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ECONOMIC EVALUATION OF POLICY MEASURES FOR ANIMAL WELFARE AND BIOSECURITY IN ANIMAL BREEDING, AND THEIR EFFECT ON THE REDUCTION OF ANTIMICROBIAL RESISTANCE IN THE ENVIRONMENT AND ALONG THE FOOD SUPPLY CHAIN

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ABSTRACT

This study aims to analyze the public costs associated with the ClassyFarm system as a tool for monitoring antibiotic use in livestock farming.

ClassyFarm is a digital platform developed in 2018 by the Istituto Zooprofilattico Sperimentale della Lombardia e dell'Emilia-Romagna (IZSLER) on the initiative of the Ministry of Health, with the goal of categorizing farms based on their risk to public veterinary health. The platform operates by applying business intelligence processes to farm-level data collected from various sources—either through field inspections or other information systems—to generate scores related to proper drug use, the implementation of adequate biosecurity protocols and compliance with animal welfare standards. Specifically, assessing the prudence of veterinary drug use by farmers allows for the estimation of each farm's risk of developing and spreading antibiotic-resistant microbial strains.

Based on the system's structure and operation, the economic evaluation considered the following parameters related to costs borne by the National Health Service (NHS):

- Development and updating of the ClassyFarm system;
- Control activities carried out by official veterinarians for data collection on ClassyFarm farms;
- Acquisition and integration of information from other sources (National Electronic Veterinary Prescription System and National Animal Registry).

Although including a benefits assessment would have strengthened the study, such analysis was limited to a qualitative approach due to the nature of the ClassyFarm system, which primarily produces information available to its users. Although the system is intended to support farmers with decision-making data to improve farm management, its use is not legally mandated, making it challenging to directly link observed improvements to its implementation. Similarly, potential benefits for the public sector—such as increased efficiency in risk-based inspections—are difficult to quantify, as they are influenced by various factors beyond the system alone. A theoretical monetary assessment of the system's benefits would require estimating the worth of the information it provides, based on users' willingness to pay for access in the absence of a centralized national infrastructure. However, this approach is prone to valuation bias, shaped more by users' perceptions of pharmacosurveillance policies and the perceived seriousness of antimicrobial resistance than by the system itself.

Despite the technical and conceptual limitations described above, this economic assessment offers an original, scientifically grounded insight into public spending on surveillance programs, which is crucial for future policy-making in the context of shrinking global healthcare budgets.

INTRODUCTION

1. Premise

Biosecurity in livestock farming refers to the set of preventive, managerial and structural measures adopted to prevent the introduction, spread and persistence of pathogens within a farm. It is generally divided into two main categories:

- External biosecurity: includes all measures aimed at preventing the introduction of pathogens from outside the farm. These include access control, quarantine for newly introduced animals, cleaning and disinfection of incoming vehicles, visitor management and protection from wild or synanthropic animals.
- Internal biosecurity: refers to the prevention of pathogen spread within the farm, between different animal groups or facilities. It involves proper management of animal, people, and material flow, adoption of cleaning and disinfection protocols, use of personal protective equipment (PPE), separation of environments and implementation of good farming practices.

As stated in Regulation (EU) 2016/429 on transmissible animal diseases, biosecurity is one of the main tools available to farmers to protect animal health and reduce the use of pharmaceuticals, thereby contributing to ensuring animal welfare. The aim of combining all biosecurity measures is to prevent both the introduction as well as the spread of infectious agent in a group of animals. As such, it targets reducing the infection pressure exerted upon the animals. It follows that good biosecurity in animal production results in improved animal health and subsequent improvements in technical performances (1). A very important additional effect is the fact that biosecurity is also an important tool in the reduction of antimicrobial use and in the fight against antimicrobial resistance (AMR). If biosecurity and disease prevention are well implemented it is possible to reduce curative treatment of diseased animals to an absolute minimum (2). As is known, the over-use of antimicrobials both in livestock and humans, can lead to the increase of AMR bacterial strains due to the genetic mechanisms underlying the resistance phenomenon. It follows that the implementation of adequate biosecurity measures at farm level is indirectly associated with a reduction of AMR through an improved animal health status and the consequent lower need for veterinary drugs (3). Moreover, recent research and field experiments have shown that improvement in biosecurity status is economically beneficial for farmers (net of the necessary investment costs) thanks to a better state of health of the animals and subsequent improvements in technical performances (4).

The implementation of biosecurity measures on farms can be further linked to the level of animal welfare provided by farm management. A recent definition of animal welfare, also adopted at European and international levels, is the one proposed by the World Organisation for Animal Health (WOAH, formerly OIE), which states that:

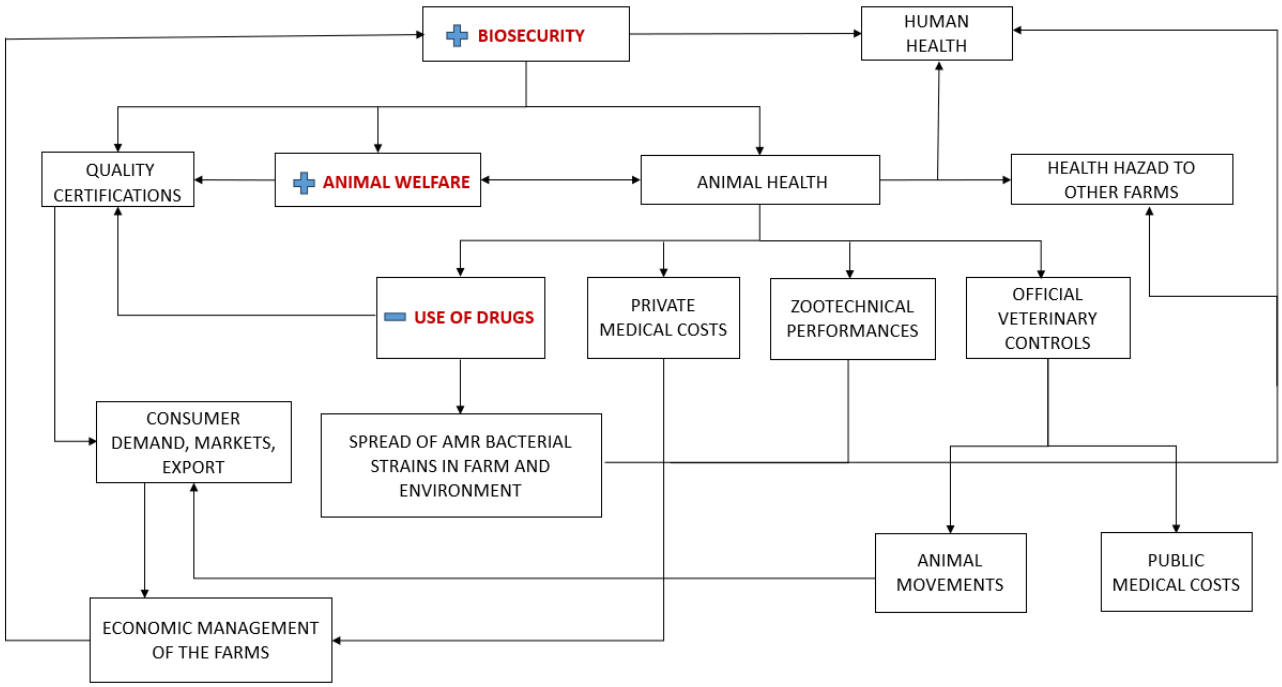
"An animal is in a good state of welfare if it is healthy, comfortable, well-nourished, safe, able to express innate behaviour and not suffering from unpleasant states such as pain, fear and distress". Considering this concept, it is easy to understand how the link between on-farm biosecurity and animal welfare is both strong and bidirectional: effective biosecurity management directly contributes to improving animal welfare, while high standards of animal welfare enhance the overall health conditions within the farm. Specifically:

- An environment protected from the introduction and spread of pathogens, through external and internal biosecurity measures, reduces the incidence of infectious diseases, limiting the need for pharmacological treatments and the isolation of sick animals—situations that can cause stress and negatively affect animal welfare.
- Animals raised in optimal hygienic and sanitary conditions, with proper infrastructure, controlled movement of people, animals and materials and a reduced environmental pathogen load, experience less stress and are better able to express natural behaviors, contributing to both physical and behavioral well-being.
- Animal welfare also influences the effectiveness of biosecurity: stressed or weakened animals have a more vulnerable immune system and increased susceptibility to infections, which can undermine the effectiveness of biosecurity measures.

Therefore, biosecurity and animal welfare must be considered synergistic elements, integrated into sustainable and ethical farm management practices focused on prevention rather than treatment, in full accordance with the principles of the One Health approach.

The following Figure n.1 summarizes the mutual connections between biosecurity, animal welfare and the prudent use of veterinary antimicrobials in animal production. As shown, improvements in these elements have impacts both at the farm level and on public health and welfare.

Figure 1 **Connections between biosecurity, animal welfare and the use of veterinary antimicrobials and their impacts**



Strengthening biosecurity measures on farms leads to improvements in the health and welfare of livestock, which in turn produces a series of effects:

1. Reduced need for pharmacological treatments, resulting in lower veterinary expenses for the farmer and a decreased risk of developing AMR;
2. Improved animal productivity, both in quantitative and qualitative terms;
3. Reduced intervention from public veterinary services, both routine (due to lower farm-level risk) and emergency (due to fewer outbreaks of notifiable diseases).

As a result, this generates savings for the National Health Service (NHS) and eliminates movement restrictions on animals that are typically imposed as a prophylactic measure.

The improved level of biosecurity and animal welfare, along with reduced use of medications, makes it possible to obtain relevant quality certifications. These certifications enable farms to target consumer segments that consider such standards an important added value in animal-derived products.

This, combined with lower private healthcare expenses, enhances the economic management of the farm, triggering a virtuous cycle through the reinvestment of resources into further improvements in biosecurity and animal welfare measures applied on the farm.

2. Objectives of the study and methodology

With the aim of improving the safety and quality of animal production in Italy and implementing the provisions of the Ministerial Decree of December 2017, regarding the epidemiological surveillance network system, the Ministry of Health introduced the ClassyFarm digital platform in 2018. Developed by IZSLER (Istituto zooprofilattico sperimentale della Lombardia ed Emilia-

Romagna) and integrated into the national veterinary portal (www.vetinfo.it), ClassyFarm collects and processes zootechnical data from official veterinary inspections, self-monitoring activities and other information systems. Based on this input, ClassyFarm provides an integrated risk assessment for public health associated with livestock farms by assigning a score related to biosecurity, animal welfare and the use of antibiotics on the farm. Farm registration is currently voluntary but mandatory to obtain the SQNBA certification and to access certain CAP measures, such as Ecoscheme and enhanced conditionality. Access to the platform is restricted to qualified individuals (official veterinarians, farm veterinarians, and farmers) and allows authorities to plan targeted, risk-based inspections, offering benefits in terms of administrative efficiency and reduced burdens for low-risk farms. For farmers, ClassyFarm also serves as a useful tool for identifying critical issues and improving farm management.

This PhD thesis is part of a broader research project aimed at estimating the economic effects generated by the implementation of ClassyFarm as a public-health risk monitoring tool linked to livestock production. However, this study specifically focuses on ClassyFarm's role in monitoring antibiotic use in farming and the potential development of antimicrobial-resistant strains, evaluating the public costs incurred for its operation. Adopting a One Health approach, the system's other components—biosecurity implementation and animal welfare—can also indirectly contribute to AMR control. As previously discussed, animals raised in healthier, higher-welfare conditions are less likely to require pharmacological treatments, which can contribute to the selection of resistant bacteria. Thus, monitoring antibiotic use in farms also provides indirect evidence on farm management practices in terms of pathogen prevention and animal quality of life.

With this in mind, the study's primary goal is to identify and estimate the costs borne by the National Health Service (NHS) for implementing and operating ClassyFarm as a surveillance system for antibiotic use in livestock. The decision to focus solely on this function is primarily driven by the significant public health impact of excessive and irrational antibiotic use in livestock. As will be explored later, this practice encourages the development and dissemination of AMR —one of the greatest threats to global health with substantial economic consequences. Another reason for this choice is the system architecture: some of the data used to calculate the risk score derive from checklists completed during field inspections. Official inspections of drug use can only be conducted by public veterinarians—according to legal requirements valid for all livestock species. Within ClassyFarm, therefore, AMR risk assessment is the only function based exclusively on data entered by public veterinarians, unlike the biosecurity and welfare scores, which also include data from checklists completed by private farm veterinarians. Consequently, in order to estimate only the public costs generated by the system, we decided—initially and for

purposes of technical clarity and robustness—to limit cost analysis to pharmacosurveillance, excluding the risk assessment functions related to biosecurity and animal welfare that also involve private-sector costs (i.e., the remuneration of private farm veterinarians).

Although including an assessment of the benefits generated by ClassyFarm would have strengthened the study, such analysis—while essential for a full evaluation of public resource use—will be developed only qualitatively. This limitation stems from the system's nature: its final product is information for veterinary authorities, farmers and farm veterinarians. Although the system was intended to provide farmers with decision-making data for improved farm management, there is currently no legal obligation to use it. Thus, any improvement observed in one of the system's evaluation areas—already difficult to quantify economically—cannot be confidently attributed as a direct benefit of a farm's participation in ClassyFarm. Similarly, potential gains for the public sector, such as improved efficiency of risk-based inspections, are hard to quantify economically. This is because possible reductions in inspection numbers and associated resource savings cannot be attributed solely to better planning; they are influenced by many factors, including farm-level management practices and the local epidemiological context. Moreover, establishing a valid reference scenario for comparison is complicated, since risk-based planning—though less structured—already existed prior to ClassyFarm.

A hypothetical monetary evaluation of the benefits generated by ClassyFarm would require calculating the value of the information the system provides to its users, which is, in fact, its only output. This process would necessarily involve consultation with the recipients of such information (farmers and public veterinary authorities) to assess how much they would be willing to pay to obtain these data—that is, to estimate the cost the system would entail if it were implemented independently in each context (in every farm or local health authority) without a centralized infrastructure shared among multiple users. The application of this methodology, already complex in itself, could nonetheless yield results affected by a valuation bias linked not to the perception of ClassyFarm itself, but rather to the perceived usefulness of pharmacosurveillance legislation and the perceived severity of the AMR issue.

Given the study's goals, the thesis begins with a review of the regulatory framework governing veterinary medicine at national and EU levels (Chapter 1). Chapter 2 examines AMR mechanisms and practices that influence its emergence and discourages misuse in both human and animal contexts. It also explores the health and economic implications of AMR, citing alarming forecasts if antibiotic misuse persists. An analysis of the Italian official veterinary inspection system follows (Chapter 3), identifying key actors and resources used for on-farm inspections, which feed into the risk classification system. Chapter 4 then describes ClassyFarm itself—its stakeholders and risk scoring methodology. The study then quantifies the public costs of

ClassyFarm by looking at both fixed implementation costs and variable operating costs (Chapter 5 and 6). This required reconstructing the system's usual operation—its processes, stakeholders, and resource use. A detailed examination showed that antibiotic use data originates from the Electronic Veterinary Prescription (EVP) system, while farm-level demographic data is sourced via interoperability with the National Animal Registry (NAR). Costs related to the development and maintenance of interfaces for data transfer from EVP and NAR were also included. Risk scores are based in part on data collected by public veterinary inspections. These inspections incur NHS costs, initially estimated using a sample of dairy farms in Parma—since detailed technical and scientific data were already available from a previous (unpublished) economic study on official bovine brucellosis inspections. This enabled a small-scale estimate of actual inspection-related costs. To broaden the economic evaluation, these estimates were then extrapolated to all pharmacosurveillance inspections on ClassyFarm-registered farms nationwide.

Though this economic assessment does not yet include a quantified benefits analysis—currently only qualitative—it offers an original, scientifically grounded insight into public spending on surveillance programs, which is crucial for future policy-making. Given the interdependence of animal, human and environmental health, events in one domain can significantly affect the others—AMR is a prime example. Moreover, with shrinking global healthcare budgets, designing cost-effective monitoring actions is essential to safeguard global health. Studies such as this one thus carry growing and strategic relevance.

CHAPTER 1. THE USE OF ANTIBIOTICS IN LIVESTOCK FARMING: EFFECTS FROM A ONE HEALTH PERSPECTIVE

1. REGULATORY FRAMEWORK FOR THE USE OF VETERINARY MEDICINES

1.1 Historical overview

The practice of administering remedies for the treatment of diseases in farmed animals is very ancient and dates back to Egyptian civilization, as documented by the discovery of papyri describing various animal diseases and the corresponding treatments that were used. For the ancient Greeks and Romans, it was also customary to use plants for therapeutic purposes in working animals. The texts of Hippocrates (460 B.C.) and other ancient physicians such as Dioscorides and Galen (1st century A.D.) mention animal- and plant-based medicines (from viper meat to honey and balms) that were used for centuries to treat both humans and animals and underwent numerous modifications according to different cultures and popular beliefs.

In the Middle Ages, veterinary knowledge was transmitted through local practitioners and relied on herbs and natural remedies to treat livestock and horse diseases, which were essential for the agricultural and military economy of the time. It was during the Renaissance that the field of veterinary medicine gained prominence, leading to more detailed descriptions of animal diseases and available treatments. This progress continued into the modern era, when the invention of the printing press enabled a wider dissemination of scientific information.

In the 19th century, the Industrial Revolution and advancements in chemistry and pharmacology led to the discovery of many active ingredients used in veterinary medicine. By the 20th century, significant progress had been made in this field, with the discovery of antibiotics, vaccines, and other therapies that revolutionized the treatment of animal diseases. This led to the introduction of strict regulations on the production and use of veterinary drugs to ensure food safety and public health.

In the United States, the Federal Food, Drug, and Cosmetic Act of 1938 included, for the first time, provisions on veterinary drugs, and similar legislation began to develop in Europe. The first specific European regulations on veterinary medicines include Directive 81/851/EEC of 1981, which established the foundation for the regulation of veterinary medicinal products within the European Community (1).

1.2 Overview of European Regulations

- **Directive 81/851/EEC**

The first European Directive regulating veterinary medicinal products was Directive 81/851/EEC, issued on September 28, 1981, with the aim of harmonizing the legislation of Member States concerning veterinary medicines. Its goal was to ensure the highest level of public health protection while not hindering industrial development or the trade of pharmaceutical products within the Community. This directive, no longer in force, included provisions for marketing authorization, which was subject to approval by the competent authority responsible for subsequent product monitoring. It also set standards to ensure the quality, safety, and efficacy of veterinary medicines.

The directive introduced a requirement for manufacturers to provide the results of physicochemical, pharmacological and toxicological tests and to ensure compliance with good manufacturing practices. Additionally, it established specific requirements for labeling and the preparation of package leaflets.

- **Directive 90/676/EEC**

Council Directive 90/676/EEC, issued on December 13, 1990, amended the previous directive by introducing stricter criteria for obtaining marketing authorization for veterinary medicines while also establishing accelerated procedures for specific emergency situations. This directive also provided further details on good manufacturing practices and clarified provisions on transparency.

- **Directive 91/412/EEC**

This directive set out fundamental principles and detailed guidelines on good manufacturing practices (GMPs), covering the entire production process of veterinary medicines from the selection of raw materials to packaging and storage.

It mandated that each manufacturing facility must have qualified personnel in adequate numbers to ensure pharmaceutical quality. The directive also emphasized the need for continuous training for industry operators.

Other provisions included specific requirements for facilities and equipment to minimize the risk of errors and ensure effective cleaning and maintenance to prevent cross-contamination and other adverse effects on product quality. Finally, manufacturers were required to maintain a documentation system to trace each production batch, ensuring that records were clear, accurate, and up to date.

- **Regulation (EC) No. 726/2004**

Regulation (EC) No. 726/2004 is a key legislative act of the European Union for the regulation of both human and veterinary medicines.

This regulation established a centralized procedure under the European Medicines Agency (EMA) for authorizing certain medicines, making them valid in all EU Member States without the need for additional national approvals.

It also provided for coordination between Member States and the EMA to ensure a harmonized approach in medicine evaluation and regulatory oversight, improving information exchange and risk management.

Furthermore, the regulation set specific rules for pharmacovigilance, requiring post-market monitoring of veterinary medicines, including adverse reaction surveillance. For medicines not covered by the centralized procedure, national authorization remained an option.

- **Directive 2004/28/EC**

This directive amended the previous Directive 2001/82/EC, updating definitions related to veterinary medicines as well as magistral and officinal preparations.

It strengthened environmental risk assessment related to the use of veterinary medicines and increased post-marketing surveillance on potential risks to human health.

Additionally, the directive introduced new rules on importation, labeling, and package leaflets, ensuring correct drug use and storage guidelines. According to this directive, the sale of veterinary medicines was only permitted through authorized channels.

- **Regulation (EU) 2019/6**

The regulation focuses on veterinary medicals repealing Directive 2001/82 EC. It sets out rules for the sale, manufacture, import/export, supply, control and use of veterinary medicinal products (VMPs), aiming to modernise legislation, stimulate innovation and increase the availability of VMPs and strengthen European Union measures against antimicrobial resistance. The regulation is part of a package of laws on improving animal and human health, which also includes Regulation (EU) 2019/4 on the manufacture, placing on the market and use of medicated feed and Regulation (EU) 2019/5 on procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency (EMA). Among its key measures, the regulation specifies clear and fully harmonised labelling requirements, implements a simpler system for decisions on exceptions and adopts a risk-based approach to pharmacovigilance and controls. The law introduces an innovative legal framework by providing that marketing authorisation of veterniary medicines must be granted by a

competent authority or the European Commission and approval is needed for conducting clinical trials, taking care to protect animals used for scientific purposes.

The regulation continues and strengthens the EU's fight against antimicrobial resistance by introducing:

- a ban on the preventive use of antibiotics in groups of animals and via medicated feed;
- restrictions on the use of antimicrobials as a control treatment to prevent a further spread of infection;
- a reinforced ban on the use of antimicrobials for promoting growth and increasing yield (in addition to the 2006 prohibition of using antibiotics as growth promoters in feed);
- the possibility to reserve certain antimicrobials for use in humans only;
- the obligation for EU Member States
- to collect data on the sale and use of antimicrobials;
- various measures aiming towards the careful and responsible use of antimicrobials.

In addition, for their exports into the EU, non-EU countries will have to respect the ban on using antimicrobials for promoting growth and increasing yield and the restrictions on antimicrobials designated as reserved for human use in the EU. This will improve the protection of consumers in the EU against the risk of antimicrobial resistance spread through imports of animals or of products of animal origin.

1.3 Overview of Italian Regulations

Italian legislation on veterinary medicinal products has undergone numerous changes over the years, starting with Law No. 615 of 1942, which regulated narcotic and hazardous substances to protect public health. The subsequent Presidential Decree (D.P.R.) No. 798 of 1956 addressed the trade and production of medicated feeds and medicated premixes, classifying them based on their active ingredients and intended use. This decree established both technical and qualitative requirements for pharmaceutical manufacturers, imposing the obligation to obtain specific authorizations and comply with good manufacturing practices to ensure the safety and quality of the final products. With the development of European legislation in this field, Italian law has been progressively adapted through national acts that transposed EU Directives and Regulations. Below is a list of the most significant regulations:

- **Legislative Decree No. 336 of 2003**

This decree transposes Directive 2001/82/EC to harmonize Italian legislation with European regulations. It defines the concepts of veterinary medicinal products, medicated premixes, and medicated feeds, establishing detailed procedures for obtaining marketing authorization. Additionally, it introduces a pharmacovigilance system to monitor adverse effects of veterinary medicines after they are placed on the market. This system requires authorization holders to report such effects and mandates periodic inspections by the competent authorities.

- **Legislative Decree No. 193 of 2006**

This decree implements European Directive 2004/28/EC (which repeals Directive 2001/82/EC) by providing even more detailed definitions than the previous legislation. The regulation includes a list of all substances that can be used as ingredients in the preparation of veterinary medicines. It also introduces the Marketing Authorization for veterinary medicinal products, defining the requirements necessary to obtain it, with provisions for centralized, decentralized, and mutual recognition procedures. The decree establishes a pharmacovigilance system, mandates compliance with good manufacturing practices (GMPs), and enforces systematic inspections to ensure compliance with the legislation, imposing penalties for non-compliance. In 2014, it was amended to introduce changes in the regulation and surveillance of veterinary medicines, but it was ultimately repealed by Legislative Decree No. 218 of 2023.

- **Legislative Decree No 147 of 2020**

This decree implements EU Regulation 2019/6 and introduces modifications to the Marketing Authorization procedure for veterinary medicines, specifying the details of the different authorization methods to ensure compliance with European regulations. The pharmacovigilance system is further strengthened, incorporating quality control systems that must meet strict standards. The regulation also establishes traceability requirements throughout the entire supply chain, reinforces the importance of compliance with labelling and packaging regulations and sets forth penalties for non-compliance with the mandatory requirements.

- **Legislative Decree No 218 of 2023**

This is the latest regulation issued in Italy regarding veterinary medicinal products. It is an adaptation decree that addresses aspects left to the discretion of individual Member States, particularly concerning stock management, drug distribution and the sanction system. It also

definitively repeals Legislative Decree 193/2006. The decree introduces new provisions on the validity of veterinary prescriptions and establishes additional detailed rules for the Marketing Authorization (AIC) of veterinary medicines in the EU and for clinical trials. The pharmacovigilance system is further strengthened, and a systematic collection of safety data is introduced into a European database.

In addition to these aspects, the key points of the regulation include:

- Promoting the prudent use of antimicrobials to prevent antimicrobial resistance, with national guidelines to be adopted for prophylaxis and metaphylaxis.
- Specific regulations for homeopathic medicines.
- New rules on advertising, allowing the promotion of veterinary medicines to professional livestock farmers, while ensuring compliance with transparency and truthfulness requirements for published information.

1.4 National-level voluntary standards

A. Strategy and National Plan for the Contrast of Antibiotic Resistance (PNCAR) 2022-2025

Antibiotic resistance occurs naturally in microorganisms as a form of adaptation to the environment and it is due to their ability to mutate and resists to molecules up to that moment capable of killing them or stopping their growth. Due to the enormous selective pressure exerted by the excessive and often improper use of antibiotics in humans, pets and livestock over time this phenomenon developed in one of the main health emergencies.

The present document follows the PNCAR 2017-2021 which represents the first attempt to put into practice the national strategy to combat antibiotic resistance. The PNCAR 20222-2025 was prepared with the aim of maintaining the effectiveness of antibiotics and providing Italy with the strategic guidelines and operational indications to tackle the problem of antibiotic resistance in the next years, following a multidisciplinary approach and a One Health vision.

The national strategy to combat AMR is based on an inclusive and integrated governance. It is divided into four horizontal areas to support all activities:

1. Training;
2. Information, communication and transparency;
3. Research and innovation;
4. National and international cooperation;

and three vertical pillars dedicated to the main prevention and control activities in the human, animal and environmental interfaces:

1. Integrated surveillance and monitoring of antibiotic resistance, of the use of antibiotics, of healthcare-associated infections (HAIs) and environmental monitoring;
2. Prevention of HAIs in hospital and community settings and prevention of infectious diseases and zoonoses;
3. Appropriate use of antibiotics in both human and veterinary field s and correct management and disposal of antibiotics and contaminated materials.

B. Guidelines for the prudent use of antimicrobials in livestock farms

The national guidelines, presented in the box below, were issued for operational purposes, aiming to summarize the critical points and recommended actions to promote the "prudent use" of antibiotics in livestock farming. They were developed by expert groups from both the veterinary public health sector (Ministry of Health, Istituti Zooprofilattici Sperimentali – IIZZSS, regional veterinary services, and local health authorities – LHAs) and the research community, with the support of private veterinary practitioners working directly on farms. These documents are intended for competent authorities, farm veterinarians and industry operators as tools to assess the rational and responsible use of antibiotics and as a means to reduce inappropriate use. In addition to guidance on diagnostic procedures and the proper use of antibiotics, the guidelines also provide information and recommendations on the correct management of animal nutrition and welfare, with the goal of preventing disease outbreaks and thereby reducing the need for antibiotics, which could otherwise contribute to the development of antimicrobial resistance. These are considered "dynamic guidelines", regularly updated in light of new scientific evidence. They focus either on specific types of farming (e.g., pigs and dairy cattle) or have been developed as "best practice manuals" to be applied across all species of zootechnical interest.

- Guidelines for the prudent use of antimicrobials in livestock farming for the prevention of antimicrobial resistance and alternative proposals;
- Biosecurity and proper, rational use of antibiotics in animal husbandry;
- Guidelines: Prudent use of antibiotics in dairy cattle farming;
- Guidelines: Prudent use of antibiotics in meat rabbit farming;
- Guidelines: Prudent use of antibiotics in pig farming;
- Guidelines: Prudent use of antibiotics in companion animals;

1.2 TRENDS IN VETERINARY ANTIBIOTIC CONSUMPTION IN ITALY

The European Medicines Agency (EMA) is a decentralised body of the European Union, mainly responsible for the protection and promotion of public and animal health through the evaluation and supervision of medicines for human and veterinary use. The founding legislation of the Agency is Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004, which establishes Union procedures for the authorisation and supervision of medicinal products for human use and sets up a European Medicines Agency. In September 2009, EMA launched the ESVAC project (European Surveillance of Veterinary Antimicrobial Consumption), following a request from the European Commission to develop a harmonised approach for the collection and reporting of data on the use of antimicrobial agents in animals by EU and European Economic Area Member States. The project collected information, on a voluntary basis, on the sales of veterinary antibiotics intended for livestock and companion animals from the Member States. The Agency published annual summary reports analysing these data, with the aim of sharing key information to identify potential risk factors in the development and spread of antimicrobial resistance in animals. The last ESVAC report was published on November 2023; it is the thirteenth report under the project and presents data on the sales of veterinary antibiotic agents from 31 European countries in 2022. These data are provided at package level in accordance with the data reporting protocol and data collection form published in March 2021. Information on country-specific trends is published separately on the EMA website in Country Individual Reports. This report focuses on the consumption of antibiotic veterinary medicinal products for food producing animals at the European level and analyses the trends it has followed since 2010. The thirteenth ESVAC report marks the end of this project and the beginning of a new phase of mandatory data collection, based on binding legislation (Regulation (EU) 2019/6 on veterinary medicinal products).

As of January 2024, all Member States of the European Union and the European Economic Area are required to report not only the volume of sales but also the use of antimicrobial medicinal products in animals. At this purpose, EMA has developed the Antimicrobial Sales and Use (ASU) Platform to support the mandatory collection and reporting of data on antimicrobial medicinal products in animals. The platform was created under the under the Veterinary Medicinal Products Regulation (Article 57 of Regulation (EU) 2019/6).

The implementation of the new monitoring system will be gradual, and the first report generated by the ASU platform will be published by 31 December 2025. During 2024, national authorities will need to start providing data on certain species: cattle, pigs, and poultry. Only in 2027 the data will

cover all species farmed for food production. From 2030, non-food-producing animals will also be included in the data collection system.

As for Italy, the last ESVAC report referring to 2022, shows a decrease of 9.2% of overall annual sales of antibiotics for food producing animals in comparison to 2021: from 173.6 mg/Population Correction Unit (PCU) to 157.5 mg/Population Correction Unit (PCU). The reduction in sales of pharmaceutical formulations used for group treatment is 10% compared to 2021 and 14.2% compared to 2020. It reaches 48.5% when compared to 2016 data. In 2022, the three highest selling antibiotic classes were penicillins, tetracyclines and sulfonamides, which accounted for 34.6%, 22.6% and 13.8% of total sales, respectively. The majority of antibiotic sales (70.9% of total sales) belonged to the EMA's Antimicrobial Advice Ad Hoc Expert Group (AMEG) category "D – Prudence", which includes medicines to be used as first line treatments, but with caution and only when medically needed. Only 1.2% of sales are represented by critically important antibiotics in human medicine, to be used only when there are no clinical effective alternatives and on the basis of antimicrobial susceptibility testing (AMEG category "B – Restrict"). Regarding the proportion of antibiotic sales by product form, oral powders, oral solutions and premixes accounted for 90.5% of total sales in 2022, while injectable drugs represented the remaining 9.7%.

Analising sales data between 2011 and 2022, in Italy sales of antibiotics used in food-producing animals decreased by 57.5% (from 371.0 mg/PCU to 157.5 mg/PCU in 2022), compared to the 53% decline recorded across 25 European countries. Sales have fallen particularly sharply for antimicrobials in AMEG Category "B – Restrict", as polymixins and quinolones.

Below is the detailed breakdown of sales reductions in Italy during the period 2011-2022:

- 6.2% 3rd and 4th generation cephalosporin sales (from 0.36 mg/PCU to 0.09 mg/PCU in 2022)
- 59.0% fluoroquinolone sales (from 2.2 mg/PCU to 0.90 mg/PCU in 2022)
- 95.9% other quinolone sales (from 9.1 mg/PCU to 0.38 mg/PCU in 2022)
- 98.1% polymyxin sales (from 30.7 mg/PCU to 0.58 mg/PCU in 2022)

1.3 TOOLS TO IMPROVE THE TRACEABILITY OF VETERINARY MEDICINES: THE ELECTRONIC VETERINARY PRESCRIPTION SYSTEM (EVP)

Law No. 167 of November 20, 2017 (European Law 2017), Article 3, concerning "Provisions on the traceability of veterinary medicinal products and medicated feed for the achievement of the objectives of Directives 2001/82/EC and 90/167/EEC", introduced a computerized system for the traceability of veterinary medicines and medicated feed. To this end, starting in 2019, the Istituto Zooprofilattico

Sperimentale dell'Abruzzo e del Molise (IZSAM) implemented the Electronic Veterinary Prescription (EVP) in Italy, which replaced all types of paper-based veterinary prescriptions, with the exception of those concerning medications containing narcotic and psychotropic substances.

The new computerized system not only changes the traditional format of the prescription, but also fundamentally transforms the previous operational model for managing veterinary medicines by fully digitizing both the prescription and the distribution of drugs. All players in the supply chain are required to upload data into the system: the veterinarian who issues the prescription, the supplier who fulfils the order, and the farmer who purchases the medicine. The competent authority (LHA veterinary services) also has access to the platform to remotely monitor the use of medicines and carry out targeted inspections in the event of anomalies.

In this way, the EVP ensures greater transparency in the drug administration process, improves control activities, and makes data available that are useful for combating antibiotic resistance. One of the aims of the new operational model introduced by the system is also to simplify and, where possible, reduce user obligations, as part of the information required to generate and archive prescriptions is automatically retrieved from data already available in the Ministry's information systems. As a result, the incidence of formal errors and the associated sanction costs are significantly reduced.

In order to complete the process of dematerializing veterinary prescriptions and promote the responsible use of medicines—especially antimicrobials—by farmers, the recording of treatments administered on farms has also shifted from paper to electronic format, as established by Legislative Decree No. 27 of 2 February 2021. The introduction of this obligation facilitates the simplification of further procedures, such as the automatic completion of slaughter declarations regarding pharmacological treatments in the dematerialized Model 4 (Declaration of origin and destination of moved animals).

CHAPTER 2. THE PHENOMENON OF ANTIBIOTIC RESISTANCE AND ITS IMPACTS

1. WHAT IS ANTIBIOTIC RESISTANCE AND HOW DOES IT DEVELOP

Antimicrobial resistance (AMR) is the inherited ability of microorganisms to grow at high antibiotic concentrations. It is typically assessed by determining the minimum inhibitory concentration (MIC) of a specific antibiotic, which reflects the lowest concentration at which the antibiotic inhibits bacterial growth. Resistant bacteria are capable of growing and reproducing at antibiotic concentrations that would normally be lethal to other strains of the same species. Antibiotic resistance can be the result of various phenomena. On the one hand, there is natural intrinsic resistance due to lack or presence of certain structures resulting in ineffectiveness of antibiotics. On the other hand, bacteria can acquire resistance via mutations in chromosomal genes or via horizontal gene transfer (HGT) of chromosomes or plasmids that lead to antibiotic resistance.

Mutations leading to antibiotic resistance usually occur in three types of genes: those encoding the targets of the antibiotic, those encoding their transporters and those encoding regulators that repress the expression of transporters or antibiotic-decontaminating elements (mainly chromosomally encoded antibiotic-modifying enzymes and multidrug efflux pumps).

The spread of such mutations occurs through vertical transmission (from one bacterial generation to the next) and is independent of the presence of the antibiotic; generally, these mutations are corrected by cellular repair mechanisms and are therefore rare (1). The phenomenon of transferable resistance, on the other hand, is more significant and involves the transfer of genetic material capable of conferring resistance between bacteria through transformation, conjugation and transduction processes. These mechanisms enable recipient bacteria to acquire the ability to activate one or more resistance strategies in order to protect themselves against antibiotic activity. In HGT, the genes involved must either have come from commensal or environmental bacteria, since they were not present in human or animal pathogens before the use of antibiotics. There is, in fact, compelling evidence that environmental bacteria are their origin (2). Since a number of antibiotics are synthesized by environmental microorganisms, it has been suggested that the origin of resistance genes must lie in antibiotic producers (if they did not possess such genes, their own antibiotic production would kill them).

2. HOW DOES ANTIBIOTIC RESISTANCE ARISE?

Potential causes of the spread of antimicrobial resistance from a One Health perspective are multiple: AMR is influenced by factors like human practices, animal-related practices and environmental factors. Below is an overview of these factors.

2.1 Human related causes of antimicrobial resistance

- **Inappropriate antimicrobial use in human medicine**

Excessive and inappropriate use of antibiotics has played a significant role in the worldwide problem of antibiotic resistance. The available evidence indicates that our heavy reliance on antibiotics, along with the interconnected relationship between human health, animal farming and animal health, has led to the emergence and dissemination of drug resistant bacteria and other organisms (3). The overuse of drugs, including self-medication, dispensing antibiotics without a prescription and over-prescription, can lead to the development of drug resistance by increasing selective pressure on bacteria and promoting the emergence and multiplication of resistant strains (4). These practices, infact, promote the survival and proliferation of germs that are resistant to antimicrobials by destroying the susceptible ones, leading to the emergence of AMR. While antimicrobials can kill certain disease-causing germs, they also eliminate beneficial germs that protect our bodies from infections. As a result, the remaining antimicrobial-resistant microorganisms survive and multiply, carrying resistance traits in their DNA that can be transferred to other microorganisms. One of the causes of excessive consumption in clinical practice lies in the empirical use of antimicrobials by physicians. Often, bacterial infections that may be life-threatening require immediate intervention, which cannot wait for an accurate diagnosis of the infectious disease, its pathogen and the microorganism's susceptibility to a specific antimicrobial therapy. Such a diagnosis would require several laboratory tests, which could take days or even weeks to complete. Consequently, in situations where rapid action is necessary, the preferred therapy often involves the simultaneous administration of multiple antibiotics, in the hope that one of them will act against the unidentified pathogen. Although these practices occur in hospital settings, are limited to specific cases, and are therefore relatively controlled, the development of accurate and rapid diagnostics could help to resolve or at least mitigate this issue. More widespread, however, is the excessive prescription of antibiotics by general practitioners. When faced with a patient presenting symptoms caused by an infectious pathogen, the physician often tends to prescribe an antibiotic therapy based on past experience and local epidemiology, without first confirming, through laboratory tests, the type of pathogen involved and its susceptibility to antimicrobials. The risk associated with this widespread practice is the failure of the initial therapy, followed by the need to prescribe additional antibiotics,

presumed to be effective against the unidentified pathogen. This exposes the patient's microbiota to repeated and intense selective pressure, a condition that greatly favors the development of antibiotic resistance (5). Moreover, it is often the patient himself who engages in the irrational use of these drugs. Although a large portion of the population takes antibiotics following a medical prescription, a fraction of individuals consume these drugs without first consulting a doctor. Self-administration of antibiotics can occur when the patient already has the drug at home (leftover from previous treatments), or when the medicine is given by a relative or friend. When it is the patient who decides which antibiotic to take, the dosage and the duration of the treatment, this often results in the use of an inappropriate drug for the current infection, in incorrect dosages and for shorter periods than actually required. Finally, an increasingly widespread practice, fueled by the growing use of the Internet, is the online purchase of medicines, which further complicates the management and control of antibiotic consumption and encourages self-medication and poor-quality treatment.

- **Inadequate sanitation and hygene in the public settings**

Poor hygiene and failure to comply with infection prevention and control measures have played a crucial role in the spread and proliferation of antibiotic-resistant microbial strains. Hospitals, in particular, have become significant reservoirs of these resistant microorganisms. This is due to the frequent and extensive use of drugs within healthcare facilities and the presence of patients, which increase opportunities for the development and transmission of resistant microbial strains. In fact, these factors contribute to the persistent dissemination of microbes resistant to various antibiotics, posing a serious threat to public health . The correlation between healthcare settings and the development of antimicrobial resistance has been known for a long time: *Streptococcus-pyogenes* resistant to sulfonamide was identified within public clinical settings in early the 19, *Streptococcus pyogenes* resistant to penicillin was noted in the 1940s and multi drugs resistant microbes were reported in the 1950s (6). In certain occasions, the extent of patient-to-patient transmission is directly proportional to the extent of hospital environment contamination : each day, thousands of staff, visitors and patients from different parts reach hospitals, each harbouring a set of the microbiome of diverse genotypes and phenotypes on their or inside their bodies as well as clothing. Microbes can disseminate in case health settings do not practice satisfactory sanitary strategies and protocols to keep up setting hygiene and culminate in further development and spread of AMR. Other public settings with a high likelihood of spreading antimicrobial resistance include buses, railway stations and subway systems due to their high population density. This overcrowding facilitates the spread of various microbial species, characterized by significant genetic diversity and the potential for genetic exchange among them. A study

conducted in Guangzhou, China, detected the presence of multi drugs resistant *Staphylococcus aureus* (MRSA) in railway stations and buses. Among the collected samples, 39,21% tested positive for staphylococci, with 75,84% identified as MRSA. This study further supports the idea that public settings play a significant role in the spread of AMR, acting as hotspots for the distribution of MRSA between humans, the environment and animals, and vice versa. The aforementioned public settings include surfaces frequently touched by many people carrying different resistant microbes to various antibiotics. This facilitates genetic exchange among microbes, allowing them to develop resistance to multiple drugs. Hand-touched surfaces can serve as a means of transmitting AMR from one individual to another, either through direct contact or when bacteria from a person's skin transfer to a surface, which is later touched by others (7). Furthermore, in crowded public places, the transmission of resistant bacteria can occur through various methods, including: the release of bacteria into the air from the skin, the inhalation of contaminated aerosols, the consumption of contaminated food.

2.2 Animal-related causes of the spread of antimicrobial resistance

The major focus on human antimicrobial consumption and inadequate antibiotic stewardship in medical setting and the community as the main drivers for the development and spread of AMR can be explained by the availability of human data compared to animal data. However, it is generally acknowledged and heavily debated that the irresponsible and excessive use of antibiotics for the control of infections in animals, combined with the administration at sub-therapeutic doses (for prophylaxis or as growth promoters) in healthy animals through feed and water, has through the years contributed to the increased resistance of some pathogens that can propagate to humans. Agriculture is still undoubtedly the most prominent consumer of antibiotics, with up to 70% of annual antibiotic usage attributed to this sector, despite policies to reduce their use in food animals (8). Moreover, differently from human medicine where patients are treated individually with low dose of antibiotics, animal producers must use mass medication since it is impractical to treat individually each animal in a group that consists of hundreds to tens of thousands. This inevitably leads to the establishment of selective pressure that promotes the selection and spread of resistant bacteria. In order to contain AMR, the scientific community has long agreed that antibiotics should be used exclusively for therapeutic purposes and that mass treatments for prophylactic and metaphylactic purposes should be avoided or strictly limited.

The European Union has embraced these recommendations, making them mandatory through two new regulations (Regulation 2019/4 and Regulation 2019/6), both in force since January 2022. From that date onward, in both Italian and European animal production systems, antibiotics are prescription-only medicines, to be administered to one or more animals for the treatment of

ongoing bacterial infections and only following a specific diagnosis. Prophylactic use (administering antibiotics before clinical signs of disease appear to prevent its onset) and metaphylactic use (administering antibiotics to a group of animals after the diagnosis of a clinical case within that group to treat sick animals and control the spread of the disease to those at risk) are permitted only under specific legal circumstances. In particular, prophylactic use is allowed only on individual animals, not for mass medication and only in exceptional cases, when the risk of infection or disease is very high and the consequences could be severe. Medicated feed containing antibiotics therefore cannot be used for prophylactic purposes. Metaphylactic use is permitted only when there is a high risk of spreading an infection or disease within the group and no suitable alternatives are available. Moreover, according to the law and with the aim of combating AMR, the use of antibiotics for metaphylactic or prophylactic purposes must never be systematic, routine or applied to compensate for poor hygiene or inadequate farming practices. It must be prescribed for a limited duration, strictly covering the period of risk. Such use must always be based on epidemiological and clinical knowledge, with documented justification and must focus on the subset of animals at greatest risk. In any case, the decision to administer antibiotics must be supported by a veterinary prescription, with documented rationale based on a bacterial disease diagnosis and a thorough understanding of the associated risk factors within the group. Antimicrobials misuse in animals and resultant AMR is a growing problem worldwide, affecting not only humans but also livestock along the entire food chain in almost every country. Genes responsible for antimicrobial resistance and drug-resistant bacteria can spread from food-producing animals to people via close contact or consumption of animal products, especially if they are not handled or cooked properly. The United States centers for disease control and prevention estimates that approximately 1 in 5 cases of resistant infections are linked to pathogen found in animals and food of animal origin (9). Furthermore, the presence of drug-resistant microbes and drug residue in animal waste is the main source of environmental AMR. From the environment, in turn, animals get these resistant microorganisms through various routes so that animals' guts and tissue harbour a high population of resistant bacteria which is further disseminated to the environment as well as to humans and vice-versa. Beyond this, administering antibiotics that are not efficient against the bacteria recorded on the label (in the absence of a specific etiological diagnosis) or when the dose on the label is inadequate (due to AMR), upshots in unnecessary antibiotic exposure and fairing AMR (10). It is crucial to note that consumers can potentially come into contact with or consume animal products carrying resistant bacteria, which adds to their exposure to such microorganisms. Actually, food of animal origin plays an important role in the transmission of AMR bacteria to humans and to the human gastrointestinal tract. Transmission of microrganisms between food and humans occurs during

handling of raw materials as well as cross- and re-contamination between different food products at production, distribution and household levels. This process is of concern due to either direct infections or the possibility of horizontal gene exchange with other, potentially pathogenic members of the gut microbiota favoured by the high cell densities found in the gut (11). In a study on consumer exposure to AMR bacteria in food at the Swiss retail level, it was found that out of 38.362 bacteria isolates and 122.438 samples of food tested, 22,9% of the bacterial isolates and 24,6% of the samples were identified as AMR positive. A significant portion of the samples (61,5%) and bacteria (70,2%) were discovered in meat products like cuts, ground pieces or meatballs. These meat products also comprised the highest percentage (88,7%) of samples with AMR and the majority (60,1%) of AMR-positive bacteria detected (12). Demonstrating that livestock products including meat, eggs and milk have been proven to be a key route of multidrug resistance pathogens, especially for *E. coli* and *Salmonella*, posing a potential health risk to consumers. Such risk for consumers is multifactorial and depends also on food preparation and consumption habits. As most raw meat products undergo a cooking step prior to consumption that reduces the bacteria quantity, the final AMR bacteria exposure level can largely vary depending on the hygiene practices employed in food handling and preparation. This is particularly linked to local culinary traditions widespread in various European countries, where shared plates or cutlery for raw and cooked meat can lead to cross-contamination from raw meat to cooked food. Raw meat products therefore represent a major factor for cross-contamination of bacteria in the kitchen or at the table to infect humans and therefore likely also for the transfer of AMR bacteria to humans (13). In contrast to raw meat or other food products undergoing a cooking step, fermented products are generally consumed without a prior heating step and feature a high level of 108-109 colony counts of technologically relevant bacteria and indicator bacteria per gram of product (14). Therefore, AMR bacteria if present might transfer in significantly higher numbers from food directly to the consumer.

2.3 Environment-related causes of the spread of antimicrobial resistance

The environment has a role both in evolution and transmission of resistance, possibly more so than has generally been recognized. AMR can arise both from mutations in the pre-existing genome of a bacterium and from the uptake of foreign DNA. Mutations readily occur in the patient or animal treated with the antibiotic due to the strong selection pressure to which commensal or pathogenic microorganisms are subjected. Although the natural production of antibiotic molecules has likely contributed to the ancient evolution of antibiotic resistance genes, external environments are generally less likely to provide a major contribution to mutation-based evolution of resistance for most pathogens. On the contrary, with regard to uptake of novel

resistance factors water, soil and other environments provide a huge gene pool with a diversity that greatly exceeds that of the human and domestic animal microbiota (15). Indeed, environmental microbiome has an immense diversity, providing numerous genes that potentially could be acquired and used by pathogens to counteract the effect of antibiotics.

Many bacterial species evolved the ability to tolerate antibiotics long before humans started to mass-produce them to prevent and treat infectious diseases. The biosynthesis of antibiotics by natural microorganisms certainly plays a role in the initial emergence of the phenomenon of AMR; however, it is not responsible for the rapid evolutionary expansion and spread of resistance factors among strains, species and environments that we have observed since antibiotics were introduced as therapeutic agents. Antibiotics produced by environmental microorganisms are widespread, but act largely on a microscale, as concentrations characteristically would be expected to drop rapidly around the producing organisms, hence limiting exposure. Man-made antibiotics, on the other hand, act on a macroscale and are typically associated with selection pressures across entire microbial communities. Antibiotics reach the environment via excretions (urine and faeces) from humans and domestic animals, through improper disposal and/or handling of unused drugs, through direct environmental contamination in aquaculture or plant production and via waste streams from the production of antibiotics. Undoubtedly, the most widespread emissions and quite plausibly the largest proportion of released antibiotics, are the result of use and excretion (16). At the same time, exposure levels via this route are always limited by, for example, the proportion of the population that is using the antibiotic at a given time, the doses used and metabolism in the human or domestic animal. Environmental concentrations of antibiotics are often lower than concentrations shown to select for resistant strains in the laboratory, but in many cases, it correlates with the abundance of AMR genes in environmental samples (17). This can be explained by different levels of pollution with human excreta, which is a source for both, rather than on-site selection of resistant bacteria in the environment by the antibiotic residues (18). Studies conducted at wastewater treatment sites have detected concentrations of antibiotic molecules higher than those considered capable of selecting for resistance, suggesting that antibiotic pollution plays a role in the evolution of resistance. Although increases in the relative abundance of certain AMR genes in such environments are reported, it is difficult to distinguish whether this is a result merely of taxonomic changes, unrelated to antibiotic selection pressures, or from direct selection of resistant strains within species. It could be plausible, but definite evidence for such direct selection in sewage treatment plants is still lacking and some evidence points to the opposite (19). On the contrary, evidence for resistance selection in environments with very high levels of antibiotics (pollution from antibiotic manufacturing) is considerably stronger than that for excreted antibiotics. This is based

on the exceedance of selective concentrations by orders of magnitude at industrially polluted sites, increased relative abundance of resistant bacteria and considerable increases in the number of AMR genes, including previously unknown AMR genes, which are not accompanied by increases in faecal contamination (20). Numerous studies have shown that the abundance of resistant bacteria and/or AMR genes increase after manure from antibiotic-treated animals is added as a fertilizer to farmland. However, in many cases it is not possible to assign such increases to selective effects of antibiotic residues in the soil, as the added manure also carries resistant bacteria. Environmental contamination with fecal bacteria creates direct contact, thereby increasing the chances of gene exchange between resident environmental bacteria and those adapted to the intestinal tracts of humans or domestic animals. Many intestinal bacteria are known to carry mobile genetic elements (such as plasmids, integrative conjugative elements, insertion sequences, transposons, or integrons), which facilitate gene acquisition and their subsequent transfer to pathogens. Studies using fluorescently labelled *E. coli* cells introduced into soil have demonstrated their ability to quickly acquire resistance traits from the soil microbiome (21). Additionally, there is a possibility that AMR genes present in fecal bacteria released into the environment may contribute to the development of clinically significant resistance by undergoing horizontal transfer to environmental pathogens that could eventually infect humans. However, the likelihood of these events occurring is significantly higher within the human or domestic animal microbiota, where selection pressures, commensal bacteria and pathogens frequently coexist. In such environments, there are no natural transmission barriers that need to be overcome, making the spread of resistance more probable. The environment can provide a route for some resistant bacteria to colonize or infect hosts. For a resistant pathogen that is already widely circulating among humans, the consequence of a single transmission event to another individual is much more limited than for an evolutionary event leading to the emergence of a new, successful resistance genotype in pathogens, with potentially global consequences. By contrast, wherever such transmission events become common, as is probably the case in many low- and middle-income countries with inferior infrastructure for handling faecal waste, environmental transmission may have profound effects on the overall resistance situation (22). There is a vast literature on how certain resistant bacteria can spread via food and through contamination on surfaces, not the least in hospitals. Exposure to surface waters heavily contaminated by faecal residues can also lead to various infections. It is plausible that resistant strains would have similar opportunities for transmission via contaminated water as sensitive strains of the same species, but dedicated studies showing that environmental exposure could be important for colonization by or infection with specific resistant bacteria are still scarce. A survey of faecal swabs from surfers from Britain, who are more likely to ingest seawater than non-

surfers, found they were more prone to carry cephalosporin-resistant *E. coli* (23). A different study found that recreational swimming might be a risk factor for urinary tract infections with extended-spectrum β-lactamase-producing *E. coli* and *Klebsiella pneumoniae* (24). More studies of this type, in both high-income and low-income settings, are needed to estimate the role of contaminated water in the transmission of resistant bacteria. At the present moment, the role of selective agents in environmental transmission is unclear. Although some pathogens (for example, *Legionella* spp. or *Vibrio* spp.) thrive in the environment, for most it is a more hostile environment than a human or domestic animal host. For those pathogens, growth in the environment is often limited. It is thus conceivable that small growth differences between resistant and non-resistant strains, caused by exposure to environmental concentrations of antibiotics, are a minor determinant for the possibility that environmental exposure becomes sufficiently high for colonization or infection of a human or animal host. Other biotic and abiotic factors, such as temperature, oxygen pressure, nutrients, predation and competition with other species, all unrelated to the antibiotic resistance profile of the bacteria, are likely to be much more important for environmental transmission opportunities for both resistant and non-resistant strains.

3. ECONOMIC COST OF AMR

3.1 AN OVERVIEW OF ANIMAL HEALTH ECONOMICS: PRINCIPLES AND APPLICATIONS

Economics is the study of how individuals and societies choose to allocate scarce resources among competing alternative uses and how to distribute the products from these resources. On the other hand, health economics is the study of how scarce resources are allocated among alternative uses for the care of sickness and the promotion, maintenance and improvement of health. In this context, plays a role animal health economics a discipline, which does not belong to the core of veterinary science but is becoming more and more important as an aid to decision
making on animal health interventions at various levels. The growing importance of animal health economics can be explained by the changes, which have occurred in the global socio-economic environment over the past 20 years. Significant shifts influencing decisions on animal health measures include (25):

- Most major epidemic diseases have been effectively controlled in developed countries. Because the benefits of their control were so clear, formal economic evaluations were often deemed unnecessary. As a result, veterinary efforts are now directed toward managing diseases with less obvious economic consequences and more complex epidemiology;

- As global market integration has progressed, national self-sufficiency in livestock production has become a lower policy priority. Consequently, political support for nationwide disease control programs has declined.
- With economic development, agriculture plays a decreasing role in national economies, intensifying competition for public funding among various sectors.
- Increasingly, responsibilities are shifting from public authorities to the private sector, which tends to focus more on measurable returns on investment.

Given these developments, providing a solid economic rationale for any proposed animal health intervention has become essential—especially to secure support from those responsible for financing such initiatives.

As previously emphasized, when adopting a One Health approach, a health issue in an animal population can both generate and be influenced by factors from the human and environmental domains**.** Considering this interdependence, the analysis of the effects of animal health issue on a regional or national economy is quite complex. In general terms, it can be stated that the effect of animal health problem in a given production system is a reduction of the efficiency with which inputs/resources are converted into outputs/products, i.e. they decrease productivity. The effects of animal disease can be classified as direct or indirect. Direct losses through diseases may occur as follows:

- at input level, disease destroys the basic resource of the livestock production process e.g. through mortality of breeding or productive animals;
- disease lowers the efficiency of the production process, and the productivity of resources employed e.g. through reduced feed conversion;
- at output level, disease may either reduce the quantity or the quality of output, in this specific case, products of animal origin;
- Reduced market access with a loss of competitiveness due to declines in production and productivity;
- Losses in business income resulting in reduced tax revenues.

The indirect losses due to disease include the following:

- losses through additional costs incurred to avoid or reduce the incidence of disease (e.g. vaccination, quarantine) or to treat cases (veterinary expenses);
- detriment of human well-being due to zoonoses: public and private healthcare costs, productivity losses due to work absences or disability, resulting in reduced income and

increased welfare interventions, which, combined with lower tax revenues, can lead to public finance;

- public costs arising from the interventions of veterinary services aimed at containing a disease outbreak and monitoring the surrounding area to detect the early emergence of new cases;

Based on the above considerations, it follows that the spread of an animal disease entails quantifiable damages in terms of both private and public costs, along with a series of broader societal effects that can also be monetized.

This insight forms the basis of the health economics perspective, which studies the economic impact of diseases, how healthcare systems and infrastructures are managed and how cost-effective certain technologies or treatments are. At the core of these analyses lies a fundamental assumption in economics: individuals have multiple needs to satisfy, but the resources available to meet those needs are limited. Therefore, it is impossible to fully meet all needs simultaneously. From this premise, economic theory has developed conceptual models aimed at identifying how to best use limited resources to achieve the highest possible level of satisfaction—solving the so-called "allocative efficiency" problem.

A key element in choosing how to use available resources is the concept of "opportunity cost", which refers to the value of what must be foregone. This means that when resources are limited, producing an additional amount of one good (e.g., Good A) requires sacrificing a certain amount of another good (Good B).

In the healthcare sector as well, the concept of opportunity cost is widely used, and it justifies the need for and role of economic evaluations. These evaluations consist of comparing different possible choices (e.g., therapeutic or preventive options in healthcare), taking into account both the costs and the outcomes they produce. According to the opportunity cost principle, investing resources in one alternative inevitably means not using them for another. This principle underpins every economic evaluation: if the first option is chosen, specific health outcomes are achieved at a given cost; if the second is chosen, different outcomes are achieved at other costs.

The comparison of costs and benefits between alternatives supports decision-making on the best use of available resources—i.e., solving an allocation problem.

From this, the main functions of this type of analysis emerge: to identify, measure, assess and compare the costs and consequences of the alternatives being considered. These are the key tasks of all economic evaluations, including those focused on healthcare services.

The following Table 2.1 describes the economic methods commonly used for decision support in the field of animal health.

Table 2.1 **Economic methods commonly used for decision support in the field of animal health. Adapted from Otte and Chilonda, 2000 (26).**

METHOD	LEVEL OF ANALYSIS	BASIC CONCEPT
Partial budget analysis	Farm/herd level	Partial budget set up over a period of one year
Enterprise budget	Farm/herd level	Gross margin analysis to compare profitability of different enterprises
Decision tree analysis	Farm level / higher level of aggregation	Calculates the value of alternative actions by including risk (probabilities) and risk attitude
Linear programming and variants	Farm level	Finds the best solution for competing activities under constraints
Dynamic programming	Farm level	Searches for the optimal solution
Simulation	Farm level / higher level of aggregation	Simulates dynamic and risk aspects of livestock disease within production systems
Cost-benefit analysis	Industry / national level	Compares benefits and costs over a period longer than one year
Cost-effectiveness analysis	All levels	Goal is to produce a desired output at least cost

3.2 THE ECONOMIC PERSPECTIVE ON THE AMR ISSUE

AMR is increasingly recognized by many international health organizations as a global public health issue and a threat to the modern health-care system that could hamper the control of many infectious diseases and dramatically set back the modern medicine. The growing ineffectiveness of antibiotics could, in the future, lead to a return to the pre-antibiotic era, in which common medical procedures such as organ transplants, cancer chemotherapy, intensive care, cesarean deliveries and the treatment of premature newborns would no longer be safely feasible. The spread of resistant bacteria and the diseases associated with them would occur unhindered, resulting in an incalculable number of infection-related deaths. Infections by antibiotic-resistant strains are associated with a reduced quality of life, with metastatic bacterial infections, an increase in recurrence rates, chronicity and future opportunistic infections with resistant organisms (27). This problem has been clearly documented by the rise of isolation of resistant human pathogens like *Salmonella*, *Campylobacter* and vancomycin-resistant enterococci (28) (some of them leading to death) associated with a high frequency of therapeutic failures, increased risk of complications, worsening of pathological conditions and death. Antimicrobial resistant organisms are found in people, food, animals, plants and the environment and can spread among different ecosystems in a global way without respecting geographical borders. Antimicrobial resistance is therefore a global public health problem that requires a global solution.

Without proper control and action, AMR will result in enormous human and economic costs. Estimates based on the European Antimicrobial Resistance Surveillance Network (EARS-Net) data from 2020 indicate that each year more than 35.000 people die in the EU/EEA as a direct consequence of antimicrobial-resistant infections. In the next 35 years, in the absence of measures, it is assumed that worldwide there will be about 300 million people who died prematurely (10 million deaths per year until 2050) with a loss of 100 thousand billion dollars of economic production; in high-income countries it is estimated that between 2015 and 2050 about 2.4 million people could die in the absence of sustained contrast measures over time (29). AMR can lead to increasing costs and the destabilization of health systems. Patients suffering from AMR nosocomial infections (mainly bloodstream infections) or who become sick due to the consumption of food contaminated by resistant pathogens experience longer recovery and a higher frequency of septicemic infections and mortality (30). In this situation, health-care costs are higher, due to extended hospital stays and the use of more expensive drugs. Moreover, there are higher risks of toxicity associated with new drugs, as well as a greater frequency of adverse drug reactions (ADRs) and collateral events. Although it is not possible to accurately estimate the expenses and losses related to this emergency, in 2017 the World Bank conducted a simulation based on reviews carried out by other research groups, concerning the future global economic consequences of AMR. The economic impact will occur through direct costs (which include resources used to treat and manage infections caused by resistant bacteria, including hospitalization and alternative drug costs) and indirect costs (which include those related to morbidity, disability, and premature death, and consequently, a decline in productivity). The World Bank projected a global GDP reduction of 0.1% in 2030 and 1.1% in 2050 compared to baseline values (i.e., a long-term global economic scenario that does not account for AMR-related expenditures). The potential impact on global economic growth was estimated by drawing a comparison with the 2008 financial crisis and it was hypothesized that the economic damage caused by AMR in the coming decades could be comparable to — if not worse than — that of the financial crisis. The substantial difference between the 2008 financial crisis and the economic crisis brought on by AMR lies in the limited possibility of a “cyclical recovery.” The financial crisis, in fact, began to resolve by 2010, whereas AMR might require much longer recovery times. The development of new drugs and vaccines could take decades and even if effective, they would be introduced in low- and middle-income countries more slowly than in high-income countries, further delaying economic recovery. This process would contribute to widening the economic gap between low-income countries and those with middle and high incomes. Moreover, the study projects that by 2050, global public and private healthcare expenditures due to AMR will increase by 8% compared to the baseline model. According to the estimate, this figure could rise up to 25% for low-income countries; for middle-income countries, the increase would be 15%, and for high-income countries, 6%. More

recent, The World Organisation for Animal Health and the World Bank have published the report "Forecasting the Fallout from AMR: Economic Impacts of Antimicrobial Resistance in Humans" (31). The document, released in September 2024, provides a detailed analysis of how antimicrobial resistance could shape global economic trajectories if left unchecked. The report uses projections from the Institute for Health Metrics and Evaluation (IHME) and combines them with economic modelling to provide a look at the impact of AMR on health systems and economies around the world. The report estimates that under a business-as-usual scenario, where resistance rates follow historical trends, the direct health costs of AMR will rise from $66 billion to $159 billion annually by 2050. Furthermore, if resistance rates increase at the rate of the bottom 15% of countries, healthcare costs could rise to $325 billion and the global economy could shrink by $1.7 trillion by mid-century. These figures underscore the profound economic and social impact of AMR. Beyond direct healthcare costs, the report emphasises that the economic impact of AMR goes beyond direct healthcare costs. The estimated losses stem not only from increased healthcare spending, but also from reduced labour force participation, lower productivity, and a decline in tourism and hospitality – industries that are particularly vulnerable to health crises. Experts consulted for the report agreed that countries with robust health systems and higher GDPs are more resilient to the economic impact of AMR, while poorer countries are particularly vulnerable. This creates a vicious circle: low-income countries, already facing significant public health challenges, will struggle even more as AMR strains their economies, limiting their ability to invest in the infrastructure and innovation needed to tackle the problem. This dynamic underscores the importance of global cooperation and support to ensure that all countries, especially those with fewer resources, can tackle AMR effectively.

Given that AMR strategies are increasingly based on an integrated One Health vision, it is essential to broaden the perspective of the AMR burden to also include how antimicrobial use (AMU) and resistance directly affect animals. Despite the potential economic impacts on food-producing animals and the spillover threats to human health and other sectors, research on the economic impacts of AMR in animal health remains limited, with only sparse relevant data. Furthermore, quantifying the exact impact of antimicrobial use (AMU) in food-producing animals on AMR in humans remains a challenge due to lack of high-quality data. Infectious diseases pose significant challenges to animal health, welfare, and productivity. The economic consequences can be considerable, depending on the nature of the pathogen, farming conditions, the mitigation strategies adopted and market circumstances. Infectious diseases in livestock can also have broader negative societal impacts due to the socioeconomic importance of animals for farmers' livelihoods and for the production of safe and affordable food. Moreover, zoonotic diseases in livestock constitute a direct public health issue. Antimicrobials are an important tool to mitigate the impact of infectious diseases at the farm level. From an economic perspective, antimicrobials represent an input to animal production and a cost

incurred to maximise production outputs by minimising infectious disease losses while enhancing animal and public health and welfare. As a production input, antimicrobials have a specific economic characteristic: they are drivers for AMR, meaning that the beneficial use of antimicrobials and their positive effects in infection mitigation may negatively affect their effectiveness in the long run (32). These negative consequences tend not to be directly accrued on the user alone, creating instead losses to society as a whole. AMR and the consequential loss of effectiveness of treatments have hence been framed as a negative externality of AMU (33). When AMR is present, it contributes to the broader burden of infectious diseases in livestock through three main pathways. The first two pathways involve increased mortality and morbidity caused by more severe and prolonged infections resulting from resistant pathogens. These negative effects, ranging from life-threatening conditions to subclinical outcomes, stem from the reduced effectiveness of treatments and have been more thoroughly documented in pet or in animals kept for sport or breeding purposes (34). In contrast, evidence on the extent of these impacts in food-producing animals remains limited. One projection estimates productivity losses of up to 11% and a decline in exports of animal products, due to trade restrictions linked to AMR (35). The third pathway relates to increased expenditures associated with treatment, treatment failures and poorer or lengthier clinical outcomes. These include repeated courses of antibiotics, use of more expensive therapeutic alternatives, additional diagnostic procedures, and veterinary labor costs. In addition, actions taken to mitigate the impact of AMR such as outbreak response, insurance-related expenses, research investments and monitoring and surveillance activities also contribute to the economic burden of AMR in livestock. However, current data quantifying these impacts in livestock remain scarce.

In a study by the WHO and the World Bank published in 2024, a macroeconomic model was developed to analyze the global economic implications of AMR (37). The research aimed to assess the economic impact of AMR on selected economic indicators, such as Gross domestic product (GDP) and covered seven regions, based on the current World Bank regional classification. In the macroeconomic model, the global economic effects of AMR in livestock sector were simulated for the period 2025–2050 under different scenarios. First, a reference scenario was established, beginning in the year 2025; this scenario was based on current levels of antimicrobial consumption and rates of resistance, to then project it for future years up to 2050. Findings from the study suggested that by 2050, the estimated cumulative global GDP loss for 2025–2050 due to AMR in livestock is US$ 575 billion (comparing the reference scenario to scenario 1 with a low resistance rate of 5%). Under the more pessimistic assumptions on the future AMR-disease burden (comparing the reference scenario to scenario 2 where AMR-attributable disease burden doubles in all regions), the estimated cumulative GDP loss between 2025 and 2050 is US$ 953 billion. The economic projections highlighted the potential economic gain from interventions that aim to reduce AMU in livestock.

Results suggest that a global reduction in AMU of around 30% is predicted to lead to a cumulative increase in the global GDP by US$ 120 billion between 2025 and 2050 (comparing the reference scenario to scenario 3). Interventions targeting AMU and AMR can mitigate resistance rates and offer economic benefits that potentially outweigh the costs of implementing these interventions.

CHAPTER 3. OFFICIAL CONTROL ACTIVITIES IN VETERINARY PUBLIC HEALTH

3.1 AN OVERVIEW OF VETERINARY PUBLIC HEALTH: DEFINITION AND SCOPE

Public Veterinary Services have always been a little-known component of the National Health Service (NHS), even though their services are often used unknowingly by both the general population and public administrations (1). Veterinary Public Health (VPH) activities, as well as the existence of a health system that ensures their organization across the territory and long-term management, are considered one of the most significant indicators for assessing the level of social and economic well-being achieved by a country (2). In line with this concept is the more recent definition of Veterinary Public Health (VPH) as the «contribution to the complete physical, mental and social well-being of people through the knowledge and application of veterinary science», formulated by WHO experts in collaboration with FAO and OIE (Teramo, 1999). In practice, veterinary services are healthcare activities primarily aimed at protecting both animal and human health, while also promoting the productivity and well-being of animal populations. As such, they play a significant economic and social role (3). In the majority of countries in the world, Veterinary Services are organized within the Agriculture Administration with the main function to assure animal health and wellbeing. On the contrary, the role of the veterinarian as a public health officer is intrinsic to the history and the culture of veterinary organization in Italy. The Veterinary service being part of the Health administration since the birth of the Italian State in the XIX Century. In the second half of the last century the birth of the Italian National Health Service confirmed that the function of the Italian veterinary service was to analyze and reduce the risks for the human population connected to the relationship man-animal-environment, animal health, food safety and security. The Italian Veterinary Medicine School curricula reflected this “model” of veterinarian as well. After the so-called “Mad-cow crisis” the awareness of the direct and essential role of veterinary services in the prevention of human illness has been officially recognized and in the third millennium the concept of “One Health” has gained popularity worldwide. The term "One Health" refers to a healthcare model that recognizes the interdependence between human, animal and ecosystem health. It is based on an integrated approach that involves multiple disciplines and sectors. Although the concept of One Health is not new, our increasing interdependence with animals and their products has spurred the medical and veterinarian professions to readdress such an approach. This approach would encourage the collaborative efforts of multiple disciplines working locally, nationally and globally to attain optimal health for people, animals and our environment. The concept of One Health originates from the idea of One Medicine, first introduced in 1984 by Calvin W. Schwabe, a veterinarian, epidemiologist and parasitologist, in

his book *"Veterinary Medicine and Human Health"*. One Medicine represents the mutual contribution that human medicine and veterinary medicine can offer to improve the health and well-being of both people and animals (4).

The terms One Health and One Medicine can be considered synonymous, as they share common foundations in the following key areas:

- The concept of population;
- The interaction with the environment;
- The use of epidemiology for the surveillance and control of shared problems (human, animal, environmental);
- The need to consider biological, chemical and physical factors;
- Preventive medicine as a fundamental goal;
- The necessity of evaluating socio-economic factors.

These aspects concern the entire field of public health, within which veterinary public health represents a specialized sector.

3.2 PUBLIC VETERINARY SERVICES IN ITALY: INSTITUITONS AND RELATED ACTIVITIES

The Italian concept of veterinary public health encompasses all veterinary activities of public relevance, with prevention as their primary goal. These activities aim to control the negative aspects arising from the human-animal relationship, while also safeguarding and promoting the positive aspects.

It covers multiple dimensions of this relationship, including:

- Animal health and welfare
- The development and regulation of veterinary medicines
- Veterinary intervention during disasters
- Urban veterinary hygiene
- Health management of wildlife populations

In Italy, the veterinary public health sector operates at the local level within the Prevention Departments of Local Health Units (LHU). It is structured into three independent units, each with technical-functional and organizational autonomy: Animal Health, Hygiene of Food of Animal Origin and Hygiene of Farms and Livestock Production. At the national level, the sector is overseen by the Ministry of Health. Other institutions involved in these activities include the National Institute of Health (NIH) and the network of Istituti Zooprofilattici Sperimentali (IIZZSS).

Below is a brief description of their respective roles and interrelationships.

- **Ministry of Health**

The Ministry of Health is the central body of Italy's NHS and is responsible for safeguarding public health, ensuring the constitutional right to health. Among its various responsibilities is veterinary health, which falls specifically under the Department of Human Health, Animal Health and Ecosystem (One Health) and International Relations. This department carries out coordination and oversight activities in areas such as animal health, veterinary medicines, and animal welfare. It is also involved in research and experimentation in the food and veterinary sectors, as well as in risk assessment related to food safety. Furthermore, the department acts as the national reference authority for the European Food Safety Authority (EFSA) and manages relations with the World Organisation for Animal Health (WOAH), the Food and Agriculture Organization (FAO) and, within its areas of competence, the European Union and other international organizations. The Head of the Department serves as the Chief Veterinary Officer (CVO) representing Italian veterinary services in European and international institutions and also acts as President of the National Centre for the Fight and Emergency Response to Animal Diseases. The department is structured into three directorates, two of which operate in the field of veterinary public health: General Directorate for Food Hygiene and Safety and General Directorate for Animal Health. The first directorate primarily deals with health aspects related to the production and marketing of food, including primary products.

Its responsibilities include:

- ❖ Preparing the Integrated National Plan (INP) every three years, which outlines the framework for official controls in the areas of food, feed, animal health and animal welfare.
- ❖ Managing the Rapid Alert System for Food and Feed (RASFF), used at the European level to report direct or indirect risks to human health related to food or feed (including foodborne zoonoses).

In addition to coordinating and overseeing the controls carried out by other bodies, this directorate also performs inspections, audits and investigations, including verifying the self-control systems implemented by food business operators (FBO) and ensuring food hygiene, especially for products intended for export. The Directorate-General for Animal Health, on the other hand, carries out epidemiological surveillance of infectious and widespread animal diseases, including zoonoses. Supervision of the national animal registry system (NAR) and control of imports and trade of animals, products of animal origin and feed. It plans and coordinates official controls relating to the use of veterinary drugs (drug surveillance) and

carries out activities aimed at identifying, evaluating and preventing adverse effects related to the use of medicines, to ensure a favourable benefit/risk ratio for the population. The Directorate defines policies and supervises official controls that verify their application also in the context of the protection of animal welfare, animal reproduction and zootechnical hygiene.

- **The National Institute of Health**

  It is the main technical-scientific body of the NHS. It carries out research, consultancy and training activities aimed at protecting public health and guiding health policies based on scientific evidence. The core functions of the National Institute of Health are organized across six departments. Among them is the Department of Food Safety, Nutrition and Veterinary Public Health, whose main objective is to protect public health through the development of knowledge, tools and strategies aimed at ensuring food safety and combating zoonoses. In addition to its scientific research activities, this department also performs operational functions. Upon request of the Ministry of Health, it conducts audits on biosafety management systems in laboratories that experimentally handle etiological agents responsible for epidemic emergencies in animal populations, including zoonotic diseases (formerly classified under List A of the World Organisation for Animal Health – WOAH).

- **Istituti zooprofilattici sperimentali (IIZZSS)**

  The IIZZSS network was founded in the early 1900s with the aim to mitigate the damage that infectious diseases were causing to the Italian livestock. Briefly, it became an integrated network of laboratory structures that was officially recognized by the Veterinary Police Regulations of 1954. Gradually, these Institutions passed through several regulatory adjustments, starting from the Law n° 745 of 1975 “Transfer of state functions to the Regions and the rules for the regionalized reorganization of the Istituti Zooprofilattici Sperimentali”, up to Legislative Decree n° 106 of 2012 " Reorganization of the entities supervised by the Ministry of Health", which is still in force.

  IIZZSS are public health institutions, funded and coordinated by the Ministry of Health. They represent an important technical-operational tool of the NHS, providing services in epidemiological surveillance, experimental research, staff training, laboratory support and diagnostics in the fields of animal health, zoonoses and food control. Their activities serve a wide range of users: the Ministry of Health, Regions and Autonomous Provinces, LHU, private veterinary practitioners, livestock sector operators, food companies and citizens.

In Italy, there are 10 IIZZSS, each responsible for 2 or 3 regions, except Sicily and Sardinia, which each have one institute. They are organized into central and peripheral offices, ensuring presence in every Italian province.

The National Reference Centres, designated by the Ministry of Health, are located within these institutes. These centres are departments with high-level expertise in specific areas of animal health, food hygiene and livestock hygiene. Each Reference Centre specializes in a specific field, such as a particular animal or zoonotic disease, a specific livestock sector or a particular diagnostic activity.

The main tasks of the Reference Centres include:

- ❖ Performing confirmatory analyses for diagnoses made by other laboratories;
- ❖ Developing official analytical methods;
- ❖ Promoting the standardization of diagnostic protocols;
- ❖ Designing intervention plans for the surveillance, control and eradication of animal and zoonotic diseases;

They also provide the Ministry of Health and other laboratories with specialized information, technical updates, and support within their areas of competence.

Some Reference Centers are also recognized as official reference laboratories by international organizations such as the European Union (EU), the World Organisation for Animal Health (WOAH), and the Food and Agriculture Organization (FAO).

- **Veterinary services (LHU)**

LHU stands for Local Health Unit, a public institution that provides health services within a geographical area typically corresponding to an Italian province. It functions as a decentralized branch of the NHS.

Each LHU is organized into various Departments, among which is the Department of Prevention, responsible for safeguarding public health through the prevention of infectious diseases, including those transmissible from animals to humans, as well as for ensuring animal health and welfare and the safety of food of animal origin.

These goals are achieved through on-site inspections carried out by veterinary staff at farms and food businesses that handle animal-based products. These inspections aim to verify compliance with regulations concerning animal health and welfare and food safety.

Operationally, official controls are conducted using specific checklists to detect non-compliances. If irregularities are found, corrective actions are proposed, which the FBO must

implement within a defined timeframe. The application and effectiveness of these corrective actions are also monitored by the Veterinary Services.

If the follow-up assessment is negative, or in the event of serious violations, administrative or criminal sanctions may be applied.

The frequency of official veterinary inspections is determined by a risk analysis, which considers both the inherent risks associated with the type of farming or food production activity and any negative outcomes from previous inspections.

The Department of Prevention is structured into three distinct Complex Units, which correspond to the Veterinary Services. These are:

1. **AREA A Animal Health Service**

Veterinarians working in Area A are responsible for:

- Epidemiological surveillance and control of highly contagious infectious animal diseases (e.g., Foot-and-Mouth Disease, Avian Influenza, Swine Fevers);
- Prevention and control of zoonoses (e.g., Brucellosis, Tuberculosis, Salmonellosis, Transmissible Encephalopathies, Rabies);
- Monitoring animal gatherings and movements, including traceability (animal identification registry), as well as import and export activities;
- Collaborating in the control of synanthropic and wild animal populations.

2. **AREA B Hygiene of Food of Animal Origin Service**

The main activities include:

- Health inspection in slaughterhouses and sanitary control of game meat intended for human consumption;
- Food safety checks in facilities that produce, process, store and market foods of animal origin;
- Sanitary certification of products intended for export and hygienic inspections of imported foods;
- Issuing hygiene and health opinions for the opening of industrial facilities requiring EU recognition for the processing, transformation and storage of animal-based food products.

3. AREA C Hygiene of Livestock and Livestock Production Service

The main responsibilities of this area include:

- Control and supervision of the distribution and use of veterinary drugs (on farms, in pharmacies, storage facilities and veterinary clinics);
- Detection of drug residues and environmental contaminants in animal products and food of animal origin through the collection of biological samples;
- Monitoring of animal feed and feed production;
- Control of animal reproduction and welfare of both livestock and companion animals.

3.3 THE EPIDEMIOSURVEILLANCE NETWORK SYSTEM AND THE ROLE OF THE COMPANY VETERINARIAN

The increase in the number of animals and animal products traded internationally, along with the growing complexity of trade exchanges in recent years, has contributed to a higher risk of pathogen dissemination, raising the level of exposure of the European Union's livestock to infectious diseases, including those originating from non-EU countries (5). In this context, the timely diagnosis and immediate reporting to the competent authorities of information related to the onset of suspected outbreaks of animal diseases is essential for implementing effective control measures.

Moreover, considering the ongoing global reduction in financial resources available for health services, the need for precise and detailed information on both human and animal populations has become crucial to secure the necessary resources for addressing potential threats to global health (6).

Lastly, the collection of epidemiological data in the veterinary field is indispensable to meet the “information obligations” that each Member State has towards international institutions such as the European Commission and the World Organisation for Animal Health (WOAH). These institutions process the collected data to periodically publish reports and bulletins on the health status of the Union.

According to the WHO definition, epidemiological surveillance is understood as “an operational methodology based on the continuous and systematic collection, analysis and interpretation of data relating to the health status of a population, which are necessary for the planning, implementation and evaluation of interventions.”

In the veterinary field, the epidemiological surveillance is a fundamental component of public health aimed at monitoring, detecting, and preventing the spread of infectious and zoonotic diseases in animal populations. Through the systematic collection, analysis and interpretation of health data, this surveillance enables early identification of outbreaks, evaluation of risk factors and implementation

of timely control measures by considering possible alternatives, along with their costs and benefits. It also plays a critical role in ensuring food safety, protecting animal welfare and preventing the transmission of diseases to humans. In the context of the One Health approach, veterinary epidemiological surveillance contribut significantly to the integrated management of human-animal-environment interface. Although they are often used interchangeably in everyday language, surveillance and monitoring actually have different meanings. Monitoring refers to the systematic measurement of various indicators and can be used, for example, to determine the prevalence level of a pathogen in an animal population or in a food product. Surveillance, on the other hand, involves the collection, analysis, interpretation and dissemination of data with the aim of assessing the evolution of a specific phenomenon over time in relation to predefined goals or requirements. Surveillance should therefore be understood as an activity that also allows for the evaluation of the effectiveness of control measures, by verifying how much they influence the development of the phenomenon under observation. It is thus a process consisting of a series of actions that generate information, the assessment of which leads to a replanning of those very actions.

To summarize, surveillance and monitoring differ in both the methods used and the objectives pursued:

- Monitoring records data on a phenomenon;
- Surveillance uses the data collected (potentially through monitoring) to evaluate the trend of a phenomenon with respect to reference standards and to make informed decisions.

In practice, surveillance activities are initiated based on a specific action or need. In other words, if carried out without the prospect of follow-up actions, they become pointless and even a waste of resources (7). Working in terms of surveillance means planning the activities of health services based on the optimization of available resources and creating a knowledge base to support decision-making processes.

In general terms, the main phases of surveillance procedures include: the systematic collection of data, their analysis and synthesis, the interpretation and dissemination of the information obtained, all aimed at supporting action, such as the implementation of short- or long-term disease control programs and strategies. This process requires an in-depth understanding of the territory, access to the target populations, a careful risk analysis, the ability to collect useful and meaningful data, validate them and make them available to the various professionals involved, and, in appropriate ways, also to the public. From an operational standpoint, there are two types of surveillance: active and passive. In active surveillance, data collection is planned in advance and requires the implementation of a specific procedure, such as conducting serological surveys, administering questionnaires to farmers or animal owners or performing regular inspections at livestock farms.

This type of surveillance involves defining in advance the target population and the sampling plan. Being systematic and organized, active surveillance allows for the analysis of trends, comparisons between areas and farms and the estimation of prevalence/incidence. It also enables the identification of infected individuals in cases of long incubation periods, subclinical forms or asymptomatic carriers. However, it is very costly and resource-intensive, both in terms of time and personnel. Moreover, if the expected prevalence is below 0.1%, the required sample size becomes unsustainable either due to excessive cost or because available tests cannot reliably distinguish between zero and very low prevalence values (8). Passive surveillance, on the other hand, is based on the voluntary or mandatory reporting to the competent authority of health data following a confirmed or suspected diagnosis of specific diseases or from routine health monitoring conducted on farms or at slaughterhouses (e.g., functional checks, linear scoring, mortality or culling reasons, pathological findings). While passive surveillance is cost-effective, easy to implement and useful for identifying new diseases for which the target is unknown, it also comes with several drawbacks. These include the risk of underreporting, particularly in the case of subclinical cases or asymptomatic carriers. Additionally, its effectiveness is variable, as it depends heavily on the willingness of the person reporting and the sensitivity of the detection system.

The importance of collecting and sharing health and livestock data within the agri-food chain has been a concern of the European legislator since the early 2000s, following the BSE crisis. This was reflected in the so-called “Hygiene Package” regulations, particularly Regulations (EC) No. 852 and 853/2004, which require FBOs who rear animals or produce primary products of animal origin to record epidemiological data and make it available to the Competent Authorities (CAs), in accordance with Regulation (EC) No. 178/2002.

These data include both health-related information, such as the onset of diseases or diagnostic test results and management-related data, such as administered medicines or the type and origin of animal feed. According to Regulation (EU) 625/2017, the information collected by FBOs as part of their self-monitoring system allows the CAs to adjust the frequency of official controls based on risk assessment in the fields of feed, food, animal health, and welfare. The surveillance obligation for operators is further reinforced by Regulation (EU) 429/2016, concerning transmissible animal diseases, which requires farmers to monitor the health and behaviour of animals under their responsibility, registering changes in production parameters or mortality rates in order to detect disease outbreaks early. In line with this regulatory framework, in December 2017, the Italian Ministry of Health issued a Decree establishing the epidemiological surveillance network system and the figure of the company veterinarian.

This system is intended for the collection, management and exchange of data and information between FBOs raising food-producing animals and the veterinary competent authorities (Ministry of

Health, Regions, the Autonomous Provinces of Trento and Bolzano and LHA). It operates via applications available on the veterinary information system portal (www.vetinfo.it), with technical support from the IIZZSS.

The Decree allows the FBO to fulfil their reporting obligations under Regulations 852 and 853/2004 by independently uploading the relevant data into the Vet info system. The goal is to encourage and facilitate the voluntary sharing of self-monitoring data by the FBO with the CA, enabling early detection of risks in farms and thereby protecting animal health, animal welfare and public health. Through the Vet info platform, data from official controls and self-monitoring (voluntarily shared by the FBO) are collected and processed to enable the risk categorization of farms. This is carried out using ClassyFarm, an application linked to the NAR managed by the Ministry of Health. The system created by the Decree offers benefits for all stakeholders. For the FBOs, the continuous flow of information to the CA strengthens their self-monitoring systems and plays a key role in the farm's risk categorization, possibly reducing the number of official inspections. For the public veterinary services, it allows more targeted and efficient inspections, saving financial and human resources.

In order for the FBO's data to be made available within the public epidemiological surveillance system, the data must be entered by a company veterinarian, who ensures the reliability and validity of the health data (Art. 2 of the Decree).

The roles and requirements of the company veterinarian are defined in Articles 3 and 4 of the Decree. The company veterinarian is a private veterinarian voluntarily selected by the FBO and acts as a consultant to the business, working to improve its health standards, while also facilitating the relationship between the FBO and public health services.

To qualify, the company veterinarian must be:

- Registered with the National Federation of Veterinary Orders (NFVO);
- Have completed a training course specified in the Decree;
- Formally appointed by the FBO through a signed designation agreement;

The company veterinarian must know the farm's health and production situation, maintain regular involvement, and may even be an employee of the FBO, provided they meet all CA requirements. As a consultant, the company veterinarian cannot have ties with companies that supply services, raw materials or products to the farm.

Company veterinarian's responsibilities include:

- Assisting with mandatory record-keeping and communications with public veterinary services;
- Ensuring compliance with mandatory disease notification regulations;
- Supporting the development of voluntary farm plans for disease control;

- Managing animal identification and registration;
- Determining causes of animal deaths;
- Supporting proper use of veterinary medicines, promoting responsible and prudent use to combat antimicrobial resistance;
- Managing drug stocks and overseeing voluntary eradication/control programs for infectious diseases;

In summary, the company veterinarian acts as a hybrid figure, both private consultant and liaison with institutions, contributing significantly to the efficiency of public veterinary health services by reducing the need for direct intervention from public authorities.

3.4 ANTIMICROBIAL RESISTANCE SURVEILLANCE IN HUMAN AND VETERINARY FIELDS

Surveillance of Antimicrobial Resistance (AMR) involves a set of activities aimed at identifying and monitoring, according to the One Health approach, the spread and evolution of bacteria resistant to currently known and used antibiotics, which are responsible for infections in both humans and animals. The data collected through surveillance are essential to guide strategies to contain antimicrobial resistance and evaluate their effectiveness, support the selection of antibiotic therapies in both human and veterinary clinical settings and steer research and development strategies for new antimicrobial agents.

AMR Surveillance in the Human Sector

In Italy, the main national surveillance systems in the human health sector are:

- AR-ISS (Antibiotic Resistance Surveillance)
- CRE surveillance (Carbapenem-Resistant Enterobacteriaceae bloodstream infections)

Both are coordinated by the NHI. The AR-ISS system, active since 2001, is based on a network of hospital clinical microbiology laboratories that annually report routine antibiotic susceptibility test data for selected pathogens of clinical and epidemiological relevance. Participation is voluntary, but regional health authorities are encouraged to recruit laboratories to ensure regional representativeness. Italy contributes AR-ISS data to EARS-Net, the European Antimicrobial Resistance Surveillance Network, coordinated by the ECDC, through the TESSy (The European Surveillance System) platform.

AR-ISS focuses on eight bacterial species from invasive infections (e.g., bloodstream infections and meningitis):

- *Staphylococcus aureus*

- *Streptococcus pneumoniae*
- *Enterococcus faecalis*
- *Enterococcus faecium*
- *Escherichia coli*
- *Klebsiella pneumoniae*
- *Pseudomonas aeruginosa*
- *Acinetobacter spp.*

The CRE surveillance system was launched in 2013 to track infections caused by carbapenem-resistant or carbapenemase-producing *K. pneumoniae* and *E. coli* across Italy. Additional systems managed by the ISS's Department of Infectious Diseases monitor AMR in specific pathogens, including: MDR tuberculosis (multi-drug-resistant TB), Neisseria gonorrhoeae, Enter-Net, which collects epidemiological and microbiological data—including resistance—for enteric pathogens (*Salmonella*, *Campylobacter*, *Shigella*, *Yersinia*, *Vibrio*, etc.). Data from these systems are also shared with ECDC for inclusion in European surveillance reports.

AMR Surveillance in the Veterinary Sector

Italy has long implemented surveillance activities within the framework of the "Harmonized Monitoring Plan on AMR in Zoonotic and Commensal Bacteria", in accordance with Decision 2013/652/EU, now replaced by Decision 2020/1729/EU.

The plan covers:

- Food-producing animals: poultry, turkeys, pigs, and calves (<1 year)
- Food of animal origin (including imported meat)

It provides accurate estimates of AMR prevalence in zoonotic bacteria such as: *Salmonella spp.*, *Campylobacter jejuni* / *coli*, *E. coli* and other Enterobacteriaceae producing extended-spectrum beta-lactamases (ESBL), AmpC enzymes or carbapenemases. The plan, issued annually by the Ministry of Health, is implemented by regions and autonomous provinces, with support from the National Reference Laboratory (NRL) and the National Reference Centre for AMR, both based at the IZS Lazio and Tuscany. Each year, raw data on resistance profiles of bacterial isolates from monitored species (alternating annually between poultry/turkeys and calves/pigs) and their derived meat are sent to the European Food Safety Authority (EFSA). These data contribute to the European Summary Reports on AMR, jointly published by EFSA and ECDC. Italy also reports these findings in its National Zoonoses Country Report, including comments and summaries from the AMR Reference

Centre. Unlike livestock, no EU-wide harmonized AMR monitoring system exists for companion animals. In Italy, as in other countries, regional and local studies based on diagnostic samples have shown the presence of multi-drug-resistant pathogens similar to those found in humans (e.g., ESBL-, AmpC- and carbapenemase-producing Gram-negatives). This confirms companion animals as a potential emerging reservoir for AMR. To support veterinary antimicrobial stewardship, it is crucial to investigate AMR profiles of clinically relevant pathogens in both livestock and pets. If laboratories use accurate and harmonized methods, susceptibility data could be processed and made available (even before diagnostic results) to guide appropriate antibiotic use. Additionally, surveillance should be accompanied by early warning systems to detect emerging resistance or genotypes. The use of Whole Genome Sequencing (WGS) for typing and tracking resistant pathogens is rapidly expanding and offers the highest resolution for strain comparison. It is recommended by both ECDC and WHO and should be further promoted.

Currently, full integration between human and veterinary AMR surveillance is difficult, due to different regulations, different objectives, different protocols and data flows. However, at the EU level, integration is progressing, especially for zoonotic pathogens (e.g., *Salmonella spp.*, *Campylobacter spp.*) and to a lesser extent for MRSA. In Italy, AMR in zoonotic bacteria is monitored through: National Salmonella Control Plans and National AMR Monitoring Plan. These results feed into both the National Zoonoses Country Report and the ECDC–EFSA Joint Reports. According to the One Health approach, targeted surveillance should focus on the movement and exchange of resistant strains or genes between the veterinary and human sectors, not only in zoonotic pathogens but also in AMR indicator microorganisms in animal production and clinically relevant human pathogens (e.g., ESBL-/AmpC-/carbapenemase-producing *E. coli*, MRSA, VRE) (14). Evaluating the bidirectional transmission potential between animal products and the human population is crucial to understanding and managing AMR risks in both sectors.

CHAPTER 4. THE CLASSYFARM SYSTEM

4.1 WHAT IS CLASSYFARM

The challenges currently facing the healthcare and agri-food sectors are becoming increasingly complex. Issues related to animal welfare, farm biosecurity and the excessive use of antibiotics generate increasingly interconnected health risks, requiring an integrated approach that involves the entire supply chain — including slaughterhouses, which are considered key epidemiological observation points. These risks are not limited to zoonoses or food safety, but also include the phenomenon of antimicrobial resistance (AMR9, which affects both human and animal health and has reached alarming levels in recent years (1). As a result, effective planning of prevention, control and risk mitigation measures has become essential and urgent. This approach has been further reinforced by the provisions of the most recent European regulations on official controls, which establish that inspections carried out by the competent authority throughout the agri-food chain must be adapted according to their relative level of risk to public health. In this context and with the aim of implementing the Minister of Health's Decree of 7 December 2017 establishing a system of epidemiological surveillance, the Ministry of Health introduced an integrated information system for risk categorization of livestock farms called ClassyFarm.

Operational since 2018, the system is the result of several projects funded by the Ministry of Health and developed by the Istituto Zooprofilattico Sperimentale della Lombardia e dell'Emilia Romagna (IZSLER), in collaboration with the University of Parma and numerous public stakeholders (Regions, LHUs, other IIZZSS, Universities) and private ones (veterinarians, farmers, trade associations). IZSLER still manages the system's overall administration and development. ClassyFarm is an IT platform included in the national veterinary portal (www.vetinfo.it), allowing for the collection, validation, and processing of data from multiple sources for the purpose of comprehensive farm evaluation. The system analyzes information collected in the field through official controls carried out by Competent Authorities, audits by certifying bodies or self-monitoring activities performed by trained freelance veterinarians such as the company veterinarian. The data concern six strategic sectors: biosecurity, animal welfare, health and production parameters, animal nutrition, drug use and lesions detected at slaughter. Once uploaded to the platform, the collected data are converted—using scientifically validated coefficients—into a numerical indicator that measures the level of risk of the farm itself. One of ClassyFarm's key features is its interoperability with other IT systems, such as the National Animal Registry (NAR), the Electronic Veterinary Prescription system (EVP) and diagnostic laboratories of the IIZZSS network. This integration allows for the inclusion of additional information related to farms and their management, enabling risk assessment even if the farmer chooses not to provide self-monitoring data. Indeed, the registration of an Italian livestock farm in

the ClassyFarm platform is currently voluntary; however, it is mandatory for obtaining the animal welfare label "Sistema di Qualità Nazionale per il Benessere Animale" (SQNBA), which has adopted the ClassyFarm system as its official tool for evaluating animal welfare conditions in order to grant or deny certification. Moreover, participation in ClassyFarm is a compulsory prerequisite to access CAP (Common Agricultural Policy) funding, particularly regarding Eco-Scheme 1 (Payments for the reduction of antimicrobial resistance and animal welfare), reinforced conditionality, and adherence to higher-level commitments that include climate sustainability actions and measures to combat antimicrobial resistance through pharmacosurveillance.

Access to ClassyFarm is reserved exclusively for certain individuals (official veterinarians, farm veterinarians and livestock farmers) upon request. In this way, the system provides competent authorities with a tool to plan more effective and targeted inspections where the risk level—assessed according to uniform and scientifically validated criteria—is higher. This results in savings for the public administration (in terms of financial and human resources) and reduces the burden on lower-risk farms by decreasing the frequency of controls to which they are subject. Through the assignment of specific scores related to the health and welfare status of farmed animals, ClassyFarm also offers participating farmers an opportunity to identify areas for improvement in their farm management strategies and to determine the most effective measures to reduce their risk level. This can also be achieved through comparison with other farms operating in the same geographical or national context. Indeed, the system, while ensuring data confidentiality, allows the visualization of aggregated data by geographical area and farm type, encouraging a virtuous cycle based on the emulation of best practices. This process benefits the economic interests of the farmer, but more importantly, it protects consumers in terms of the safety and quality of the food produced. In fact, in the context of animal health and welfare, the economic performance and productivity of a farm are closely linked to its overall health status, its capacity to implement preventive measures to reduce risk, ensure animal welfare and make prudent use of veterinary drugs.

Information on how the system works, as well as the checklists currently in use can be freely consulted on the website: www.classyfarm.it

4.2 CLASSYFARM OPERATION AND ACTORS

The ClassyFarm system collects a wide range of data related to farm management in order to develop a risk assessment for public health associated with livestock farms through the assignment of a score. This risk is essentially categorized into three main areas:

1. Sanitary risk related to the spread of diseases in the animal and human population, estimated through the assessment of the level of biosecurity implemented on the farm.

2. Risk of the occurrence of ethically unacceptable farming conditions that may compromise the physiology and productive capacity of the reared animals. This risk is quantified by considering the level of animal welfare allowed by the farm's conditions.
3. Risk of emergence and spread of antimicrobial-resistant bacterial clones, assessed by analyzing the practice of veterinary medicines use.

The elements necessary to enable an objective risk assessment come from official inspections conducted on farms by the competent veterinary authorities, from self-monitoring activities carried out by farmers and from official databases (primarily NAR and EVP system). Both public and private veterinarians collect data using specific checklists dedicated to different thematic areas, so that the assessment process is simplified and conducted according to uniform and transparent criteria.

Inspections carried out by public veterinarians are official controls performed to ensure compliance with legislation on food and feed, as well as with animal health and welfare regulations. Since they are legally mandated under European Regulation 625/2017, these inspections follow the same criteria for all farms, regardless of whether the business participates in the ClassyFarm system.

In contrast, checklists completed by the farmer through the company veterinarian represent a voluntary activity aimed at gathering rational information to improve farm management and reduce the frequency and burden of official inspections, provided that the checklists indicate a low level of risk. According to the Ministerial Decree of 7 December 2017, voluntary controls within the ClassyFarm system are carried out by freelance veterinarians who act as consultants to the farmer in the role of company veterinarian. The requirements to obtain this qualification and the formal relationship to be established with the farmer are specified in the same Decree. By law, performing the self-monitoring, completing the checklists and subsequently entering the data into the ClassyFarm portal is the exclusive responsibility of the company veterinarian, ensuring the accuracy and consistency of the information uploaded and made available to the competent authorities.

An additional data stream that feeds the system derives from inspections carried out at the slaughterhouse. These findings, collected as part of official controls, provide valuable information to assess both the health status and the level of animal welfare. Through the examination of anatomopathological lesions on carcasses, it is possible to identify subclinical or chronic diseases, as well as pathognomonic signs of poor welfare conditions (2).

Given the dual nature of the inspections just described, even farms that do not actively participate in ClassyFarm can be classified according to the system's own metrics. This is achieved by calculating a risk score based on the results of official controls and by integrating data from other databases of the national veterinary information system (e.g. NAR or EVP system), to which all farms are legally required to report data. Data from various sources—gathered from the field via checklists, at

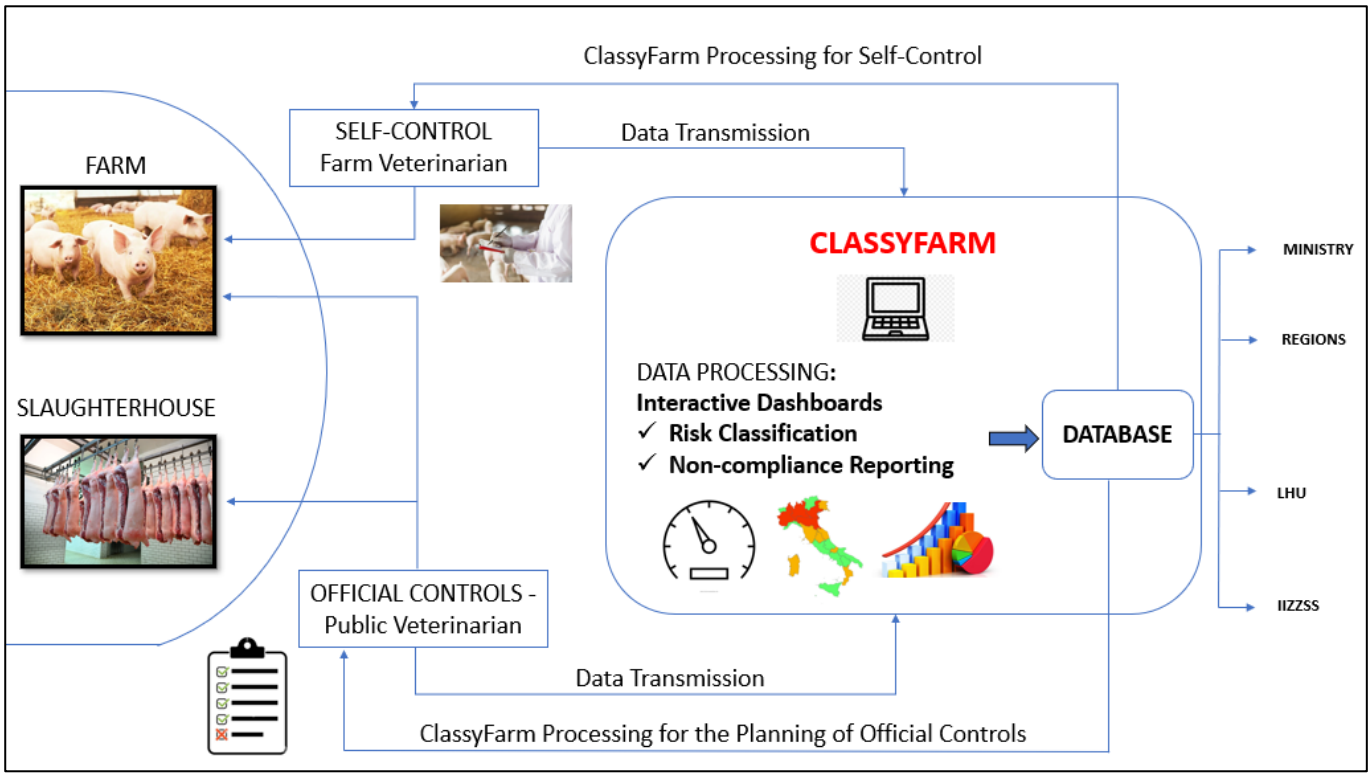
slaughterhouses or retrieved from official information systems—are compiled within ClassyFarm and processed using business intelligence tools. The system generates a score indicating the level of public health risk associated with each farm, based on three key assessment areas: biosecurity, animal welfare and antibiotic use. These scores are made available to registered users (public veterinarians, farmers and company veterinarians) through interactive dashboards, graphs and downloadable summary reports. The data viewable via the dashboards varies according to the area of focus. For antibiotic consumption, information can be consulted both in aggregate form and at the individual farm level. In the former case, data refers to farms within the same LHU or to those under the care of a specific company veterinarian, depending on the user's role (LHU or company vet). In both display modes, the following information is made available: overall antimicrobial use, detailed use by drug criticality category (critically important/highly important/important as per WHO classification), active substance, administration route, antibiotic class and livestock category. Users can filter by year and compare their data with national, regional or provincial medians. The system also provides multi-year trends, filterable by antimicrobial class or active substance. For biosecurity and animal welfare, data can also be visualized in aggregate form or at the individual farm level. Graphs and statistics correspond to each checklist question, with responses categorized as insufficient, acceptable or optimal. The three evaluation types are also displayed as percentage distributions by farm or by LHU. The overall score, based on all checklist responses, is shown in bar chart form, highlighting stratified scores by questionnaire macro-areas (e.g., internal and external biosecurity or, for animal welfare, structures, management, major risks and animal-based measures). Stratified scores can be compared with average values at national, regional or LHU level.

Authorized users of the system include public veterinarians working for institutions involved in veterinary public health (Ministry of Health, regional and local veterinary services and IIZZSS) and private veterinarians acting as consultants for farmers. ClassyFarm's data therefore serves different purposes depending on the type of user. For official veterinarians, the system supports risk-based control planning, provides field evidence for policy development and allows for evaluation of intervention effectiveness. For farmers and their company veterinarians, ClassyFarm scores can highlight weaknesses in farm management and support targeted improvements. The system offers farmers a comprehensive, regularly updated snapshot of their farm's status. By analyzing risk scores and trends over time, users receive direct feedback on the impact of improvements made in specific areas (e.g., biosecurity or animal welfare) and the resulting effects on other sectors. For instance, investing in farm biosecurity may reduce the risk of pathogen spread, which over time can lower antibiotic usage due to fewer disease cases among animals. Reduced drug use, in turn, may decrease the likelihood of developing antibiotic-resistant bacterial strains, benefiting both animal and human

health. In this regard, ClassyFarm aligns with the principles of One Health, recognizing the interdependence of human, animal, and environmental health.

The following Figure 4.1 describes the operating of ClassyFarm.

Figure 4.1 **The functioning of the ClassyFarm system**



4.3 MAIN DATA CATEGORIES AND ASPECTS CONSIDERED IN CLASSYFARM

4.3.1 ANIMAL WELFARE

There are numerous scientifically recognized definitions of animal welfare, many of which are based on the concept of absence of deprivation regarding the fundamental freedoms defined in the Brambell Report (1965), namely:

1. Freedom from hunger, thirst, and malnutrition;
2. Freedom from pain, injury, and disease;
3. Freedom from fear and mental suffering;
4. Freedom to live in an appropriate physical environment;
5. Freedom to express normal species-specific behaviours.

Determining what constitutes a good level of welfare for farmed animals is undoubtedly complex, as one may confuse their actual living conditions with one's own expectations and specific knowledge in the field of animal husbandry (3). From a medical-scientific standpoint, the "diagnosis" of an animal's welfare level must be based on the analysis of many factors related to its living conditions, fulfilment of needs and adaptability to the environment. All these elements must be recorded and

assessed through specific indicators and the results must be analysed using a method that is as objective and scientific as possible.

The ClassyFarm system includes species-specific checklists for assessing animal welfare, available to official veterinarians when controls are mandated by law or to farm veterinarians for self-monitoring purposes. These documents were developed by the National Reference Centre for Animal Welfare (CReNBA), based at the IZSLER, taking into account general and specific legislation on the protection of farm animals and the latest authoritative scientific evidence. The ultimate goal of using these checklists, beyond identifying hazardous situations for animal welfare, is to categorize farms into risk levels and allow comparisons between farms using uniform criteria, ensuring the highest level of objectivity in welfare evaluations.

The system classifies farms according to three risk levels:

- Level 1 – High risk: unacceptable or negative conditions indicating that some animals are or may be experiencing distress due to the inability to enjoy one or more of the five freedoms;
- Level 2 – Controlled risk: acceptable condition, where all animals in the herd can fulfil their five freedoms and are not subject to stress;
- Level 3 – Low risk: optimal, positive condition due not only to the full adaptation of the animals to their environment and fulfilment of the five freedoms but also to the ability to experience positive and rewarding situations that result in "eustress."

For evaluation purposes, two groups of data are analysed: those related to environmental conditions (management, structures, equipment, and microclimate) and those based on direct indicators of welfare or animal-based measures (ABMs) from recent scientific literature. The first group is divided into three risk areas:

- Area A – Farm management and personnel;
- Area B – Structures and equipment;
- Area – Major risks and alarm systems.

The second group, involving direct observations and measurements on animals to assess their welfare, falls under:

- Area C – Animal-based measures.

The final result of applying the checklists is a global numerical welfare index that indicates the farm's risk level. The partial result of each area (A, B, C, and Major Risks) provides insight into the weight and significance each area contributes to the final welfare risk index.

At the end of the entire evaluation process, a final report is generated, summarizing the collected data and identifying the critical points. The report includes:

- A list of critical points, i.e., criteria with non-compliant or insufficient responses;
- The overall risk level related to the welfare conditions of the animals present on the farm;

- The risk level of the animals in relation to each of the four assessment areas.

4.3.2 BIOSECURITY

Biosecurity refers to the combination of all the different measures implemented to reduce the risk of introduction and spread of disease agents through an area where farm animals are present (4). Implementing biosecurity involves providing facilities and adopting behaviour to reduce the risk of infection in all activities involving animal production. It can be divided into main components: external and internal biosecurity. The first one includes all measures taken to prevent the introduction of infectious agents into farms and it is associated with all actions where there is contact between the farm and the outside world such as infrastructure aspects, organisation of the farm buildings, presence of entrance restriction for animals and persons (e.g. hygiene lock, quarantine pen). Internal biosecurity, on the other hand, consists of all the measures taken to prevent spread of infectious agents within the farm from one age category to another or from one production group to another. Internal biosecurity measures are strongly linked to farm management and daily practise of animals' carers (e.g. hygienic measures between compartments, working lines, cleaning and disinfection practices, etc.).

As with the other areas of investigation included in the ClassyFarm system, biosecurity measures applied on farms are also assessed using specific checklists designed to evaluate the risk associated with biosecurity deficiencies for each farm. The checklists addressed to official veterinarians for the assessment of legally required biosecurity standards apply to pig and poultry farms.

In the case of pig farming, the checklist includes questions related to the minimum requirements applicable across the entire national territory (in accordance with the recent Ministry of Health Decree of 28/06/2022, "Biosecurity requirements in establishments housing pigs") as well as measures required in enhanced biosecurity zones due to outbreaks of African swine fever in the same or neighbouring areas (Implementing Regulation (EU) 2023/594). The checklist was developed with the principle of maintaining a single format, adapted to the production type and capacity of the farm. Production types are divided into housed and semi-free-range farms, which are further classified by capacity into high and low capacity. In this regard, the Ministerial Decree of 28/06/2022 defines a "high capacity" farm as one capable of housing 300 or more animals.

For poultry species, the checklists for public veterinarians are based on the mandatory biosecurity measures provided by the Ministry of Health Decree of 30 May 2023, "Application procedures for biosecurity measures in poultry farms." These measures, verified through the checklists, concern both ordinary management and emergency situations involving disease outbreaks, in which stricter measures are required. Specific requirements are also considered for backyard flocks, outdoor systems and holdings with fewer than 250 birds. In addition to the mandatory requirements, the checklists include further questions relevant to assessing the risk of major poultry diseases (such as Influenza and Salmonella).

In addition to official control, the ClassyFarm system also provides tools for assessing the level of farm biosecurity on a voluntary basis, carried out by the company veterinarian. In this case, the reference species is the pig, and the checklist used is the one developed by Ghent University.

The Biocheck.UGent system is a risk-based scoring system to quantify the on-farm biosecurity. It does not start from a specific disease but rather approaches biosecurity in general and focusses on those aspects that are common for the transmission of many different types of infectious diseases. The survey is divided into several subcategories for internal and external biosecurity. The answer to every question results in a score between zero (when this measure is not implemented at all or the least optimal answer is given) and one (when the measure is fully implemented). Depending on the importance of a particular biosecurity measure, the score per question is multiplied by a weight factor. As such, the Biocheck.UGent scoring system provides a risk-based score which takes into account the relative importance of all different biosecurity measures. The final score for both internal and external biosecurity can range from zero, indicating a total absence of the described biosecurity measures, to 100, indicating a full application of the described measures. The average of internal and external biosecurity results in a score for the total biosecurity. Except for certain specificities related to the species and the livestock category involved, the checklists developed for official or voluntary controls in pig and poultry farming share a similar structure in the questions proposed. The verification elements concern both external and internal biosecurity and include structural and management-related measures.

Main general requirements referring to external biosecurity focus on:

- Farm location and environment;
- Access and control of visitors;
- Employed workers and foreign labour;
- Purchasing policy - introducing new animals to the farm;
- Control of transport vehicles;
- Control of feed and water;
- Pest control;
- Management of cadavers;

As for internal biosecurity, the questions focus on three main areas: hygiene control (cleaning and disinfection of stable and equipment), handling sick animals (i.e. the presence of sickbays and the use of dedicated equipment to handle sick animals) and disease management (i.e. the implementation of all-in/all-out systems or different rooms to keep animals of different ages).

4.3.3 USE OF DRUGS AND PHARMACOSURVEILLANCE

Over the past 20 years, control activities in farms raising animals for food production regarding the use of veterinary medicinal products have been mainly focused on compliance with legal requirements—particularly the proper management of medicines, record-keeping obligations and adherence to withdrawal periods before sending animals to slaughter. More recently, the concept of food safety has significantly evolved: it is no longer sufficient to ensure the absence of pharmacologically active residues in food of animal origin; it is also necessary to demonstrate that drug treatments are carried out appropriately in order to prevent the emergence of AMR, a phenomenon whose health and economic consequences are becoming increasingly alarming.

In this context, the ClassyFarm system includes a specific checklist as a tool to record the outcomes of official pharmacosurveillance inspections. Together with data from the EVP system on the quantity and types of antibiotics used, it enables risk assessment of farms related to improper drug management. Therefore, the collection of data on this risk is carried out exclusively by public veterinarians across all species raised in farms participating in the system.

The checklist, developed in accordance with the latest regulatory provisions (Regulation (EU) 2019/6 and Legislative Decree of 7 December 2023, No. 218), is structured into four assessment areas:

AREA A: STOCK OF VETERINARY MEDICINES

AREA B: USE OF VETERINARY MEDICINES

AREA C: HORMONAL TREATMENTS

AREA D: AMR RISK ASSESSMENT

When performing inspections in verification areas A, B and C which concern mandatory legal requirements, official veterinarians may identify non-compliances categorized as either minor or major. A minor non-compliance typically results in a formal warning, that is, a request to implement a corrective action within a given time frame. However, repeated violations automatically lead to a more serious classification. In the case of a major non-compliance, in addition to a possible warning, an administrative or criminal sanction may be imposed if provided for by law.

Assessment area D, on the other hand, is used to assess risk behaviors related to antimicrobial resistance. Unlike the other areas, the items in this section are not assessed for compliance but are instead assigned numerical scores, which vary depending on whether the behavior is considered to pose a lower or higher risk.

- **OPTIMAL** (low risk)
- **IMPROVABLE**
- **INSUFFICIENT** (high risk)

The sum of the scores assigned will allow the farm to be classified into a specific risk category, which may subsequently influence the frequency of official inspections. According to the 2024–2026 National Pharmacovigilance Plan, in fact, 60% of the farms to be inspected annually are selected based on the risk categorization developed by the ClassyFarm system.
The main elements considered in each section of the checklist are summarized as follows:

1. **AREA A: STOCK OF VETERINARY MEDICINES**

   AREA A is completed only in farms where the competent authority has authorized the storage of appropriate reserves of veterinary medicines in accordance with Legislative Decree 218/2023. This section assesses the proper storage of these reserves, the types of medicines present (as some antibiotics may not be stored in reserve), and their correlation with a veterinary prescription. During the inspection, the adequacy between the quantity of stored medicine and the number of animals (species/category) to which the medicine is intended is also verified, in order to assess its actual appropriateness.

2. **AREA B: USE OF VETERINARY MEDICINES**

   This section of the checklist verifies whether the obligation to register the medicines used in the Electronic Veterinary Prescription system (EVP) has been properly fulfilled and whether the medicines present, associated with a veterinary prescription, are being used in compliance with the conditions established by their marketing authorization. It also checks for the proper identification of treated animals, compliance with withdrawal periods for animals sent to slaughter, the absence of unauthorized pharmacological substances and the correct management of leftovers and expired drugs. Some questions also assess whether the use of antibiotics for prophylactic or metaphylactic purposes occurs strictly within the limits defined by law.

3. **AREA C: HORMONAL TREATMENTS**

   The points considered in this case concern compliance with the legal provisions regulating the use of hormonal treatments (Legislative Decree 158/2006) and the correct identification of the animals to which such treatments are administered.

4. **AREA D: AMR RISK ASSESSMENT**

   AREA D assesses whether the use of antimicrobial drugs on the farm is conducted in accordance with the prudence criteria set out in relevant regulations and national guidelines.

Specifically, it evaluates how often antibiotic treatments are preceded by a clinical and laboratory diagnosis, including antimicrobial susceptibility testing (antibiograms); the methods of milk disposal in the case of antibiotic treatment of lactating animals; and the implementation of disease prevention measures, such as vaccination or enhanced biosecurity protocols exceeding the legal minimum. Finally, it checks for the presence of standard operating procedures that ensure compliance with the conditions of use for medications administered via drinking water or liquid feed, and that the risk of cross-contamination during the distribution of medicated feed is properly managed.

CHAPTER 5. CLASSYFARM COST ASSESSMENT

5.1 COST CLASSIFICATION

As previously described, ClassyFarm is an integrated surveillance system for monitoring the Italian livestock farms on risks related to antimicrobial use (AMU) and other indicators, such as animal welfare and farm biosecurity. It is the result of various projects funded by the Italian Ministry of Health and it was developed by the Istituto Zooprofilattico Sperimentale della Lombardia e dell'Emilia Romagna (IZSLER) in collaboration with the University of Parma. The system processes data on AMU, farm biosecurity, animal health and welfare collected by the competent veterinary authorities during official controls and those resulting from self-control, recorded by the farm veterinarians. Such data are integrated with further information acquired by the databases of other systems in the National Veterinary Information system such as the National Animal Register (NAR) and the database of the National Electronic Veterinary Prescription system (EVP). As for the internal organisation, ClassyFarm can be described as an information hub which processes information from both existing IT facilities and ad hoc information provided by private and public institutions (farm vets, public health vets, public institutions). Based on this input data, the system is able to provide an integrated assessment of the health risk to which a livestock farm may be exposed, by assigning a score related to the level of biosecurity, animal welfare and use of antibiotics within the farm.

Authorized users of this information include farmers and their respective company veterinarians, as well as competent veterinary authorities at both the local level (Local Health Authorities – LHAs, regional veterinary services, staff from the Experimental Zooprophylactic Institutes – IIZZSS) and the central level (Ministry of Health). In light of the scenario just described, it is possible to reconstruct the standard operation of the ClassyFarm system, identifying its component processes, the stakeholders involved and the resources used. The following Table 5.1 outlines the activities carried out within the system and specifies who is responsible for each.

Table 5.1 **Operative phases of the ClassyFarm system**

WHAT						
ACTORS INVOLVED	Data collection	Data entry	Data processing	Development and updates	User support	Data visualization
Company veterinarians	X	X				X
Competent veterinary authorities	X	X				X
ClassyFarm personnel	X	X	X	X	X	X
Ministry of Health				X		X
Farmers						X
IIZZSS	X	X				X

For the purpose of an economic evaluation of the system, it is necessary to take into account the costs related to data collection on farms, the development and operation costs of the IT platform and the costs associated with the integration of information coming from other databases within the national veterinary portal.

Below is a brief description of the costs analysed.

1. **Costs of on-site inspections carried out by public and private veterinarians**

A significant portion of the data used by ClassyFarm for risk classification originates from on-site inspections conducted by public and private veterinarians. In these cases, veterinarians carry out visual inspections, measurements and document checks on the farm with the goal of completing specific checklists related to the various areas evaluated within the system. These activities entail economic costs associated with the labour performed and the use of materials, such as personal protective equipment (PPE) — coveralls, boots, gloves etc. — worn to safeguard the operator's health and to prevent contamination of the farm environment or the animals themselves. As it is known, inspections can be carried out by company veterinarians when done on a voluntary basis, or by official veterinarians when required by law. In the first case, the costs related to inspections were not included in the evaluation, as the economic estimate developed in this study only considers public system costs. Moreover, this activity is not technically separable from the broader range of tasks carried out by the veterinarian responsible for the animal health and farm management on behalf of the farmer. In most cases, it is the same freelance veterinarian who provides routine care to livestock that also assumes

the role of company veterinarian as defined by the Decree of 7 December 2017 (the regulatory foundation of ClassyFarm), i.e., a specially trained and officially designated figure responsible for performing ClassyFarm checks. These control activities are often conducted alongside other duties, without specific remuneration, and thus cannot be economically isolated or assessed separately. By contrast, such an evaluation can be developed for inspections conducted by public veterinarians, whose on-farm work consists exclusively of official duties. In this case, the cost categories considered for the economic estimation were identified as follows:

A. Labor: This category includes the remuneration paid to official veterinarians for carrying out on-farm inspection activities and the related office work. Before conducting field inspections, veterinarians perform preparatory document checks in the office. The field activity is also followed by the entry of completed checklists into the ClassyFarm portal. With a few exceptions depending on the internal organization of the various local health LHAs, even the office work is generally carried out entirely by veterinarians rather than administrative staff.

B. Logistic costs: Veterinarians travel to farms using company vehicles. This cost category includes the operating costs of the vehicles (fuel, maintenance and vehicle depreciation) as well as the personnel cost for the time required to travel.

C. Materials: This includes the cost of consumable materials (mostly single-use personal protective equipment) needed to carry out the inspections and the cost of disposing of those materials.

2. Implementation and operation costs of the ClassyFarm system

This category includes both investment costs and operating costs of the system. The former refer to fixed costs for the development of the platform, which do not vary with the volume of services provided and are shared across several functions of ClassyFarm. In this case, they consist of costs incurred for instrumental resources such as appropriate IT equipment, software licenses, cloud-based service delivery, etc. Operating costs, on the other hand, are variable or semi-fixed costs necessary for the operation of ClassyFarm, assuming a standard operating regime after all the investments have been made over time. These are mainly represented by software maintenance costs (developmental, adaptive and corrective maintenance) and user assistance costs. Table 5.2 below describes the activities corresponding to the cost categories.

Table 5.2 **Description of the operating costs of the ClassyFarm system**

COST CATEGORIES	DESCRIPTION
Developmental maintenance (DM)	• Software analysis, design and development; • Adjusting system functionality by adding or removing features to meet user needs (e.g. following regulatory changes or requests from the competent authority);
Adaptive and corrective maintenance (AM)	• Correction of failures and errors in a part of the system with a potential impact on the functionality of the software in general; • Adapting the system to evolving technologies as well as software-related policies and rules;
End user assistance (UA)	• First level help desk service to manage requests for intervention and assistance relating to the application software; • Specialist support service to provide users with technical-operational assistance;

3. Costs for integrating data from other information systems

As previously highlighted, a significant feature of the ClassyFarm platform is its interoperability with other databases included in the Vet info portal, specifically NAR and EVP system. In order to enable a continuous flow of data from the aforementioned sources to the ClassyFarm system, specific IT procedures were developed by the information systems staff of the Istituto Zooprofilattico Sperimentale dell'Abruzzo e Molise (IZSAM), which is responsible for the technical management of all Vet info applications. Since 2018, a development process for the data transmission service has been implemented, as illustrated in the following diagram 5.1.

Diagram 5.1 *Timeline of service implementation*

YEAR 2018			YEAR 2019		
I Quarter	II Quarter	III Quarter	I Quarter	II Quarter	III Quarter
Identification of ClassyFarm's requirements	Creation of software procedures for data extraction from NAR and EVP	Implementing a system for sending files	Software update to comply with current regulations and the evolving needs of the ClassyFarm project		
Identification of the necessary data and definition of the IT traces		Extraction and transmission of data files according to defined IT traces	Extraction and transmission of data files according to defined IT traces	Extraction and transmission of data files according to defined IT traces	Extraction and transmission of data files according to defined IT traces
Definition of transmission requirements and file delivery methods			Non-stop monitoring of the process and timely resolution of any mistakes	Non-stop monitoring of the process and timely resolution of any mistakes	Non-stop monitoring of the process and timely resolution of any mistakes

Based on the information presented in the diagram, it can be observed that after an initial phase of software design and development (in 2018 and the first quarter of 2019), the activities required for the full operation of the service are essentially related to the maintenance of the extraction and transmission process. This maintenance is aimed at correcting any technical errors in the system and implementing changes to improve its efficiency. The costs incurred for carrying out these activities have been included in the economic assessment of the ClassyFarm system. This is because the data integration process is a crucial element for risk categorization, as it provides registry information and specific data concerning the administration of veterinary medicines and medicated feed on farms. The following Table 5.3 describes the estimated cost categories.

Table 5.3 **Description of costs for data integration from NAR and EVP**

TYPE OF COST		DESCRIPTION
FIXED COSTS Investment costs for the development of the system, which do not vary with the volume of services provided	Software	Development of data processing algorithms and transfer services, purchase of licenses, systems for cybersecurity and for data backup and recovery etc..
VARIABLE COSTS System operating costs (data flow from NAR and EVP to ClassyFarm) assuming a standard operating regime	Management of hardware and software equipment	Maintenance and verification of IT services, updates, repairs etc...
	Personnel	Personnel for maintenance and verification of services

5.2 RESULTS OF THE ECONOMIC ANALYSIS

Following the description of the ClassyFarm system and the processes it comprises, the economic analysis was developed by evaluating the resources used to the corresponding economic cost categories identified for each process. As previously mentioned, the collection of technical and economic data was organized by distinguishing the different operational phases of the farm classification process as follows:

- On-site inspections carried out by veterinarians for the completion of checklists;
- Implementation and operation of the ClassyFarm system;
- Integration of data from different information systems (NAR and EVP).

For each identified phase, the costs necessary to carry out the respective activities were obtained through direct interviews with veterinary and IT personnel from the operational units responsible for

them. The following section presents the details of the data collected and the subsequent analyses, organized according to the framework described in the previous paragraph.

5.2.1 Costs of field inspections

For the purposes of this study, the economic evaluation of inspections focused exclusively on activities carried out by official veterinarians and on the area of pharmacosurveillance. The first of these choices stems from the very purpose of the research, which aims to assess the costs of ClassyFarm borne by the National Health System (NHS). As previously discussed, there are also technical limitations involved, namely the inability to isolate ClassyFarm checks and their related costs from the broader range of duties performed by private farm veterinarians. The decision to narrow the scope of the investigation to pharmacosurveillance is instead linked to the structure of ClassyFarm, in which antibiotic use inspections fall exclusively under the responsibility of public veterinarians, due to the potential impact that improper use of such drugs may have on public health as a whole. The cost assessment of official on-farm inspections was carried out based on the categories identified in paragraph 5.1: labour costs of veterinarians for field inspections and related office work, logistic costs to reach the farms and the cost of materials used during inspections. The data required for this estimation were drawn from the accounting records of the LHAs of Parma and Romagna, as well as expert opinions collected by interviewing their veterinary personnel. The province of Parma was selected as the territorial reference unit for the economic evaluation due to its prominent role in the Italian livestock sector. This area hosts approximately 20% of cattle and 10% of pigs raised in Emilia-Romagna—a region that, together with Lombardy and Veneto, is among the most livestock-intensive in the country (NAR Statistics). Within the province of Parma, the cost estimate included official pharmacosurveillance inspections carried out on dairy cattle farms that participated in the ClassyFarm project between 2021 —when this type of checklist has been fully operational within the system—and 2022. The selection of the livestock species and production orientation is based on the composition of the regional livestock sector. In the province of Parma alone, around one-fifth of the region's cattle farms are located, accounting for a total of 134.000 head raised for milk production (NAR Statistics). Consequently, around 80% of the pharmacosurveillance inspections conducted for the ClassyFarm system between 2021 and 2022 involved this type of farm. For greater clarity, the indicators relating to the economic analysis of inspections will be presented by separating the logistic costs incurred for travel (Table 5.4) from those associated with field inspection activities (Table 5.5).

Table 5.4 *Logistic costs for carrying out official controls*

INDICATORS	MOVEMENTS FOR PHARMACOSURVEILLANCE INSPECTIONS (YEAR 2021)	MOVEMENTS FOR PHARMACOSURVEILLANCE INSPECTIONS (YEAR 2022)
Total farm inspections (N°)	294	188
Personnel involved: veterinarians (N°/inspection)	1	1
Average hourly cost vets (€/hour)	65,15	65,15
Average route taken for inspection (km/inspection)	14	14
Total km travelled for farm inspections (km)	4116	2632
Average cost per kilometer for vehicle use (€/km)	0,4	0,4
Average travel time per kilometer traveled (1'30" converted to hours) (hours)	0,025	0,025
Total travel time (hours)	102,9	65,8
Personnel travel cost (€)	6.703,93	4.286,87
Cost of vehicle use (€)	1.646,4	1.052,8
Total travel cost (€)	**8.350,33**	**5.339,67**

Tab. 5.5 **Farm inspections costs**

INDICATORS	FARM INSPECTIONS (YEAR 2021)	FARM INSPECTIONS (YEAR 2022)
Total farm inspections (N°)	294	188
Personnel involved: veterinarians (N°/inspection)	1	1
Average time spent on conducting a farm inspection (hours/inspection)	2	2
Office work related to inspections carried out by veterinarians (hours/inspection)	3	3
Average hourly cost vets (€/hour)	65,15	65,15
Cost of PPE (€/inspection/vet)	1,79	1,79
Cost of PPE disposal (€/inspection/vet)	0,14	0,14
Total hours for inspections	588	376
Total hours for office work	882	564
Total veterinary costs (€)	**95.770,5**	**61.241**
Total material costs (€)	**567,42**	**362,84**
Total farm inspections costs (€)	**96.337,92**	**61.603,84**
Average cost for inspection (€)	**327,68**	**327,68**

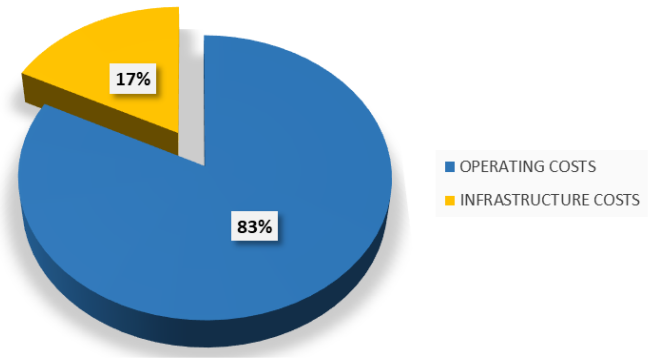
5.2.2 Implementation and operation costs of the ClassyFarm system

The collection of economic data was carried out through interviews with the veterinary and IT staff of IZSLER, which was commissioned by the Ministry of Health to develop the initial version of the system and is still responsible for its management. Table 5.6 presents the infrastructure costs (instrumental resources for the development and maintenance of the system) and operating costs, broken down into maintenance costs (developmental and adaptive) and user assistance costs. The time considered spans from 2018, the year the system was launched, to 2022. The subsequent Chart 5.1 shows the percentage distribution of total costs over the entire study period.

Table 5.6 **Infrastructure and operating costs of ClassyFarm – years 2018-2022**

COSTS CATEGORIES	2018	2019	2020	2021	2022	TOT
Developmental maintenance (€)	217.200	434.400	606.410	258.015	779.000	2.295.025
Adaptive and corrective maintenance (€)	0	10.000	20.000	42.000	56.000	128.000
End user assistance (€)	30.069,07	60.138,15	60.138,15	60.138,15	60.138,15	270.621,67
TOTAL OPERATING COSTS	247.269,07	504.538,15	686.548,15	360.153,15	895.138,15	2.693.646,67
Infrastructure (€)	33.529,41	13.4117,65	13.4117,65	13.4117,65	13.4117,65	570.000,01
TOTAL COSTS (OPERATING + INFRASTRUCTURE)	280.798,48	638.655,8	820.665,8	494.270,8	1.029.255,8	3.263.646,68

Chart 5.1 **Percentage Distribution of Infrastructure and Operating Costs of the ClassyFarm System (Total Costs 2018–2022)**



Based on the data just presented, it is evident that the operating costs of the system are predominant compared to the infrastructure costs, accounting for 83% of the total cost. This has been attributed to the ongoing need to modify the software's features to keep it aligned with the evolving needs of users, which stem from changes in regulations concerning biosecurity requirements on farms, animal welfare and the use of veterinary medicines. These considerations have led to the development of a new vision for ClassyFarm—conceived as a dynamic system in continuous evolution, capable of maintaining functionality in line with updates to veterinary legislation. Below is the breakdown of costs associated with the different system versions (ClassyFarm 1.0, 2.0, and 3.0) introduced during the study period.

Table 5.7 **Operating and infrastructure costs of ClassyFarm – versions 1.0, 2.0, 3.0**

TYPE OF COSTS	CF 1.0	CF 2.0	CF 3.0
DEVELOPMENTAL MAINTENANCE (€)			
Parameterization and customization (€)	204.500	296.125	779.000
Analysis, design and development of custom software (€)	277.500	0	0
Application management and user support (€)	228.000	60.000	0
Infrastructure technical management (€)	64.000	0	0
Process review (€)	169.000	32.065	0
Architectural support (€)	143.000	41.835	0
ADAPTIVE AND CORRECTIVE MAINTENANCE			
Management and maintenance (€)	128.000	0	0
END USER ASSISTANCE			
Thematic and functional support (€)	176.000	37.955	56.666,67
TOT Operating Costs (€)	**1.390.000**	**467.980**	**835.666,67**
INFRASTRUCTURE			
Instrumental resources (€)	250.000	160.000	160.000
TOT Costs (operation + infrastructure) (€)	**1.640.000**	**627.980**	**995.666,67**

5.2.3 Integration of data from different information systems (NAR and EVP)

The Information Systems Unit operating at IZSAM manages, on behalf of the Ministry of Health, numerous applications included in the Vet Info portal, among which are the NAR and the EVP system. Since 2018, under commission from the Ministry, the Institute has developed software procedures for extracting and transmitting data required by the ClassyFarm project from the two sources (NAR and EVP). The implementation and management of this service required the use of financial resources, as previously described. Table 5.8 presents the estimated costs for the integration of data into ClassyFarm for the period between 2018 and 2022. The cost categories identified refer to the classification described in paragraph 5.1.

Table 5.8 **Infrastructure and operating costs of data integration services**

TYPE OF COSTS	2018	2019	2020	2021	2022	TOTAL
Software (€)	7.800	7.900	2.000	2.100	2.200	22.000
TOT Infrastructure costs (€)	**7.800**	**7.900**	**2.000**	**2.100**	**2.200**	**22.000**
Management of hardware and software equipment (€)	3.400	3.500	3.600	3.700	3.800	18.000
Personnel for maintenance and verification of services (€)	3.600	3.600	3.600	3.600	3.600	18.000
TOT Operating costs (€)	**7.000**	**7.100**	**7.200**	**7.300**	**7.400**	**36.000**
TOT COSTS (€) (OPERATING + INFRASTRUCUTRE)	**14.800**	**15.000**	**9.200**	**9.400**	**9.600**	**58.000**

The technical and economic data required to produce the above cost estimate were gathered through interviews with Information Services staff. The following assumptions were made in calculating the costs:

- An indicative cost of managing the overall equipment of the Data Centre (Information Systems) was estimated at € 1.000/day, with a slight annual increase and a share allocated to services developed for ClassyFarm equal to 1%;
- An indicative cost of licenses was estimated at approximately € 550/day, with a slight annual increas, and a share allocated to ClassyFarm equal to 1%;
- It was assumed that throughout the entire study period, one day per month (12 man-days) would be devoted to the verification and maintenance of services, at an indicative cost of €300/day;
- Costs related to facilities, training, and consumables were not considered, as they are negligible compared to the rest and can be assumed to be included within the other listed cost categories.

5.3 SUMMARY

The economic analysis of ClassyFarm was developed by first identifying the processes into which the system is structured, in order to recognize and quantify the resources used. Three main operational phases were identified that lead to the assignment of a risk score for the farms participating in the system. These are:

- Collection of information through on-site inspections;
- Processing of the collected data;
- Integration of findings observed on the farm with information from other databases within the veterinary information system Vet Info.

The costs required for the implementation of each phase were estimated as follows:

1. Costs of field inspections based on the selected sample

The evaluation was limited to official pharmacosurveillance inspections carried out on dairy cattle farms in the province of Parma. As previously discussed, the sample selection was constrained by the objective of the study and is rooted in the characteristics of the Italian livestock sector, which reaches its highest level of development in certain regions of Northern Italy. During the two-year study period (2021–2022), the costs related to inspection activities—including office work carried out before and after field visits—were estimated at € 96.337,92 in 2021, and € 61.603,84 in 2022. Additional costs for the travel of veterinary personnel to the farms must be added to these amounts. These travel costs were: € 8.350,33 in 2021, and € 5.339,67 in 2022. Therefore, the total cost of field inspections for the reference period, including both inspection and travel costs, was estimated at € 104.688,3 in 2021 and € 66.943,51 in 2022.

2. Implementation and operation costs of the ClassyFarm system

To assess the economic impact of the data processing phase for the information collected in the field, both investment costs (resources required for the technical infrastructure) and operating costs of the system related to software maintenance and user support were taken into consideration. These costs were evaluated as follows.

Table 5.9 **ClassyFarm system cost summary**

TYPE OF COSTS	2018	2019	2020	2021	2022	TOT
TOT OPERATING COSTS (€)	247.269,07	504.538,15	686.548,15	360.153,15	895.138,15	2.693.646,67
TOT INFRASTRUCTURE COSTS (€)	33.529,41	134.117,65	134.117,65	134.117,65	134.117,65	570.000,01
TOTAL COSTS (OPERATING + INFRASTRUCTURE)	280.798,48	638.655,8	820.665,8	494.270,8	1.029.255,8	3.263.646,68

The same costs described above were further estimated with reference to the different versions of the ClassyFarm system developed during the study period, in response to changes in the international epidemiological context, regulatory developments and specific needs of users of the digital platform. The total cost (system operation and infrastructure) estimated for the three

versions of ClassyFarm (CF 1.0, CF 2.0, CF 3.0), introduced between 2018 and 2022, amounts respectively to: € 1.640.000 for CF 1.0, € 627.980 for CF 2.0 and € 995.666,67 for CF 3.0.

3. Data Integration costs from different information systems (NAR and EVP).

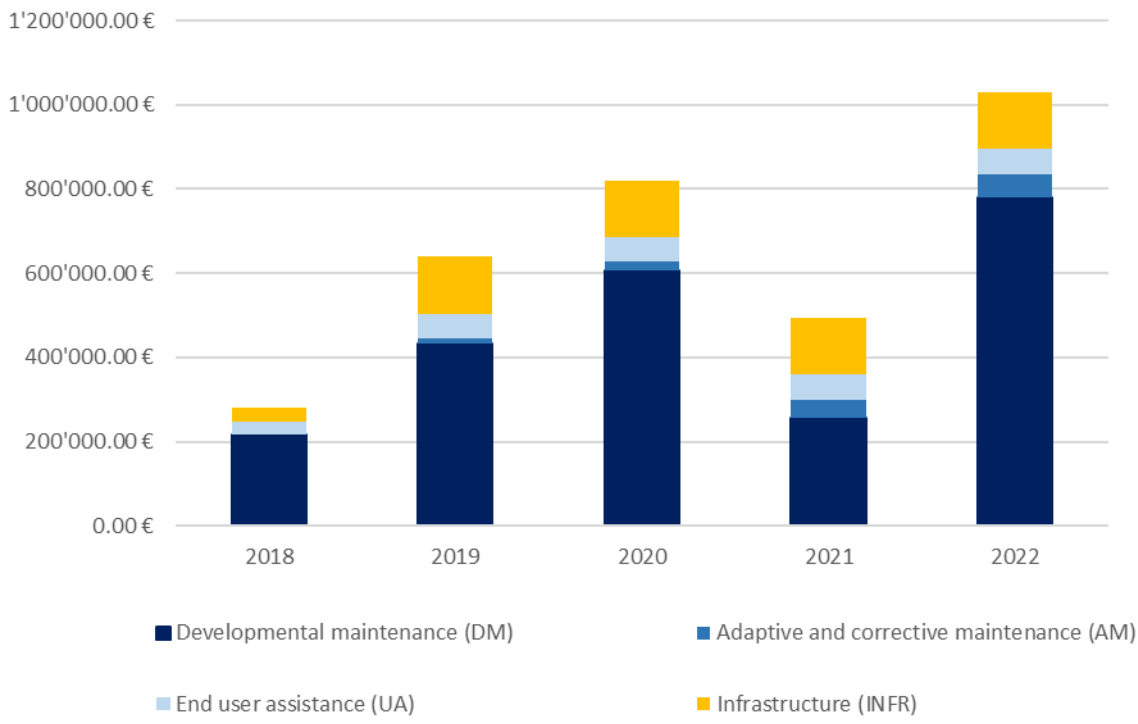
The process of extracting and transmitting registry and health information to the ClassyFarm system from applications within the Vet Info veterinary portal required the use of financial resources for the development and management of dedicated software. These costs were assessed as fixed costs for software development and the purchase of IT equipment and as variable costs including the maintenance of software and hardware systems. For some of these indicators, values were calculated as a percentage of the corresponding total cost incurred by the Information Systems Data Centre for carrying out its functions. The total investment and operating cost for services related to the integration of data from NAR and EVP was estimated at: € 14.800 in 2018, € 15.000 in 2019, € 9.200 in 2020, € 9.400 in 2021, and € 9.600 in 2022. Finally, the total value of all costs incurred over the entire study period was estimated at € 58.000.

CHAPTER 6. DISCUSSION OF RESULTS AND FINAL CONSIDERATIONS

5.2 ESTIMATE OF PUBLIC COSTS OF THE CLASSYFARM SYSTEM

As already illustrated in the previous chapter, the development and operation of the ClassyFarm system required financial investment from the National Health Service (NHS). The incurred costs were classified as infrastructure costs, related to the instrumental resources necessary for the creation of the IT platform and operating costs, associated with software maintenance and end user assistance. Within the time frame covered by this study — from 2018, the year the system was launched, to 2022 — infrastructure costs amounted to € 570.000,10, while maintenance costs were estimated at € 2.693.646,67, bringing the total cost to € 3.263.646,68, with an average annual cost of € 652.729,33. Figure 6.1 below shows the annual distribution of these costs over the reference period. Maintenance costs were analitically broken down according to the different activities: developmental maintenance, adaptive and corrective maintenance and end user assistance.

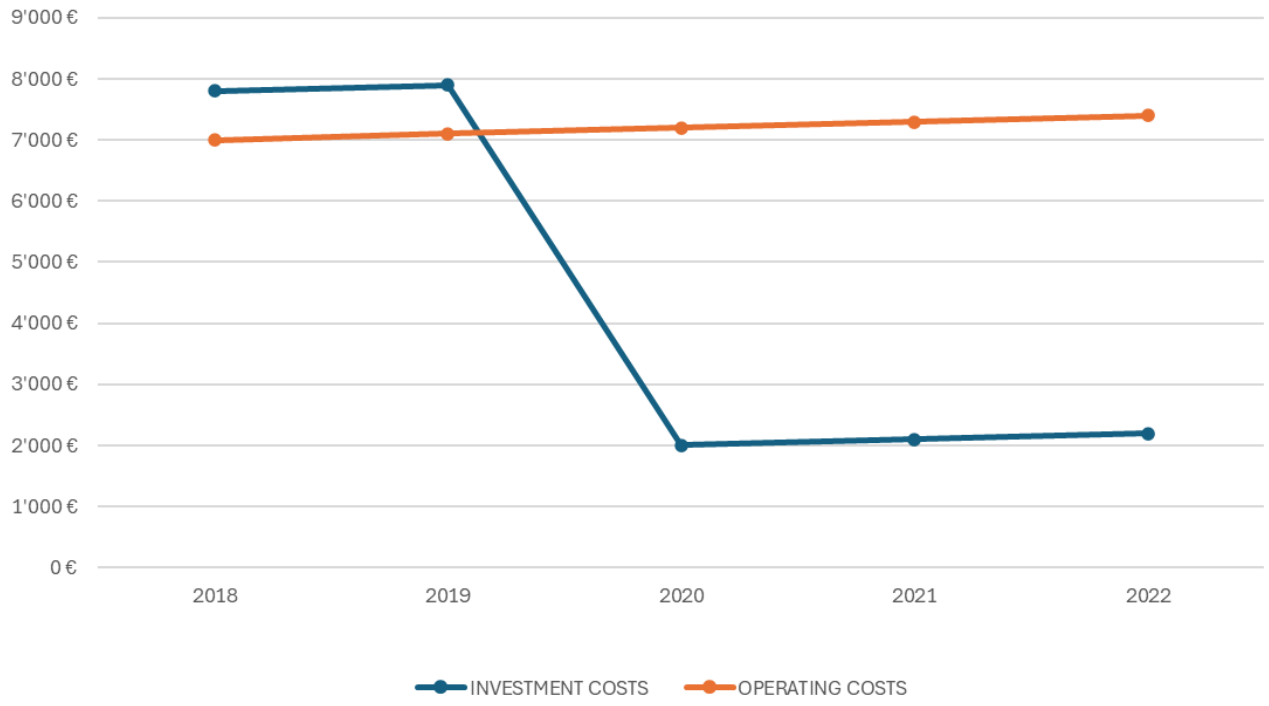
Figure 6.1 **Annual distribution of infrastructure and operating costs of the ClassyFarm system – years 2018–2022**



As shown in the previous chart, operating costs consistently outweighed infrastructure costs throughout all the years considered, accounting for more than 80% of the total cost. Within the operating costs alone, the most significant category was developmental maintenance, which includes all activities required to integrate software modules that were not part of the original system design, in order to promptly respond to the evolving needs of system users.

Over time, changes in legislation and the international epidemiological context necessitated adjustments to the system, such as the inclusion of new animal species and the development of new checklists for both official and voluntary controls. The composition and temporal trend of costs therefore reflect the dynamic nature of ClassyFarm, which is continuously updated to maintain functionality in line with developments in veterinary legislation. As previously highlighted, a key feature of the system that greatly enhances its risk categorization potential is the interoperability of the platform with other tools within Vet Info, the national veterinary information system. In particular, the integration of data from the National Animal Register (NAR) and the National Electronic Veterinary Prescription system (EVP) allows the system to assign scores even to farms that do not actively participate in the ClassyFarm program. This makes it possible to produce a more robust and consistent AMR (antimicrobial resistance) risk assessment, compared to evaluations based solely on the outcomes of official drug use controls. However, this process entails costs, as it requires the development of software capable of periodically extracting and transferring data, enabling communication between different IT systems. These costs were estimated as investment costs for software development and operating costs related to hardware and software management, during the same time frame used for the economic evaluation of the algorithms that form the basis of the ClassyFarm system. The total cost of data integration services over the period 2018–2022 was calculated at € 58.000, with investment costs amounting to € 22.000 (38%) and operating costs to € 36.000 (62%). Figure 6.2 illustrates the trend of investment and operating costs related to the data extraction process.

Figure 6.2 **Trend in costs of the data extraction and transmission service to ClassyFarm; years 2018 – 2022**



From the analysis of Figure 6.2, it is clear that investment costs decreased by approximately 75% starting in 2020 and then remained stable. In fact, during the first two years of the service's activation, about 80% of the total costs were attributed to personnel compensation for the design and development of the algorithms necessary for data transmission — a component that was no longer required once the system became fully operational.

In contrast, operating costs, mainly related to the maintenance of software and hardware components, remained virtually unchanged throughout the entire period under consideration.

This cost trend differs from the one observed for the ClassyFarm risk categorization applications, where maintenance costs have shown significant fluctuations over time, due to the release of multiple system versions. This difference likely stems from the limited impact of regulatory changes on the volume and type of data extracted from the NAR and EVP, compared to the impact such changes have had on the development of new ClassyFarm functionalities.

With reference to the first five years of ClassyFarm's operation (2018–2022), the average annual cost of the system — including public spending on the development and maintenance of the IT platform, as well as the expenses for data integration services from external applications — was estimated at € 664.329,30.

This cost is broken down as shown in Figure 6.3 and Table 6.1, distinguishing between: costs directly attributable to the ClassyFarm system itself, costs associated with the data flow from NAR and EVP and, for each of these, the distinction between investment costs and operating costs.

***Figure 6.3 %* Composition of the average annual cost of the ClassyFarm system in the first 5 years of activation; years 2018 - 2022**

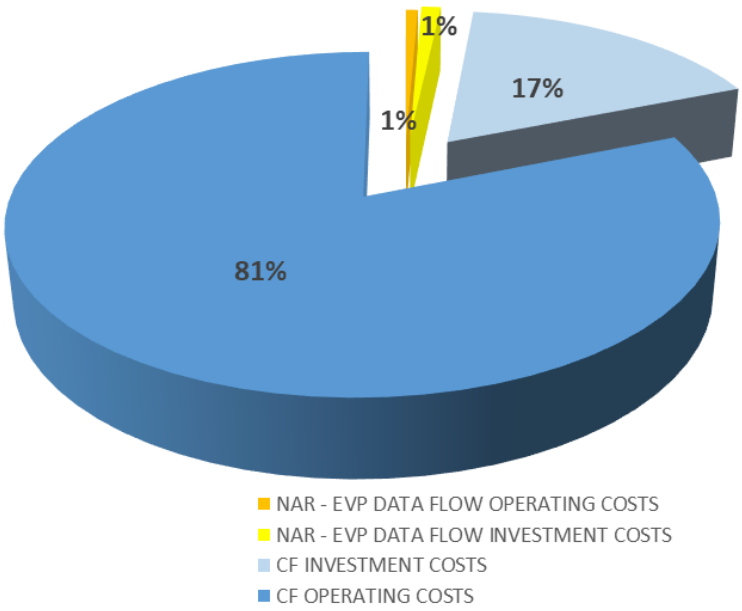


***Table 6.1* Average cost composition (€) of the ClassyFarm system; years 2018 – 2022**

TYPE OF COSTS	AVERAGE ANNUAL COST (€)
NAR-EVP DATA FLOW OPERATING COSTS	4.400
NAR-EVP DATA FLOW INVESTMENT COSTS	7.200
CF-INVESTMENT COSTS	114.000
CF-OPERATING COSTS	538.729,3
TOTAL	**664.329,3**

The risk-based classification process implemented by the ClassyFarm system is powered by a combination of data from other information systems and field data collected by either company veterinarians or official veterinarians. The cost of inspection activities of public veterinarians has been estimated as part of the costs borne by the NHS for implementing ClassyFarm as a surveillance tool to monitor the development of AMR risk. The sample selected for the analysis referred to

pharmacosurveillance inspections carried out on dairy cattle farms located in the province of Parma during the 2021–2022. The reasons for this choice — already discussed in Chapter 5 — are based on the strategic importance of the Emilia-Romagna region and, within it, the province of Parma, in the context of Italian livestock production. Over the study period, a total of 482 inspections were conducted, with an average cost of € 356,08 per on-site visit. For the purpose of the economic evaluation, costs were broken down into logistics and on-site inspection costs.

Logistical costs include:

- the usage cost of vehicles provided by AUSL-Parma (calculated using standard parameters, including fuel consumption, vehicle management and depreciation costs);
- the time required for travel to reach the farms.

Based on the data presented in Table 5.4 of Chapter 5, the average travel cost per pharmacosurveillance inspection conducted under the ClassyFarm system was estimated at € 28,40 per visit. Table 6.2 below provides a detailed breakdown of this cost.

Table 6.2 **Logistical cost estimate: average cost per trip**

Average travel time for inspection (minutes)	21
Average personnel cost for travel (€/trip)	22,80
Average cost of vehicle use (€/trip)	5,60
Average total cost (€/trip)	**28,40**

The costs related to on-farm inspections include both the remuneration of veterinarians and the cost of materials required to carry out the controls. Based on the data collected, the average cost of an on-farm inspection, excluding previously calculated travel expenses, was estimated at €327,68, of which only 0.6% corresponds to material costs. This is due to the fact that an official pharmacosurveillance inspection does not involve collecting biological samples from animals or the environment, but rather consists solely of visual inspections and document checks. Therefore, the only materials needed are personal protective equipment (PPE), which are routinely used for visitor access to farms. Below is a summary of the parameters considered for estimating the average cost of an inspection (Table 6.3).

Table 6.3 **Estimated costs of inspections – average cost of a farm inspection**

N° of inspections performed	482
Total hours spent on inspections	964
Total hours spent on office work related to inspections	1.446
Total veterinary costs (€)	157.011,5
Total material costs (€)	930,26
Total farm inspections costs (€)	157.941,8
Average cost per animal checked (€/head)	**1,31**
Average cost per inspection (€/inspection)	**327,68**

The data presented in the table above highlight how office work related to inspections involves a significant time investment, accounting for 60% of the total hours in which veterinary personnel are engaged. This type of activity includes both a preparatory phase prior to the farm visits and a follow-up phase, during which the information collected in the field is entered into the IT portal using checklists. The pre-inspection phase is the exclusive responsibility of official veterinarians, as it is aimed at guiding the inspection process itself — a task that only public veterinarians are authorized to carry out. However, the office work following the inspections (e.g., data entry into the system) could potentially be carried out by administrative staff, whose compensation is generally lower than that of a veterinary officer employed by the Local Health Authority (LHA). This reallocation of tasks could lead to significant savings in public resources dedicated to inspections of farms enrolled in the ClassyFarm system. Nevertheless, the possibility of dividing tasks between different professional roles, as described above, remains at the discretion of each LHA, depending on the availability of personnel and the internal organizational structure.

Another potential opportunity to reduce personnel costs would be to enter checklist results into the IT portal directly during the on-farm inspection, thus eliminating the need for post-visit office work and achieving a clear saving in billable hours. However, this option may not be feasible due to technical constraints between field inspections and data entry activities. Additionally, it would require equipping veterinarians with portable electronic devices (e.g., tablets or laptops), resulting in further costs and may not always be practical in cases of unreliable internet connection in rural areas.

Table 6.4 below summarizes the results of the economic evaluation of pharmacosurveillance inspections carried out in dairy cattle farms enrolled in ClassyFarm in the province of Parma over the reference period (2021 and 2022)

Table 6.4 **Summary of the economic assessment results of public pharmacosurveillance controls in the sample of ClassyFarm companies – years 2021/2022**

N° of inspections performed	482
N° of animals checked	120.045
Total logistical costs (€)	13.690,01
Total farm inspections costs (€)	157.941,8
Total cost of pharmacosurveillance controls (€)	**171.631,8**
Average cost per pharmacosurveillance control (€/control)	**356,08**
Average cost per animal checked (€/head)	**1,42**

In order to develop a comprehensive economic evaluation of the system, the cost estimation approach described above was extended to include all pharmacosurveillance inspections carried out on ClassyFarm-registered farms, thus overcoming the geographical and zootechnical limitations of the previously considered sample. The total cost estimate of the inspections was recalculated by maintaining the two components: the cost of on-farm inspections and the logistics cost.

For the on-farm inspection cost, the unit cost was kept constant, based on the value calculated for inspections in dairy cattle farms in the province of Parma. As previously noted, this cost mainly reflects the remuneration of veterinarians involved in performing the inspections. The average duration of inspections was considered comparable to the value derived from expert opinion by LHA veterinarians in Parma, and individual variability in the speed at which inspections are performed was considered negligible.

The decision to adopt the cost estimated from the sample under analysis as the standard unit cost for performing a pharmacosurveillance inspection is justified based on the following assumptions:

a. The remuneration of LHA veterinarians was considered uniform at the national level, as it is established by the National Collective Labour Agreement (NCLA) and regional regulations. Although individual regions may introduce specific additions or variations in the application of these contracts, the NCLA sets a minimum wage threshold that is always guaranteed.
b. The checklist used for pharmacosurveillance inspections does not vary depending on the species being farmed.
c. The size of the farm, in terms of the number of animals, does not significantly affect the duration of the inspection, considering the nature of the parameters being assessed. The

elements being verified mainly concern the methods of antibiotic use, which do not differ whether treatment is administered to one or multiple animals.

Given that, over the reference period, a total of 26.585 pharmacosurveillance inspections were carried out in ClassyFarm farms across the country, the total cost of on-farm inspections amounted to €8.711.372,8 for the period 2021–2022, with an average cost per inspection of € 327,68.

As for logistics costs, the previously estimated unit value (€/trip) was not adopted as a national standard reference, since the distance between the farm and the LHA office can vary considerably from one province to another, depending on the local distribution of the ends of the route.

Therefore, in order to identify a national average value for this parameter, the following considerations were made:

a) The average number of intensive farms (including bovine, buffalo, poultry, equine, lagomorph, swine, sheep and goat species) within the jurisdiction of an LHA district at national level is estimated at 600. This figure was calculated using the total number of facilities registered as "farms" in the NAR database for the previous species and the number of health districts across the country (1 per 100.000 inhabitants, as defined by Legislative Decree 502/92);
b) The number of farms per LHA district in the province of Parma can be considered comparable to the national average, as it is only slightly higher (+8%);
c) Assuming an inverse proportionality between the farm density per km² (D) and the average distance between farm and LHA district office (d), based on points a and b the following proportion can be set:

$$d_1 * D_1 = d_{TOT} * D_{TOT}$$

Table 6.5 **Description of the formula**

D_1	Average number of farms per km² in the province of Parma	0.7
D_{TOT}	Average number of farms per km² at national level	1.1
d_1	Average distance between farms and LHA headquarters in the province of Parma (km)	7
d_{TOT}	Average distance between farms and LHA headquarters at national level (km)	-

d) Starting from the formula just described, it is possible to derive the parameter d_{TOT} as follows:

$d_{TOT} = D_{1*} d_{1/} D_{TOT}$

$d_{TOT} = 0.7*7/1.1 = 4.4$ km

Using the value obtained through the procedure described above, the average cost per trip was estimated based on the total number of pharmacosurveillance inspections conducted nationally on ClassyFarm farms in the years 2021 and 2022, resulting in a value of € 17,85 per trip.
This estimate was calculated based on the data presented in Table 6.6 below.

Table 6.6 **Indicators for the estimation of logistics costs – national inspections 2021–2022**

INDICATORS	MOVEMENTS FOR PHARMACOSURVEILLANCE INSPECTIONS at national level years 2021 and 2022
Total farm inspections (N°)	26.585
Personnel involved: veterinarians (N°/inspection)	1
Average hourly cost vets (€/hour)	65,15
Average route taken for inspection (km/inspection)	8,8
Total km travelled for farm inspections (km)	233.948
Average cost per kilometer for vehicle use (€/km)	0,4
Average travel time per kilometer travelled (1'30" converted to hours) (hours)	0,025
Total travel time (hours)	5.848,7
Personnel travel cost (€)	381.042,805
Cost of vehicle use (€)	93.579,2
Total travel cost (€)	**474.622,005**

Extending the cost estimation of official pharmacosurveillance inspections on ClassyFarm farms to the entire national territory, the total cost of inspections for the 2021–2022 biennium amounted to €9.185.994,805

This figure includes:

- logistics costs: € 474.622,005 (5,2% of the total)
- on-site inspection costs: € 8.711.372,8 (94,8% of the total)

resulting in an average cost per inspection of € 345,53.

6.2 CONCLUSIONS

The estimation of public costs for the ClassyFarm system, developed according to the methodology described so far, produced the following results:

1. **Costs for the implementation and operation of the IT platform (2018–2022):**
   Total: € 3.263.646,68 (average annual cost: € 652.729,33), of which:
   a. € 570.000,10 for infrastructure
   b. € 2.693.646,67 for system maintenance

2. **Costs for data integration from other VetInfo applications (2018–2022):**
   Total: € 58.000 (average annual cost: €11.600), of which:
   a. € 22.000 for investment costs
   b. € 36.000 for operating costs

3. **Costs of pharmacosurveillance inspections:**

   - In dairy farms in the province of Parma (2021–2022): € 171.631,8 (average cost per inspection: € 356,08)
   - In all ClassyFarm farms nationwide (2021–2022): €9.185.994,805 (average cost per inspection: € 345,53)

As outlined in the research objectives, this study focuses on evaluating the costs associated with the use of the ClassyFarm system as a tool for monitoring antibiotic use in farms. The decision to restrict the cost analysis to the pharmacosurveillance function stems from the significant impact that irresponsible use of veterinary antimicrobials can have on animal and public health, through the development and spread of AMR bacterial strains. However, as discussed in the introduction, the administration of antibiotic therapies can be heavily influenced by other aspects of farm management — such as biosecurity and animal welfare — which are also evaluated by ClassyFarm. Animals raised

in conditions of high biosecurity and good welfare generally experience better health, and therefore require fewer medical treatments. To maintain the study's focus on pharmacosurveillance — specifically, the evaluation of antibiotic use on farms — the estimated development and operational costs of the IT risk classification system should ideally reflect only the resources dedicated to antibiotic scoring. However, since it is technically impossible to isolate system costs by specific verification areas, it was assumed that the total system cost should be evenly distributed among the three evaluation areas (biosecurity, welfare and pharmacosurveillance), given no clear reason to believe that any area requires disproportionately more resources.

Based on this assumption, the revised estimation of public costs for the ClassyFarm system related specifically to antibiotic use surveillance is as follows:

1. **IT platform implementation and operation costs (2018–2022):**
   Total: € 1.087.882,23 (average annual cost: €217.576,44), of which:
   a. € 190.000 for infrastructure
   b. € 897.882,23 for system maintenance

2. **Costs for data integration from Vet Info applications (2018–2022):**
   Total: € 19.333,33 (average annual cost: €3.866,67), of which:
   a. € 7.333,33 for investment
   b. € 12.000 for operating costs

Assuming the first two years (2021–2022) of pharmacosurveillance inspections on farms participating in the ClassyFarm system as the reference period, the average annual cost of these inspections was estimated at € 4.592.997,40

In conclusion, considering the three categories of costs analysed so far — the implementation and operation of the IT platform, namely data integration from other Vet Info applications and official pharmacosurveillance inspections — the average annual public expenditure for operating the ClassyFarm system as a surveillance tool for antibiotic use in farms was estimated at € 4.814.440,51. In light of these estimated costs, it would be advisable to extend the economic evaluation to include the benefits generated by the application of the system. However, although this step is essential to complete the assessment of public resource investment, it is not considered feasible beyond a qualitative approach. This limitation is inherent in the functioning of the system itself, which — as previously mentioned — mainly generates information as its final output, made available to veterinary authorities, farmers and their respective farm veterinarians. The benefits that system users can derive from accessing risk classification data for their farm can be summarized as follows:

A. Farmers/Farm veterinarians

The assignment of scores in the system's assessment areas (biosecurity, animal welfare, antibiotic use) provides the farmer with an up-to-date overview of the overall condition of their farm in relation to the potential exposure to various types of risks (health, poor animal welfare, development of AMR). This information can be contextualized both locally and nationally by comparing the farm's score with average values, and it can be broken down into components, enabling the farmer to identify specific shortcomings. In this way, the data obtained by participating in the ClassyFarm system can be used as a tool to improve livestock management, increasing farm efficiency and generating positive effects on both animal and human health, as well as economic outcomes. Although this was the institutional goal behind the system's design, there is currently no legal requirement regarding how farmers must use the information they receive. Therefore, any improvement observed in one of the system's assessment areas — already difficult to quantify economically — cannot be definitively considered a direct benefit of the farm's participation in ClassyFarm. While using the system's data to guide farm management is not a direct consequence of being enrolled in ClassyFarm, it is reasonable to assume that farmers may be interested in doing so, with the dual aim of reducing the number of veterinary inspections (as a higher score lowers the risk index and reduces inspection frequency) and qualifying for CAP payments (to be eligible, farms must be enrolled in ClassyFarm and report DDD — average days of treatment per year — equal to or below the regional median). An additional benefit that farmers may gain from the scores provided by the system is the potential facilitation of quality certification processes related to antibiotic use or the level of animal welfare ensured by the farm. In this sense, ClassyFarm could prove to be a strategic operational tool for identifying critical points that need intervention and for measuring any improvements achieved. Although the incentives listed above can be considered strong motivations for ensuring ClassyFarm operates as intended, the resulting positive effects are difficult to quantify in monetary terms — both within the livestock sector and for public health more broadly.

B. NHS/Public veterinary services

From an institutional standpoint, the system was designed to achieve a series of objectives aimed at fully implementing the recent European legislation on Animal Health Law (Regulation (EU) 2016/429). These objectives include:

a) Improving dialogue between the farmer, their veterinarian, and the Competent Authorities to optimize antimicrobial use and animal welfare.

b) Making aggregated information available at various geographical levels (national, regional, local) to enable territorial monitoring and comparisons across different areas.

c) Allowing for the planning of official controls on animal welfare, pharmacosurveillance and biosecurity, targeted at farms with higher risk indexes.

Achieving the goal described in point c) implies an improvement in the efficiency of the control system, as it allows available economic resources to be concentrated where they are most needed, minimizing waste and maximizing effectiveness — that is, the ability of surveillance activities to detect regulatory violations that could pose a risk to public health and to promptly prescribe corrective actions. This aspect is even more relevant given the growing international trend of reducing financial resources allocated to health prevention and monitoring policies. It is important to note, however, that risk-based planning of inspections had already been established in Italy prior to the introduction of ClassyFarm, although based on less rational and uniform criteria. Based on these observations, the data provided by the ClassyFarm system offer the public veterinary authorities a twofold benefit: they help to optimize the scheduling of inspections and provide a scientifically validated dataset — processed through ClassyFarm's algorithms — to support policy-making. As already discussed in the private sector context, these benefits — although clearly significant from a qualitative perspective — are, in our view, difficult to quantify economically. The resulting public health outcomes (e.g., reduction of AMR, lower pathogen circulation, improved livestock productivity, etc.) are multiple and heavily influenced by countless external factors.

In conclusion, the actual benefit generated by the ClassyFarm system is an informational asset whose economic value is difficult to estimate within the decision-making processes of public and private actors. However, assuming a scenario in which ClassyFarm data were not made available to its users, these users would have to implement their own autonomous monitoring systems to obtain the same information. This alternative could potentially be more costly overall (i.e., summing the individual costs of each user) than the centralized system implemented by ClassyFarm, based on the principle of economies of scale. A rough estimate of the value of this information could only be obtained through a detailed survey of users to ultimately determine their willingness to pay for such information (a qualitative-quantitative assessment of the utility of the information). Even this evaluation might not be conclusive, as it could reveal a valuation bias stemming from the farmers' perception not so much of the ClassyFarm system itself, but rather of the legislation on pharmacosurveillance and the perceived magnitude of the AMR problem.

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