number of *Salmonella* strains isolated from poultry from the Pathogen Reduction Program conducted by MAPA. The resistance profile reported for 1 939 strains isolated between 2004 and 2011 is depicted in Table A.B.3. Comparing both studies, it can be seen that there is a common trend in the resistance profile.

Regarding pig-related samples, Almeida et al. (2016) conducted a study comparing the antimicrobial resistance profile of *Salmonella* strains isolated from pigs and humans between 2000 and 2012. However, a lower number of strains were tested in this study and no temporal analyses were conducted. The results (Table A.B.4) demonstrated a trend of higher resistance of the human strains to Nalidixic acid, while the porcine strains showed the highest resistance against Tetracycline. Both groups showed a common profile against Chloramphenicol, Ampicillin (intermediary resistance level) and Ciprofloxacin (low resistance level). The results related to Nalidixic acid resistance in human strains are in accordance with the findings of Fitch et al. (2016).

Table 7. Average antimicrobial resistance of non-typhoidal *Salmonella* isolated from poultry and humans, 1995 to 2014

Antimicrobial	Poultry % (n)	Human % (n)
Ampicillin	14.8 (1048)	24.5 (833)
Cefalotin	24.2 (592)	12.6 (295)
Chloramphenicol	2.9 (1026)	15.2 (833)
Ciprofloxacin	1.4 (1060)	0.5 (242)
Gentamicin	6.6 (1141)	13.3 (323)
Streptomycin	22.5 (1000)	12.4 (609)
Sulfonamide	44.3 (684)	46.4 (428)
Tetracycline	35.6 (1136)	28.0 (747)
Trimethoprim/sufamethoxazole	8.2 (879)	14.8 (398)

Source: Adapted from Voss-Rech et al. (2017).

In 2016, the World Health Organisation published a list of drugs considered the Highest Priority Critically Important (HPCI) Antimicrobials in the so-called WHO list of Critically Important Antimicrobials for human medicine (CIA list, 2016). The CIA list is intended for public health and animal health authorities, practicing physicians and veterinarians, and other interested stakeholders involved in managing antimicrobial resistance to ensure that all antimicrobials, especially critically important antimicrobials, are used prudently in human and veterinary medicine. This list is a reference to help formulate and prioritize risk assessment and risk management strategies for containing antimicrobial resistance mainly due to non-human antimicrobial use. The HPCI antimicrobials belong to the following groups: *quinolones*, cephalosporins (3rd and higher generation), *macrolides* and *ketolides*, *glycopeptides*, and *polymyxins* (WHO, 2017). The HPCI antimicrobials are of utmost importance for treating human patients with severe infections, mainly those admitted to Intensive Care Units (ICUs).

The Health Surveillance Agency (ANVISA) published in the Patient Safety and Quality in Health Services Bulletin #16 the frequency of antimicrobial resistant bacteria in the period of January to December 2016. The data were collected and reported by hospital infection control committees of around 56% of the hospitals with beds of Intensive Care Unit (ICU). The bacteria included in the report represented the most frequent causes of primary infection of the bloodstream associated with central venous catheter in Brazilian hospitals. The data obtained from notifications demonstrated the high selection of strains resistant to a number of antimicrobials occurring in ICUs. In 2016, the National Program for the Prevention and Control of Infections in Health Care was launched by ANVISA. The program targets, amongst other goals, was to achieve 80% of the hospitals (by 2020) with ICUs adopting a standard protocol for antimicrobial use and sending data on antimicrobial resistance to ANVISA.

Studies published in scientific journals have reported data on HPCI antimicrobial resistance in bacteria isolated from food animals and humans in Brazil. In order to gather data published between 2016 and 2018 a systematic review of databases was conducted. Information on resistance against the HPCI was searched in food. The animal data were searched at CABI, Pubmed, Scielo, ScienceDirect, Scopus and Web of Science (only original articles). For human data the searched database were Pubmed and Science Direct (only original articles). In both cases, articles without quantitative data (frequency of resistant strains) and with less than five strains tested were excluded from the analysis.

The results obtained in poultry, swine, cattle and human are presented in Table A.B.5 to A.B.8. The data should be analysed with caution since there is a high variability in tested bacteria, sampling strategies and number of strains tested. Studies assessing human strains were mostly conducted in bacteria isolated from hospital settings, where the selection pressure is high and the patients are suffering severe clinical infections. Strains originating from poultry and swine were most frequently isolated at slaughter or from healthy animals on farms. For instance, non-typhoid *Salmonella* usually causes an asymptomatic infection in both chickens and pigs. The studies reporting resistance on strains isolated from cattle were obtained from dairy cattle, and the isolates frequently originated from the udder of cows with subclinical mastitis.

Policy on antimicrobial use in animals and the National Action Plan on Antimicrobial Resistance

The regulation on antimicrobials use in animals started in 1969, with the Decree-Law 467 (BRAZIL, 1969) which established the mandatory inspection of the industry, commerce and use of veterinary products throughout the national territory. This inspection covers all the establishments that manufacture, fractionate, market or store products for veterinary use, encompassing their manipulation, packaging and use. Moreover, veterinary medicines produced in the country or imported must be licensed and registered by the Ministry of Agriculture and Livestock. The technical responsibility rests with the veterinarian, pharmacist or chemist, depending on the product. In 2004, the Regulation on Inspection of Veterinary Products was published (BRASIL, 2004), and establishes standards on facilities infrastructure, product registration, technical responsibility, inspection and penalties.

Antimicrobial products for veterinary use via feed were specifically regulated by the Normative Instruction 65 of 2006 (MAPA, 2006), which approved the Technical Regulation on the procedures for the manufacture and use of veterinary drugs intended for inclusion in animal feed. This Regulation established the criteria and procedures for the marketing and use of feed for farm animals containing veterinary medicines of the antimicrobial and anti-parasitic classes. Products are included with indications of administration via feed for the purpose of prophylaxis and treatment of diseases. The antimicrobial growth promoters are not covered by this regulation. The regulation covers the rules for the production of medicated feed, the cleaning of equipment, the requirement of a prescription by a veterinarian, and mandatory inspection. This regulation was extended to owners and independent producers of food animals by the Normative Instruction 14 of 2016 (MAPA, 2016), which will enter into force on 18 July 2019. After this date, according to the IN14/2016, medicine (antimicrobials and anti-parasitic drugs) for food animal use and administered in feed will be marketed to the owners or holders of the animals only by means of a prescription by the veterinarian responsible for the management of the property. In this sense, all antimicrobials administered via feed for prophylactic and therapeutic purposes will need a veterinary prescription. It should be noted that AGPs are not included in this regulation.

The first programme regarding the use of antimicrobials in food animals focused on the control of residues in food. In March 2005, based on Decree No. 5,351, the Coordination for Control of Residues and Contaminants (CCRC) was created to implement and monitor programmes related to the control of residues and contaminants in agricultural products. Regarding the presence of antimicrobial residues in food of animal origin, MAPA acts through the National Plan for the Control of Residues and Contaminants (PNCRC) and through active participation in the working groups of the Codex Alimentarius, both in the Veterinary Drugs Residues in Food and in the Antimicrobial Resistance Task Force. The National Program for the Control of Residues in Products of Animal Origin (PNCRC/Animal), established by Ordinance No. 50/2006, is based on risk analysis and determines maximum limits of residues and amounts of samples to be collected. Samples are taken by federal inspectors on rural properties and processing establishments registered in the Federal Inspection Service (SIF). Similar to all Brazilian legislation dealing with feed additives, this programme was based on Codex Alimentarius recommendations. The laboratory analyses are carried out in official MAPA laboratories or in laboratories accredited by them. Every year, a Sampling Plan is established by MAPA's Normative Instruction and the results analysed for the previous year are published on the MAPA's website. For 2016, there was no nonconformity regarding antimicrobial residues in the samples collected from cattle (0/592) and low levels of nonconformities in chicken (1/607) and swine (4/603) samples. The published results of the PNCRC of 2016 and the sampling plan established by IN09 of February 2017 can be assessed at <http://www.agricultura.gov.br/assuntos/inspecao/produtos-animal/plano-de-nacional-de-controle-de-residuos-e-contaminantes/documentos-da-pncrc/pncrc-2017.pdf/view>.

The first official initiative to monitor antimicrobial resistance in animals was instituted by IN 30 of 2014 of the Ministry of Fisheries and Aquaculture, which instituted the National Program for Monitoring Antimicrobial Resistance in Fishery Resources. This program aimed to guarantee the sustainability of the systems for the production of aquatic animals and the health of fishery resources. The Program is mandatory to all farms of aquatic animal cultures in the national territory. It was expected that target microorganisms, sample plans and methodologies would be defined in complementary acts. In 2015,

however, the Ministry of Fisheries and Aquaculture was abolished, and monitoring competency was transferred to MAPA. To date the complementary Act has not been published.

The fighting of antimicrobial drug-resistant infection spread was the theme of the high-level meeting of the United Nations (UN) in September 2016. Brazil participated in the meeting and ratified the fight against antimicrobial resistance. In 2017, Brazil was a signatory to the G20 Leaders' Statement, whereby antimicrobial resistance was recognized as a growing threat to public health and economic growth. In this meeting, countries reaffirmed the goal of having National Action Plans based on the "One Health" approach in an advanced phase by the end of 2018. The leaders also stated they would promote the prudent use of antibiotics in all sectors and make efforts to restrict their use in veterinary medicine exclusively for therapeutic purposes. However, they also declared that the prudent and responsible use of antibiotics does not include its use for growth promotion in the absence of a risk analysis (Ministério das Relações Exteriores, 2017). According to the Ministry for Agriculture Livestock and Supply (MAPA), the decision concerning the withdrawal of the antimicrobial use in Brazil will be based on scientific studies and risk analysis, and that the discussion of the use of Critically Important Antimicrobials for humans will be prioritized (BRESLAU, 2017).

On 23 October 2017, the Normative Instruction 41 was published. This established the National Programme for Prevention and Control of Antimicrobial Resistance in Agriculture (AgroPrevine) under the coordination of the Ministry for Agriculture, Livestock and Supply (MAPA, 2017). This program attempts to strengthen measures for the prevention and control of antimicrobial resistance in livestock, within the concept of "One Health" which establishes the interdependence between human, animal and environmental health through activities of education, surveillance and monitoring. The coordination of the programme is under the responsibility of the Department of Inspection of Livestock Inputs of MAPA and it aims to promote activities related to the objectives and strategic interventions established in the National Plan of Action for the Prevention and Control of Antimicrobial Resistance (PAN-BR Agro): health education; epidemiological studies; surveillance and monitoring of antimicrobial use; strengthening of infection prevention and control measures implementation; and promotion of the rational use of antimicrobials. On 16 May 2018, the PAN-BR Agro was launched during the agriculture fair (Agrobrasília), which took place in the Brazilian cerrado. This is the first version of the PAN-BR AGRO (MAPA, 2018) and covers the years 2018-2022. The Plan targets five strategic objectives aligned to the Global Plan (WHO / FAO / OIE), and includes eight main objectives, 15 strategic interventions, and 21 activities. The five strategic objectives, as well as the specific objectives and interventions planned are listed in Table A.C.1.

5. Conclusion

After an extensive search of data on antimicrobial use and resistance, it is possible to summarize the information found as follows. Antimicrobial use for therapeutic, prophylactic or growth promotion in food animals is not prohibited in Brazil. However, over the last decades many antibiotic drugs have been withdrawn as growth promoters by specific legislations.

The volume of antimicrobials used is not officially published. There are only some estimates or data originated from case studies conducted on a limited number of farms. The distribution of the antimicrobials used among the therapeutic, prophylactic and growth promotion purposes is not published.

Antimicrobial resistance among bacteria isolated from human and animals has been of increasing concern among health professionals and the scientific community, and frequently discussed in congresses and workshops. Professionals working in food production are informed about this topic, as well as about the resistance mechanisms and hazards of the massive use of antimicrobials in animal production. Regarding information provided to the public, fewer initiatives have been taken. The Health Surveillance Agency (ANVISA) provides, on its website, information about responsible antimicrobial use in human medicine and the hazards of resistance and selection of multi-resistant bacteria. These aspects have been highlighted since the adoption of mandatory medical prescriptions for antimicrobials in pharmacies. The use of antimicrobials in animal production is less discussed, but some articles or interviews have been published

in newspapers and on the web. Usually these articles refer to the “One Health” approach on antimicrobial resistance and the animal-human-environment interface.

The great concern among stakeholders in the food animal production chain is the possible increase of production costs if antimicrobials are withdrawn from use in animal production. Several ongoing studies aim to estimate the impact of such withdrawal, and more data will be available soon. There are many alternatives available on the market which claim to be capable of replacing antimicrobials. Among these, probiotics, prebiotics, phytotherapies and organic acids marketed by different companies are advertised on their websites. In recent years, the industry and producers have adopted feed additives to improve intestinal health, as well as to prevent and manage health problems such as post-weaning diarrhoea in pigs or dysbiosis in broilers. The replacement of AGPs is a new concept and will depend on studies that demonstrate their efficacy and the costs/benefits in the context of Brazilian livestock production.

The National Action Plan on Antimicrobial Resistance in Agriculture was launched in 2018 and presents objectives, strategies and activities to be implemented up to 2022. The plan targets health education, epidemiological studies, surveillance and monitoring of antimicrobial use, strengthening infection prevention and implementation of control measures, and promotion of the rational use of antimicrobials in animals. It can be expected that the data gaps on antimicrobial use will be solved by these activities. Moreover, the regulation of antimicrobial use, such as the need of veterinary prescriptions, the research of alternatives for AGPs, and education programs will contribute to the prudent use of antimicrobials.

Since 2016, under the co-ordination of the Ministry of Health, Brazil has been working on elaborating its National Action Plan (Plano de Acao Nacional – Pan-BR). The Plan is in line with the Global Action Plan on the “One Health” concept and involves co-ordination with the Brazilian Ministry of Health, The Health Regulatory Agency (ANVISA), the Ministry of Agriculture, the Ministry of Science, Technology, Innovations and Communications (MCTIC), the Ministry of Cities, The Ministry of Education, and the Ministry of the Environment. This Plan is in the final validation phase at the Ministry of Health. In 2017, ANVISA published its sectorial plan and in May 2018 the Ministry of Agriculture published the PAN-BR Agro. These two sectorial plans will be integrated into the PAN-BR.

The Plan encompasses nine objectives, 13 interventions and 20 activities, and aims to increase the awareness of health professionals about: antimicrobial use and resistance; the monitoring of antimicrobial resistance in humans; the hygiene and infection programs in hospitals and clinics; the control of antibiotics prescription and sales, research on antimicrobial resistance; and the monitoring of antimicrobials residues in foods. Both plans aim to tackle the antimicrobial resistance problem in Brazil. There is no published plan that targets the environment, although the Agroprevine has some activities related to controlling the discharge of antimicrobial residues into the environment. Agriculture is an important driving force of the Brazilian economy, so any aspect related to this area is critical for the country. Although there is further room for improvement, these aforementioned initiatives show the growing importance of public health in agriculture.

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Annex A. Some economic indicators on agriculture in Brazil

Table A A.1. Evolution of Brazilian export and import of additives for animal feeding

USD millions

		2000		2005		2011	
		Import	Export	Import	Export	Import	Export
Aminoacids		77.17	8.51	120.75	44.74	298.85	285.90
Growth promoters anticoccidial drugs		23.03	6.56	34.78	8.78	81.41	63.02
Vitamins		57.17	0.86	64.83	2.06	153.81	2.81
Enzymes		12.71	7.05	19.62	32.28	84.82	101.79
Others		25.27	11.01	71.99	33.96	160.29	97.61
TOTAL		195.35	33.99	311.97	121.82	779.18	551.13

Source: Ministério do Desenvolvimento Indústria e Comércio Exterior (2012).

Table A A.2. Stages of the Brazilian pig production chain and their percentage share in the total financial movement

Stage	Description	Financial movement (USD billions)	% of total financial movement
After the farm	Industrial processing and commercialization	35 276	78.58
On-farm	Activities conducted in the farms	4 828	10.76
Before the farm	All needed production inputs	4 240	9.44
Facilitating agents	Transportation, technical assistance, softwares, registrations and port costs	0 548	1.22
Total		44 892	100

Source: ABCS (2017).

Table A A.3. Items included in the “Before the farm” stage and their percentage share in the total financial movement

Item	Financial movement (USD billions)	% of total financial movements of this stage
Genetics	135.94	3.20
Boars	20.64	0.48
Sows and gilts	66.20	1.56
Breeding overhead	35.59	0.84
Semen	7.06	0.17
Imported pigs	1.03	0.02
Artificial insemination products	5.42	0.13
Medicines and vaccines	182.80	4.31
Biologics	50.58	1.19
Endoparasitic medicines	0.77	0.02
Ectoparasitic medicines	0.40	0.01
Antimicrobials	62.82	1.48
Therapeutic drugs	6.02	0.14
Supplements	1.41	0.03
Environmental use products (disinfectants, water purification, etc.)	3.59	0.08
Feed additives	15.96	0.38
Others	41.25	0.97
Feeding	3,706.24	87.41
Corn	1,618.03	38.16
Soybean meal	1,166.45	27.51
Other feed concentrates	368.73	8.70
Amino acids	118.32	2.79
Dairy by-products	87.29	2.06
Premix	347.42	8.19
General costs	78.88	1.86
Electricity	34.58	0.81
Fuel	12.23	0.29
Repairs and maintenance	32.07	0.76
Infrastructure	136.14	3.22
Piglets Production Unit	84.74	2.0
Fattening	51.46	1.21
Total	4,240	100

Source: Adapted from (ABCS, 2017).

Table A A.4. Composition of the Effective Production Cost of dairy farms in January and February, 2017

Brazilian average

Item	% of effective operational cost
Concentrate feeds	44.3
Mineral supplements	2.8
Labour	15.5
Milking products	3.0
Medicines	3.5
Maintenance and improvements	2.1
Forages	2.3
Silage	12.4
Electricity/ Fuel	3.2
Taxes, administration fees, etc.	4.4
Other	6.5

Source: Adapted from CEPEA (2017).

Annex B. Data on antimicrobial resistance

Table A B.1. Frequency (%) of antimicrobial resistance of 250 *Salmonella* sp. strains isolated from frozen chicken carcasses sampled in Brazil, 2004 to 2006

Antimicrobial	% Resistant strains in each year		
	2004	2005	2006
Ampicillin	79.5	62.3	8.5
Aztreonam	0	29.9	17.0
Cefoxitin	20.5	14.6	19.1
Cephalothin	15.4	19.6	2.1
Ceftriaxone	0	11.1	8.5
Ceftiofur	17.9	19.6	28.7
Ciprofloxacin	0	0	1.1
Chloramphenicol	0	0	0
Enrofloxacin	64.1	17.1	1.1
Florfenicol	92.9	84.6	13.8
Gentamicin	0	6.0	0
Nalidixic acid	51.3	36.7	50.0
Nitrofurantoin	50.0	10.7	4.8
Streptomycin	35.9	100.0	100.0
Sulphonamide	56.4	66.6	86.2
Sulpha/Trimethoprim	0	6.8	14.9
Tetracycline	20.5	15.4	2.1
Trimethoprim	2.6	9.4	15.9

Source: ANVISA (2008).

Table A B.2. Frequency (%) of antimicrobial resistance of *Enterococcus* strains isolated from frozen chicken carcasses sampled in Brazil, 2004 to 2006

Antimicrobial	<i>E.faecalis</i> (n='1,501')	<i>E.faecium</i> (n='82')	<i>E.gallinarum</i> (n='400')	<i>E.casseliflavus</i> (n='106')
Ampicillin	0	0	0	0
Chloramphenicol	27.8	29.3	26.0	22.6
Ciprofloxacin	26.7	56.1	43.0	33.0
Erythromycin	58.5	65.9	62.0	45.3
Gentamicin	10.1	8.5	24.7	6.6
Linezolid	1.1	2.9	3.6	2.5
Quinupristin/ Dalfopristin	98.2	70.6	59.9	53.3
Streptomycin	29.8	37.8	30.3	14.2
Teicoplanin	0.3	24.4	0	0
Tetracycline	79.7	89.0	89.0	49.1
Vancomycin	0.3	24.4	0	0

Source: ANVISA (2008).

Table A B.3. Antimicrobial resistance profile of 1 939 *Salmonella* strains isolated from poultry in Brazil, 2004-2011

Antimicrobial	% of resistant <i>Salmonella</i> strains
Ampicillin	10.0
Ceftriaxone	5.2
Chloramphenicol	3.5
Ciprofloxacin	0.6
Gentamicin	4.7
Tetracycline	20.9
Trimethoprim/sulfamethoxazole	6.0

Source: Adapted from Fitch et al. (2016).

Table A B.4. Antimicrobial resistance profile of 70 *Salmonella* strains isolated from swine and humans in Brazil, 2002 to 2012

Antimicrobial	Swine % resistant (n=27)	Human % resistant (n=43)
Ampicillin	44.4	39.5
Chloramphenicol	37.0	34.8
Ciprofloxacin	3.7	0
Nalidixic acid	22.2	55.8
Tetracycline	51.8	9.3
Trimethoprim/sulfamethoxazole	29.6	44.1

Source: Adapted from Almeida et al. (2016).

Table A B.5. Frequency of selected antimicrobial resistance profiles in bacteria involved in primary infection of the bloodstream associated with central venous catheter in intensive care units for adults and children from Brazilian hospitals, 2016

Bacteria	Adult intensive care units	Pediatric intensive care units
Coagulase-negative <i>Staphylococcus</i> resistant to Oxacilin	78.7	75.0
<i>Staphylococcus aureus</i> resistant to Oxacilin	63.1	54.0
<i>Enterococcus</i> resistant to Vancomycin	25.8	10.9
<i>Escherichia coli</i> resistant to 3 rd and 4 th generation Cephalosporins	33.3	22.9
<i>Escherichia coli</i> resistant to 3 rd and 4 th generation Cephalosporins and Carbapenem	9.9	4.2
<i>Klebsiella pneumoniae</i> resistant to 3 rd and 4 th generation Cephalosporins	27.8	29.1
<i>Klebsiella pneumoniae</i> resistant to 3 rd and 4 th generation Cephalosporins and Carbapenem	46.8	19.3
<i>Enterobacter</i> spp. resistant to 3 rd and 4 th generation Cephalosporin	28.1	24.3
<i>Enterobacter</i> spp. resistant to 3 rd and 4 th generation Cephalosporins and Carbapenem	18.2	1.7

Table A B.6. Results of resistance frequency (%) Highest Priority Critically Important Antimicrobials in bacteria isolated from poultry in Brazil reported in original articles, 2016-2017

Authors / year	Bacteria	Strains (n)					Frequency of resistant strains (%)											
2016			AZI	CAZ	CEP	CIP	COL	CRO	CTF	CTX	ENO	ERI	FLU	POL	NAL	NOR	POL	
Bezerra et al.	<i>Escherichia coli</i>	174	48.8	-*	-	91.4	-	-	42.5	-	-	-	-	-	-	-	1.1	
Braga et al.	<i>Escherichia coli</i>	15	-	-	-	-	-	-	54.5	-	54.5	-	80.0	-	80.0	-	-	
Fitch et al.	<i>Salmonella spp.</i>	1.939	-	-	-	98.6	-	93.6	-	-	95,1	-	-	-	-	-	-	
Furian et al.	<i>Pasteurella multocida</i>	56	-	-	-	-	-	-	1.8	-	23.2	5.3	-	-	-	-	-	
Mion et al.	<i>Salmonella spp.</i>	18	-	-	-	0	-	-	11.1	-	0	-	-	-	-	-	-	
Nepomuceno et al.	<i>Escherichia coli</i>	130	-	-	-	13.1	-	-	16.2	-	33.1	-	-	-	-	-	-	
Neves et al.	<i>Salmonella Heidelberg</i>	54	-	-	-	0	-	9.3	31.5	-	0	-	-	-	66.7	0	-	
Palmeira et al.	<i>Salmonella spp.</i>	135	-	-	-	0	3.0	-	1.0	-	0	-	-	0	49.0	0	-	
Panzenhagen et al.	<i>Campylobacter spp.</i>	82	-	-	-	100	-	-	-	-	100	-	-	-	-	-	-	
Penha Filho et al.	<i>Salmonella enterica</i>	41	-	0	0	34.1	-	-	0	-	21.9	-	-	-	39.0	-	-	
Sierra-Arguello et al.	<i>Campylobacter jejuni</i>	50	-	-	-	94.0	-	-	-	-	-	2.0	-	-	90.0	-	-	
Yamatogi et al.	<i>Salmonella spp.</i>	196	-	-	-	1.0	-	-	4.6	-	6.6	-	-	-	28.1	0.5	-	
Ziech et al.	<i>Salmonella spp.</i>	98	-	-	-	-	-	-	7.0	-	2.0	-	-	-	95.0	-	1.0	
2017																		
Borges et al.	<i>Salmonella Enteritidis</i>	148	-	-	-	41.9	-	-	4.1	-	17.6	-	-	-	-	-	-	
Giuriatti et al.	<i>Salmonella Heidelberg</i>	18	-	100	-	-	-	94.4	100	100	38.9	-	-	-	100	-	-	
Koerich et al.	<i>Salmonella enterica</i>	60	-	-	-	-	27.0	-	8.0	-	83.0	96.0	-	-	-	90.0	-	

Authors / year	Bacteria	Strains (n)															
Rodrigues et al.	<i>Salmonella enterica</i>	60	-	-	-	-	-	-	-	13.3	-	-	-	-	-	-	-

Source: *Not tested. AZI –azithromycin; CAZ –ceftazidime; CEP –cefepime; CIP – ciprofloxacin; COL – colistin; CRO – ceftriaxone; CTF –ceftiofur; CTX – cefotaxime; ENO – enrofloxacin; FLU – flumequine; NAL – nalidixic acid; NOR – norfloxacin; POL – polymyxin B

Table A B.7. Results of resistance frequency (%) Highest Priority Critically Important Antimicrobials in bacteria isolated from pigs in Brazil reported in original articles published, 2016-2017

Authors/Year	Bacteria	Strains (n)					Frequency of resistant strains (%)							
2016			CAZ	CEP	CIP	CRO	CTF	CTX	ENO	ERI	NAL	NOR	TI	
Furian et al.	<i>Pasteurella multocida</i>	40	-*	-	-	-	22.5	-	22.5	40.0	-	-		
Guerra Filho et al.	<i>Salmonella spp.</i>	20	0	0	90.0	5.0	-	10.0	-	-	80.0	-		
Lima et al.	<i>Salmonella spp.</i>	357	-	-	0.2	0.6	-	-	-	-	25.0	-		
2017														
Pissetti et al.	<i>Escherichia coli</i>	228	0.9	-	1.3	-	-	1.3	-	-	75.9	-		
Poor et al.	<i>Corynebacterium spp.</i>	11	-	-	-	-	0	-	63.6	100	-	-		
Souto et al.	<i>Salmonella enterica</i>	39	-	-	-	-	-	-	-	-	33.3	2.5		

Note: *Not tested. CAZ –ceftazidime; CEP –cefepime; CIP – ciprofloxacin; CRO – ceftriaxone; CTF –ceftiofur; CTX – cefotaxime; ENO – enrofloxacin; ERI – erythromycin; NAL – nalidixic acid; NOR – norfloxacin; TIL – tylosin

Table A B.8. Results of resistance frequency (%) Highest Priority Critically Important Antimicrobials in bacteria isolated from cattle in Brazil reported in original articles published, 2016-2017

Authors / Year	Bacteria	Strains (n)	Frequency of resistant strains (%)							
			CIP	CTF	ENO	ERI	NAL	NOR	TEI	VAN
2016										
Oliveira et al.	<i>Staphylococcus spp.</i>	269	-*	7.0	-	11.0	-	-	-	0
Palma et al.	<i>Listeria monocytogenes</i>	11	9.1	-	-	9.1	100	0	-	0
Porto et al.	<i>Enterococcus spp.</i>	53	-	-	-	60.4	-	17.0	9.4	11.3
Santos et al. (a)	<i>Staphylococcus spp.</i>	170	-	-	0	7.6	-	-	-	-
2017										
Haubert et al.	<i>Staphylococcus aureus</i>	31	-	6.0	6.0	35.0	-	-	42.0	-
Souto et al.	<i>Escherichia coli</i>	61	-	-	-	-	54.1	21.3	-	-
Vargas Júnior et al.	<i>Escherichia coli</i>	15	-	-	20.0	-	-	-	-	-

Note: *Not tested. CIP – ciprofloxacin; CTF – ceftiofur; ENO – enrofloxacin; ERI – erythromycin; NAL – nalidixic acid; NOR – norfloxacin; TEI – teicoplanin; VAN- vancomycin.

Table A B.9. Results of resistance frequency (%) Highest Priority Critically Important Antimicrobials in bacteria isolated from humans in Brazil reported in original articles published, 2016

Authors / year	Bacteria	Strains (n)	Frequency of resistant strains (%)																
			AZI	CAZ	CEF	CEP	CIP	COL	CRO	CTX	ERI	LEV	MOX	NAL	NOR	OFL	POL	TEI	VAN
2016																			
Araujo et al.	<i>Pseudomonas aeruginosa</i>	242	- *	-	-	34.3	42.6	-	-	-	-	-	-	-	-	-	0	-	-
Barbosa-Ribeiro et al.	<i>Enterococcus faecalis</i>	20	0	-	-	-	0	-	-	-	0	-	5.0	-	-	-	-	-	0
Barros et al.	<i>Streptococcus agalactiae</i>	98	-	-	-	-	-	-	-	-	14.3	-	-	-	-	-	-	-	-
Braun et al.	<i>Klebsiella pneumoniae</i>	14	-	100	-	85.7	100	-	-	100	-	-	-	-	-	-	50.0	-	-
Capett et al.	<i>Escherichia coli</i>	115	-	-	-	-	66.9	-	-	-	-	-	-	-	-	-	-	-	-
Cardoso et al.	<i>Acinetobacter baumannii</i>	31	-	48.4	-	100	96.8	-	-	83.9	-	83.9	-	-	-	-	0	-	-
Carrilho et al.	<i>Enterobacteriaceae</i>	127	-	-	-	-	-	21.3	-	-	-	-	-	-	-	-	-	-	-
Carvalho et al. (a)	<i>Escherichia coli</i>	61	-	11.4	-	9.8	18.0	-	18.0	13.1	-	-	-	-	-	-	-	-	-
Carvalho et al. (b)	<i>Acinetobacter spp.</i>	34	-	100	-	100	100	-	100	-	-	-	-	-	-	-	0	-	-
Cunha et al.	<i>Escherichia coli</i>	653	-	-	-	9.2	24.4	-	7.2	-	-	-	-	31.6	20.4	-	-	-	-
Dias et al.	<i>Acinetobacter baumannii</i>	44	-	100	-	100	100	-	-	-	-	-	-	-	-	-	0	-	-
Fraga et al.	<i>Clostridium difficile</i>	50	-	-	--	-	-	-	-	-	-	-	8.0	-	-	-	-	-	58.0
Freire et al.	<i>Acinetobacter baumannii</i>	92	-	-	-	-	-	-	-	-	-	-	-	-	-	-	3.3	-	-
Gallo et al.	<i>Stenotrophomonas maltophilia</i>	100	-	79.0	-	-	-	-	-	-	-	9.0	-	-	-	-	-	-	-
Gushiken et al.	<i>Staphylococcus aureus</i>	42	-	-	-	-	-	-	-	-	95.2	-	-	-	-	-	-	-	-

Authors / year	Bacteria	Strains (n)	Frequency of resistant strains (%)																
			AZI	CAZ	CEF	CEP	CIP	COL	CRO	CTX	ERI	LEV	MOX	NAL	NOR	OFL	POL	TEI	VAN
Leite et al.	<i>Acinetobacter baumannii</i>	20	-	-	-	-	-	35.0	-	-	-	-	-	-	-	-	-	-	-
Matos et al.	<i>Staphylococcus aureus</i>	128	-	-	-	-	56.0	-	-	-	68.0	-	-	-	-	-	-	0	-
Neves et al.	<i>Acinetobacter baumannii</i>	43	-	-	-	-	-	-	-	-	-	-	-	-	-	-	7.0	-	-
Palma et al.	<i>Streptococcus salivarius</i>	22	-	-	-	-	-	-	-	-	90.9	-	-	-	-	-	-	-	-
Pereira et al.	<i>Staphylococcus spp.</i>	103	-	-	-	-	-	-	-	-	54.3	-	-	-	-	-	-	-	-
Pieri et al.	<i>Staphylococcus spp.</i>	43	49.3	-	-	-	52.4	-	-	-	-	-	-	-	-	-	-	-	0
Rocha-Castro et al.	<i>Salmonella spp.</i>	32	-	-	-	-	3.0	-	0	-	-	-	-	-	-	-	-	-	-
Rodrigues et al.	<i>Escherichia coli</i>	1.654	-	-	-	-	28.9	-	-	-	-	-	-	-	30.7	-	-	-	-
Santos et al. (b)	<i>Pseudomonas aeruginosa</i>	9	-	6.7	-	4.5	56.0	100	-	-	-	-	-	-	-	-	-	-	-
Santos et al. (c)	<i>Klebsiella pneumoniae</i>	34	-	-	-	-	87.5	0	-	-	-	-	-	-	-	-	-	-	-
Souza et al.	<i>Streptococcus dysgalactiae</i>	44	-	-	-	-	-	0	-	-	18.2	0	-	-	-	-	-	-	0
Tuon et al.	<i>Klebsiella pneumoniae</i>	14	-	-	-	-	92.8	100	-	-	-	-	-	-	-	-	-	-	-
2017																			
Aires et al.	<i>Klebsiella pneumoniae</i>	16	-	100	-	100	75	-	-	100	-	-	-	-	-	-	12.5	-	-
Campana et al.	<i>Pseudomonas aeruginosa</i>	25	-	0	-	0	20	-	-	-	-	-	-	-	-	-	-	-	-
Capizzani et al.	<i>Burkholderia cepacia</i>	24	-	29.5	-	-	-	-	-	-	-	82.4	-	-	-	-	-	-	-
Carrilho et al.	<i>Enterobacteriaceae</i>	27	-	-	-	-	-	100	-	-	-	-	-	-	-	-	-	-	-

38 | ANTIMICROBIAL USE, RESISTANCE AND ECONOMIC BENEFITS AND COSTS TO LIVESTOCK PRODUCERS IN BRAZIL

Authors / year	Bacteria	Strains (n)		Frequency of resistant strains (%)															
				AZI	CAZ	CEF	CEP	CIP	COL	CRO	CTX	ERI	LEV	MOX	NAL	NOR	OFL	POL	TEI
Castilho et al.	<i>Acinetobacter baumannii</i>	56	-	92.8	-	96.4	91.0	-	-	-	-	35.7	-	-	-	-	8.9	-	-
Lorenzoni et al.	<i>Enterobacteriaceae</i>	70	-	98.6	-	97.1	94.3	8.6	95.7	-	-	-	-	-	-	-	-	-	-
Pfaller et al.	<i>Pseudomonas aeruginosa</i>	213	-	33.0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Rechenchoski et al.	<i>Enterobacter spp.</i>	40	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1.5	-	-
Rosa et al.	<i>Enterobacter spp.</i>	103	-	-	-	10.5	-	-	-	-	-	-	-	-	-	-	1	-	-
Rossi et al. (b)	<i>Klebsiela pneumoniae</i>	27	-	13.0	-	15.6	-	4.8	-	-	-	19.3	-	-	-	-	-	-	-
Rossi et al. (c)	<i>Enterobacteriaceae</i>	16.533	-	-	-	-	-	1.0	-	-	-	-	-	-	-	-	-	-	-
Santos et al.	<i>Enterococcus spp.</i>	132	-	-	-	-	8.2	-	-	-	18.6	1.6	-	-	7.4	-	1	1	-
Vasconcellos et al.	<i>Acinetobacter baumannii</i>	71	-	15.8	-	17.2	00	1	-	18.6	-	14.4	-	-	-	-	1	-	-
2018																			
Abboud et al.	<i>Enterobacteriaceae</i>	30	-	-	-	-	-	-	-	-	-	-	-	-	-	-	40.0	-	-
Bazzo et al.	<i>Neisseria gonorrhoeae</i>	550	6.9	-	0	-	55.6	-	0	-	-	-	-	-	-	-	-	-	-
Gorla et al.	<i>Neisseria meningitidis</i>	2.888	-	-	-	-	0.07	-	0	-	-	-	-	-	-	-	-	-	-
Marchi et al.	<i>Enterococcus spp.</i>	86	-	-	-	-	-	-	-	-	-	-	-	-	-	-	83.7	100	-
Martins et al.	<i>Enterobacteriaceae</i>	499	-	-	-	-	-	33.0	0	-	-	-	-	-	-	-	-	-	-
Medeiros et al.	<i>Shigella spp.</i>	63	-	20.6	-	-	-	0	- 0 - - - 0	-	-	-	-	-	-	-	-	-	-

*Not tested. AZI –azithromycin; CAZ –ceftazidime; CEF- cefixime; CEP –cefepime; CIP – ciprofloxacin; COL – colistin; CRO – ceftriaxone; CTX – cefotaxime; ERI= erythromycin; LEV- levofloxacin; MOX- moxifloxacin; NAL – nalidixic acid; NOR – norfloxacin; OFL- ofloxacin; POL – polymyxin B; TEI- teicoplanin; VAN- vancomycin

Annex C. The strategic objectives and interventions of the National Action Plan on AMR

An operational plan was drawn up to achieve each of the strategic objectives. It included the planned activities, the managers, the execution period, the estimated cost, and the source of financing. Table A.C.1 lists the activities and implementation periods for each strategic intervention.

Table A C.1. The five strategic objectives, as well as the specific objectives and strategic interventions planned on the National Action Plan on Antimicrobial Resistance

Strategic objective	Specific objective	Strategic intervention
To improve awareness and understanding of antimicrobial resistance through effective communication, education and training	#1 To promote strategies for communication and health education for health professionals, health managers, regulated sector and society in order to increase the awareness on the resistance to antimicrobials	# 1.1 Establishment of communication actions on resistance to antimicrobials for health professionals, health managers, regulated sector and society
	#2 To improve information and training in resistance to antimicrobials of professionals and managers in the area of animal health	#2.1 Promotion of continuous training of animal health professionals and managers on antimicrobial resistance
		#2.2 Updating and improvement of the curriculum of Veterinary Medicine courses by the inclusion of topics related to antimicrobial resistance
#2 To strengthen knowledge and scientific based information through surveillance and research	#3 To build and establish the National Integrated Surveillance and Monitoring of Antimicrobial Resistance	#3.1 Establishment of an integrated surveillance and monitoring system of antimicrobial resistance #3.2 Development of a system for surveillance and monitoring of resistance to antimicrobials in the context of farming #3.3 Development of a monitoring system of antimicrobial use in the agriculture sector #3.4 Evaluation of the quality of antimicrobials for veterinary use
#2 To strengthen knowledge and scientific based information through surveillance and research	#3 To build and establish the National Integrated Surveillance and Monitoring of Antimicrobial Resistance	
	4 To improve and expand the scientific knowledge about resistance to antimicrobials	#4.1 Development of a research agenda on antimicrobial resistance #4.2 Development of research and innovation in resistance to antimicrobials
#3 To reduce the incidence of infections by effective hygiene and prevention measures	#5 To strengthen the implementation of preventive and control measures of livestock infections	#5.1 Strengthening of good agricultural practices adoption
#4 To optimize the antimicrobial use	#6 To promote the rational use of antimicrobials in the agricultural sector	#6.1 Strengthening of regulatory actions to promote the rational use of antimicrobials in animals #6.2 Supporting the development of recommendations for rational antimicrobials use in animals
	#7 To promote the adequate veterinary antimicrobials waste management	#7.1 Supporting the adequate management of wastes from antimicrobials used in veterinary

Strategic objective	Specific objective	Strategic intervention
#5 To prepare economic arguments for sustainable development and investment in new medicines, diagnostics and vaccines, as well as other intervention for implementation of the National Action Plan for Prevention and Control of Antimicrobial Resistance	#8 To develop the financial plan for the implementation of the National Action Plan for Prevention and Control of Antimicrobial Resistance to be included in the federal budget planning	8.1 Setting the annual budget for implementation of the National Action Plan for Prevention and Control of Antimicrobial Resistance to be included in the federal budget planning #8.2 Definition of alternative funding sources

Strategic intervention 1.1: Establishment of communication actions on resistance to antimicrobials for health professionals, health managers, regulated sector and society

Activity 1.1.1 Elaboration and implementation of a national communication plan for animal health professionals, animal health managers, rural producers, professionals working in the production and processing chain of animal products and other professionals in the regulated sector to raise awareness of: antimicrobial resistance; prevention and control of infections; rational use of antimicrobials in animals; the need for increased veterinary supervision of antimicrobial use in animals and the correct disposal of antimicrobial drugs.

1.1.1.1 Development of the communication plan about antimicrobial resistance in agriculture, containing objectives, strategies, target audience, channels of communication, and execution schedule. This activity will be conducted in the first semester of 2019.

1.1.1.2 Implementation of the communication plan about antimicrobial resistance in agriculture. This will be a continuous activity conducted between the second semester of 2019 and the second semester of 2022.

Strategic intervention 2.1: Promotion of continuous training of animal health professionals and managers on antimicrobial resistance

Activity 2.1.1 Promotion of ongoing capacity building in antimicrobial resistance for animal health professionals and managers working in animal health.

2.1.1.1 Meeting with involved areas and bodies to harmonization of guidelines for the continuous training on antimicrobial resistance. This activity will take place in the first semester of 2019.

Strategic intervention 2.2: Updating and improvement of the curriculum of Veterinary Medicine courses by the inclusion of topics related to antimicrobial resistance

Activity 2.2.1 Encouragement of the inclusion of the antimicrobial resistance and related topics in the undergraduate curriculum of Veterinary schools.

2.2.1.1 Meeting with involved areas and bodies to harmonization of guidelines for the inclusion of antimicrobial resistance and related topics in the curriculum of Veterinary schools. This activity will take place in the first semester of 2019.

Strategic intervention 3.1: Establishment of integrated surveillance and monitoring of antimicrobial resistance

Activity 3.1.1 Establishment of an inter-ministerial structure for definition, institution, implementation and follow-up of integrated surveillance and monitoring

3.1.1.1 Holding a meeting with other involved governmental organizations and areas in order to establish an inter-ministerial committee, with the definition of their goals and competencies within the National Integrated Program on Surveillance and Monitoring of Antimicrobial Resistance. This activity will take place in the second semester of 2019.

Strategic intervention 3.2: Development of a system for antimicrobial resistance surveillance and monitoring in agriculture

Activity 3.2.1 Implementation of an antimicrobial resistance surveillance program for bacteria isolated from broilers on farm, from chicken processing plants and from feed mills

3.2.1.1 Conduction of a survey of antimicrobial resistance in bacteria isolated from broilers in 2016-2017. This activity was planned for the first semester of 2018.

3.2.1.2 Workshops to develop a surveillance program on antimicrobial resistance of bacteria isolated from broilers on farm, from chicken processing plants and from feed mills. This activity will take place in the second semester of 2018.

3.2.1.3 Implementation of the surveillance program on antimicrobial resistance of bacteria isolated from broilers on farm, from chicken processing plants and from feed mills. This activity will take place between the first semester of 2019 and the second semester of 2022.

Activity 3.2.2 Implementation of antimicrobial resistance surveillance programs for bacteria isolated in official pathogen monitoring programs targeting other animal species

3.2.2.1 Workshops to develop a surveillance program on antimicrobial resistance of bacteria isolated in official pathogen monitoring programs targeting other animal species. This activity will take place in the second semester of 2019.

3.2.2.2 Implementation of the surveillance program on antimicrobial resistance of bacteria isolated in official pathogen monitoring programs targeting other animal species. This activity will take place between the first semester of 2020 and the second semester of 2022.

Activity 3.2.3 Development of the structure needed for surveillance and monitoring of antimicrobial resistance in agriculture within the National Agricultural Laboratories network

3.2.3.1 Planning the laboratory capacity strengthening for surveillance and monitoring of antimicrobial resistance in the National Agricultural Laboratories network. This activity will take place in the second semester of 2018.

3.2.3.2 Implementation of the laboratory capacity strengthening for surveillance and monitoring of antimicrobial resistance in the National Agricultural Laboratories network. This activity will take place in the first semester of 2019.

Strategic intervention 3.3: Development of a monitoring system for antimicrobial use in agriculture

Activity 3.3.1 Implementation of an antimicrobial use monitoring program in animals

3.3.1.1 Workshops for discussion of guidelines for the monitoring program on antimicrobial use in animals. This activity will take place in the second semester of 2018.

3.3.1.2 Development of the monitoring program on antimicrobial use in animals according to the defined guidelines. This activity will take place in the second semester of 2018.

3.3.1.3 *Implementation of the monitoring program on antimicrobial use in animals using a computerized system. This activity will take place between the first semester of 2019 and the second semester of 2022.*

Strategic intervention 3.4: Evaluation of veterinary antimicrobials quality

Activity 3.4.1 Improvement of quality monitoring of veterinary antimicrobials

3.4.1.1 *Setting priorities for improvement of quality monitoring of veterinary antimicrobials. This activity will take place in the second semester of 2019.*

3.4.1.2 *Implementation of quality monitoring of veterinary antimicrobials in accordance with the defined priorities. This activity will take place between the first semester of 2020 and the second semester of 2022.*

Activity 3.4.2 Development of the structure needed for quality monitoring of veterinary antimicrobials within the National Agricultural Laboratories network

3.4.2.1 *Planning the laboratory capacity strengthening for quality monitoring of veterinary antimicrobials in the National Agricultural Laboratories network. This activity will take place in the second semester of 2019.*

3.4.2.2 *Implementation of the laboratory capacity strengthening for quality monitoring of veterinary antimicrobials in the National Agricultural Laboratories network. This activity will take place in the first semester of 2020.*

Strategic intervention 4.1: Definition of an antimicrobial resistance research agenda

Activity 4.1.1 Definition of research priorities on antimicrobial resistance, considering the topics: resistance profile of bacteria from animals; dynamics of transmission of resistance; new diagnostic methods, vaccines, therapeutic alternatives and new antimicrobials; impact on human and animal health from exposure to water, soil and food contaminated with antimicrobials and/or resistant micro-organisms; and, economic and public health impact of the use and restriction of the use of antimicrobials in animal production

4.1.1.1 *Workshop to set priorities for research on antimicrobial resistance in agriculture. This activity will take place in the second semester of 2018.*

Strategic intervention 4.2: Encouragement of research, development and innovation in antimicrobial resistance

Activity 4.2.1 Evaluate public and / or private ways to induce funding for priority lines of research on antimicrobial resistance

4.2.1.1 *Holding a meeting with involved areas and bodies in order to evaluate ways to induce funding for AMR research in the scope of agriculture. This activity will take place in the second semester of 2018.*

Strategic intervention 5.1: Strengthen the adoption of good agricultural practices

Activity 5.1.1 Promotion of sanitary and biosecurity management practices implementation for the prevention and control of infections in animals

5.1.1.1 *Dissemination of manuals and other literature targeting recommendations on animal health and biosecurity management practices for prevention and control of infections in animals. This activity will take place between the second semester of 2018 and the second semester of 2022.*

5.1.1.2 Workshops to plan guidelines and encourage the development and dissemination of recommendations on animal health and biosecurity management practices for prevention and control of infections in animals, prioritizing poultry, swine, cattle and aquaculture. This activity will take place between the first semester of 2019 and the second semester of 2022.

5.1.1.3 Set of recommendations for sanitary and biosecurity management for prevention and control of infections in animal health, prioritizing poultry, swine, cattle and aquaculture. This activity will take place between the second semester of 2019 and the second semester of 2022.

Activity 5.1.2 Evaluate and propose the adoption of policies of good agricultural practices

5.1.2.1 Workshops to set guidelines for the preparation of regulations on mandatory good agricultural practices. This activity will take place between the second semester of 2018 and the second semester of 2021.

5.1.2.2 Preparation of a normative act to establish the mandatory good agricultural practices. This activity will take place in the second semester of 2022.

Strategic intervention 6.1: Strengthening of regulations to promote the rational use of antimicrobials in animals

Activity 6.1.1 Evaluate and propose the adoption of policies to strengthening the veterinary supervision of antimicrobial use in animals

6.1.1.1 Workshops to set guidelines for the preparation of regulations aiming to strengthening the veterinary supervision of antimicrobial use in animals. This activity will take place in the second semester of 2018.

6.1.1.2 Preparation of a normative act to strengthen the veterinary supervision of antimicrobial use in animals. This activity will take place in the first semester of 2019.

Activity 6.1.2 Update of current legislation on veterinary antimicrobials advertising

6.1.2.1 Workshops to set guidelines for the update of current legislation on veterinary antimicrobials advertising. This activity will take place in the second semester of 2018.

6.1.2.2 Preparation of a normative act to updating the current legislation on veterinary antimicrobials advertising. This activity will take place in the first semester of 2019.

Strategic intervention 6.2: Development of recommendations for the rational use of antimicrobials in animals

Activity 6.2.1 Promote the development of protocols for the rational use of antimicrobials in animals

6.2.1.1 Workshops to set guidelines and to promote the development of protocols for the rational use of antimicrobials in animals. This activity will take place in the first semester of 2019.

Strategic intervention 7.1: Supporting the adequate management of wastes from antimicrobials used in veterinary practice

Activity 7.1.1 Promote the preparation of solid waste management plans by the regulated sector, including the provision of collection points for the disposal of antimicrobials used in veterinary practice and their packaging

7.1.1.1 Holding a meeting with involved areas and bodies in order to promote the elaboration of solid waste management plans, including the provision of collection points for the disposal of packaging and antimicrobials used in veterinary practice. This activity will take place in the first semester of 2019.

Strategic intervention 8.1: Setting the annual budget for implementation of the National Action Plan for Prevention and Control of Antimicrobial Resistance to be included in the federal budget planning

Activity 8.1.1 Provide a specific Internal Plan for the activities of the National Action Plan for Prevention and Control of Antimicrobial Resistance to be included in the MAPA Annual Operational Plan

8.1.1.1 Establish a specific Internal Plan for the activities of the National Action Plan for Prevention and Control of Antimicrobial Resistance. This activity will take place in the second semester of 2018.

Strategic intervention 8.2: Definition of alternative funding sources for implementation of the National Action Plan for Prevention and Control of Antimicrobial Resistance

Activity 8.2.1 Evaluation of public and/or private funding alternatives for implementation of the National Action Plan for Prevention and Control of Antimicrobial Resistance

8.2.1.1 Articulate with public institutions and/or private organizations involved in combating resistance to antimicrobial agents, financial support for the implementation of the National Action Plan for Prevention and Control of Antimicrobial Resistance. This activity will take place between the first semester of 2019 and the second semester of 2022.

Activity 8.2.2 Set up of partnerships with international organizations for the implementation of the National Action Plan for the Prevention and Control of Antimicrobial Resistance.

8.2.2.1 Articulate with international organizations involved in combating resistance to antimicrobials, alternatives of financial support for the implementation of the National Action Plan for Prevention and Control of Antimicrobial Resistance. This activity will take place between the first semester of 2019 and the second semester of 2022.