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Reduction of antimicrobial use in the monogastric sector: progress and prospects

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■ **Antimicrobial use in the monogastric sector has fallen sharply in recent years. This article analyses how this was achieved in France, the actions taken and the results obtained, and outlines the prospects for the future.**

Introduction

Faced with the development of antimicrobial resistance, major efforts have been made over the past ten years in France to optimise the use of antimicrobials in the livestock sector. A previous article (David *et al.*, 2019) discussed the situation in the French cattle industry. In monogastric livestock (pigs, poultry and rabbits), indicators used to monitor veterinarian drug sales show that animal exposure to antimicrobials increased up to the mid-2000s (Anses, 2021a). In response to this rise, health and animal stakeholders mobilised, undertaking a series of coordinated actions within the framework of the first EcoAntibio plan (2012-2017).[1] These led to a massive reduction in the use of antimicrobials across production sectors. The plan's target of reducing antimicrobial use by 25% within five years was thus largely exceeded. The second EcoAntibio plan (EcoAntibio 2, 2017-2021)[2] encouraged the continuation of these activities to sustain the progress made, with a particular focus on certain important antimicrobials in human health.

Monogastric species are mainly reared in standardised intensive production systems, in which the use of antimicrobials once was an effective tool for controlling common livestock diseases, especially during delicate phases (e.g. chick settling or piglet weaning). In the past, antimicrobials were used regularly in a metaphylactic approach (treatment of the entire batch of animals when a few individuals are ill), or even prophylactically (treatment as a preventive measure, during a risk period, for diseases occurring at a specific age and on a recurring basis on certain farms). Changing this vision of antimicrobial use would have to address certain technical constraints (ageing buildings), economic constraints (cost-benefit ratio of antimicrobial therapy and alternative approaches), and the weight of habits.

Changing practices requires the removal of obstacles and the evolution, in parallel with the technical progress achieved, of the perceptions of farmers and their technical-sanitary supervisors regarding animal health, their understanding of antimicrobial therapy and its impact, and their apprehensions

1 https://agriculture.gouv.fr/plan-ecoantibio-2012-2017-lutte-contre-lantibioresistance
2 https://agriculture.gouv.fr/le-plan-ecoantibio-2-2017-2021

about eliminating antimicrobial use, which is considered as a kind of "safety insurance". Nevertheless, the structure of these organised sectors means that incentives and actions undertaken at the level of the entire sector or of production organisations can have an effective and rapid impact.

The aim of this article is to review the use and evolution of antimicrobials in the monogastric sector in France, to present the efforts undertaken and the different approaches developed since the 2000s in terms of the prevention of health problems and evolution of antimicrobial therapy practices, and to consider the prospects for the future.

1. Evolution of antimicrobial use in the monogastric sector

■ 1.1. National monitoring of antimicrobial sales

The tonnage of antimicrobials sold (Anses, 2021a) has decreased considerably since 1999, when the monitoring of antimicrobial sales based on manufacturers' declarations first began. However, these tonnages do not accurately reflect antimicrobial use levels. To monitor usage accurately, it is necessary to consider both the animals' exposure to antimicrobials, taking into account the dosage and duration of administration of the different antimicrobials, and the evolution of the animal population over time. The ALEA (Animal Level of Exposure to Antimicrobials) indicator, which relates the live weight of treated animals to that of all animals – the potentially exposed population – is the most frequently used exposure indicator in France. Between 2011 and 2020, it decreased, all classes of antimicrobials combined, by 56% for pigs, 64% for poultry and 40% for rabbits. Pigs and poultry are mainly treated orally. The use of premixed drugs is decreasing and the ALEA of this pharmaceutical form had decreased by 78%, 69% and 55% in 2020 compared to 2011 for pigs, poultry and rabbits, respectively (Anses, 2021a).

The classes of antimicrobials used and the associated changes differ between species. According to 2020 ALEA values, pigs were treated mainly with tetracyclines, penicillins, polymyxins, followed by macrolides, sulphonamides and trimethoprim. Poultry were treated mainly with polymyxins, penicillins and tetracyclines, then sulphonamides and trimethoprim. Rabbits were treated mainly with tetracyclines, sulphonamides and trimethoprim, followed by aminoglycosides, polypeptides and pleuromutilines.

Exposure to critically important antimicrobials – meaning ones used as a last resort in the treatment of certain infectious diseases in humans – decreased dramatically compared to 2013 data. In 2020, for fluoroquinolones, the decrease was 92% in pigs and 76% in poultry, and for 3rd and 4th generation cephalosporins (not authorised for poultry), the decrease was 96% in pigs. Exposure to colistin, which is not listed as a critically important antimicrobial but is subject to enhanced monitoring, decreased by 75% for pigs and 63% for poultry compared to the average exposure calculated for 2014 and 2015. The objective set by the 2017-2021 EcoAntibio 2 plan to reduce exposure to this antimicrobial by 50% over five years therefore was exceeded in the pig and poultry sectors, which are the main users.

■ 1.2 Measuring antimicrobial use

Different systems can be used to complete the overview obtained from monitoring antimicrobial sales (Anses, 2021a); these include studying data at a finer scale (farms) and adding further information (physiological stage, reason for use, etc.). In addition to monitoring sales, three types of systems can be identified in France (Table 1).

The panels and observatories run by interprofessional organisations and technical institutes, and initiated with the assistance of the French Agency for Food, Environmental and Occupational Health and Safety (ANSES), aim to provide reference data on antimicrobial use based on a sample of farms on which various exposure indicators are calculated using a standardized method. The INAPORC panel (Hémonic *et al.*, 2019) measures antimicrobial use on a representative sample of randomly selected pig farms. The data, collected periodically (in 2010, 2013, 2016, 2019), make it possible to describe changes in antimicrobial use by molecule, pharmaceutical form, physiological stage, target disease and type of treatment (preventive, metaphylactic, curative). The RefA^{2}vi network (Rousset *et al.*, 2019) has similar objectives for the poultry industry (turkeys and broilers, all types of production combined). In 2018, a first pilot phase of data collection was carried out with 11 voluntary production organisations. In Label Rouge poultry production, a collection system initiated by SYNALAF (*Syndicat National des Labels Avicoles de France*) provides a quarterly indicator of the frequency of antimicrobial use, distinguishing between the different production phases and certain families of antimicrobials. Since 2010, the rabbit industry has been equipped with a tool to quantitatively monitor antimicrobial use through the recording of IFTAs (Index of

Table 1. ***Devices for measuring antimicrobial use in livestock.***

	Forces	Weaknesses
ANSES-ANMV – sales data provided by the pharmaceutical industry	Exhaustiveness of the data collected Homogeneity of the indicators calculated (comparability) Age and permanence of the system Possible comparison on a European scale (ESVAC)	Low level of detail Aggregation of different species and physiological stages Sales data (may differ from actual use)
Panels and observatories	Representativeness Homogeneity of calculated indicators (comparability) Details of uses	One-off view (quarterly, annual, etc.) Variable membership of farmers or producer organisations Data collection not fully automated and tedious
Studies, one-off surveys	Representativeness Detail of uses Allows cross-referencing of antimicrobial uses and explanatory variables	Point-in-time view (cross-sectional or limited to a given period of time) Tedious data collection with little or no automation
Livestock monitoring software	Continuous collection of data from veterinary prescriptions and/or from the register of treatments in the farm Details of uses Interface for "piloting" purposes, usable by farmers, technicians and veterinarians	Heterogeneous calculation methods the indicators Variable adherence of the actors Accessibility of the data

Frequency of Antimicrobial Treatment) for each rabbit flock (Fortun-Lamothe *et al.,* 2011) under a national plan initiated by CLIPP (the French Interprofessional Committee for Broiler Rabbits).

Specific studies and surveys, based on data collected on farms or from veterinarians, make it possible to obtain a detailed analysis of antimicrobial use and to study the effect of different determinants of this use. Under the MINAPIG project, the study of antimicrobial use on 227 pig farms in four European countries showed that many factors are associated with use, and that it is difficult to identify generic explanatory elements. One of the main determinants was the occurrence of clinical respiratory or nervous signs in growing pigs (post-weaning and fattening) (Collineau *et al*., 2018).

Software for monitoring use in livestock farming enables farmers and veterinarians to continuously monitor the use of veterinary medicines (antimicrobials, but also vaccines, deworming agents, etc.) in real time. There are many purely private initiatives to collect data, either from veterinarians based on their prescriptions (INDICAVET, COOPERL, EVELUP, Certiferme software for the Michel Group, for example) or from farmers based on the record of the treatments they have administered. The GVET (*Gestion des traitements vétérinaires*) approach, developed for pig farming by IFIP, ANSES and ISAGRI, is a computerised version of the register of treatments administered on the farm (quantities of treatment administered, dates, reasons and animals concerned) which aims to replace the paper-based system.

■ 1.3. Variability of antimicrobial use in livestock

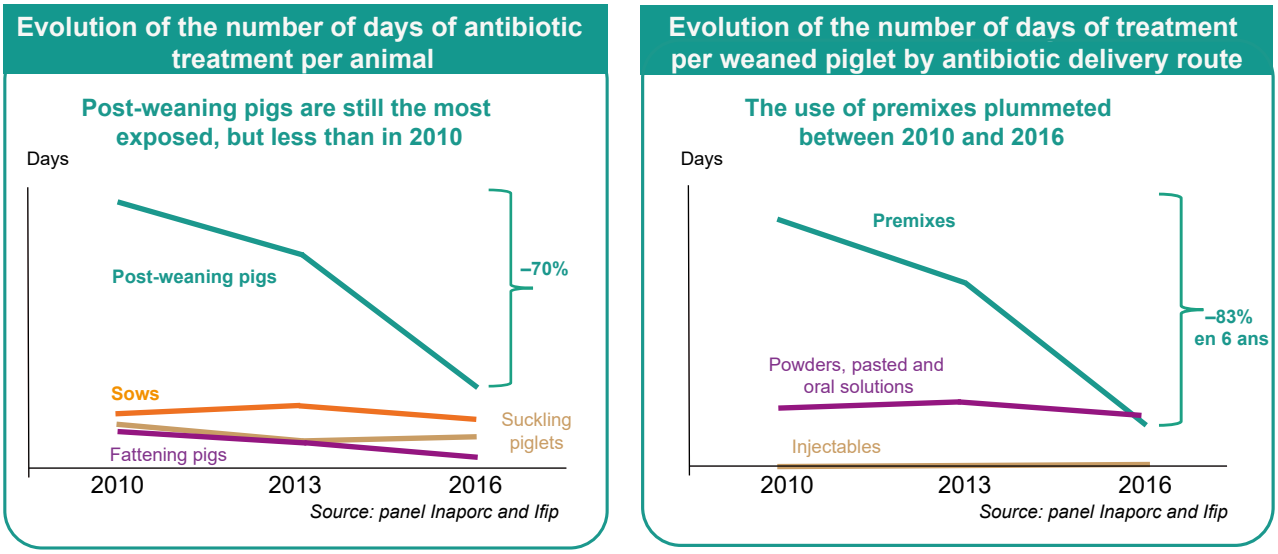
a. Poultry production: diversity of evolutionary paths between species and productions

The French poultry industry is characterised by a wide variety of species (broilers, turkeys, laying hens, palmipeds, guinea fowl, pigeons, quails, etc.) and production methods (operating or not under a quality label, providing or not access outdoors). One of the main limitations of the ANSES-ANMV sales monitoring data is the aggregation of data concerning all these species and production methods in the same "poultry" category. In addition, data from the RefA^{2}vi observatory show a difference in exposure between the two species mainly raised for meat (chicken and turkey) (RefA2vi, 2019).

In broiler turkey, a pharmacoepidemiological study (Vove, 2019) conducted on 1,209 batches between January 2015 and December 2017 reveals that, regardless of the type of production (standard, certified baby), all batches studied received at least one antimicrobial treatment. The most commonly used families of antimicrobials were the betalactams (amoxicillin, ampicillin and penicillin), cyclins and polypeptides (colistin). Exposure to colistin dropped considerably, with the percentage of batches treated falling from 79% to 39% in three years.

In standard broiler chicken, the RefA^{2}vi observatory, considering data

Figure 1. ***Evolution of antimicrobial exposure in pigs (Source: INAPORC Panel, 143 farms).***



equivalent to 37% of broiler production, found a reduction in antimicrobial exposure of 30% to 32% between 2018 and 2020 depending on the indicators used (nDDkg[3] and nCDkg). In 2020, penicillins were the most used antimicrobials, polypetides represented 10% of total uses (mainly colistin) and fluoroquinolones 2%. Furthermore, antimicrobial prescription data collected in two producer organisations in the Grand Ouest region of France show a change in the age profile of treatment (Jacque, 2021, personal communication). Between 2013 and 2016, there was a clear decrease in very early treatments (D0-D1), which fell from 17% to 9% of treatments administered.

b. Pig production: marked differences between physiological stages

In pig production, it is widely recognised that antimicrobial use is not evenly distributed between the different production stages (Sjölund *et al.*, 2016, Hémonic *et al.*, 2019). Data from the INAPORC panel (Figure 1) show how the trajectories of usage change differ between physiological stages (Hémonic *et al.*, 2019). In 2016, post-weaning piglets remained the physiological stage using the most antimicrobials (47% of total treatment days on the farm), mainly for digestive problems (52% of total piglet exposure time) ahead of respiratory problems (20% of total). However, the overall use of antimicrobials in this segment of production decreased by 70% between 2010 and 2016, with a more pronounced evolution between 2013 and 2016 (–63%) than between 2010 and 2013 (–19%). The most striking result is the sharp decline in the use of premixes, particularly colistin-based premixes. The rate of farms using premixes fell from 84% to 32% between 2010 and 2016, and the exposure time of piglets was reduced by 83%. This is partly due to the European Commission's decision in March 2015 to remove the indications for preventive use of oral colistin and to limit treatments to seven days (EMA, 2015). This reduction in colistin premixes has not resulted in a shift in use to other oral routes, nor to other digestive antimicrobials. Compensation with a zinc oxide premix, authorised in France in January 2016 and then banned again, was only slightly widespread (16% of farms concerned). This result suggests that digestive problems were managed by other preventive measures, such as vaccination, feeding, biosecurity or other aspects of farm management.

Overall antimicrobial use in fattening pigs also decreased by 71% between 2010 and 2016, with a more pronounced decrease between 2013 and 2016 than between 2010 and 2013 (Hémonic *et al.*, 2019). This resulted in a decrease in the exposure times per animal and the percentage of farms affected by each type of treatment. Respiratory disorders were the most common reason for treatment.

In farrowing sows, which accounted for 29% of total antimicrobial exposure time on farms in 2016 (Hémonic *et al.*, 2019), overall antimicrobial use decreased by 7% between 2010 and 2016. The major reason for use was urogenital disorders. Use also decreased in piglets in the maternity ward (28% decrease between 2010 and 2016). This decrease took place over the period 2010 – 2013, with use remaining stable

3 nDDkg and nCDkg are indicators of antimicrobial exposure: nDDkg is the live weight treated-day, representing the recommended amount of active ingredient per day of treatment of one kilo of live weight; nCDkg is the live weight treated for one treatment, which incorporates the duration of treatment.

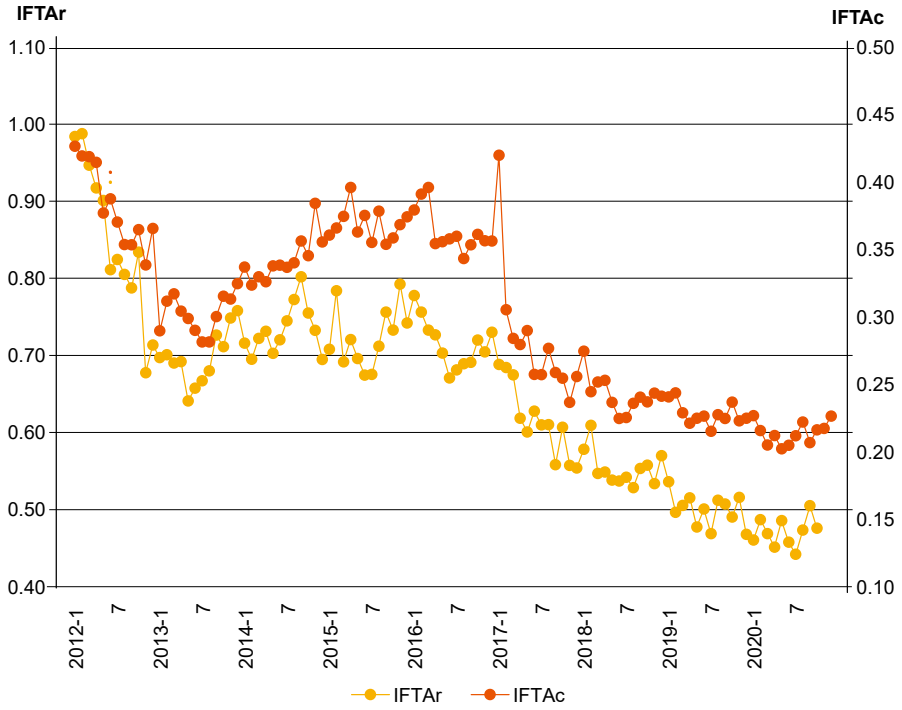
between 2013 and 2016 (+1%). For sows and piglets in the maternity ward, the drop in the use of critically important antimicrobials (CIA) was very clear over six years (respectively -80% and -83% for fluoroquinolones and -100% and -98% for last generation cephalosporins). Two reasons are the moratorium established by veterinarians and breeders in 2010 for cephalosporins (Verliat *et al.*, 2021), followed by the decree issued in 2016 extending the restriction of use to other CIAs such as fluoroquinolones (Decree n° 2016-317). For piglets in the maternity ward, the other major result is the cessation of the administration of antimicrobial premixes, which was a risky practice in terms of antimicrobial underdosing due to the small quantities of solid "first age" feed ingested by these animals.

c. Rabbit production: initial use differs little from one farm to another

Most rabbit farms in France are farrow-to-finish. A study carried out in 2009 and 2010 on 113 farms (Chauvin *et al.*, 2011) found that female rabbits were more exposed to antimicrobials than male rabbits, with a mainly respiratory target for female rabbits and a mainly digestive target for male rabbits – the period around weaning being a critical stage for the latter. The same study revealed a high initial use, but also a clear decrease between the two years of the study: a 15% decrease in the amount of active substances was noted between 2009 and 2010 on 91 farms.

Since this study, sector professionals have been monitoring IFTA indicators to measure the use of antimicrobials on breeding animals (IFTAr) and on growing animals (IFTAc). These indicators are calculated from the treatments given to rabbits regardless of whether the products' marketing authorisation is for rabbits or for other species. The curves (Figure 2) show a 47% drop in IFTAr and 44% drop in IFTAc between 2012 and 2020. A clear plateau is observed between 2014 and 2017, which can be linked to a very unfavourable sanitary context (epizootic of Viral Haemorrhagic Disease due to a new viral genotype); however, the drop resumes after 2017. It should be noted, however, that the exposure of rabbits to antimicrobials has remained stable for several years according to the ALEA indicator used by ANMV (Anses, 2021a) on a national scale, calculated on sales declared by the pharmaceutical laboratories.

Figure 2. ***Evolution of antimicrobial use in rabbits between 2012 and 2020 (IFTAr for breeding females and IFTAc for growing animals) (ITAVI-CLIPP data).***



2. Drivers of change in antimicrobial use: the role of regulation and private initiatives

Sociological studies (Ducrot *et al.*, 2018) have shown that different personal contexts (e.g. succession, health problems on the farm, health problems in the family) lead farmers to think differently about how and when to use antimicrobials on their farms. A personal decision is primarily responsible for initiating a process of change. Nevertheless, several factors have been instrumental in facilitating this evolution in thoughts and actions over recent years.

Since 2012, the EcoAntibio plans have created an arena in which all stakeholders concerned by antimicrobial use in livestock farming are engaged. The obligation to fight antimicrobial resistance in animal production has enabled broad consultation between stakeholders. However, collective initiatives already had begun even before these plans were launched. For example, the rabbit industry took collective action in 2011 (launch of an interprofessional plan for rational medication, signing of an interprofessional charter by all the players in the industry), with a commitment to do everything possible to reduce the consumption of antimicrobials, set up monitoring indicators, adopt the recommended good usage practices, and implement technical progress actions.

This approach was well received by technical advisors, which then led to a collective mobilisation of the farmers.

At the same time, regulations have been tightened on certain points (Rostang *et al.,* 2022, this issue), particularly concerning the rules for the use of medicated feed, critical antimicrobials and colistin. In the pig sector, the evolution of regulations on critical antimicrobials was preceded by a joint initiative in 2010 by farmers and veterinarians for a "moratorium on the use of C3G and C4G" (3rd and 4th generation cephalosporins), an action that was decisive in changing behaviours, especially regarding metaphylactic use in "key" phases of rearing and preventive use for arthritis in suckling piglets (Verliat *et al.,* 2021).

Lastly, in response to consumer demand, downstream actors -- supermarkets and certain international restaurant chains – have exerted strong pressure since the early 2010s to reduce the use of antimicrobials in livestock farming (Ducrot *et al.,* 2019; Hercule and Rousset, 2021). In response to these developments and as part of a competitive positioning approach, "antimicrobial-free" specifications and value chains have multiplied (Roguet and Hémonic, 2021; Hercule and Rousset, 2021; Roguet and Hémonic, 2022).

Changing the use of antimicrobials represents a risk for farmers, particularly in the case of preventive treatments. This raises the question of how to support farmers in reducing the use of antimicrobials without penalising animal health, welfare and technical and economic performance. Various actions have been undertaken by farmers, veterinarians, livestock advisors and cooperatives. The following two chapters present a summary analysis.

3. Development and improvement of preventive actions

Various preventive approaches have been tested and deployed in the monogastric sectors, both within the framework of action research and through initiatives undertaken by the stakeholders themselves, independent of research activities. They are based on a multifactorial approach to health, the establishment of a sound diagnosis of the main health problems on a farm, and work on their underlying causes to define preventive measures adapted to the health context of the farm.

■ 3.1. Multifactor and participatory approach

The work of the EFFORT and MINAPIG European projects provides insight into the key factors for success in reducing antimicrobial use in pig farming (Collineau *et al.,* 2016; Sanders and Chauvin, 2019). In these two projects, an intervention plan specific to each farm was defined with the aim of reducing antimicrobial treatments and implementing alternative measures. Under the EFFORT project, an inventory of the 293 measures described in the 41 documented action plans showed that the measures were divided between farm management (50% – e.g. management of pens, ventilation, feed, water), disease management (34% – e.g. infection prevention, vaccination, improved diagnosis), antimicrobial treatment management (12% – e.g. modification of treatments and proposal of alternatives) and staff training (5%). An analysis of the action plans of 54 broiler farms (French, Belgian and Spanish) showed that 98% of the farms aimed to improve farm management. Of the actions outlined in the plans, 50% targeted the quality of the environment (ventilation); the remainder concerned the distribution and quality of feed, water, litter. Furthermore, an alternative to antimicrobials (prebiotic, probiotic, organic acid, etc.) had been proposed by a veterinarian or technical advisor on 60% of the farms. Training of farmers, particularly in monitoring and recording quality or clinical signs in chicks and chickens, also was frequently recommended. Finally, on 18 farms, measures to improve biosecurity, cleaning and disinfection, and hygiene practices were identified. In the MINAPIG project, an intervention study on 19 French farrow-to-finish pig farms was conducted to identify key factors for the success of an antimicrobial use reduction plan (Collineau *et al,* 2016). The factors identified included: *i)* establishing a good diagnosis of the main health problems on the farm and their causes; *ii)* ensuring that the farmer is ready to commit to improving the health of the herd; *iii)* having a controlled and stabilised health situation; *iv)* defining the procedure to follow in the event of the reappearance of clinical signs despite the measures implemented (e.g. use of a dosing pump); and *v)* assessing the risk perceived by the farmer who commits to reducing antimicrobial treatments. In addition to these data, an analysis of possible action levers is presented by Fortun-Lamothe *et al.* (2022), this issue.

■ 3.2 Vaccine innovations

For pig, poultry and rabbit production, the reduction in the use of antimicrobials over the last ten years has taken place against a backdrop of vaccine innovations. In the pig sector, for example, in addition to an already extensive vaccine arsenal (Mycoplasma, PRRS (porcine reproductive and respiratory syndrome), Circovirus, *Actinobacillus pleuropneumoniae*, *Lawsonia intracellularis*...), the arrival on the market between 2013 and 2015 of new anti-

colibacillary vaccines for post-weaning piglets has enabled a breakthrough in the control of digestive disorders and problems related to oedema disease. A study evaluating the effect of a vaccine to prevent weaning colibacillosis on 45 farms showed an increase in growth rate, a decrease in post-weaning mortality after vaccine application, and a strong reduction (-65%) in the use of digestive antimicrobials (Gauvrit *et al.,* 2021). The results show that the vaccine's positive effects were particularly pronounced when poor health conditions prior to vaccination had impacted technical performance, illustrating the importance of a precise diagnosis prior to the implementation of appropriate preventive measures. In chicken and turkey farming, a live anti-colibacillary vaccine, administered as a spray or in drinking water, has been marketed in recent years; it is increasingly used, even without a marketing authorisation, for other poultry species, especially species with a fairly long lifespan. Vaccination against coccidiosis is also being developed to control a parasitic infestation that is conducive to bacterial infections.

The development of autovaccines also makes it possible today to better control diseases that have a strong impact on animals. Examples include *Escherichia coli* in all long-lived poultry, *Pasteurella multocida* and *Riemerella anatipestifer* in ducks, *Ornitobacterium rhinotracheale* in turkeys, *Streptococcus suis* and *Glaesserella parasuis* in pigs, and *Staphylococcus aureus* (Highly Virulent strains) in rabbits. This "tailor-made" approach, using a strain and a vaccine protocol specific to each farm, is based on a precise diagnosis and support, as its effectiveness is variable and may depend on the control of other farming factors, such as the effectiveness of colostrum intake (Rémond *et al.,* 2021) and intercurrent sanitary factors (viral diseases against which, here too, vaccine prophylaxis plans have been reinforced).

■ 3.3. Use of alternative substances: prebiotics, probiotics, organic acids, plant extracts

Progress also is being made in the use of so-called "positive" flora, the addition of ingredients beneficial to digestive health such as prebiotics, probiotics, organic acids and plant extracts. Some studies show beneficial effects on the intestinal health of piglets, but not always real preventive or curative properties. Work on the gut microbiota may provide a better understanding of the mechanisms involved in the action of these alternatives (Guevarra *et al.*, 2019; Luise *et al.,* 2021). Nevertheless, an in-depth review of the existing literature has recently shown that it remains extremely difficult to assess the effectiveness of these different products (prebiotics, probiotics, organic acids and plant extracts) as alternatives to antimicrobials due to the lack of sufficient documentation (Anses, 2018). This does not necessarily mean that these products are ineffective, but it does highlight the need to encourage research in this field to identify promising products, characterise their effects and better analyse their safety. The 2018 survey conducted by a group of experts also highlighted the difficulties in positioning these products from a regulatory point of view, with many claims leading to the products concerned being classified as veterinary drugs, even though their intended function is slightly different (Anses, 2018).

■ 3.4. Livestock management

In addition to the above-mentioned innovations, various levers relating to husbandry and zootechnics have been mobilised to improve animal health on farms, and thus reduce the use of antimicrobials. For example, a case-control study conducted on chicken farms operating under a quality label showed that the use of antimicrobial treatments was significantly lower on farms using starter paper when chicks arrive (Adam *et al.,* 2019). This device is used by farmers to attract chicks to a place in a building where all of the elements essential for their survival (heating, feed, water) are grouped together. The importance of getting chicks off to a good start and satisfying their physiological needs is unanimously recognised as an important factor in the success of the batch, meaning the technical performance of the batch, mortality, etc. (Yassin *et al.,* 2009).

Improved nutrition plans also play a favourable role in the reduction of antimicrobial use in livestock. Different actions based on the optimisation of nutrition have been implemented to manage digestive disorders during the weaning phase of piglets, which is a critical stage in the use of antimicrobials in piglets. Better knowledge of nutritional requirements has helped to improve the quality of feed at weaning and to use so-called "safe" feed for this phase (lower protein content) (Sauzea *et al.*, 2020). In addition, to limit the anorexia period at this time and the subsequent risk of diarrhoea, but also to improve piglet performance, it has been shown to be beneficial to give piglets solid feed during the lactation period (development of the digestive tract and its enzymatic capacities, limitation of the proliferation of pathogenic bacteria) (Lalles *et al.,* 2004; Pluske *et al.,* 2007).

In the pig, poultry and rabbit sectors, major efforts have been made to address the quality of drinking water (microbiological and biochemical

quality), which is also unanimously recognised as an important factor in health management. This includes better application of water treatment or pipe cleaning-disinfection processes (Leblanc-Maridor *et al.,* 2019). Measures to check the absence of biofilm along water lines are now widely used in animal husbandry. In addition, the acidification of water to stabilise the digestive flora of animals is a common practice (Sauzea *et al.,* 2020). Finally, special efforts have been made to improve equipment and associated rearing techniques, with improved comfort thanks to the control of the environment and ventilation, and the use of concrete floors in poultry farming.

■ 3.5. Biosecurity and farm sanitation

In addition to improving animal rearing conditions (density, ventilation, flock management, feeding strategies), major efforts have been made to improve biosecurity and sanitation on farms with regard to certain pathogens. These efforts have been particularly strengthened in recent years following new regulatory requirements (Biosecurity Order of 8 February 2016 for poultry farms[4]; Biosecurity Order of 16 October 2018[5] for pig farms) aimed at protecting farms from the introduction of regulated infectious diseases (particularly avian influenza and African swine fever). Biosecurity is defined as the application of a set of measures to prevent the risks of introduction and spread of pathogens on a farm (Guériaux *et al.,* 2017). It combines the application of a set of physical measures (such as the spatial division of the farm into different health status zones or zoning of entry gates) and practices (e.g. change of clothing and cleaning-disinfection methods).

The literature shows that the effectiveness of biosecurity measures goes far beyond the framework of regulated diseases and makes it possible to prevent and limit the impact of a range of pathogens, including endemic ones. When properly applied, biosecurity measures are associated, in the long term, with a reduction in costs (treatments) and losses (mortality) generated by disease outbreaks (Gifford *et al.,* 1987; Fasina *et al.,* 2012). Studies of pig farming have shown that biosecurity practices can reduce the risk of infection and antimicrobial consumption without negatively affecting the production parameters of a farm or economic gains (Rojo-Gimeno *et al.,* 2016; Postma *et al.,* 2017; Collineau *et al.*, 2017; Stygar *et al.,* 2020). In poultry farming, results suggest a similar trend between biosecurity and reduced antimicrobial use (Gelaude *et al.,* 2014).

Good compliance with biosecurity measures is essential for these measures to be effective. However, studies assessing compliance with biosafety measures in livestock production show that practices vary greatly in different countries and for different species, with some measures being better or less well respected than others (Brennan and Christley, 2012; Backhans *et al.,* 2015; Racicot *et al.*, 2011). The effective implementation of biosecurity on farms, and in particular daily compliance, requires a diagnosis of each situation and the definition of an action plan targeted at the specificities of the farm. With biosecurity as the theme in 2020-2021, mandatory pig health checks (known as Pig Health Visits) were an opportunity for veterinarians and farmers to discuss this issue and, following an audit, to draw up an improvement plan. Three axes have been implemented in pig farming in terms of biosecurity. The improved health status of genetic stocks means that many breeding farms are now free of the main bacterial diseases, in particular the different serovars of the actinobacillosis agent (*Actinobacillus pleuropneumoniae*) and *Mycoplama hyopneumoniae*. Voluntary efforts to eradicate PRRS are increasingly common, as this disease has a strong impact on curative health care expenditures. When farms are renovated or reorganised, restocking is increasingly carried out to eradicate certain chronic bacterial diseases that are often treated with antimicrobials. Finally, in pig farming, attention has also been paid to the mixing of animals from different batches or origins, as breeding sites can be divided by physiological stage into different sectors (separation of farrowing and fattening).

In the poultry industry, major efforts have been made in recent years to improve farm biosecurity. These efforts were reinforced markedly under the threat of the highly pathogenic avian influenza epizootics. Action plans have been drawn up in close consultation with professionals and government departments, and adapted to the different species and production sub-sectors. The repeated occurrence of epizootics makes it difficult for the time being to assess the effect of these measures on technical performance and antimicrobial use. Overall, the application of these preventive measures has been strongly reinforced in the monogastric sectors due to the specific health context of each one, and a certain number of measures are now mandatory, which contributes to better health prevention.

4 JORF n°0240 of 17 October 2018: https://www.legifrance.gouv.fr/jorf/id/JORFTEXT000037501487
5 https://groupecristal.fr/alterbiotique/la-solution-alterbiotique/

4. Evolution of antimicrobial therapy practices

■ 4.1. Changes in veterinary prescribing practices

For many years, the rearing of large numbers of animals has made it possible to use bacteriological examinations, which complement the orientation diagnosis (clinical, lesion) for bacterial diseases, in certain production sectors. Bacterial isolation is interpreted by experienced bacteriologists in the light of the clinical elements of suspicion and the characteristics of the bacterial growth (pure culture, abundant, etc.). It is completed by an antibiogram for the germs deemed of interest by the veterinarian. A qualitative study conducted in France among veterinarians practising in different sectors (production, companion and sport animals) highlighted the specificities of the monogastric sectors with regard to the use of the antibiogram (Bourély *et al.,* 2018). This study shows that in these sectors, which require a collective approach to diseases, the ratio between the cost of the additional examination and the expected benefit of investigating the cause to save the rest of the batch or flock is largely favourable. In the poultry sector, and to a lesser extent the pig sector, the long-standing link between analysis laboratories and veterinary practices helps to facilitate the use of antimicrobial susceptibility testing, particularly in high production areas.

Based on these test results and the clinical evolution of the batch, an antimicrobial treatment can be prescribed and implemented. The veterinarian then monitors the evolution of the batch's health status and technical parameters during and at the end of the treatment. In the poultry and pig sectors, unlike in other sectors, the use of antimicrobial susceptibility testing does not systematically imply the subsequent use of an antimicrobial (Bourély *et al.,* 2018). The annual statistics on the sensitivity of bacteria to antimicrobials, carried out on several thousand antibiograms and compiled by the laboratories, can also be used to guide the implementation of a first-line antimicrobial treatment after clinical and lesion diagnosis, if a batch's state of health justifies a very rapid response. The annual reports provided by the national antimicrobial resistance surveillance network (Résapath), which collects antibiogram data on pathogenic bacteria of animal origin in France (Anses, 2021b), are also a useful source of information to guide veterinary practitioners in their therapeutic choices (Bourély *et al.,* 2020). For diseases for which treatment is based exclusively on clinical examination (diseases caused by bacteria that cannot be cultured or are very difficult to culture), and for which antimicrobial treatments are deemed necessary, a prescription is made when necessary.

The veterinary profession has been very dynamic in engaging in extensive reflection and taking consensual decisions on the approaches and protocols to be implemented in different contexts, which has led to decision rules, the need for complementary examinations and the performance of antibiograms. This desire for consensus is reflected in the "Recommendations for good practice in the use of antimicrobials" published by the SNGTV for each sector. In pig production, the moratorium on the use of 3rd and 4th generation cephalosporins, and the limitation of antimicrobial treatments via feed, have contributed to a reduction in metaphylactic treatments for entire herds, with farmers moving towards more targeted treatments at the trough or in the pen. The veterinary profession also has taken a cautious stance on the use of zinc oxide, used to prevent post-weaning diarrhoea in piglets. Unlike several European countries, this substance has been prescribed sparingly in France to limit the risk of ecotoxicity. In the poultry and pig sectors, veterinarians also have supported farmers in these changes, in particular through the use of new devices to better manage collective treatments such as dosing pumps (Fortané et al., 2014) (Figure 3). At the same time, work has been done to make better use of the pharmaceutical speciality available. The administration of antimicrobials at the right dose is essential to avoid therapeutic failures and the development of antimicrobial resistance. However, underdosing sometimes occurs on farms for various reasons, such as poor

Figure 3. ***Installation of a dosing pump to delivery antimicrobials in drinking water (photo Anne Hémonic). More flexible and responsive than administration in feed, the administration of antimicrobials in drinking water using a dosing pump has made it possible to reduce the use of antimicrobials in the monogastric sector.***

assessment of animals' weight, calculation errors, poor storage or preparation of medicines. Some errors are easy to correct, while others require further study.

■ 4.2. Health monitoring devices

The evolution of antimicrobial therapy practices also must be based on better health monitoring tools. These tools enable the health status of animals to be monitored precisely, changes to be noted at an early stage, and swift reaction in the event of an alert, and can serve as a basis for discussions with farmers. The regulations concerning the prescription of antimicrobials outside of a clinical examination require veterinarians to carry out an annual Farm Health Check (FHC), accompanied by the drafting of a treatment protocol for priority diseases on the farm, as well as one or more additional follow-up visits (Order of 24 April 2007, see article on veterinary pharmacy in this special issue). The FHC and the associated visits provide valuable opportunities for the farmer and the veterinarian to discuss a wide range of issues and a global approach to health management. This system offers a useful framework to discuss reduced antimicrobial use and the means of achieving this while taking into account the specific features of the farm visited. For instance, the FHC provides an opportunity for the farmer and the veterinarian to discuss optimal control strategies. In the pig sector, a move from an "antimicrobial" protocol for controlling a bacterial disease to the introduction of vaccination for all animals can, for example, be envisaged, particularly for chronic diseases such as leptospirosis in sows or proliferative ileitis in pigs. In addition, global approaches to meet societal expectations, particularly regarding antimicrobial use and animal welfare, are undertaken by the majority of structures involved in organised animal production. An example is the Alterbiotic approach,[6] with a notable development of phytotherapy.

In poultry production, the need to be more reactive and proactive has given rise to the interest of "end of batch" assessments, carried out in a tripartite manner with the farmer, the producer organisation and the veterinarian. These assessments, led by the veterinarian, allow for the rapid implementation of corrective actions in poultry farming for the next batch, and to measures to support farmers in changing their practices. In addition to these various assessments, predictive modelling approaches have been developed on a pilot basis in the broiler sector. Predictive models, built from large retrospective databases, can be used to reconstruct the mortality curve during the first week of life (Gall, 2015). Combined with a necropsy examination (weight in relation to the standard, hydration status and consumption of digestive fillers, infectious lesions), these references constitute safeguards against possible premature recourse to antimicrobial treatments.

5. Supporting farmers in reducing the use of antimicrobials

■ 5.1. Awareness-raising and training schemes for preventive approaches

Preventive actions are even more effective if they are implemented in a coordinated manner by the three key players – farmers, veterinarians and technicians – to facilitate farmers' adherence and compliance. These actions are accompanied by collective awareness-raising, training, incentives and technical and economic support, with the aim of adding value to products. To this end, various individual and collective support mechanisms are made available to farmers (Sulpice *et al.,* 2005; Kling-Eveillard and Frappat, 2010; Ruault, 2015). This support is provided through three main channels: information, training and exchange (Ruault *et al.,* 2016).

Participatory meetings and practice exchange groups are increasingly being proposed to and mobilised by farmers (Ruault, 2015; Ruault *et al.,* 2016) with the aim of continuously improving practices. The multi-partner project UniFilAnim Santé (*Union des Filières Animales pour la Santé*), co-financed by the Pays de la Loire region and Europe, was set up within this context. It is a multi-sector project (ruminant and monogastric sectors) which aims to help farmers and their stakeholders to develop new perspectives regarding animal health management by considering the needs and expectations of farmers in terms of support (Gambara, 2020; Manoli *et al.,* 2020). Similarly, educational tools are proposed for biosecurity in pig farming (collected on the same website[7]), in poultry farming (e-learning modules, audit tools, technical sheets, videos of testimonies from farmers who have succeeded in reducing their use of antimicrobials, economic simulator of the cost of biosecurity) and in rabbit farming (set of 21 biosecurity sheets resulting from a collaboration between ITAVI CLIPP SNGTV).

6 http://biosecurite.ifip.asso.fr/

7 https://opera-connaissances.chambres-agriculture.fr/doc_num.php?explnum_id=154052]

The training of farmers and technicians is a starting point for a coherent discourse between all actors, especially for a better use of antimicrobials (Piel *et al.,* 2019a; Piel *et al.*, 2019b). Courses can focus on different topics involving animal health (animal welfare, biosecurity, water quality...) and on tools for monitoring antimicrobial consumption. Several studies highlight that reducing antimicrobial use does not lead to a degradation of technical performance (Lopez *et al.,* 2017; Piel *et al.,* 2019a, 2019b; Poissonnet *et al.,* 2021). This counter-intuitive result is probably the result of combined actions, such as the implementation of more effective preventive measures. In any case, this result constitutes a strong argument in discussions between veterinarians and farmers during an antimicrobial use reduction process.

■ 5.2. Factors favouring a farmer's adherence to changes in antimicrobial therapy practices

In all of the production sectors studied, farmers identify the veterinarian as their main contact for health issues, and it is the veterinarian who is best placed to set up a personalised monitoring plan with the farmer, with support from technicians. A key to success in improving antimicrobial therapy practices is the development of working relationships within the trio formed by the farmer, the veterinarian and the livestock advisor, in order to collectively construct solutions (Ducrot *et al.,* 2019). In addition to establishing a sound diagnosis of a farm's health problems and defining the approach to follow in the event of a recurrence of clinical signs, it is also necessary to ensure that farmers are ready to commit to the approach and to assess the risks they perceive to be involved in reducing antimicrobial treatments. This last point deserves to be explored further to provide stakeholders with tools to best support the process of reducing antimicrobial use (Collineau *et al.,* 2014). A study by Gery-Choquet *et al.* (2019) analysed the factors that prevent and motivate farmers to implement preventive measures against avian colibacillosis. Their analysis revealed different farmer profiles that can be distinguished by their motivation to change their practices, and suggested that advice should be adapted according to this typology. Drawing from studies in different animal sectors, Ducrot et al (2019) reported various factors motivating farmers, including: the adequacy of the reduction of antimicrobial use with the representation of "doing the right thing"; the notion of control perceived by farmers, i.e. the confidence they have in the existence of possible alternatives to antimicrobials, therapeutic or otherwise; the perception of stress as a driving force in work (challenges to be taken up); and financial incentives.

Reducing the use of antimicrobials in livestock farming is part of complex organisational changes. The quality of the farmer-veterinarian relationship, and in particular the trust placed in farmers, is a key factor in obtaining farmers' support for an approach to reduce antimicrobial use or, more generally, for compliance with recommendations (Racicot *et al.,* 2012; Fortané *et al.,* 2015; Collineau *et al.,* 2017). In human medicine, the trust granted to practitioners by patients has been the subject of numerous studies leading to the establishment of validated and robust trust evaluation grids (Hillen *et al.*, 2012; Muller *et al.*, 2014). In veterinarian medicine, on the other hand, this subject has not yet been explored extensively. The European project ROADMAP ("Rethinking of antimicrobial decision-systems in the management of animal production") explores a new research frontier on the importance of trust between farmers and their animal health advisors for better compliance with recommendations in pig farming. The results should help improve knowledge on the sociological and psychological factors of the trust relationship and its implementation in a farmer-veterinarian-technician working relationship (Drouet *et al.,* 2020).

6. Discussion and perspectives

The approaches implemented to rationalise antimicrobial use combine preventive measures adapted to the context of each farm with the judicious use of antimicrobials when they are deemed necessary. Farmers may be concerned that a reduced use of antimicrobials may lead to a deterioration in their animals' health and welfare, and to a decline in their technical and economic performance. However, several studies have shown the technical and economic effectiveness of intervention plans undertaken by farmers with the support of veterinarians (Poisonnet *et al.,* 2021). This type of action nevertheless requires more technical expertise, regular monitoring of the situation with permanent adaptations, and a strong relationship of trust between the farmer, the veterinarian, other technical supervisors and production organisations.

However, due to self-censorship on the part of some farmers and veterinarians, there may be an increasing possibility that antimicrobial treatments are not used even when they are necessary. Experience in the field shows

that market segmentation around "antimicrobial-free" specifications also can have perverse effects in terms of animal welfare and suffering. In some situations, farmers and veterinarians opt to euthanise sick animals, which may be a better strategy than sometimes futile attempts to treat them or a complete lack of action, leaving animals to suffer.

In the future, the development of alternative livestock rearing systems consistent with certain societal expectations (access of animals to the open air, provision of straw....) is likely to have very heterogeneous impacts on animal health and antimicrobial use (Delsart *et al.,* 2020). For example, rearing pigs on litter provide certain benefits in terms of welfare, offering better comfort than concrete (fewer foot injuries) and a larger surface area per animal; on the other hand, straw is risky in terms of mycotoxins (with deleterious consequences on immunity and disease resistance), rodents (carriers of pathogenic germs), heat stroke and finally hygiene when it is not provided in sufficient quantity or renewed sufficiently often. Various projects are underway to carry out a multi-criteria evaluation of new livestock systems by studying the impact on animal welfare, health, the environment, the economy and work ergonomics (e.g. the Pigal, BP 2022[8] and Physior projects).

Today, it seems difficult to imagine a further reduction in the quantities of antimicrobials used on monogastric farms. In the pig sector, an analysis of a 2018-2019 health survey on antimicrobials and antimicrobial resistance revealed that few farmers believe that they can still reduce their use (Pandolfi *et al.,* 2021). Only 28% of farmers thought they could still reduce their antimicrobial use (results for 1,480 farms selected at random out of 11,465 visits carried out). Progress is nevertheless possible through improved compliance with treatments (dose, duration), and the application of targeted measures on the farms that use the most antimicrobials. After a phase of "massive reduction" of antimicrobial use, we are now moving towards a qualitative analysis and adjustment of antimicrobial use to maintain a good level of health while guaranteeing respect for animal welfare, which requires the monitoring of use at a fine scale and analysis adapted to each farm situation.

Moving in this direction requires solid coordination between stakeholders, adjustments in practices that may involve different actors in the production chain, and the involvement of stakeholders in these changes. To this end, participatory approaches are worth considering. For example, the European research project ROADMAP[9] addresses possible ways to further refine and reduce the use of antimicrobials in livestock farming. It is based on a participatory research scheme (Living Lab) involving the main stakeholders in the pig and poultry sectors. The objective is to define a vision shared by the different partners involved – practising veterinarians, industry representatives, technical institutes, government – of what we want to achieve in terms of antimicrobial use, to define the pathway to get there, and to implement actions or conduct research to remove obstacles (Belloc *et al.*, 2022, this issue). Depending on the direction taken, stakeholders from the retail sector and representatives of citizens and consumers could also be mobilised. These reflections should inspire the partners to help define the next EcoAntibio plan's objectives and means of action.

At the same time, research and new initiatives are tackling diverse issues. Some concern the risks of antimicrobial resistance, such as the risk of resistance selection linked to the use of zinc oxide or disinfectants, the orientation of the intestinal microbiota, a search for a compromise between minimal antimicrobial use and preservation of animal health and welfare, the relationship between antimicrobial use in animal production and resistance of bacteria to antimicrobials, and the effectiveness and safety of alternative solutions. Others concern health management, including continuous data analysis for health monitoring and reflection on management and decision-making indicators, evaluation of the health situation in the innovative livestock systems that are emerging (winter gardens – access to an outdoor space such as a veranda or covered area – and perches for broiler poultry; differentiated areas, straw and access to the open air for pigs) and their selection pressure on antimicrobial resistance. More generally, questions are being raised about the compatibility between natural farming methods and reduced antimicrobial use; the financing of changes in the trajectory for livestock farmers (more expensive buildings, bedding, cost of alternative measures, etc.); the recurring issue of financing veterinary services and the territorial coverage of veterinary practitioners; and the balance between the welfare and health of animals and the well-being, health and job satisfaction of farmers.

8 https://www.legouessant.com/actualites/rd-un-elevage-porc-pilote-dici-fin-2021/

9 https://www.roadmap-h2020.eu/

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Abstract

In France, the quantity of antimicrobials used in monogastric production (swine, poultry and rabbit) has dropped since the 2000s, and is now relatively stationary. Successive EcoAntibio plans strengthened the momentum and contributed to a drastic reduction in the use of critically important antimicrobials. This progress is the result of a combination of factors, including regulatory changes, private voluntary actions implemented in different sectors, as well as collective and individual professional initiatives. Different preventive approaches have been implemented in France based on a multifactorial approach to animal health, a more refined diagnosis and analysis of livestock health disorders, and the definition of suitable preventive measures. The emphasis has been put on farm management, hygiene, biosecurity, vaccination, nutrition, and the use of alternative products. Antimicrobial prescription practices also have evolved, with the establishment of consensual good treatment practice guidelines, the generalization of bacteriological testing and antibiograms, correct compliance with dosage, and closely monitoring animal health to tailor treatments. These changes rely on good relationships between farmers, veterinarians and technicians, which have been reinforced through the support and training of farmers. Further rationalization of antimicrobial use needs to target "at-risk farms" and tailor-made actions.

Résumé

Réduction de l'usage des antibiotiques en filières monogastriques : état d'avancement et perspectives

La quantité d'antibiotiques utilisés dans les filières monogastriques (porcs, volailles et lapins) a chuté fortement à partir des années 2000, et connaît une relative stabilisation depuis quelques années. Les plans EcoAntibio successifs ont renforcé la dynamique et contribué à réduire drastiquement l'usage des antibiotiques critiques. Cette évolution est la résultante combinée d'évolutions réglementaires, d'actions volontaires privées mises en œuvre dans les filières de production, et de démarches professionnelles collectives et individuelles. Différentes actions ont été mises en place, reposant sur une approche multifactorielle de la santé, l'établissement d'un diagnostic fin des troubles sanitaires de l'élevage, et un travail sur leurs causes sous-jacentes pour définir des mesures préventives adaptées. L'accent est mis sur la conduite d'élevage, l'assainissement vis à vis d'agents pathogènes particuliers, la biosécurité, la vaccination, la nutrition, et l'usage de substances alternatives. Les pratiques d'antibiothérapie ont aussi évolué, avec la mise en place de guides de bonnes pratiques consensuels, la généralisation de l'examen bactériologique et de l'antibiogramme, la bonne observance des posologies, et le suivi précis de la santé pour adapter les traitements. La mise en place de ces évolutions repose par ailleurs sur un bon rapport de confiance entre éleveur, vétérinaire et technicien d'élevage, l'accompagnement des éleveurs ayant aussi été renforcé via des dispositifs de sensibilisation et de formation. La poursuite de la rationalisation des usages reposera sur le ciblage des exploitations à risque au regard des usages d'antibiotiques et la mise en place d'actions sur-mesure.

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