

ROADMAP

Rethinking of antimicrobial decision-systems in the management of animal production

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Report on the cost-effectiveness analyses and marginal abatement cost curves determined with associated data and data collection protocols

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About the ROADMAP research project

The overall aim of ROADMAP is to **foster transitions towards prudent use of antimicrobials (AMs) in animal production in different contexts to manage antimicrobial resistance (AMR). Prudent antimicrobial use (AMU) will be achieved by enhancing antimicrobial decision-systems along the food and drug supply chains.** ROADMAP will focus on supporting animal health and welfare through prevention and health promotion actions.

AMR is recognized as a significant threat to global public health and food security. Overuse and improper use of AMs in many parts of the world contribute to the emergence and spread of AMR. Although human and animal health require AMs, it has been estimated that two thirds of the future AMU growth worldwide will be in animal production. Improving the management of AMU in farm animals is therefore a critical component of dealing with AMR and optimizing production in the livestock sector. Nevertheless, the variety of contexts of AMU in the livestock sector is a major challenge to managing AMR. **There is no “one-size-fits-all” solution to improve AMU and strategies must be contextually developed** (for instance, strategies used in the Danish pig industry are difficult to adapt and adopt in the French free-range poultry farming). Successful solutions must be combined and tailored to the production systems and the social and economic context in which they operate.

ROADMAP will meet three general objectives, in line with the EU AMR Action plan: i) **Rethink AM decision-systems and animal health management;** ii) **Develop options for encouraging prudent AMU in animal production;** iii) **Engage all actors in the food and drug supply chains in fostering a more prudent use of AMs.**

Project consortium

Part . N°	Participant organisation name (acronym)	Country
1	Institut National de Recherche pour l'Agriculture, l'Alimentation et l'Environnement (INRAE) **	France
2	Association de coordination technique agricole (ACTA) ***	France
3	Centre de coopération internationale en recherche agronomique pour le développement (CIRAD) **	France
4	University of Liverpool (ULIV) *	United Kingdom
5	Cardiff University (CU) *	United Kingdom
6	James Hutton Institute (HUT) **	United Kingdom
7	Alma Mater Studiorum - Università di Bologna (UNIBO) *	Italy
8	Aarhus Universitet (AU) *	Denmark
9	Eigen Vermogen van het Instituut voor Landbouw en Visserijonderzoek (EV-ILVO) **	Belgium
10	Research Institute of Organic Agriculture (FiBL) **	Switzerland
11	Stichting Wageningen Research (WR) *	Netherlands
12	Swedish University of Agricultural Sciences (SLU) *	Sweden
13	Southern Agriculture and Horticulture Organization (ZLTO) ***	Netherlands
14	European Forum of Farm Animal Breeders (EFFAB) ****	Netherlands
15	Fundacion Empresa Universidad Gallega (FEUGA) ****	Spain
16	Dierengezondheidszorg Vlaanderen (DGZ) ***	Belgium
17	INRAE Transfert (IT) ****	France

* Universities/veterinary schools

** Research institutes specialized in both fundamental and applied agricultural and veterinary sciences

*** Public and private advisory services Organisations

**** Knowledge transfer and Innovation organisations

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List of acronyms and abbreviations

AB – Antibiotic

AH - Anthelmintic

AM – Antimicrobial

AMR – Antimicrobial Resistance

AMU – Antimicrobial Use

CBA – Cost-benefit analysis

CEA – Cost Effectiveness Analysis

CIA – Critically Important Antibiotics

CS – Case Study

EC – European Commission

EFSA - European Food Standards Agency

EGGVP - European Group for Generic Veterinary Products

EMA - European Medicines Agency

ESVAC - European Surveillance of Veterinary Antimicrobial Consumption

EU – European Union

FAO - Food and Agricultural Organisation of the United Nations

FCR – Feed conversion ratio

LL – Living Labs

MS – Milestone

WHO – World Health Organisation

WOAH – World Organisation for Animal Health

Summary

The ROADMAP project aims to develop interventions/solutions for encouraging prudent antimicrobial use (AMU) in animal production. The objective of activities conducted under WP5 is to determine the costs of implementation and the impact on the critical outcomes required by the stakeholders across the food and drug supply chain using data collected by other work packages. The aim of this deliverable D5.4 was to provide **cost-effectiveness analyses and marginal abatement cost curves determined with associated data and data collection protocol.**

There was limited data for conducting a cost-benefit analysis on the strategies to reduce AMU in food-producing animals., which hampered the capacity to deliver the proposed product. As an alternative a scoping literature review on the impact of alternatives to AMs and intervention to reduce their usage in food-producing animals was conducted, alongside the development of a calculator to estimate the costs of implementing strategies to reduce AMU in such contexts. Additionally, and to further understand the poorly known key factors for the success of national-level policies to reduce AMU in livestock production and their socio-economic effects, a socio-economic assessment on the French Ecoantibio 1 programme. The report presents the results of such an evaluation, based on a qualitative survey conducted among the actors of the French pig production. The outcomes shed a light on the key factors for the success of these policies and their socio-economic effects.

1 Introduction

Like other chemical inputs, antimicrobials, thanks to their capability to control infectious diseases, were part of the green revolution, which allowed for a drastic increase in farm productivity and made food of animal origin more affordable (Bentley and Bennett 2003, Steinfeld and Gerber 2010, Pingali 2012). In swine production, antimicrobials are used in three circumstances: (i) in individual medicine to treat a sick animal, (ii) in collective medicine (to treat batches of animals) when a percentage of animals in the batch is sick (metaphylaxis), (iii) in prevention before the appearance of the disease, on all the animals of a batch on which the probability of disease appearance is considered high (prophylaxis). By treating or seeking to prevent the occurrence of certain diseases, antimicrobial use (AMU) respond to several challenges: (i) animal welfare, in the context of optimizing the quality of care, (ii) economics, since diseases impact food products value chain through change in quantity and quality, and (iii) public health, in the fight against contagious infectious diseases and particularly zoonoses (animal diseases that can be transmitted to humans) (Lhermie, Grohn et al. 2017). Although relatively effective and inexpensive products, their use is not risk-free. In the short term, the direct risks of using antimicrobials in livestock production for animals and/or consumers, associated with antimicrobial toxicity, overdose and/or presence of antimicrobial residues, are very low. In France, as in many countries, their market is regulated by the Public Health Code. This regulation sets maximum residue limits in food products of animal origin for all drugs used in livestock production, in order to guarantee food safety (LegiFrance 2021a, LegiFrance 2021b). For ensuring the above, a withdrawal period – time between the last administration of a veterinary medicine and the slaughter of the animal – is established according to the competent authorities (European Parliament and the Council of the European Union 2019). In addition, adverse effects reported by owners of animals who have been treated by antimicrobials are very rare (ANSES 2021). With the growing consciousness of the mid and long-term impact of antimicrobial misuse, present concerns are focused on the increased indirect risk of the selection of antimicrobial-resistant pathogens, leading to a progressive decrease in the effectiveness of antimicrobials in treating bacterial diseases.

Resistant bacteria can be transmitted to humans, either by direct animal-human contact, or via the environment, or via the food chain (Williams-Nguyen, Sallach et al. 2016). Public health costs due to antimicrobial resistance (AMR) take different forms, monetary and non-monetary. This resistance leads to increased lengths of hospital stay, greater morbidity and mortality, and increased costs of care. In 2019, the global number of deaths associated with antimicrobial-resistant bacteria was estimated at 4.95 million (3.62–6.57), which included 1.27 million (95% Uncertainty Interval 0.911–

1-71) deaths attributable to antimicrobial-resistant bacteria (Murray, Ikuta et al. 2022). According to the World Bank, by 2050, the yearly increase in healthcare cost in the public sector due to antimicrobial resistance can range from US\$300 billion to more than US\$1 trillion (Ahmad and Khan 2019). In France, recent studies estimate that infections with resistant bacteria represent around 140,000 cases, 5,500 deaths and a total cost of 290€ million per year (Touat, Opatowski et al. 2019). Globalisation and international trade also play a role in this emerging health concern, with food supply chains and transport routes offering the means to move the risk of disease due to resistant bacteria between regions and countries. This is particularly relevant considering the uneven national legislations regulating the use of antimicrobials in livestock production (Avraam, Lambrou et al. 2021).

Although the contribution of the use of antimicrobials in agriculture to antimicrobial resistance in human health is ultimately poorly quantified (Landers, Cohen et al. 2012, Singer and Williams-Nguyen 2014, Chang, Wang et al. 2015), the public health risk justifies that all agricultural sectors make an effort to reduce its use. As such, public policies aimed at reducing the use of antimicrobials in animal production have been put in place to mitigate this public health risk in many countries. For example, the European Parliament banned the use of antimicrobials as growth promoters in animal feed in 2000 (European Union 2003). Several countries have now set up plans to control antimicrobial resistance, which is also the subject of actions coordinated worldwide by the World Health Organization, the World Organisation for Animal Health, and the Organization for Food and Agriculture (FAO 2016, OIE 2016, World Health, Food et al. 2016).

In France, several regulatory and voluntary measures have been implemented. A moratorium to reduce the use of third and fourth generation cephalosporins, led by the French pig farmers and vicenarians, came into light in 2011 within the pig value chain, which agreed on using these antimicrobials solely at last resort (Hémonic, Chauvin et al. 2018). In 2012, the French government launched the five-year program Ecoantibio 1 programme that aimed at reducing the consumption of antimicrobials in livestock sectors by 25% (ANSES 2011). This plan is a voluntary programme set up on the initiative of the Ministry of Agriculture in 2012 (Ministère de l’Agriculture de la Pêche et de la Ruralité 2011). Many actors from the pharmaceutical system and the food system have been involved in this. Some recommendations made by the programme were juridically anchored in the so-called Future Law for Agriculture, Food and Forestry, which was enforced in January 2015 (Ministère de l’Agriculture de la Pêche et de la Ruralité 2014). Although not specifically targeting AMU, it has provided the legal basis for regulating the use of critically important antimicrobials. Noteworthy measures were the mandatory use of sensitivity tests before prescribing antimicrobials, their prescription only after clinical examination of the animals, and the ban of a certain type of discounts

by resellers. The Ecoantibio 1 plan was a great success, with a decrease in AMU by 35 % in 5 years. The swine sector was a heavy AMU user before the Ecoantibio 1 plan, and remains high at the end of the plan in spite of an important decrease. In 2018, 35% of the tonnage of antimicrobials sold by veterinary pharmaceutical laboratories were intended for pigs (around 167 tonnes), 29% for cattle and 18% for poultry (ANSES 2019). Overall, AMU in the pig sector fell by 47% over the period of 2010-2016, and the use of medicated premix plummeted (-74% over 2011-2018).

This rapid and massive reduction in use raises questions about its effects for the various stakeholders. If all things were kept equal, reducing or removing the use of antimicrobials in pig production could hamper farmers' ability to manage disease pressure, with an increase in morbidity and mortality affecting the productivity of the animals. Studies in the US have estimated the ban in the use of antimicrobials for growth promotion (AGP) in the swine sector to increase production costs and decrease net profits. In Denmark, a study led by a WHO panel has indicated similar findings resulting from the same policy, with net production costs per pig produced increasing 1.04€ (Laxminarayan, Van Boeckel et al. 2015). On the other hand, improved biosecurity and adequate and effective vaccination plans could replace AMU in pig production in a cost-effective manner, even with added labour costs (Dewulf, Joosten et al. 2022). Reducing AMU in pig production could also mean less income from their sales to veterinarians. If this is their main revenue stream, the impact would be substantial. Contrarily, moving away from antibiotic sales to increased farm advisory could mitigate the impact to the veterinary business.

The aim of this study is to carry out a retrospective assessment of the Ecoantibio 1 programme over its implementation period in the pig sector through a qualitative research approach, and evaluate its impact in stakeholders across the value chain. In this article, we present and discuss the results of semi-structured interviews, intended to collect information on 6 evaluative questions: (1) the effects of the program on the different actors (changes in practices, interplay between actors, structural effects); (2) effects on farm incomes; (3) effects on other supply chains; (4) acceptability and most influential measures; (5) effects on pig health; (6) and the effects of alternatives to antimicrobials.

2 Materials and Methods

2.1 Data collection

Semi-structured interviews were conducted, in order to collect information (i) that could provide explanations or factual elements on the role of the Ecoantibio 1 plan in reducing AMU in the sector swine and (ii) reveal indirect effects of the plan. Six blocks of questions were developed for the semi-structured interviews, with priority questions (presented below) and follow-up questions (see supplementary material).

Q.1: what were the effects of the Ecoantibio 1 programme on the various players in the sector? Do some benefit more than others, if so which ones, why and how? For example, is this the case for veterinarians (in terms of advice, consultation and sales) and sanitary defence groups?

Q.2: How does the Ecoantibio 1 programme act on the different types of costs and benefits of a pig farm?

Q.3: Has the application of the Ecoantibio 1 programme to the pig sector had positive or negative repercussions on the cattle and poultry sectors (for example in terms of purchasing substitutions)?

Q.4: Which measures of the Ecoantibio 1 programme have had the most positive or negative influences, by acting in what ways and on what?

Q.5: What were the consequences of the Ecoantibio 1 programme on the health and growth of pigs?

Q.6: Have alternative measures been taken to reduce AMU, for example the use of probiotics or other growth factors, biocontrol, health measures, etc.?

The data collection was carried out between December 2020 and March 2021, on a convenient sample of thirty-three participants, holding various positions in the sector. The interviews lasted between 24 and 90 minutes, for a total of 23 hours 10 minutes, and took place remotely (by videoconference or telephone). The interviews were recorded through Zoom and transcribed. Selected participants were contacted by phone or email to provide information on the rationale of the study. At the beginning of

the interview, participants were informed that the conversation would remain anonymous, and that any material leading to a potential identification of the individual would be removed from the analysis.

2.2 Data treatment

Verbatim interviews were manually transcribed. Responses were then analysed for themes and topic areas that are echoed by many respondents, as well as areas that they highlight as critical or most important. Text fragments were identified in relation with the 6 overarching questions. Triangulation principle was applied to ensure construction of coherent themes. A member checking was done by presenting the results during one stakeholder meeting, gathered by the French Ministry of Agriculture, as stipulated in the grant agreement funding the study.

3 Results & Discussion

3.1 Changes in farmers' practices

The Ecoantibio 1 plan has encouraged farmers to change their view of their farming practices, in favour of a more rational use of antimicrobials. Indeed, the psychological trigger of the actors in the field is a key lever for a sustainable change in farming practices.

The vaccination strategy is the main alternative used to limit the use of antimicrobials, but it started long before the start of the plan. During the Ecoantibio 1 plan, stakeholders reported that vaccination has mainly been developed for the respiratory axis (circovirus, PRRS), the digestive axis (colibacilli) and piglet edema, helping to improve health advice, among other things. Vaccines began replacing antimicrobials by playing a “patch” role, without considering all the risk factors. Moreover, it is often in the face of poor animal husbandry practices that vaccination is adopted. Even if the Ecoantibio 1 plan has been able to play an accelerating role in the spread of vaccination, it has settled into a dynamic already at work, of rising prices of medicated feed, reducing specialties available, and raising awareness among farmers.

Another practice for optimising the use of antimicrobials was highlighted during our investigation: that of the use of dosing pumps. A dosing pump is a farming tool that allows direct targeting of animals and application of the treatment dose for a health problem, by strongly limiting systematic treatment through feed. The dosing pumps were generally already installed before the implementation of the plan. According to a survey participant, about 3% of farmers would have equipped themselves during the period. However, the Ecoantibio 1 plan was able to play an accelerating role in their installation in post-weaning, and therefore in the prescription of the associated oral powders. The spread of pumps can also occur after discontinuation of the use of antimicrobials in food supplementation or following the appearance of new solutions and new products using pumps. Dosing pumps mainly play a role of “transitional safety measure” towards the discontinuation of medicated feed.

Developed by feed manufacturers, safe feeds have the role of strengthening the immune system of piglets during their first age. However, raw materials are generally replaced by cheap materials; the adaptation of piglets to these changes is often difficult, leading to digestive drifts. Some cooperatives have marketed secure feed with a low protein content, causing slower growth in piglets. This type of problem may have caused dissatisfaction among farmers or even a return to antimicrobials, but it is not a significant phenomenon over the period of the plan. These feed solutions were largely developed counter-current to the plan; they took place in a context of reduced use of antimicrobials, promoted

by an improvement in awareness and demand from groups in terms of specifications. Although farmers may perceive secure feed as less effective than antimicrobials, the increasingly limited use of antimicrobials has fostered the search for alternatives. Safe feeds have been more widely adopted in the phases of discontinuation of antimicrobial use, such as when stopping early colistin supplementation. During the Ecoantibio 1 plan, a significant drop in the quantity and number of medicated feed specialties was observed, which may be correlated with the implementation of the plan. However, the reduction in the use of medicated feed may have encountered certain difficulties, in particular because this type of supplementation was integrated into farming practices.

The Ecoantibio 1 plan has helped to revise these farming practices and put zootechnicians back at the centre of discussions on risk management. Even if part of an ongoing dynamic, zootechnicians are increasingly committed to the reduction on the use of antimicrobials, through the adoption of good farming practices and prophylactic measures. Given the multifactorial nature of health problems, it is possible to address them upstream through the management of zootechnical factors. However, economic factors must also be taken into account; for example, reducing the density of animals in a building improves welfare and can limit the spread of disease, but handling costs are then higher (Jones, Grace et al. 2013, Schodl, Wiesauer et al. 2021, Hayek 2022). Among the zootechnical measures, a greater weight of piglets at weaning makes it possible to limit digestive problems, but too much time spent in the weaning room can also have significant impacts on technical and economic performance.

Biosafety has not been placed at the heart of the plan, but it is an essential tool for achieving a sustainable reduction in the use of antimicrobials. Cleaning and disinfection, ventilation and loading must be put at the centre of the sanitary conduct, among others. However, too much investment in air filtration and improving pig comfort may weaken their immune system.

Herbal medicine is probably developed; but these products do not have any Marketing Authorization (AMM), which makes it difficult to quantify the flows intended for them and there is little information on this subject. Even if the demand increases among farmers, the lack of control remains in terms of safety and effectiveness. Herbal medicine is generally used as an adjunct to vaccination, to regulate the intestinal flora for example. It is then not a question of a pure substitution, but of a complement.

3.2 Structural transformations induced by the plan

The decline in the use of antimicrobials is generally considered to be the result of a collective approach between food manufacturers, farmers and veterinarians. Thanks to the financing of projects, the plan has promoted better veterinary supervision in the event of the occurrence of a health crisis.

Some stakeholders mention that the issue of the reduction in the use of antimicrobials is not the reduction in quantities but, above all, veterinary practice, as well as the improvement of animal welfare and health. The logic of administering medicinal inputs by default has gradually shifted towards responsible veterinary practice. Generally, the farmer places great trust in the veterinarian, who plays the role of preventive health adviser. These two stakeholders play an important role in responding to public health issues. The relationship between veterinarians and farmers has not fundamentally changed, although some stakeholders in the pig industry believe that their bond has been strengthened. This observation is even truer in farms where the objective was already to reduce the use of antimicrobials before the plan was implemented. In the pig sector, farmers did not question the role of the veterinarian because he was generally perceived as being at the initiative of stopping supplementation.

When it comes to antimicrobial usage, farmers can be divided into two categories: those willing to change their antimicrobial usage habits, and those more reluctant to do so (often farmers at the end of their career). Initially, the veterinarians accompanied farmers within the first category. Then, the snowball effect involved most farmers in the dynamic towards reduced antimicrobial usage. The last remaining in the second category are usually those with poor technical management of their post-weaning room. To foster the reduction in the use of antimicrobials, veterinarians adopt several strategies: they reassure farmers by providing guarantees, or they refuse to sign prescriptions for the most reluctant, for example. A small pool of farmers has reportedly maintained their practices, in which case some veterinarians may choose to refuse to sign prescriptions.

For feed manufacturers, the development of medicated feed leads to a stock break in manufacturing, as well as a risk of pollution of the production plants. It is therefore not desirable on their part to produce medicated feed; it is a service provided to farmers. The relationship between veterinarians and feed mill technicians seems to be the most negatively impacted by the plan and, more broadly, by the decline in the use of antimicrobials. However, the turnover and the pedagogy made it possible to accompany the changes in a gentle manner.

The arrival of antimicrobial-free product labelling has accelerated the decline in use, in particular thanks to Cooperl and Fleury Michon. Even if a hesitation period was observed at the start due to

poorly applied and costly solutions, products with a "pigs without antimicrobials" labelling finally served as buffer in the face of increasingly demand on the consumers end. Generally, however, the specifications do not impose a definitive discontinuation of antimicrobials, as a farmer retains his freedom to treat animals if their health situation deteriorates.

3.3 Economic effects of the plan

Most actors agree that the Ecoantibio 1 plan only had a very moderate economic impact and, at most, transitory. According to those surveyed, the plan did not have a significant impact on the income of farmers. Farmers highlight that other elements, such as building governance, feeding and breeding management are much more impactful. The direct costs as well as the indirect costs, such as the workload of farmers, were only slightly affected, subject to compliance with preventive measures, such as biosecurity or vaccination strategies. "Safe" feeds sold by feed manufacturers may have represented an additional cost. However, these feeds with higher nutritional value limit digestive problems and therefore the associated expenses. Ultimately, the Ecoantibio 1 plan had no significant impact on pig growth. When a reduction in productivity has been observed, the causes are multifactorial. For example, safe feeds may have led to a reduction in the size of piglets when they contain too low a protein level. A cooperative actor reports that during de-medication after 2012, the average daily gain fell from 810 to 801 grams, to return to its initial value today. The fattening loss rate was 3.2%. Some of the farmers who noticed a decline in growth wanted to return to medicated feed, but most preferred to maintain the change in practice. These have mostly seen compensatory growth during the fattening phase.

The veterinarians do not declare having encountered any real economic difficulties after the implementation of the plan. While the drop in revenue generated by curative treatments (sale of antimicrobials) is real, it was partly offset by the sale of preventive products (vaccines, alternatives, diagnostics) over the period of the plan. However, some independent veterinarians have seen their profitability erode, in particular due to the fact that preventive drugs are also marketed by farmers' groups. In addition, some veterinary groups who have seen their income related to antimicrobials decrease have compensated by asking farmers to participate in livestock health assessments. As for the reduction in the prescription of medicated feed, it often did not affect the veterinary activity as it is feed manufacturers who mostly deal with its trade. Faced with this decrease, veterinary structures sold more oral powders intended for dosing pumps. Some practicing veterinarians have stated that

the decrease in turnover per farmer is an opportunity to free up more time for other farmers, in order to balance the overall turnover.

There was no significant economic impact for medicated feed manufacturers. It should be noted that the number of specialties has dropped. Supplementation with medicated feed is considered as a service provided to farmers, even if medicated feed leads to stock breaks in manufacturing, as well as risks of pollution at the factory level.

Although the economic effects for consumers and distributors are beyond our study, it is interesting to note that during the plan, several specifications were drawn up, such as the "pig confidence"- U system and the labels "antimicrobial-free after 42 days" and "without medicated feed".

3.4 Success factors of the Ecoantibio 1 plan

In this section, we highlight the relevant facts which seem to have led, according to the declarations of the people surveyed, to the success of the Ecoantibio 1 plan, in its component of quantitative reduction in antimicrobial use, as well as the broad support of the stakeholders.

3.4.1 Direct State investment and coordination role

Two million euros are allocated per year by the Ministry of Agriculture to research projects and actions aimed at research, knowledge transfer and communication (Figure 1). This allows plan's partners to implement tools such as good practice guides, smartphone applications (Porcisante, GVET) and regulations to prohibit the use of certain critical antimicrobials.

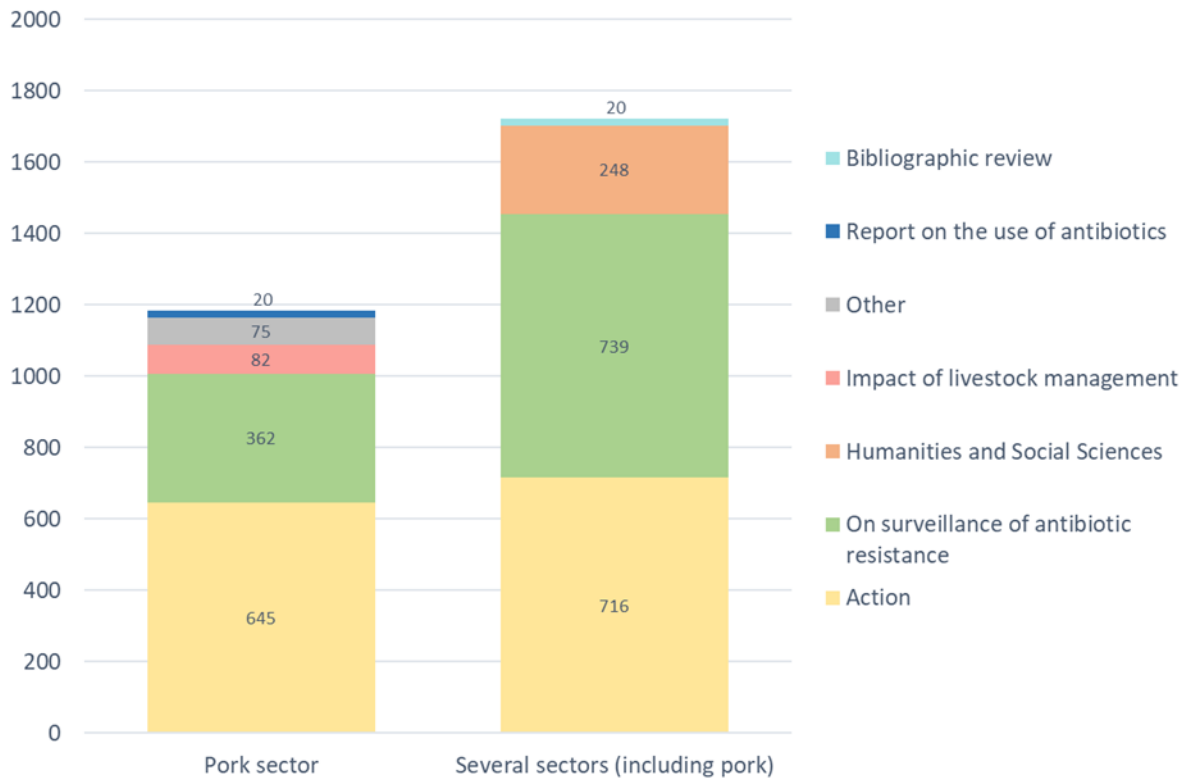


Figure 1. Budgets allocated to projects financed by the Ministry of Agriculture and Food for the Ecoantibio 1 plan (x €1000).

Trainings and meetings between stakeholders seem to have played a role in the effectiveness of the plan. An Ecoantibio module is included in the training intended for veterinarians for the sanitary control of farms. In order to develop new non-critical antimicrobials, meetings have been organized by the Syndicate of the Veterinary Medicines Industry (SIMV) to encourage public-private partnerships. In addition, the annual conferences organized by ANSES helped to explain the views of the stakeholders present on the topics of antimicrobial resistance, which has now become central to the work of the veterinary profession. Notwithstanding the ability of private actors to support the change in the practices of farmers, it clearly appears, in our study, that the State plays a key coordinating role. This role had already been highlighted by Ducrot et al., (2019)(Ducrot, Adam et al. 2019), who had also described the State in its different roles –regulatory power, incentive power, and coordinating power.

3.4.2 Dynamics in place

The Ecoantibio 1 plan was implemented when a dynamic was already largely at work around a sanitary framework: reduction in the use of antimicrobials, awareness, implementation of specific practices by groups of farmers, improving animal welfare and health.

The use of alternatives to antimicrobials was already widespread before the plan was implemented. Historical solutions to limit the use of antimicrobials, such as the implementation of biosecurity or the adjustment of the nutritional quality of feeds have been adopted at a moderate pace, for reasons of economic balance between the cost of antimicrobials and the cost of the measures. Since 2011, ahead of the plan, certain veterinary structures have offered farmers a first-line approach without antimicrobials before considering collective treatment. Faced with a gradual increase in the prices of medicinal premixes and more generally of antimicrobials, as well as a drop in the number of specialties available, pharmaceutical companies have developed their vaccine portfolio. For a sustainable change in practices, and an effective reduction in the use of antimicrobials, the Ecoantibio 1 plan has been able to contribute to strengthening the role of veterinarians as health and zootechnical advisers and to encouraging farmers to change their practices.

In addition to the Ecoantibio 1 plan, there are other factors that explain its success. Indeed, regulatory efforts from the public sector (ban the use of growth promoters in animal feed in Europe in 2006) and initiatives from private sector (prudent use of third and fourth generation cephalosporins in 2010) were already in place before 2012 (Table 1).

Table 1. Private initiatives and public policies governing the use of antimicrobials in France

Date	Initiative/Policy
1st January 2006	application of the ban on the use of growth promoters in animal feed (European regulations).
24th January 2007	the Riaucourt ruling of the Council of State reframes the practice of veterinary pharmacy, by prohibiting veterinarians employed by groups of farmers from selling antimicrobials. In response to this ruling, most veterinarians left the groups to join SELAS ¹ , in order to continue to provide comprehensive services to farmers who are members of cooperatives.
1st July 2010	the moratorium on the ban on third and fourth generation cephalosporins comes into force for the pig sector.

Date	Initiative/Policy
25 th October 2012	the prescription circuit is modified, making it more complex and contributing to the reduction in the use of medicated feed.
September 2012	the <i>Cooperl</i> 's farmers launched its production of whole males; this then represented 4% of slaughtered carcasses (10% in 2014 and 12% in 2016). However, no studies exist on the effects of castration on the health of pigs.
January 2014	part of the CASDAR ² budget (130 million euros in total) for the new CAP ³ reform is used for projects aimed at reducing the use of antimicrobials in the pig industry. However, this concerns only one or two research projects
13 th October 2014	The Future Law for Agriculture prohibits laboratories from back discounting on antimicrobials; all customers must now pay the same price
June 2014	<i>Cooperl</i> markets “pork without antimicrobials”.
16 th March 2016	the decree on critical antimicrobials comes into effect. Drugs containing one or more critical antimicrobials are then prohibited for preventive use
June 2016	the group of European Medicines Agency experts AMEG ⁴ chooses not to prohibit the use of colistin for food-producing species, in order to avoid increasing pressure on critical antimicrobials (c3g ⁵ , c4g ⁶ , fluoroquinolones). The group of experts has set a European objective of reducing use by 65% over a period of three to four years.

¹ SELAS: Private practice company by Simplified Action. SELAS veterinarians are former employees of groups of farmers. It was in 2007 that the Riaucourt rulling of the Council of State prohibited these veterinarians from practicing veterinary pharmacy, in the case where the drugs were bought and/or sold by the group and not by the prescribing veterinarian ² CASDAR: Agricultural and Rural Development Special Account ³ CAP: Common Agricultural Policy ⁴ AMEG: Antimicrobial Advice Ad Hoc Expert Group (AMEG) ⁵ Third generation cephalosporin ⁶ Forth generation cephalosporin

Stakeholders came together when ANSES reported the emergence of resistance to third- and fourth-generation cephalosporins in human medicine. By creating a surveillance network for resistant bacteria of animal origin in the 1990s, and setting up the Inaporc panel in the 2010s, the pig industry and ANSES have been able to regularly observe the progress made. Some agricultural unions report

that the decline in antimicrobial consumption began before the plan, with a significant shift in the purpose of their use - from 70% curative to 30% preventive in the years 1990-2000 to 70% preventive to 30% curative in the 2010s.

The reduction in the use of antimicrobials is the result of a collective approach, combining farmers and veterinarians in the field. Nevertheless, two groups of farmers can be distinguished with regards to antimicrobial usage: those more willing to change their practices and those more fearful. Overall, the veterinarians supported the former, from which a snowball effect converted the latter. The consistency of the responses of the people surveyed, who almost unanimously mentioned this dynamic, echoes the notion of trajectory of change, developed by Fortané et al. (2015)(Fortané, Bonnet-Beaugrand et al. 2015). These authors have shown the importance of networks or economic and technical objectives in shaping trajectories of change. The role of actors who provide farmers with diversified resources in terms of methods and knowledge also seemed central to them.

Policies related to the plan have also contributed significantly to the decline in the use of antimicrobials, such as the moratorium on the latest generation cephalosporins (2010), the modification of the prescription circuit (2012), the Future Law for Agriculture (2014) and the the decree on critical antimicrobials (2016). The moratorium on latest-generation cephalosporins, for example, led to a reduction in pig exposure of more than 60% between 2010 and 2012, while the number of growing pigs treated fell by 73.3% over the same period (ANSES 2013). Other private initiatives, such as the production of whole males or the production of antimicrobial-free pigs by Cooperl, have contributed to reducing the use of antimicrobials. For example, Cooperl aimed for the share of animals raised without antimicrobials to reach 10% of the cooperative's production in 2015, with a steady increase in the following years (Process alimentaire 2014). Several television stories, such as "Assiette tous risque" broadcast on France 3 in 2014, have also contributed to the decline in use. The plan was then able to benefit from the built momentum and from the awareness of the stakeholders. Despite some reluctance at the announcement of the quantified objectives of the plan, livestock professionals and veterinarians have been helpful and constructive in applying the reduction in the use of antimicrobials. The success of the plan is the responsibility of each stakeholder, thanks to communication and training.

3.4.3 Frail or transitory technical and economic effects

The technical effects of the plan remain limited, as they were added to the initiatives taken previously in terms of vaccination strategy, feed, zootechnics, installation of dosing pumps and commercial labelling of products. Between 2012 and 2016, avoided the use of antimicrobials, but was mainly adopted to counterbalance poor farming practices. Several vaccines have been developed on the respiratory and digestive axes and on piglet edema and several specific practices have been drawn up by producer groups. The quantity of medicated feed and the number of specialties fell ahead of the plan. Farming practices were revised and zootechnicians was placed back at the center of risk management.

The economic effects of the plan remain weak concerning the income of farmers, veterinarians and manufacturers of medicated feed. It would seem that the insurance role of antimicrobials has been offset by the implementation of a vaccine strategy at an equivalent cost. Our results are consistent with those of Collineau et al. (2017), who highlighted the possibility of reducing the use of antimicrobials by cost-efficiently implementing biosecurity and vaccination practices (Collineau, Rojo-Gimeno et al. 2017). Similarly, the IFIP indicates that the drop in the use of antimicrobials does not seem to have deteriorated the technical and economic indicators of pig farmers (IFIP 2021).

4 Conclusions

This retrospective evaluation addressed the need for information on the socio-economic, individual and structural effects of the Ecoantibio 1 plan on the French pig sector. It is an original approach because, to date, there has been no socioeconomic evaluation of public policies to reduce the use of antimicrobials in France. The socio-economic impacts of the Ecoantibio 1 plan appear moderate, both in terms of changes in practices, structural transformations and economic effects. The plan is part of a professional dynamic, initiated by other public policies and private initiatives. From a technical point of view, most of the alternatives to antimicrobials existed before the implementation of the plan and were being used. Relations between stakeholders in the pig industry have been little impacted by the plan or have been strengthened, so no overall negative impacts were detected.

A limitation of the study was a lack of quantitative data. Therefore, as this assessment was based largely on qualitative interviews with stakeholders in the pork industry, our results must be extrapolated with caution. Even if the collection of qualitative data is not exhaustive, it was based on the players a priori most impacted by the Ecoantibio 1 plan. The specific economic impacts of the

Ecoantibio 1 plan remain difficult to estimate, because they are confounded by other initiatives and changes in the pork sector. In order to have relevant and quantifiable indicators for conducting retrospective analyses, the authors recommend including a reflection on the evaluation of their effects when designing public policies to reduce the use of antimicrobials.

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6 Delays and contingency plan

As outlined throughout the project, the SARS-Cov-2 pandemic made the development of the activities with LL and CS difficult. This made empirical data required by WP5 unavailable. A contingency plan was outlined and performed accordingly – a SLR was conducted and a cost-calculator developed. Additionally, a retrospective socio-economic assessment of the Ecoantibio 1 programme was conducted.

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