

# ÉCOANTIBIO

RÉDUIRE L'UTILISATION DES  
ANTIBIOTIQUES VÉTÉRINAIRES



## NATIONAL ACTION PLAN **FOR THE REDUCTION** OF THE RISKS **OF ANTIBIOTIC RESISTANCE** IN VETERINARY **MEDICINE**



MINISTÈRE  
DE L'AGRICULTURE  
DE L'AGROALIMENTAIRE  
ET DE LA FORÊT

**AGRICULTURES  
PRODUISONS  
AUTREMENT**



# NATIONAL ACTION PLAN FOR THE REDUCTION OF THE RISKS OF ANTIBIOTIC RESISTANCE IN VETERINARY MEDICINE

## Background

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Antibiotics are medicinal products capable of achieving the destruction or cessation of multiplication of microorganisms. After its discovery in 1928 by the Scottish biologist and pharmacologist Sir Alexander Fleming, penicillin (penicillin G), an antibiotic produced by the *Penicillium* mould capable of preventing the development of certain bacterial cultures, came on to the market in 1940.

Research and development for new classes of antibiotics followed this discovery and led to the production and use of antibiotics against a diverse range of conditions such as tuberculosis, pneumonia, skin infections, and so on.

For less than a century the use of antibiotics has been developing not only in human medicine as the population has grown and healthcare has improved, but also in animal medicine.

Antibiotics are now widely prescribed in both the curative and preventive treatment of human beings and animals. In all these cases, their use is capable of leading to the emergence of resistance in bacteria, thus allowing them to spread.

This is because so-called antibiotic-resistant bacteria exist, that is to say bacteria that are neither killed nor inhibited by the antibiotic doses administered.

Such resistance is a natural phenomenon given that certain bacteria are not naturally sensitive to certain antibiotics. However, resistance can be acquired by previously sensitive bacteria. This phenomenon of acquired resistance stems from the species selection mechanism, especially as certain bacteria can exchange their resistance genes at a distance. Any inappropriate use of antibiotics in human or veterinary medicine can encourage the selection of resistant bacteria.

For example, certain families of antibiotics are no longer effective against certain species of bacteria. Although the discovery of penicillin, followed by the various families of antibiotics, made it possible to combat very effectively many infectious diseases that have been a scourge for both human beings and farm livestock, the corollary is that the simultaneous development of mechanisms for resistance to antibiotics constitutes a new threat to the animal health and public health.

Antibiotic resistance is probably one of the major medical challenges of the 21st century. The European Commission estimates on the basis of a publication of the European Centre for Disease Prevention and Control (ECDC) that for all the Member States of the Union the infections caused by microorganisms resistant to antimicrobial drugs are responsible for the deaths of 25,000 patients each year and an additional cost of € 1.5 billion arising from healthcare and lost productivity due to these phenomena.

The transfer of genes for resistance through the environment and the food chain, the potential for development of such bacteria and the appearance of therapeutic failures in human medicine notably due to zoonotic bacteria constitute major health issues for livestock farming sectors.



## Programmes already under way :

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Internationally, there was a great deal of reflection under the auspices of international organisations such as the FAO, WHO and OIE during the 1990s on how to combat antibiotic resistance. This has led to the definition of guidelines for the surveillance of antibiotic resistance and consumption in veterinary medicine, risk analysis and the prudent use of antibiotics. The OIE emphasises the major benefits of antibiotics for animal health and welfare (of which health is a key component). In 2004 that organisation set up an ad hoc group and published standards and guidelines for the assessment of the risks of antibiotic resistance induced by the use of antibiotics in animals, plus a list of antibiotics crucial to veterinary medicine. A similar approach is currently being applied to the use of antibiotics in aquaculture. Another recent example is the adoption in July 2011 of guidelines for risk analysis of food-related risks arising from antimicrobial resistance by the Codex Alimentarius Commission (an organisation set up by the FAO and WHO).

Similarly, European bodies are now closely involved in this area, mobilising the institutions concerned by these issues, ranging from the European Medicines Agency (EMA), the European Centre for Disease Prevention and Control (ECDC), the network of Heads of Medicines Agencies (HMA) and the European Food Safety Authority (EFSA). Recommendations on the prudent use of antibiotics have been published and a draft European action plan is on the point of adoption. The agreement of November 2009 on the setting up of a US/Europe “task force” to combat antibiotic resistance is a further instance of this broader determination to coordinate activity.

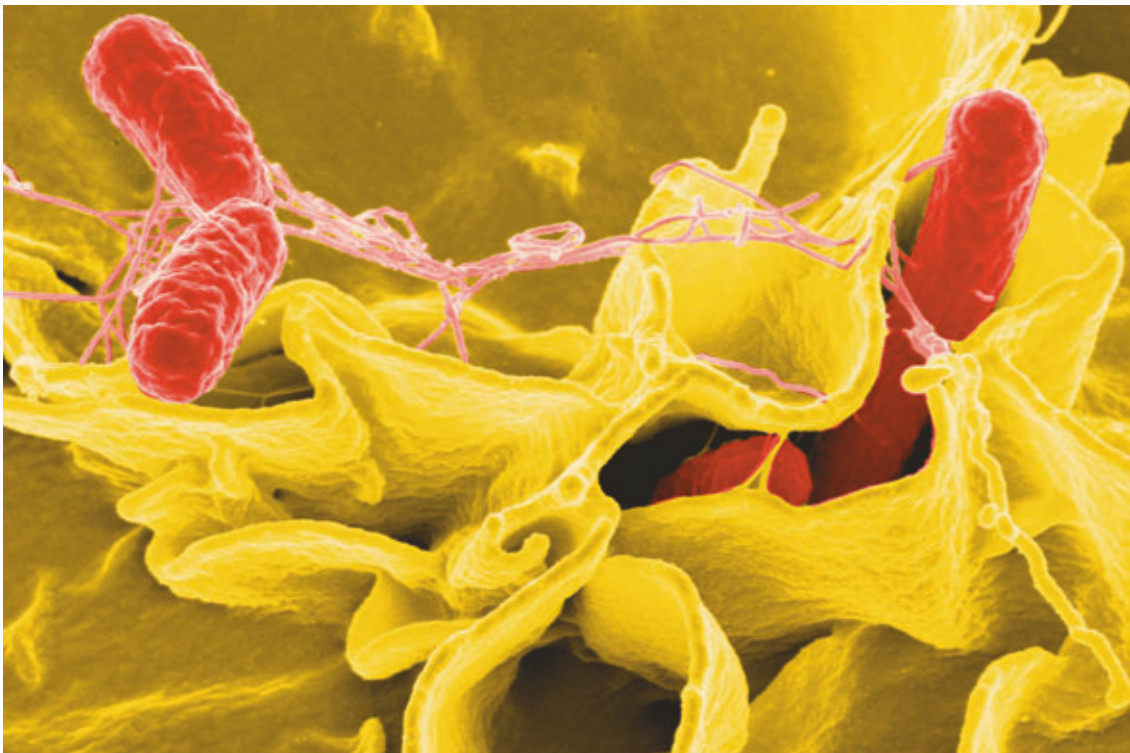
At the national level in the area of human medicine the ministry responsible for health has implemented, starting in 2001, a national plan to preserve the effectiveness of antibiotics which has since gone through two phases (2001-2005 and 2007-2010). Over the years 1999 to 2009, consumption of antibiotics in human medicine declined from 37.1 to 30.4 defined daily doses per 1,000 inhabitant-days (DDD/1000/Day; the dosage involved is a standard quantity for a 70kg adult), which represents a fall of 16% (Source: AFSSAPS report published 21 June 2011 under the title *Dix ans d'évolution des consommations d'antibiotiques en France* [Ten years of changing antibiotic consumption in France]).

In the veterinary domain, several programmes have been initiated by the authorities for the monitoring of developments in antibiotic resistance (the setting up of networks, surveillance programmes and farm surveys coordinated by the ministry of agriculture and ANSES<sup>1</sup>) and by concerned sector professionals in order to promote the proper utilisation of antibiotics (livestock farming sectors, veterinarians, pharmaceutical industry). Additionally, the use in livestock farming of antibiotics to promote growth has been banned in the European Union since 2006.

Starting in 1999, the Ministry of Agriculture has been funding the implementation by ANSES/ANMV of the monitoring of sales of veterinary medicinal products containing antibiotics. This monitoring is conducted in conjunction with the SIMV (Syndicat de l'Industrie du Médicament Vétérinaire et réactif – Industry federation for veterinary and reactive drugs) according to OIE guidelines on the “Monitoring of the Quantities of Antimicrobials Used in Animal Husbandry” (OIE Terrestrial Animal Health Code 2010 – chapter 6.8). The “ALEA” (Animal Level of Exposure to Antimicrobials) is the most reliable indicator for such monitoring since it is directly correlated with the percentage of animals treated in relation to the total animal population. This general level of animal exposure to antibiotics rose, taking all families together, by 27.9% between 1999 and 2009. From 2007 to 2010 it fell by 12.2% to a value of 0.62. The decline in the level of exposure over these last three years, although the trend remains to be confirmed, reflects an awareness of these new concerns on the part of sector professionals and the effects of their initial commitment to reducing exposure to antibiotics (source: the ANSES-ANMV Report published in November 2011 under the title *Suivi des ventes de médicaments vétérinaires contenant des antibiotiques en France en 2009 – volumes et estimation de la consommation d'antibiotiques chez les animaux* [Monitoring of sales of veterinary drugs containing antibiotics in France in 2009 – volume figures and estimation of animal antibiotic consumption]).

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<sup>1</sup> The AFSSA report of January 2006 on the “Veterinary uses of antibiotics, bacterial resistance and the consequences for human health” [in French], the ANSES report of November 2010 “FARM – French programme of surveillance of antibiotic resistance of animal origin 2007-2008 [in French] and the 2009 overview report by RESAPATH (Réseau d'Épidémiologie de l'Antibiorésistance des bactéries PATHogènes animales / Network for epidemiological surveillance of antibiotic resistance in pathogenic animal bacteria) published in November 2010.



## Definition of a national plan for the reduction of the risks of antibiotic resistance :

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Encouraged by the above concerns and the inception of the first initiatives, the Ministry of Agriculture set out to mobilise in a sustained and consistent manner all the professionals involved in the implementation of a national action plan for the reduction of the risks of antibiotic resistance in veterinary medicine.

On 18 November 2009 the French Directorate-General for Food called the first meeting of the National Coordination Committee for the judicious use of antibiotics in veterinary medicine, in which all the concerned actors are participants ; the main working focuses were defined at this meeting. The present plan is the outcome of the work done over the last two years.

The action plan has two objectives :

- Firstly, to reduce the contribution to bacterial resistance made by the antibiotics used in veterinary medicine and its consequences for public health,
- And secondly, to preserve the therapeutic arsenal on a sustainable basis, especially given that the prospects for development of new antibiotics are limited in veterinary medicine.

It aims to achieve a reduction of 25% in use over five years by developing alternatives capable of protecting animal health while avoiding recourse to antibiotics.

Indeed, antibiotics are special medicinal drugs that must be seen very much as a common good that it is important to preserve since they are indispensable to human and animal health. For that reason there must now be a change in the attitude to their use. Recourse to antibiotics must be prudential and targeted, with the prescription and administration of no more than the quantities strictly necessary to meet the therapeutic need. The objective is therefore not simply quantitative; it is also qualitative.

Prior to their implementation, certain measures will be the subject of further scientific evaluation and impact studies. In particular, the conclusions reached by ANSES, publication of which is expected in 2013, may lead to changes in the proposed measures.

This approach is in line with the policy directions defined by the European Parliament's resolutions of 12 May and 27 October 2011, the recommendations of the European Commission of 27 October 2011 on antibiotic resistance and generally the policy directions defined by the FAO, WHO and OIE, which recommend that countries adopt safeguard measures for antibiotics.

In this connection, France will contribute actively to the Strategic Research Agenda defining requirements and objectives for medium- and long-term research in the area of antibiotic resistance.



## AXIS 1

# PROMOTION OF GOOD PRACTICE AND RAISING THE AWARENESS OF THE ACTORS TO THE RISKS ARISING FROM ANTIBIOTIC RESISTANCE AND THE NEED TO PRESERVE THE EFFECTIVENESS OF ANTIBIOTICS

Adherence to the rules of good practice for hygiene and asepsis, the design and upkeep of suitable buildings and health-care establishments, application of biosafety measures and good sanitary monitoring are all effective ways of preventing and combating microbism and infection, the ultimate result of which is a reduction in the use of antibiotics. Dissemination of such good practice associated with the raising of the awareness of all the actors are priorities under the plan.

### **Measure n° 1 : Design and distribution of tools for raising awareness of the risks arising from antibiotic resistance and for the promotion of good practice to prevent recourse to antibiotics, for a target audience of livestock farmers**

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Efforts to counter antibiotic resistance must involve the greatest possible number of users ; the promotion of programmes relating to this topic must make use of suitable and instructive tools such as guides to good hygiene practice, articles in the specialist farming press and information brochures distributed by organisations in the sanitary field and chambers of agriculture.

Specifically, guides to good husbandry practice are an important tool for improving user practices. The inclusion of a chapter on antibiotic resistance must be considered when drafting all new guides and when updating existing guides.

### **Measure n° 2 : Development of an offering of continuous training on biosafety and proper use of antibiotics**

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Raising the awareness of and training livestock farmers and technicians involved in husbandry work is imperative if behaviour is to be changed.

Veterinarians will be associated with the organisations and establishments responsible for this training: this will unify the messages communicated on prevention of the use of antibiotics, promotion of good practice for use and treatment observance, adherence to hygiene measures and knowledge of the regulations.

### **Measure n° 3 : Raising the awareness of husbandry professionals to the risks arising from antibiotic resistance starting with their initial training**

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Proper use of antibiotics and good practice must also be addressed right from the stage of the initial training of husbandry professionals.

Existing course modules must be added to and improved to meet the specific needs of agricultural teaching establishments : agricultural high schools, technical training colleges (IUT), engineering schools, and the like.

## **Measure n°4 : Ensuring that the veterinarian’s visit provides a special point of contact between farmers and veterinarian for discussion of issues relating to antibiotic use**

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Visits by veterinarians to livestock farms must provide a special opportunity for dialogue on antibiotic therapy between prescriber and user.

Each livestock farmer must therefore have during sanitary visits to their farms the benefit of advice from a veterinarian on the right practices for achieving control over the quality of their production in sanitary terms.

Sanitary visits to farms will now include a chapter on the “Use of antibiotics in animal husbandry and antibiotic resistance”. This will look at solutions for problems that may arise before they can lead to dangers for consumer or livestock, and indeed before they are picked up by an official inspection.

## **Measure n°5 : Creation of self-assessment tools for livestock farmers and veterinarians**

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In order to allow veterinarians and farmers to assess their own usage on a voluntary basis, to identify possible room for progress and to encourage them to change their habits, benchmark indicators for the prescription and usage of antibiotics and medicated feed on farms will be defined and suggested.

## **Measure n°6 : Development of guides to good antibiotic prescription practice with a primary focus on pathologies identified by the working groups (cf. Measure n°27)**

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Carrying forward the approach already under way with the publication of the guide to good practice in antibiotic therapy for the use of veterinarians, professional veterinary organisations must adapt this guide for use in all sectors of activity. A consensus will need to be built on the treatment of pathologies, the categorisation of antibiotics by therapeutic indication (antibiotic treatments of choice, antibiotics for restricted and conditional use, antibiotics whose use is not recommended, antibiotics never to be used).

## **Measure n°7 : Reinforcement of veterinarians’ continuous training and information, and specifically the “veterinary pharmacy” module proposed for “sanitary mandate” training**

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Continuous vocational training on the judicious use of antibiotics must be reinforced. Such training will address various topics such as epidemiology, regulations, and so on, and must be adjusted in line with the objective of reducing the use of antibiotics and the development of alternatives that meet veterinary requirements. The training must provide reminders of the factors for the risk of appearance of bacterial resistance and the need to preserve the effectiveness of antibiotics crucial to the protection of human health.

In particular, the veterinary pharmacy module proposed in the “Sanitary Mandate” course will address the topics of judicious antibiotic therapy and antibiotic resistance.

## **Measure n°8 : Reinforcement of veterinarians' initial training on antibiotic resistance, and especially on applied antibiotic therapy**

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Proper utilisation of antibiotics must be addressed right from the stage of veterinarians' initial training. The recent recommendations of the High Level Committee on the veterinary training programme are a step in this direction. Similarly, students must be introduced to the tools made available to veterinarians by veterinary technical bodies.

A working group comprising representatives of official departments, teachers and veterinary technical bodies will prepare the implementation of a module devoted to antibiotic therapy for future veterinarians in schools.

This module, which will address the pharmacological and regulatory aspects and well as those relating to management of medicinal products in professional establishments, could be dispensed at the end of the course when students come into contact with medical practice and are writing their first prescriptions, the aims being the following :

- firstly, to ensure greater consistency between the theoretical teaching dispensed at the beginning of the course and the practical training at its end for students destined to become drug prescribers ;
- secondly, to allow greater consideration to be given to the public health risks arising from treatment decisions ;
- and to bring the guides on judicious antibiotic therapy to their attention (cf. Measures 1 and 6).

## **Measure n°9 : Ensuring that pharmacists are better informed and more aware of antibiotic resistance in veterinary medicine**

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The training of pharmacists is ill-suited to the specific features of pathologies encountered in livestock farming and veterinary medicine. The existence of specific rules in veterinary pharmacy and in particular the obligations concerning prescription, pharmacovigilance and the risks arising from antibiotic resistance must be fully mastered when dispensing medicinal products intended for animals in pharmacies.

Initially, pharmacists will therefore be made more aware of the requirements of examination of veterinary prescriptions in order to ensure that they possess the same expertise as they do for prescriptions in human medicine, as well as of the issues surrounding the renewal and substitution of veterinary antibiotics.

## **Measure n°10 : Enhanced scientific communication targeting prescribing and dispensing professionals, and the provision to professionals of resistance data**

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The provision of information on resistance to antibiotics from surveillance networks, notably RESAPATH (*Réseau d'Épidémiologie de l'Antibiorésistance des bactéries PATHogènes animales* / Network for epidemiological surveillance of antibiotic resistance in pathogenic animal bacteria), the network set up by ANSES, to veterinarians and possibly to livestock farmers, is judged to be inadequate.

For this reason, data on strain sensitivity and resistance will be provided to prescribers and users, with a reminder of the fundamental difference between epidemiological resistance and clinical resistance. This will encourage veterinarians to make more use of antibiograms, facilitate diagnosis and promote the judicious use of antibiotics by prioritising the use of narrow-spectrum types.

The relationship between veterinary diagnostic laboratories and prescribing veterinarians must also be developed since this is an especially useful channel for information relevant to greater vigilance on the part of practitioners. The data collected by the RESAPATH network will be more effectively circulated.

## **Measure n° 11 : Encouragement of laboratories carrying out antibiograms to use methods validated for veterinary medicine and to develop inter-laboratory networks**

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A number of supplementary tests, for canine veterinarians in particular, are carried out by human biology laboratories applying methods inappropriate to veterinary medicine (unsuitable germs and antibiotics tested). Antibiograms must be executed and interpreted using validated methods specific to veterinary medicine offering sufficient guarantees of reliability.

Veterinarians will be made aware of the need to use laboratories that have developed veterinary competencies for their tests, thus enabling proper interpretation of the results.

## **Measure n° 12 : Continuation of discussions between partners on issues arising from antibiotic resistance, using platforms such as working groups deriving from the National Coordination Committee for the judicious use of antibiotics in veterinary medicine**

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Continuing the approach undertaken for the adaptation of the guide to good practice in antibiotic therapy for use by veterinarians, working groups on the use of critical antibiotics have been set up in all sectors. They will meet annually to survey the whole range of existing practices, identify areas for progress, and to design and disseminate consensus-based prescription procedures for defined situations.

## **Measure n° 13 : Promotion of the proper use of antibiotics targeting the owners of pet animals by means of a public communication programme**

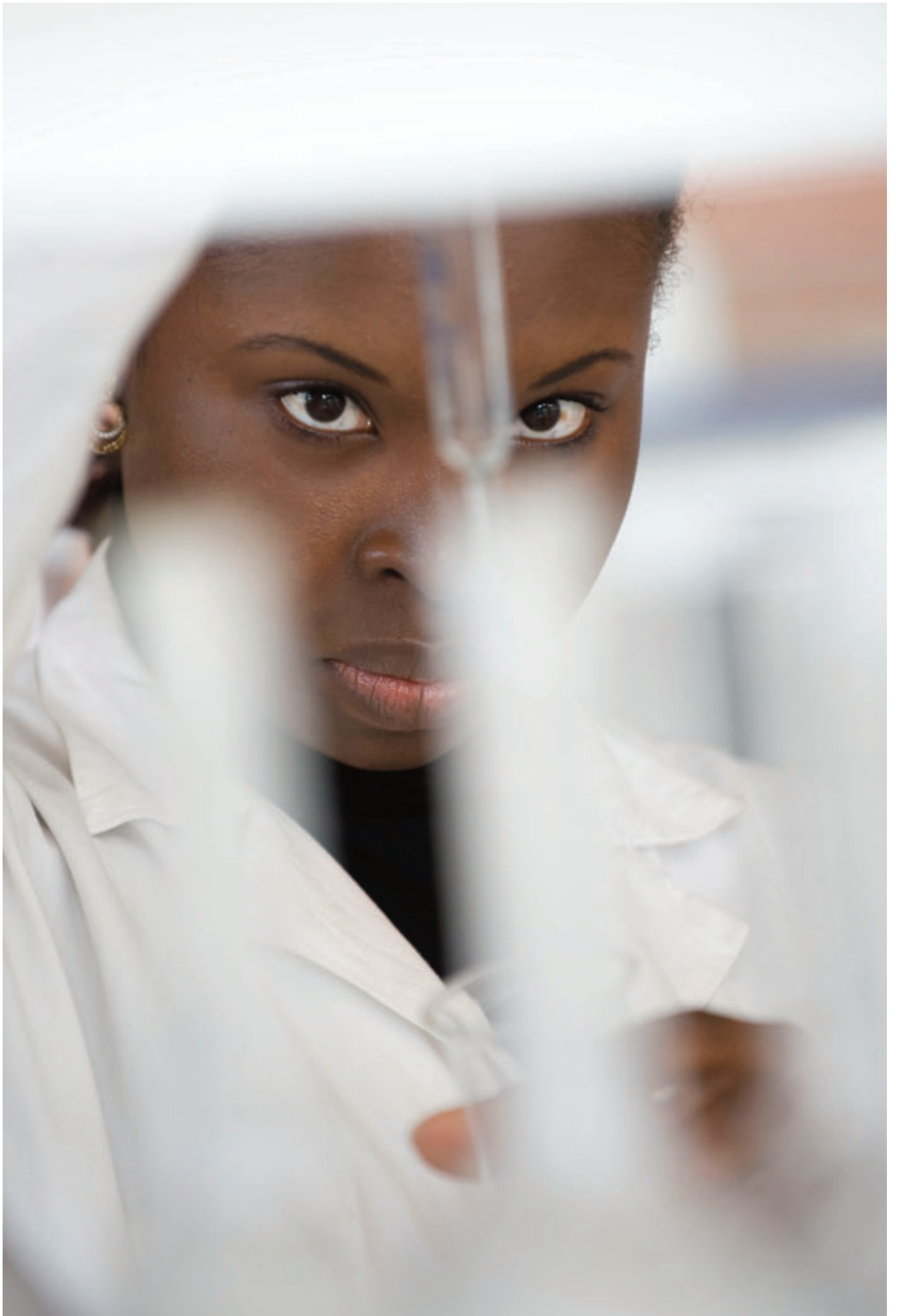
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The livestock farming world is not alone in being concerned by the proper use of antibiotics and the need to counter antibiotic resistance. Indeed, where pet animals are involved it is necessary to make their owners more aware of the therapeutic importance of antibiotics. In particular, emphasis should be placed on the veterinarian's diagnostic approach and proper observance of treatment protocols. The aim here is to convince pet owners :

- that improper use of antibiotics undermines their effectiveness just as it does in human medicine,
- and that when an antibiotic treatment is applied, its success will depend on adherence to the prescription, observance and follow-up visits during the treatment.

There is a need to encourage targeted communication campaigns in the specialist pet press and on posters in canine veterinary establishments.





## AXIS 2

# DEVELOPMENT OF ALTERNATIVES FOR AVOIDANCE OF THE USE OF ANTIBIOTICS

Limitation of the use of antibiotics and promotion of good practice cannot be fully justified in the absence of development of a varied range of alternatives that matches the constraints applicable to animal production and care sectors. Experimental and research programmes may be necessary to arrive at new solutions for pathologies encountered in animals and to gain more knowledge of their resistance mechanisms.

### **Measure n° 14 : Development of sanitary prophylaxis tools and zootechnical measure**

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Adherence to the rules of good practice for hygiene and asepsis is effective in preventing and combating microbism and infection and will encourage reduced use of antibiotics.

These measures must be set out in guides to good husbandry practice drafted by professionals in order to promote sanitary prophylaxis, biosafety measures and, on the basis of known data, building design.

Work will begin on consolidation of the development of husbandry protocols that allow the use of antibiotics to be reduced.

### **Measure n° 15 : Promotion of research on immunity and the use of vaccines and auto-vaccines**

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Research in the field of specific immunity must be developed in order to promote the preventive use of vaccines to replace antibiotic treatments, including markets of limited economic viability.

Recourse to vaccination must be encouraged where it is possible for the prevention of certain pathologies in the husbandry context as well as for pet animals. The use of vaccines must be made more competitive compared with antibiotics in prophylaxis and the financial brakes on use must be removed. In the event of lack of availability, and following scientific evaluation, imports for therapeutic purposes of vaccines authorised in other Member States will be facilitated.

Subject to scientific validation of their therapeutic value and in the absence of authorised vaccines, recourse to auto-vaccines will be considered.

### **Measure n° 16 : Development of fast diagnostic tools validated for defined sectors**

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The development of validated “instant” tests for fast diagnostic guidance on viral or bacterial aetiology for certain diseases, in neonatal calf diarrhoea and certain respiratory conditions for example, must also be given priority.

Some of these tests already exist and are used routinely in other States, which should facilitate their validation at national level.

## **Measure n° 17 : Ensuring maintenance of marketing authorisations (AMM) for non-critical older antibiotic molecules**

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The use of older molecules should be encouraged in order to avoid use of more sensitive recent molecules, where evaluation has not revealed any risk of cross- or co-resistance. Pharmaceutical firms will be encouraged to collect information on the effectiveness of specialities containing older molecules with a view to possible applications for AMM amendments. In particular, attention must be paid to ensuring the revalidation of therapeutic schemes.

## **Measure n° 18 : Support for research into new antibiotic molecules reserved for veterinary use and non-critical in human medicine**

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With a view to less but better use of antibiotics, the alternatives considered may provide replacements for so-called critical antibiotics or antibiotics generating major resistance in gut flora by other non-critical antibiotics that do not lead to resistance in flora.

The search for new molecules would make it possible to expand the therapeutic arsenal and thus provide access to new alternatives. This research and its application to veterinary medicine will be developed, with consideration being given to the importance and impact of the relevant molecules in human medicine.

## **Measure n° 19 : Evaluation of the benefit of alternative treatments enabling antibiotic use to be reduced**

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Research into alternative products will be the subject of studies that take into account the benefits they offer with regard to reducing antibiotic use. As an example of this in the pig farming sector, the advantages of use of zinc oxide in reducing the incidence of piglet diarrhoea will be the focus of an ANSES risk/benefit study.

## **Measure n° 20 : Research into solutions for minor species in the context of availability of veterinary medicinal products**

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Lack of availability of antibiotics is a difficulty encountered in the rearing of minor species. Several causes have been identified for this:

- ▶ Disappearance of the indication applicable to minor species in the marketing authorisation (AMM): in the case of certain medicinal products an indication for minor species was included at the time of issuance of the initial AMM. This indication has been lost when the AMM was reviewed or when the summary of product characteristics (RCP) was drawn up due to lack of data on the minor species concerned ;
- ▶ Abandonment of the term “volaille” in French, which provided a generic umbrella heading for a number of species, led to the sole inclusion of those species covered by the data supplied by the holder of the marketing authorisation (usually the poultry species *Gallus gallus*) in its AMM marketing application, with the result that all other species such as duck, guinea fowl or turkey have been left out.

It is necessary to promote the development or the amendment of existing AMMs and to continue the work on MRL extrapolation for minor species.

Additionally, application of the standard withdrawal period imposed in the event of use of the replacement or off-label use provisions encourages the use of critical antibiotics with a withdrawal period that is either very short or zero days. A revision of the European regulations on the standard withdrawal periods should be undertaken for related species.

## **Measure n°21 : Research : coordination for reducing antibiotic use in farm livestock**

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Studies of the mechanisms that lead to resistance and those for its transmission via genes and genetic media, contact, food or the environment must be continued, especially for zoonotic bacteria.

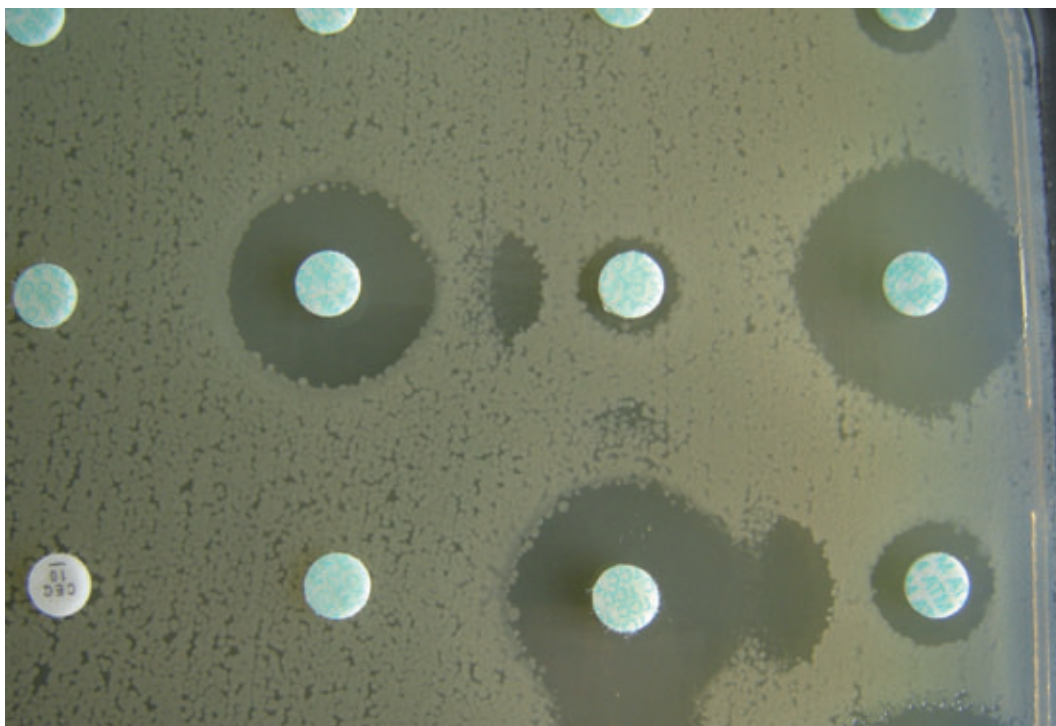
High-risk practices leading to selection of multiresistant bacteria need to be defined and the effects of prophylactic, metaphylactic or curative use of antibiotics, according to indication, quantified in order to validate therapeutic schemes. This measure must be operational in the short term and is part of ANSES' examination of antibiotic resistance.

In addition, study of the mechanisms whereby resistance transmission chains can be broken is an avenue that may lead to alternative treatments for infections of bacterial origin. This is a long-term research project for which it is imperative to coordinate the programmes of private operators and those of the authorities.

## **Measure n°22 : Consideration of the desirability of a levy dedicated to funding the preventive actions under the Plan, essentially the implementation of the recommendations in guides to good husbandry practice and the development of alternative techniques for reduction of antibiotic use**

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The General Council on food, agriculture and rural areas and the general financial inspectorate will be charged with examining the advantages of a national levy on sales of antibiotics. Such a levy would provide funding for the measures under Axis II of the present Plan and the information campaigns.





## AXIS 3

# REINFORCEMENT OF CONTROLS AND REDUCING HIGH-RISK PRACTICES

If the effectiveness of antibiotics, and especially the effectiveness for human beings of the most “critical” of those products, is to be preserved, it will be necessary to limit their use. The changes in EU and national regulations recommended under the Plan are intended to permit :

- an improvement in the conditions for evaluation of the marketing of such antibiotics and the conditions for the provision of information and advertising targeting prescribers and rights holders ;
- and, secondly, reinforcement of controls over commercial practice and prescription rules.

### **Measure n°23: Greater consideration for the risk arising from antibiotic resistance in the evaluation or re-evaluation of marketing authorisation applications (AMM), especially in the case of generics.**

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Antibiotics are a class of veterinary medicinal product for which the risk/benefit assessment needs to be carried out according to specific rules.

Application of this measure will require changes in EU regulations. This is so because it is necessary to modify the existing regulatory framework in order to make it possible to reject or to amend an AMM application for an antibiotic on the basis of risks related to antibiotic resistance. Specifically, greater consideration must be given to issues of antibiotic resistance in order to limit the marketing of generics that will drive increased consumption.

The CNMV (*Commission Nationale du Médicament Vétérinaire* / National veterinary drug commission) will be consulted for its view on whether it is appropriate to define and take into account a concept of “actual medical benefit” that would apply to antibiotics.

### **Measure n°24 : Improved information in summaries of product characteristics (RCP) and the inclusion of a health education message in product leaflets.**

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The inclusion of a health education message in the outer wrappings of antibiotics and in package leaflets along the lines of “inappropriate use of antibiotics is a cause of microbial resistance” must be made mandatory in order to prevent self-medication, among other things. Such a measure is already planned for medicinal products intended for human use.

Directive 2001/82/EC on the Community code relating to veterinary medicinal products provides in Article 26 that marketing authorisations should require the holder to indicate on the immediate packaging and/or the outer wrapping and the package leaflet other particulars essential for safety or health protection; those particulars do not currently include antibiotic resistance.

As part of the process of revision of the directive recently initiated in 2011 it would be useful to consider an amendment to this article in order to allow for the possibility of requiring the inclusion of medical education message relating to antibiotics intended for veterinary use.

Application of this proposal requires a change to EU regulations. In the meantime, the pharmaceutical industry will be encouraged to commit to including messages of this kind.

## **Measure n° 25 : Establishment of a list of “critical” antibiotics for which preservation of effectiveness in human medicine is a priority**

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The antibiotics concerned are the third- and fourth-generation cephalosporins and fluoroquinolones with the exception of intramammary ointment presentations. This list is open to change. It will be reviewed following the conclusions reached by ANSES in its examination of this area and work done by FAO/WHO/OIE.

## **Measure n° 26 : Restrictions on prescription of “critical” antibiotics for which preservation of effectiveness in human medicine has high priority**

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The prescription of critical antibiotics must be made conditional upon the prior execution of supplementary testing (e.g. antibiogram) in compliance with the opinion notified by the European Commission’s Committee for Medicinal Products for Veterinary Use (CVMP) and the recommendations issued by meetings of EU Chief Veterinary Officers. This requirement of supplementary testing before prescription will be rolled out progressively to all sectors.

## **Measure n° 27 : Improved prescription of antibiotics based on specific measures to match each species**

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The first meetings of the four groups (pigs, poultry, veal calves, dairy cows and pet animals) set up following the meeting of the Committee on 18 January 2011 led to the detailed definition of specific proposals concerning the use of certain antibiotics (the priorities being third- and fourth-generation cephalosporins and fluoroquinolones, the subject of macrolides also being raised). Listed in Annex 1, detailed actions will be supplemented on the basis of the conclusions to come later from the working groups dedicated to the rabbit, horse and fish farming sectors.

## **Measure n° 28 : Improved control of the prescribing of antibiotics without prior clinical examination, within the framework, firstly, of the treatment protocol and, secondly, livestock farming health programmes**

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In addition to the measures on critical antibiotics contained in the preceding proposals (cf. measures 15,16 and 17), control of provisions concerning the prescription without clinical examination and livestock farming health programmes (most notably, the positive list of substances approved for inclusion in livestock farm health programmes and able to be issued by groupings) will be reviewed in light of the conclusions reached by ANSES.

## **Measure n° 29 : Revision of the control of commercial practices associated with the sale of antibiotics, and specifically an end to promotional campaigns and limitation of profit margins likely to influence prescription**

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Veterinarians must be freed of commercial practices that may influence their product procurement. To that end, new provisions in Article R. 242-46 of the code of professional ethics for veterinarians and Article R.5141-87 of the public health code concerning the advertising of veterinary products will be adopted by an official decree in the Council of State in order to ensure that rights holders do not obtain procurement under contracts making financial benefits conditional on quantities of medical products purchased and that they do not enter into commercial cooperation contracts with pharmaceutical firms.

Inspection tasks will also be entrusted to the General Council on food, agriculture and rural areas for the definition of rules for greater transparency with regard to the character of contractual agreements already in place.

## **Measure n°30 : Adaptation of packaging for optimized use**

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Product unit price is often lower for veterinary products sold in large packages than for the same products in small packages. Moreover, the presentation of such products in large packages may encourage use of the totality of the product independently of any duly prescribed course of treatment.

Veterinary pharmaceutical companies will be encouraged to commit, based on the drafting of an ethical charter, to going down the road of developing product packaging that is more effectively adjusted to the quantities being dispensed, thus allowing optimum use as strictly required for the treatment and pricing policies that do not penalise packages of smaller quantities of product.

## **Measure n°31 : Stronger controls on antibiotics advertising ; promotion of vaccination**

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Stricter controls will be applied on advertising in order :

- to reinforce the conditions for the control and examination of advertising by the ANMV (French national agency for veterinary medicinal products),
- to ensure mandatory insertion of a health message along the following lines: “inappropriate prescription and dispensing of antibiotics leads to the appearance of microbial resistance”.

On the other hand, the communication and advertising rules applicable to pharmaceutical firms will be made more flexible to ensure that the advertising of vaccines targeting livestock farmers can be authorised and to promote the prevention of sanitary risks.

## **Measure n°32 : More effective prosecution of illegal use and trafficking**

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Detection and prosecution of the illegal use of veterinary medical products will be a priority for the BNEVP (*Brigade Nationale d'Enquêtes Vétérinaires et Phytosanitaires* / National veterinary and phytosanitary investigation unit). OCLAESP (*Office Central de lutte contre les atteintes à l'environnement et à la santé publique* / Central office for combating damage to the environment and public health) and the customs authorities will be asked to undertake specific enquiries.

## **Measure n°33 : Reinforcement of controls on the prescription, dispensing and use of antibiotics**

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Adherence by veterinarians and pharmacists to proper procedures for antibiotic prescription, both on farms and on the premises of manufacturers of medicated feed, is key to controlling antibiotic consumption.

Inspection will be stepped up, with priority being given to prescription content in order to ensure that prescriptions do not permit self-medication, use of antibiotics as growth promoters or unjustified access to these medicinal products.



## AXIS 4

# CONSOLIDATION OF THE SYSTEM FOR MONITORING ANTIBIOTIC CONSUMPTION AND ANTIBIOTIC RESISTANCE

The objective of this plan axis is to assess the impact of the steps taken.

The monitoring of antibiotic sales and use continues to be essential and the data currently being collected make it possible to track the quantities used and the exposure for individual species generally over time, but they do not provide effective monitoring taking account the age of the animals treated or therapeutic indications.

This plan axis must be aligned with the EU approach coordinated by European Medicines Agency (ESVAC project). Such intensification of monitoring activity to include the age of the livestock treated and therapeutic indications is an essential step.

This approach will be applied both to productive and pet animals.

To that end, it is proposed to set up an observatory for antibiotics use in the ANMV (French national agency for veterinary medicinal products).

European and national surveillance programmes are already providing data on the prevalence of resistance in zoonotic, pathogenic and commensal bacteria deriving from productive livestock. The aim now is to widen the scope of those programmes to include the links in the food supply chain judged to be relevant, in line with EFSA recommendations in this area.

### **Measure n° 34 : Continuation of the monitoring of antibiotic sales and exposure ; creation of a usage observatory in ANSES-ANMV and analysis of data on medicated feed**

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The objective of this measure is to create the conditions for exhaustive collection of data on antibiotic sales in France. Although the present system for voluntary notification of information on antibiotic sales to ANSES-ANMV has given satisfaction, it must be extended with a view to shared transparency.

The information provided by the manufacturers of medicated feed must be more detailed. This could be a source of additional data on the use of antibiotics for preventive purposes, the development of which it is important to be able to monitor. And lastly, the monitoring of off-label usage will be included.

Thought will also be devoted to modern tools for the harmonised collection of information used for the recording of data on prescriptions and the dispensing of veterinary medicinal products. In this respect better use should be made of DATAMATRIX (barcode) data.

A cost/benefit analysis must be done for the implementation, maintenance and operation of a system of this kind. Following completion of this impact study, systematic feedback of prescription and administration data by rights holders could be envisaged for one or more sectors, beginning with those in which consumption is highest.

## **Measure n°35 : Organisation of regular surveys of representative samples of veterinarians and farmers and extension of pharmacoepidemiological surveys to include all sectors**

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INAPORC and veterinary technical bodies in the pig farming industry (SNGTV, AVPO, AFMVP) are currently helping to implement voluntary restrictions on the prescription and use of third- and fourth-generation cephalosporins in pig farming. In conjunction with ANSES and the technical institutes, they are defining detailed procedures for monitoring the dispensing of products, along with their use by a representative sample of pig farmers.

This type of monitoring involving the representative farming bodies needs to be extended to include other molecules and other sectors.

In the case of other sectors, it will be necessary to determine the most appropriate ways in which prescription and use can be tracked.

Pharmacoepidemiological studies make it possible for a given production system to characterise the types of livestock farm that consume the largest quantities of antibiotics where repeated use is considered to be a strong indicator of dysfunction.

Subsequently, the risk factors within those holding types will be identified and taken into account to ensure that targeted corrective action is taken with the support of veterinarians and technical institutes.

Periodic surveys such as those already conducted for poultry, rabbits and pigs will be continued and new surveys implemented along the same lines for cattle and pet animals.

## **Measure n°36 : Intensified monitoring of antibiotic resistance**

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The monitoring of development of resistance is the subject of annual surveillance plans driven by DGAL (the French directorate-general for food) and implemented by ANSES, which provide resistance data on one or more species and commodities for each year of collection.

Cooperation between the national and European bodies already involved (EFSA, centres of reference, ENV (French national veterinary school), networks for the surveillance of sentinel bacteria and pathogens) will be stepped up, especially in order to ensure the availability of surveillance data to permit comparison between the situation in France and other Member States.

Additionally, the results of antibiotic resistance surveillance will be compared with data on sales of antibiotics. This is the purpose of the ESVAC project.

In order to facilitate shared reflection, comparative monitoring tables for antibiotic consumption and bacterial resistance in human and veterinary medicine will be drawn up and circulated.

## **Measure n°37 : Examination of the impact of antibiotics use in the livestock farm environment**

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Reflection on the use of antibiotics and efforts to counter antibiotic resistance must take account of antibiotic persistence and resistant bacteria spread in farm slurries, effluent, water, and so on.

Further studies should be undertaken in this area.





## AXIS 5

# PROMOTION OF EUROPEAN APPROACHES AND INTERNATIONAL INITIATIVES

Antibiotic resistance knows no borders, either between species or between countries. The French national level is therefore very much part of an international context in which France expects the same efforts to be made by its European and international partners.

### **Measure n°38 : Arguing for French policy directions in European and international discussions**

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As has been stressed in the introduction to the Action Plan, the topic of resistance to antibiotics is a matter for discussions and projects both within the European Union and internationally.

It is appropriate for France to present the policy directions described in the Plan to its partners and suggest that they pursue together their efforts to resolve these issues.

It is also France's wish that these specific topics should continue to be addressed internationally (OIE, WHO/FAO and notably the work done by the Codex Alimentarius, WTO) and within the framework of TATFAR (TransAtlantic Task Force on Antimicrobial Resistance: a contact body between the United States and the European Union) and will contribute to the definition of international standards based on its expertise and experience.

Regular status reviews of the national plan will be published in order to highlight and quantify the efforts deployed by France, and thus increase consumer and customer confidence in French agriculture.

### **Measure n°39 : Improvements in technical watch activities and international regulations.**

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A regular watch will be kept on ongoing developments in Europe and internationally relating to subjects touching on resistance to antibiotics or their judicious use and this will be reflected in regular publication of a bulletin for all actors in the plan.

One of the objectives of this kind of watch activity is to ensure swift dissemination of alternatives proposed in other States and which would be needed by industry sectors in France, and to identify the levers that can be exploited to allow use of the tools concerned.

It will also ensure improvements in the information on the whole range of regulatory developments and European discussions currently under way concerning antibiotic resistance.

Maintenance of the use of antibiotics as growth promoters (in the United States for example) will be monitored specifically.

## **Measure n° 40 : Reinforcement of the programme of surveillance of livestock, animal feedstuffs and commodities traded or imported in the European Union**

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The quality of the work undertaken in France by prescribers and users in connection with the judicious use of antibiotics and combating antibiotic resistance increases the need to apply reciprocity rules applicable to the introduction of commodities from countries that are less advanced on these issues.

In February 2011 France asked the European Commission to work on a strengthening of import regulations and controls applicable to inputs used in animal production in non-EU countries. France also seeks stronger rules on indications of origin in labelling.

Based on the model already existing in other countries such as Denmark, and after a reasonable period of application of the Plan, it will be useful to set up a wider programme of surveillance of resistance to antibiotics in sentinel and zoonotic bacteria relating to commodities and animals produced in, introduced or imported into France.



# ANNEX

## Pet animals

- ▶ Adjustment of the system of pharmacovigilance (feedback on therapeutic failures, and successes in the case of use on new domestic animals).
- ▶ Drafting of prescription guides for each speciality along the lines of the work done in dermatology.
- ▶ A formal request to ANSES to consider the possible use of metronidazole in the treatment of pet animals.

## Cattle

- ▶ Development of vaccination strategies, especially for the allotment of veal calves and beef cattle.
- ▶ In order to limit group treatment of fattening livestock, application of risk analysis to incoming cattle lots.
- ▶ Limitation of use of fluoroquinolones, these being widely used for the treatment of neonatal diarrhoea, by redefining good husbandry practice.
- ▶ Promotion of practices for differentiated treatment relating to drying off (antibiotic therapy reserved for livestock detected as infected or animals presenting a particular risk of contracting a further infection during drying off).

## Pigs

- ▶ An end to use of third- and fourth-generation cephalosporins for preventive purposes in connection with piglet procedures (tail docking, castration and tooth clipping) and their use solely as a second line treatment after identification and demonstration of the sensitivity of a strain by means of an antibiogram. This approach has already begun to be applied by industry bodies and veterinary technical organisations in the sector.
- ▶ An end to the use of fluoroquinolones other than for curative purposes, with utilisation being limited to second line treatment following prior additional testing.
- ▶ Limitation of use of macrolides, these being widely employed at the present time in treating digestive conditions at weaning, by redefining good husbandry and prescription practice, given that nutritional and therapeutic alternatives are available.
- ▶ A formal request to ANSES to consider use of zinc oxide on piglets for the reduction of diarrhoea, while limiting its use in feedstuffs for growing pigs in order to avoid increased discharge into the environment.
- ▶ Encouragement for the introduction of plans for the control of viral agents conducive to bacterial superinfection (PRRS).
- ▶ Introduction of indicators for the level of animal exposure to antibiotics enabling objective assessment of the progress made at each husbandry stage (exposure of nursery piglets to cephalosporins, to macrolides at weaning and sows to fluoroquinolones). The industry organisations have begun this work.
- ▶ Comparison across Europe of the medicinal products available in other Member States, notably with regard to “older” molecules and vaccines.

## Poultry

- ▶ And end to the use of third- and fourth-generation cephalosporins in ovo and on one day-old chicks in hatcheries, except for specific export requirements.
- ▶ Introduction of indicators for monitoring antibiotic use in hatcheries and ESBL resistance genes in indicative flora sampled on farms.
- ▶ Improved availability of autovaccines, which seem to offer a useful alternative in sectors of more minor importance (duck, guinea fowl, turkey) subject however to prior risk/benefit assessment.
- ▶ Consideration of arrangements to permit use of bacitracin zinc.





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