Impact matrix analysis and cost-benefit calculations to improve management **pr**actices regarding health status in **o**rganic dairy farming

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- Deliverable -

D9.6 - Report describing the options and limitations in the use of alternative remedies to reduce the use of antibiotic

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Deliverable Author(s):	A. Sundrum

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Executive Summary

Because of public concern regarding the increase of antibiotic resistance, the question arise whether the use of alternative treatments particularly homeopathy and phytotherapy holds potential to replace the use of antibiotics in treating bacterial infectious diseases. This question cannot simply be answered with “yes” or “no” but depends on different prerequisites, including the efficacy of medicinal products under standardised conditions, the effectiveness of products under heterogeneous farm conditions, the availability of expertise to ensure therapeutic success, a cost-benefit outcome relationship where positives outweigh negatives, and last but not least keeping negative side effects that might compromise the issues of animal health and welfare (AHW) to a minimum. To deal with the main question, a comprehensive pilot project was initiated and produced the following results:

At the beginning, two comprehensive literature reviews were conducted on previous scientific studies on the efficacy of homeopathy and phytotherapy in farm animals. In the case of homeopathy, search results revealed a total number of 52 trials performed within 48 publications fulfilling the predefined criteria. Twenty-eight trials showed a significantly higher efficacy of the homeopathic remedy in comparison to a control group, whereas 22 showed no medicinal effect. Cure rates for the treatments with conventional remedies, homeopathy or placebo varied to a high degree. Looking at all the studies, not even one study was repeated under comparable conditions. Consequently, the use of homeopathy lacks any reproducibility and cannot claim to have sufficient prognostic validity where therapeutic efficacy is concerned. When striving for high therapeutic success in treatment, the employment of homeopathy in replacing or reducing antibiotics requires evidence of efficacy confirmed by Randomised Controlled Trials under modified conditions.

Where phytotherapy was concerned, the majority of the 53 scientific studies identified showed limitations in the study design as well as for presentation and standardisation of the botanical remedies studied. This makes it impossible to compare studies on remedies derived from the same plant as well as reproducing these studies in the future. Although most studies tend to conclude that phytotherapeutic remedies have potential, it is not possible to draw firm conclusions. None of the scientific studies with homeopathic or phytotherapeutic products have been re-produced.

In the past, only few research bodies in Europe have been involved in research on veterinary homeopathy and phytotherapy, with little manpower dedicated to the area. Insufficient support from funding bodies seems have led to a poor research infrastructure, although many of those questioned clearly expressed the need for more research in the area. This limits opportunities for efficient research on veterinary homeopathy and phytotherapy.

Evaluations on organic dairy farms in Germany, France and Spain revealed that there were no uniform procedures for homeopathic treatment in the case of mastitis. It seemed that each farmer had developed his/her own homeopathic treatment strategy; regardless of the principles of homeopathy. According to assessments by homeopathic experts, most farmers showed only a poor level of awareness of the homeopathic principles. In many cases, farmers were acting illegally by using homeopathic products which carried no approval for food-producing animals. Early detection monitoring was rarely conducted. A follow-up check was often only performed visually by the farmers themselves and the results seldom documented. The results indicate that the degree of efforts needed to comply with the EC-Regulation on organic agriculture, demanding immediate treatment and particular attention to the minimising of diseased animals’ is left to the subjective decisions of the farmers.

To gain insight regarding the current use of phytotherapeutic remedies on conventional pig and poultry farms in France, Germany, Netherlands and Spain, and the context in which these remedies are used, a questionnaire was circulated. The results showed considerable heterogeneity in the use of phytotherapeutic products, but the main purpose seemed to be prevention. In many cases, essential prerequisites for the target-oriented and effective use of phytotherapeutic products were

missing. Inappropriate diagnostic procedures and monitoring of treatment success as well as the limited availability of expertise made it hard to establish an appropriate level of therapy success on the farm level.

The effectiveness of alternative treatments in farm practice is highly context-dependent and is doubtful without the consistent implementation of *lege-artis* procedure, including early registration of symptoms, detailed diagnostic procedure, removal of the main causes, selection of the appropriate remedies, follow-up check of the recovery progress and documentation of the success of therapy. Thus, the employment of homeopathy or phytotherapy in favour of conventional products cannot be sanctioned unless these alternative products are administered by highly skilled and responsibly operating people. Otherwise, alternative treatments might enhance the risk for increasing health and welfare problems due to lack of therapeutic success and thus extended suffering of diseased animals.

Apart from the significant uncertainties regarding the effectiveness of alternative treatments in farm practice, differences in their mode of action make alternative treatments largely unsuitable for the replacement of antibiotics for group treatment, being the main scope of application for antibiotics.

Improving preventive measures on the farm level and increasing therapeutic success by implementing a *lege-artis* treatment procedure requires considerable labour time and cost. In this conflicting area, farmers neither benefit when their animals have a high level of therapeutic success and low prevalence of production diseases (PDs) nor face penalties when they deviate considerably from the average. Furthermore, retailers do not offer adequate incentives and do not cover the additional costs which are necessary to improve the success rates of therapy. The farmers are thus left alone in managing the trade-offs.

Remedies are means to an end. However, the end result can vary widely, ranging from a missing to a complete recovery from problematic issues. Therapeutic success in the individual and cure rates on the herd level do not only depend on selecting the appropriate remedy but on the herd level, they are the result of the overall effort invested in the prevention and treatment measures. And vice versa, the level of envisaged cure rate determines the means and the degree of effort required to achieve the target sets in the context of the farm system involved. Deciding which level of therapeutic success and what prevalence of PDs is acceptable should not be left to each farmer to decide for themselves. These values are essential to the common good and should be set using external reference values.

Organic livestock production shows that enhanced basic standards cannot be expected to result in improved therapeutic success and the reduction of PDs. The impacts of the various influencing factors should be validated by studying the outcomes of the highly complex processes instead of focussing primarily on input criteria. The way farm specific disease prevention and treatment measures are managed certainly influences the prevalence of selected PDs and the issues of animal welfare and food safety. Thus, systems for monitoring selected PDs are urgently needed to provide orientation for all stakeholders, to check whether targets set are being achieved and to reduce unfair competition when animal products from farms with quite different levels of PDs and therapeutic success gain the same market price. Lacking economic incentives for successful and evidence based animal health management and penalties for the significant impairment of common goods, the current market conditions support unfair competition between farmers at the cost of animal health and welfare of farm animals.

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1 Introduction

Remedies are a means to an end when it comes to food production. In general, remedies are intended to support diseased animals in their efforts to recover from illness or disease. On the one hand, treatment is focussed on the individual animal's specific state of illness at a given time. Remedies are, however, also used for preventive and metaphylactic purposes. If used, remedies should be the most effective for both the purpose and for the context where they are applied. Whether this goal is fully achieved or only to some degree is dependent on many factors within a complex interrelationship of physiological processes. To deal with the complexity of the issue, it is first of all necessary to differentiate between the efficacy and between the effectiveness of remedies. Efficacy describes the capacity an intervention (e.g. a drug) has for beneficial change (or therapeutic effect). When talking in terms of efficacy vs. effectiveness, effectiveness relates to how well a treatment works in the practice (on the farm level), as opposed to efficacy, which measures how well treatment works in clinical trials or laboratory studies (Thaul, 2012).

Antimicrobial drugs have been used in livestock production for decades as the first (and often only) effective option for individual or group treatment of infectious bacterial diseases. However, the use of antibiotics in food-producing animals has become unpopular amongst many consumers (Midan Marketing, 2014; Mintel Group, 2015; Niamh, 2015). "Antibiotic-free" or "raised without antibiotics" labelled products are enjoying increased popularity in both Europe and in the United States. This development is fuelled (amongst others) by the mis- and overuse of antibiotics in human and animal medicine, which has provoked a selective advantage for resistant strains of bacteria worldwide (Laxminarayan et al., 2013). The fundamental concern over antimicrobial use in food-producing animals is the potential for resistant microorganisms on farms being transferred to humans via direct or indirectly (e.g. ingestion of contaminated food and water) contact. Correspondingly, the emergence of microorganisms that are resistant to antibiotics has become a growing public health concern.

One reason for the considerable interest in alternatives like homeopathy and phytotherapy might be the concerns and doubts over conventional treatment strategies. Consequences from the overuse of antibiotics in animal production threaten the efficacy of antibiotics in successfully treating humans and animals; an ongoing increase in antibiotic resistance to bacteria. Despite a tremendous increase in knowledge about the causes and pathophysiological development of disease, the incidence of productions diseases has not declined but increased and therapeutic treatment often fails (Rauw et al., 1998; Østerås et al., 2007; Knaus, 2009; Ivemeyer et al., 2012; Perry et al., 2013).

To address this important issue, scientists are searching for alternatives to antibiotics. While the use of phytotherapeutic products in food producing animals seems to be widely accepted within the scientific community and has been the topic of numerous International Conferences, e.g. of the World Organisation of Animal Health (OIE, 2012), the use of homeopathy is highly controversial and often received with much scepticism about the mode of action (van Sluijs, 2005). On the other hand, there is evidence that in some European countries homeopathic remedies are widely used in food producing animals; either by the farmers themselves, by non-veterinary practitioners or by veterinarians (Hovi, 2001; ECCH, 2007; Ullman, 2010; Keller et al., 2016).

In the case of organic livestock production, farmers are even encouraged to consider the use of homeopathy and phytotherapy by legislation. According to the Commission Regulation (EC No 889/2008, Art. 24(2)) on organic agriculture, homeopathic and phytotherapeutic products should be used in preference to chemically-synthesized allopathic veterinary treatment, provided that the resultant therapy is effective for the species of animal and the condition for which the treatment is intended. Chemically synthesised allopathic veterinary medicinal products (including antibiotics)

may be used where necessary and under strict conditions, when the use of phytotherapeutic, homeopathic and other products is inappropriate (EC No 834/2007, Art. 14(1)). However, it is also emphasised in the Commission Regulation (EC No 889/2008, Art. 24(1)), that if animals become sick or get injured, despite preventive measures to ensure animal health as laid down in Article 14(1)(e)(i) of Regulation (EC) No 834/2007 they should be treated immediately, if necessary in isolation and in suitable housing. The general outline of the EC regulation and the principles of organic agriculture (IFOAM, 2006) suggest that alternative remedies should only be seen as a valid alternative if the alternatives do not jeopardise animal health and welfare (AHW) through extended suffering if the remedies are not effective. Thus, the effectiveness of homeopathic and/or phytotherapeutic products in comparison to conventional therapy is crucial when asking whether they can be used to replace antibiotics when treating farm animals. However, whether a treatment is effective is not just related to the efficacy of the medicinal products itself but depends on the intentions and the context in which these remedies are used. From the AHW perspective, it should be ensured that animals receive the most effective therapy possible. Correspondingly, in the case of bacterial infections alternatives to antimicrobials remedies ought to be at least as effective.

In line with the European Parliament resolution of 12 May 2011 on antibiotic resistance in which a reduction in the use of antibiotics in livestock farming and an increase in the employment of alternative methods was called for, a pilot project was initiated to coordinate research on the use of homeopathy and phytotherapy in livestock farming. In this pilot project, the role of alternative options to reduce the use of antibiotics in organic and conventional livestock farming (cattle, pig and poultry production) were assessed using:

- Reviews of research projects in the field of homeopathy and phytotherapy;
- Investigations on the cooperation between research bodies;
- Workshops with both proponents and opponents of alternative methods;
- Research on the pre-existing conditions and diagnostic procedure for the use of homeopathic and phytotherapeutic treatments according to the state of the art in pig and poultry production;
- Economic impacts of the use of homeopathic and phytotherapeutic treatments in conventional pig and poultry production.

The following report guides the reader through this complex issue and through the results obtained from the pilot project's various areas of focus and summarises the main results. Finally, general conclusions are drawn on how to improve the effectiveness of treatments for illness and how to establish goals and standards to benefit AHW providing orientation for all stakeholders involved.

Detailed results of research work in WP9 are outlined in the following Deliverables:

D9.1. - Report on research projects in the field of homeopathy, cooperation between research bodies and initiatives to reduce use of antibiotics by using homeopathic remedies,

D9.2. - Report on research projects in the field of phytotherapy cooperation between research bodies and initiatives to reduce the of antibiotics by using phytotherapeutic remedies,

D9.3. - Report exploring the effectiveness of alternative treatment in livestock systems incorporating a variety of different experts' views and perspectives,

D9.4. - Report on the preconditions for an effective use of phytotherapy in pig and poultry production,

D9.5. - Normative simulation models for the economic evaluation of therapies in broiler and pig farms.

2 Efficacy of remedies

Remedies differ considerably in their mode of action and thus are not interchangeable; the general principles of each remedy need to be understood. Before the results of the reviews conducted on the efficacy of remedies are provided, the mode of action of antibiotic, homeopathic and phytotherapeutic products are outlined. Furthermore, factors that affect the therapeutic success of treatment are discussed.

2.1 Principles of treatment strategies

2.1.1 Principle of antibiotic therapy

Antibiotics are some of the most frequently prescribed remedies. They work by killing bacteria or preventing bacteria from multiplying and spreading. However, antibiotics also require the host's immune system to be functioning in order to aid the elimination of bacteria and, thus, achieve a successful cure in order to be effective. Although antibiotics are useful for a wide variety of infections, it is important to recognise that antibiotics only treat bacterial infections and are useless for viral infections. Antibiotics come in various forms: oral, topical or as an injection via needle, either subcutaneous, into the muscle or via drip infusion directly into the blood. In growing livestock, especially in poultry and pigs, oral medication is the method of choice for the application of antibiotics. The majority of antimicrobial products sold for use on farm animals are for pigs; the majority of these products are for designed to be administered via medicated feedstuffs and drinking water (Coyne, 2014). Antibiotics used in veterinary medicine are largely the same as those used in human medicine.

Each antibiotic is only effective for certain types of infection. In most cases, a veterinarian will choose an antibiotic based on the most likely cause of infection. Good knowledge of the prevalence of different pathogens, and their antimicrobial resistance patterns, within the herd is important to share an "educated guess" which species of bacteria is causing an infection before choosing an antibiotic. Thus, routine antimicrobial susceptibility testing is commonly requested for treatment of individual cases (FVE, 2016). The risk for development of resistance in micro-organisms of the individual animal, the population of animals and the risk for transfer to other populations should be considered. Generally, antibiotics with a broad spectrum of activity lead to development of resistance in non-target microorganisms more rapidly than those with narrow spectrum, because they exert a selection pressure on a greater number of micro-organisms. In order to minimise the likelihood of broad antibiotic resistance developing, where an appropriate narrow spectrum agent is available, it should be selected in preference to a broad spectrum agent.

Antimicrobial resistance is the temporary or permanent ability of an organism and its progeny to remain viable and/or multiply under conditions that would destroy or inhibit other members of the species (Cloete, 2003). Resistance in pathogens emerges when members of a particular strain are not susceptible to the antimicrobials used in clinical practice. Antimicrobial resistance narrows the choice of treatment options and is a problem recognised worldwide in both human and veterinary medicine. Antimicrobial stewardship is defined as the process of reducing the development, continuation and dissemination of resistance through the reduction of the inappropriate and excessive use of antimicrobials, along with the targeted selection of antimicrobials, their dosage and treatment duration (Prescott, 2008).

2.1.2 Principles of homeopathy

Homeopathy is a method developed by Samuel Hahnemann in the year 1796 to treat disease in humans. Hahnemann (1810) described health as a dynamic process and homeopathy as a way of

stimulating self-healing or regulatory processes in the body. Thus, poor treatment conditions for homeopathy would be when the body system is not able to react appropriately, e.g. in the case of severe tissue damages or organ failures.

Homeopathy is based on three main principles: The first is the principle of Similarity, the so called "Simile-Rule" ("*similia similibus curentur*") stating that a substance which causes certain symptoms when administered to healthy subjects will be able to cure the manifestation of a disorder and corresponding symptoms in sick individuals. The second principle is individualisation. It refers to the fact that in the case of illness, every individual exhibits symptoms unique to themselves, the "clinical picture". While individuals may suffer from diseases stemming from the same cause, symptoms may differ considerably in some (if not all) cases. The "homeopathic drug picture" of the chosen remedy should be aligned as near as possible to the symptoms in the "clinical picture" presented by the patients. The closest match is called the "simillium". The third principle involves the use of the Smallest Dose. The minimum dose of a substance that is still sufficient to cause a reaction in an organism without being harmful is selected. Homeopathic remedies are used in a more or less dilute form due to the potentiation procedure described in the homeopathic pharmacopoeia. The doses range from those similar in concentration to some conventional medicines to very high dilutions (above C12 or D24 resp. a 1: 1024 dilution) containing no material trace of the starting substance. "D" for decimal, means a remedy diluted by a factor of 10 and "C" for centesimal describes diluting a substance by a factor of 100 at each stage. Homeopathic remedies are administered via contact with the mucous membranes (mouth, nose, and vulva) or according to the medical product leaflet (Schmidt & Bär, 1998).

Furthermore, three strategies of homeopathic treatment have to be differentiated: In the case of classical or individualized homeopathy, every individual and illness is unique and so is the chosen remedy. It considers the individual reactions of a patient towards the cause of diseases (individualised treatment). The "clinical picture" approach covers inter alia the causa (any influences that caused the disease), modalities (temporal, physical, physiological or psychological circumstances under which the symptoms increase or decrease), (extraordinary) behaviour, constitution, general symptoms, symptoms of organs, frequency of symptoms and the tendency or disposition for infection. In clinical homeopathy or organotrophic homeopathy, the remedies are chosen due to the symptoms in individual organs. Complex homeopathy (or combined-remedy-homeopathy) is not as holistic as different ingredients for the disease and its symptoms are combined. This approach is often used in livestock production when information about the symptoms and the modalities of every individual animal are lacking. (For further details see Deliverable D9.1.)

2.1.3 Principles of phytotherapy

The Encyclopaedia Britannica defines phytotherapy as a science based medical practice where medicines derived from plants are used in the treatment and prevention of diseases by defining and standardizing the active substances within through pharmacological tests and clinical trials. This is in many ways very similar to the development of chemosynthetic pharmaceuticals where an active substance is identified and purified. However, the encyclopaedia also recognizes that there is great confusion regarding the terminology and that herbalism, botanical medicine and phytotherapy are often confused; it may be difficult to separate different types of approaches from one other. Furthermore, as botanical medicines are important in many traditions, there are numerous remedies, preparations and applications (as well as indications and theories related to their use) that may or may not have been subject to pharmacological tests and clinical trials, which further complicates the terminology (Wynn & Fougère, 2007).

When it comes to farm animals, the use of plant-derived medications varies immensely. Some therapists use commercial products for specific conditions, just as they would employ synthetic drugs, while others prescribe or prepare traditional herbal medicines following ancient theories. According to a text-book on veterinary herbalism (Fougère, 2007), the pillars of modern phytotherapy involve taking the individual patients' unique symptoms, general health and environment (season, food, emotions) into account to enable the prescription of a remedy specifically designed to the individual. Thus, there is not only one correct system of prescribing but several different formulas of prescription.

According to Fougère (2007), veterinary herbal practice is "empiric, adaptive and experiential by nature" and it is the responsibility of practitioners, relying on their own experience and the patient's knowledge, to diagnose, determine dosage and define the best treatment for each individual patient, and to take all appropriate safety precautions. However, this approach stands in opposition to the definition of phytotherapy by the Encyclopaedia Britannica as a science based medical practice. When relying primarily on empirical findings, it would be impossible to conduct tests and RCT's and the decisions regarding the use of phytotherapeutic products would be left to self-referential estimations.

Furthermore, the professional should be very aware that chemical compounds in plant medicines may have additive, antagonistic, or synergistic effects. The origin and type of plants, the parts used, the extraction process and the preparation of the herbal remedies all vary greatly. Sometimes fresh or dried plants are used without further processing but extraction of the active ingredients using alcohol, or oil also occur (Schmidt et al., 2012; Disler et al., 2014). The most common ways of administration are topical, oral and (sometimes) intra uterine treatment. (For further details see Deliverable D9.2.)

2.2 Review on clinical control trials

2.2.1 Efficacy of homeopathic products

Up till now, only four scientific publications had reviewed the efficacy of homeopathy in animals (Kowalski, 1989; Hektoen, 2005; Rijnberk & Ramey, 2007; Ruegg, 2008), quoting diverse results. A review of the previous scientific results, achieved in Workpackage 9.1, has been recently published by Doehring & Sundrum (2016). Quality and risk of bias in randomised controlled trials on veterinary homeopathy were previously reviewed by Mathie & Clausen (2014; 2015), who demanded the need for new and higher quality research in veterinary homeopathy. There has been no review of peer-reviewed publications conducted on the efficacy of homeopathy in food-producing animals. The aim of the review performed within IMPRO (Deliverable D9.1) was therefore to systematically evaluate existing knowledge on the efficacy of homeopathic remedies used for the prevention or treatment of disease in livestock by studying more scientific publications (incl. doctoral thesis) and employing a comprehensive timeframe from 1980 to 2014.

Taking into account the amount of time the homeopathic treatment strategy has existed and its use in livestock production, only a comparatively small number of good scientific studies focussing on the efficacy of homeopathy have so far been conducted. As the extended literature used multiple sources, it can be assumed that nearly all peer-reviewed articles on homeopathy in livestock matching the search criteria were considered. Thus, this review can claim to be the most comprehensive review on homeopathy in food producing animals so far.

327 abstracts/full text articles from a total number of 4448 records screened by title and keywords were seen as applicable and thus evaluated eligibility. Only articles in peer reviewed journals and

doctoral theses were considered for further analysis, finally resulting in a total number of 62 studies, dealing with homeopathy in cattle, pigs and poultry. Study descriptions were assessed according to various criteria, among others: purpose of application, disease in focus, exclusion of experimental animals, diagnostic method and person diagnosing, remedy used, as well as origin, ingredients and potency of the remedy, means of administration, study design and control groups, measurement methods, and finally the outcome of the studies. From the 62 studies that fulfilled the standards required, only 31 studies concluded that homeopathy was more efficacious than a control group, whereas 23 studies exhibited no medicinal efficacy and 8 studies reported an indifferent effect.

The cure rates for treatment with conventional remedies, homeopathy or with a placebo varied greatly. The results revealed that in a considerable number of studies, a significantly higher efficacy was recorded for homeopathic remedies than for a corresponding control group. Therefore, the potential medical efficacy of homeopathy under certain conditions cannot be ruled out. However, this does not necessarily imply that homeopathic remedies are effective under different farm conditions. This is especially true for the context-sensitive treatment strategy in homeopathy, which considers (besides symptoms and the pathogen responsible) behaviour, constitution and the conditions the animal is living in. The review revealed that all studies included were conducted under very specific conditions but that no trial had been repeated in a comparable manner. While the use of homeopathy lacks reproducibility, the previous results cannot be generalized and thus have to be regarded as single case studies.

The first priority when medically treating animals should always be finding the most effective treatment or remedy and thus preventing the animal's unnecessary suffering - if only for the reasons of animal welfare. As it is hard to always tell how effective homeopathy has been on farms as a whole, this can only be achieved by appropriate control and monitoring of treatment success in farm practice. Otherwise, homeopathic remedies could start to be blamed for increasing health and welfare problems instead of solving or reducing them. Due to a lack of prognostic validity, replacing or reducing antibiotics with homeopathy cannot be properly recommended unless evidence of efficacy is seen in further RCTs and its effectiveness is proven in various farm practice conditions.

2.2.2 Efficacy of phytotherapeutic products

The aim of the review of existing phytotherapeutic studies was to provide a comprehensive overview of the evidence based literature available on treatment using phytotherapeutic remedies in practice. Thus, only studies in which phytotherapeutic remedies were used to treat or prevent a specific disease were included. In total, 53 scientific studies were identified that fulfilled the requisite standards. The main focus was on therapeutic success, studies on how phytotherapeutic remedies influence general parameters (such as growth, mortality and other physiological changes or effects on immune system and changes in microbiota not associated with clinical symptoms) were excluded from the review. Even so, the excluded studies were sorted into two categories, production related measures and physiological measures, respectively, to illustrate the number of publications available in this area. The studies finally included were categorised depending on whether the phytotherapeutic product was used to prevent or treat disease. 'Treatment' was defined as using the remedy on animals with an established case of disease, meaning they had developed clinical symptoms or other pathological changes detected by analytical diagnostic methods. 'Prophylactic use' was defined as the use of a phytotherapeutic remedy to prevent or reduce the effect of infection by a specific pathogen/pathogens or to lower the incidence of disease in a population. (For further details see Deliverable D9.2).

The majority of the studies contained limitations in their: design, presentation and standardisation of the botanical remedies studied. This makes it impossible to compare the studies using remedies

derived from the same plant as well as to reproduce studies in the future. Overall, the majority of studies tend to conclude that botanical compounds have potential. However, most studies focus on the prevention of disorders. Thus, the extent to which the products could be successfully employed in treating acute diseases is not clear. In addition, the effect the treatment had towards solving the disorders remains uncertain in the majority of studies and the study design was often seen to lack blind trials, control groups and other measures to assure confidence in the result. Yet, there are some indications that certain botanical products may be useful in the prevention of some disorders and thus could be used to decrease the use of antibiotics. However, so far this information is very vague and limited, especially when compared to the large number of botanical drugs used in practice. The limitations are mainly due to the fact that (in general) knowledge of the essential requirements for ensuring success when treating farm animals under practical conditions is not yet sufficient. These requirements include knowledge of ingredients, the correct dose, mechanism of action, interaction with other treatment (allopathic or phytotherapeutic), etc. In addition, it is not clear whether the botanicals deliver any more than an unspecific and/or supportive effect or whether they can actually heal specific disturbances and disorders shown by diseased farm animals. Because the studies conducted on the efficacy of botanical products were not repeated under the same (or comparable) conditions, the use of phytotherapy lacks reproducibility. This means that it cannot be claimed that the results of the studies have relevant prognostic validity. Thus, it is not recommended that medical laypeople make use of phytotherapy instead of allopathy for treating acute disease in farm animals; as has been suggested by the EU Regulation on organic farming. However, medically trained people should at least be capable of diagnosing when an ineffective treatment should be discontinued, which is essential to preventing prolonged suffering in diseased animals. A medical professional should therefore be consulted if phytotherapy is being considered. Used inappropriately, phytotherapy risks being blamed for decreasing health and welfare instead of improving them, regardless of the potential of a particular product.

2.2.3 Current stand of research in Europe regarding the use of alternatives

A survey on the research situation on the European level regarding the use of alternatives to antibiotics was conducted, but no comprehensive conclusion can be drawn due to the small number of answers received in the course of a questionnaire. However, the answers from different institutions indicated that only a few institutes and individuals are involved in active research on veterinary homeopathy and the research network was regarded as either poor or insufficient by three-quarters of the respondents. Three-quarters of them also saw a need for more research on homeopathy, especially of high quality studies. The main constraints mentioned were lack of funding and the reluctant attitude research colleagues/superiors or practising veterinarians had towards homeopathy. (For further details see Deliverable D9.1).

In the case of veterinary phytotherapy, there are also just a few research bodies involved in research in Europe, with little manpower dedicated to the field of research. Insufficient support from funding bodies has led to poor research infrastructure (especially on a human resource level) despite of a need clearly expressed by the respondents. Lack of funding thus limits opportunity for efficient research on veterinary phytotherapy. (For further details see Deliverable D9.2).

2.2.4 Conclusions drawn from the perspective of different experts

Two expert's workshops were arranged to gain feedback on current scientific reviews on the efficacy of homeopathy and phytotherapy, as well as to identify important factors influencing the effectiveness and use in research and farm practice. The workshops took place in Germany and each workshop (focusing on homeopathy and phytotherapy, respectively) lasted one day. For each workshop, twelve participants from 6-8 European countries with differing expertise, background in

research or veterinary practice, and varying opinions on homeopathy or phytotherapy were invited to share and discuss their views and opinions, guided by a professional moderator. Core questions were: What is needed to scientifically validate the efficacy of homeopathy/phytotherapy? Which conditions influence an effective on-farm treatment? What has to be altered in future, both with respect to homeopathy/phytotherapy and in relation to a more successful treatment, improved AHW and reduced antibiotic use? The results of the workshops are presented in further detail in the Deliverable D9.3.

The participants in each workshop confirmed that the studies evaluated in the reviews exhibited various weak points in study design. In studies on homeopathy, the individualized homeopathic treatment procedure was usually not considered appropriately. In studies testing phytotherapy, the description of remedies' composition and dosage of the applied botanical was generally poor.

According to the workshop participants the main obstacles homeopathic treatment face are the lack of expertise when choosing the correct remedies. The use of homeopathy by veterinarians in practice is also influenced by national legislation (supporting or declining homeopathy). Homeopathic remedies for humans which farmers obtain over the counter currently fill gaps in availability for the use in food producing animals as they are comparably cheap and simple to employ. They are usually applied without expert advice or the veterinarian prescription required by legislation.

Products of phytogenic origin are listed under various terms and the same botanicals are used as remedies and feed additives. Only few registered veterinary phytotherapeutic products are available, possibly due to the high costs of obtaining legislative approval combined with small profits and no protection or patent for the product composition or content. Thus investment in research and development is not attractive for manufacturers. As a consequence, botanical products are sold and used as feed additives, which leaves decisions on indication for treatment and dosage to the farmer. Without knowledge regarding which level of efficacy can be expected from different botanicals and which dosage is required to achieve it, it is not possible to identify results-driven ways of using the products in practice.

A general estimation was that vets and other users often lack sufficient expertise in phytotherapy and homeopathy. General knowledge about how effective on-farm treatment is does not exist and documentation of treatment especially of the outcomes is not established on farms.

The experts were in favour of further farm animal studies in order to find alternative strategies to reduce antibiotics. The efficacy of alternative treatments, as well as dosage and indications for treatment, should be scientifically proven using an appropriate study design, particularly RCTs. According to the workshops, this type of study design can be used for homeopathic and phytotherapeutic products, although some alterations to fit the specific needs of a homeopathic treatment procedure or phytotherapeutic guidelines are required. Guidelines for standardization of phytotherapeutic remedies regarding content and ingredients or - for multicomponent herbs - by metabolomic fingerprinting, could support transparent research, reasonable use and appropriate dosage. Currently, homeopathic and phytotherapeutic products are often not registered for veterinary use and therefore not available when veterinarians treat patients. The adaptation of legislation to allow better categorisation of phytotherapeutic remedies as a class of products and to fit in with human regulations was proposed. A registration procedure for the use of veterinary homeopathic and phytotherapeutic remedies on a European level could improve the availability of these remedies for veterinarians.

The effectiveness of any treatment applied in practice (whether conventional or alternative) depends upon several external factors. Thus, promising results on the efficacy of remedies in scientific studies concerning requires further evaluation of the effectiveness in practice. It is necessary to monitor the use and effectiveness of treatments across Europe. This could be achieved by establishing a monitoring program, documenting the use of treatments (alternative as well as conventional), combined with monitoring of production diseases. Such information would be essential for farm as well as for large scale studies to assess the impacts of (new) treatments, interventions or diseases for the benefit of AHW.

Homeopathy and phytotherapy are mostly employed by lay people as established and standardised expertise and training is not available. Standardised expertise and training, however, is critical for appropriate and effective use; especially with respect to the animal welfare issue, as ineffective treatments extend the suffering of diseased animals. Expertise on therapy and knowledge on the efficacy and effectiveness of treatments should be improved by standardized training courses. Veterinarians trained on these courses should also supervise the treatment of food-producing animals with homeopathy or phytotherapy. As a first step, it is necessary to establish a monitoring system to assess the effectiveness of treatments.

3 Factors affecting therapeutic success

According to the principles of Evidence-Based-Medicine (EBM), RCTs are the best method and the standard means of proving a remedy's clinical efficacy (van Sluijs, 2005). However, the EBM-method is also prone to errors (e.g. by taking too few factors/ a limited perspective into account and providing no information about the scope of application) which causes misleading conclusions or results claiming efficacy where there might be none (Weymayr, 2013). While the previous reflections are focussing on the potentials of alternative products as means to achieve the purpose of therapeutic success it has to be taken into account that remedies are not the only factors that count when striving for therapeutic success. To achieve this aim, many other factors are important in terms of initial or boundary conditions. It is by far beyond the scope of this report to reflect on all the influencing factors in the necessary depth. Thus, only the most relevant factors are addressed briefly in order to bridge the gap between an evidence based approach by RCTs and the need to consider also the context in which treatments takes place.

When faced with facultative or obligate pathogen germs, the body is usually able to mount both an effective and efficient immune response. The elimination of intracellular pathogens generally requires infected cells to be destroyed by phagocytic and cytotoxic immune cells. This process is called a 'cell-mediated immune response'. In contrast, extracellular pathogens and soluble antigens are more effectively controlled by 'antibody-mediated immune responses'. Other mediators play an important role in orchestrating adaptive immune responses by promoting host immune responses tailored to the pathogen encountered. Mobilisation of energy and an alteration in priorities for the utilisation of nutrients are key features of the non-specific defence response (Colditz, 2002). Defence of the animal's integrity via physiological and immune functions is an amalgamated strategy progressing from high input non-specific responses on initial exposure to lower input, more specific on re-exposure to the stressor (Colditz, 2008). The refinement of responses through experience and reactive learning enables to become more specifically suited to eliminate or diminish the impact of the noxious invaders.

The ability of the immune system to function affects therapeutic success considerably. This can be greatly influenced by various animal related factors and factors emanating from their living conditions. These conditions include: nutrient supply, housing, climatic conditions or stress caused

by behavioural interactions within a herd. Immunosuppression can occur when prior diseases reduce the ability of the animal to respond to infections. In general, animals in a higher parity have a lower cure rate than those in a lower parity (Zadoks et al., 2001). While the severity of some infectious diseases is governed predominantly by animal related factors, others are driven more by the pathogenicity of the germs (Burvenich et al., 2003). On a farm, there is usually a mixture of pathogens present. The bacteria vary in prevalence and virulence. The severity of infections differs between farms. Some of these pathogens can be destroyed through self-cure; however, others require more sensitive treatment. Inter alia, cure rates are affected by the time and duration of treatment, the quality of active ingredients in the drug applied, and the sensitivity of the germs to the antibiotic (Hoe & Ruegg, 2005). Farm management, pathogen, drug formulation, the individual animal or the herd/flock to which the patients belong should all be examined to locate the cause of disease (Melchior et al., 2006; Wright 2007). Many studies have shown a positive correlation between length of treatment and likelihood of cure. Early detection and duration of therapy remain the most important aspects in the treatment with antimicrobials (Maxwell et al., 2015).

A critical flaw in the current trials on efficacy is that they are conducted under standardised conditions and do not consider the specific situation which farm animals experience. The focus is mainly on the remedy without taking into account the interaction between animals and their living conditions and animals' differing ability to react to certain pathogens. In RCTs, both inclusion and exclusion criteria are used to narrow down the heterogeneity of the individuals in the trials and to exclude animals which are expected to be resistant to a therapy or might not be able to react adequately to a stimulus. In farm practice, this procedure is generally not possible and thus, the likelihood of therapeutic success is expected to be lower in farm practice compared to RCTs. E.g., in the case of mastitis, treatment of chronic infections yields poor results with clinical cure rates often <35% and bacteriological cures nearing zero (Maxwell et al., 2015).

The reactions of the animals to remedies are largely influenced by the context (when and how does the treatment occur), the affective state and the residual adaptive capacity of the diseased animal. An animal expends much effort in regulating its internal environment. The effort required increases in increments according to the load (in terms of stressors) and/or decrements in terms of residual adaptive capacity. During life on a farm, farm animals are exposed to many potential stressors, which can negatively impact their physiological, behavioural, and affective states, resulting in reduced production and poor AHW. An individual's response to external stimuli is influenced by numerous factors including ontogeny, prior experiences, behavioural type, genetics, age, gender, physiological status, and affective state (Colditz & Hine, 2016). The affective state influences the perception of stimuli and also influences the likelihood of the animal recovering quickly. The position of the individual within the group's social hierarchy can influence both physiological and immune response and disease outcomes (Hessing et al., 1995; Tuchscherer et al., 1998). Furthermore, individual variation can occur at each level of the response, sensor stimulation, perception, reaction and outcome (Moberg, 2000).

Living conditions of farm animals vary widely between farms, inter alia regarding diagnostic procedure and regarding the method whereby the most suitable remedy or means of treatment are decided. The person performing the diagnostic procedure will have varying judgement according to education and experience. The complexity of factors resulting in a cure and the performance of different diagnostic measures may distort the resultant efficacy of the remedy applied. Expertise is a prerequisite in choosing the appropriate remedy and helps inform any running adaptions of the treatment when necessary. However, when any factors which cause disease are left undiscovered and thus are not instantly removed, animals may still remain ill. If farm animals are kept under living conditions where their immune systems are under strain or exhausted, neither conventional nor

alternative remedies will be able to provide a sufficient cure rate. Thus, a remedy which proved efficacious in a scientific trial may not be effective under farm conditions.

4 Legal conditions

4.1 Legislation concerning the use of homeopathy

4.1.1 Homeopathic products under EU law

A homeopathic veterinary medicinal product is defined as “any veterinary medicinal product prepared from products, substances or compositions called homeopathy stocks in accordance with a homeopathy manufacturing procedure described by the European Pharmacopoeia or, in the absence thereof, by the pharmacopoeias currently used officially in the Member States” (2004/28/EC/Art.1(8). The pharmaceutical sector legislation for medicinal products for veterinary use is covered by Directives and Regulations, compiled in volume 5 of the publication "The rules governing medicinal products in the European Union" (COM, 2010). While Regulations are binding, directly applicable without the need for national legislation, Directives set out a goal that all EU countries must achieve, leaving the implementation of national regulations to the Member States.

Rules on the production and distribution of veterinary medicinal products in the EU are aimed at safeguarding public health and ensuring the development of industry and trade in medicinal products within the Community (Directive 2001/82/EC (2, 3)). For homeopathic remedies, a simplified registration procedure (in comparison to an officially approved registration) is possible. This procedure takes into account the particular characteristics of homeopathic products, such as the very low level of active substances and the difficulty of applying conventional statistical methods to them (2004/28/EC (20)). Registration schemes for homeopathic remedies are operated nationally and involve the submission of a relatively limited amount of information. Such information has to ensure the pharmaceutical quality and a batch-to-batch homogeneity.

In all EU regulations dealing with veterinary medicinal products (including homeopathic products), a basic distinction is made between products used in food-producing animals and those used in non-food producing animals. In general, all veterinary medicinal products for food producing animals require a veterinary prescription for dispensing to the public (2001/82/EC/Art.67). To avoid unacceptable suffering of animals where no authorised veterinary medicinal product is available, Directive 2004/28/EC/Art.11 has established a cascade of rules to be followed in exceptional cases. These rules stated that remedies dedicated for another species or a different indication may be used. However, a prescription from a veterinarian is always required and minimum withdrawal periods apply. Although, article 16 of Directive 2001/82/EC (consolidated version) allows deviation from the “rules of cascade” for homoeopathic veterinary medicinal products, provided that the active constituent in the product is mentioned in Regulation (EEC) No 37/2010 on “Pharmacologically active substances and their classification regarding maximum residue limits in foodstuffs of animal origin”. For food producing animals, only remedies included in the annex of Directive 37/2010/EC from a D4 dilution (one part per 10,000 of the mother tincture) upwards, and only under the supervision of a veterinarian, may be used (2004/28/EC/Art.17). About 40 homeopathic products based on non-toxic substances are allowed even in lower potency than D4. They can stem from a mother tincture, or be employed as a D1-D3. Some substances are completely forbidden (such as *Aristolochia* and *Colchizine*) due to their toxic effects and the fact that a maximum residue limit cannot be established for them (37/2010/EC/Annex/Table 2). Directive 2006/130/EC allows a veterinary prescription for food-producing animals to be omitted, if the remedies pose no direct or indirect risk for animals, humans or the environment, even if administered incorrectly. However,

homeopathic remedies are not mentioned here explicitly. Remedies used in food producing animals must always be documented (96/23/EC and 90/676/EEC).

An ongoing Revision of the legal framework for veterinary medicinal products aims to “increase the availability of veterinary medicinal products, to reduce the administrative burden on enterprises, to improve the functioning of the internal market for veterinary medicinal products and to assess the opportunities for an improved response to antimicrobial resistance related to the use of veterinary medicines”. The Proposal for a joint Regulation by the European Parliament and the Council on Veterinary Medicinal Products (COM 2014) will alter the legislation on veterinary medicinal products to a regulation instead of a directive.

4.1.2 National legal conditions in 21 European Countries

Knowledge of the legal conditions on the use of homeopathy in the EU member states is scarce. Specific national regulations which consider homeopathic medicinal products for food producing animals do not exist in every European country. As a result, the availability and use of homeopathic remedies in food producing animals differs considerably depending on existing national regulations. Therefore an overview and comparison between European countries was developed. (For further details see Deliverable D4.4.)

While the use of homeopathic products is regulated in most European countries, the extent of usage varies greatly between countries. Homeopathy can be used for treating food-producing animals in all European countries, from which feedback was provided. In these countries (except Sweden), veterinarians are allowed to prescribe and administer homeopathy. Farmers are also allowed to administer homeopathy, except for in Estonia, Latvia and Lithuania. There is no obligation for veterinarians to undergo training when they want to prescribe homeopathic remedies. The obligation to keep records and their resultant monitoring is dealt with quite differently. The same is true for the more specific regulations concerning homeopathic remedies and the related educational requirements. There are hardly any unitary remedies (without indication) registered for veterinary use in the Member States, although veterinarians who specialize in homeopathy generally prefer to work with these remedies. It seems that the costs of registration are far too high in relation to the potential earnings from the remedies and are thus mainly avoided by manufacturing companies. In Member States with a tradition of homeopathic remedies use, there are homeopathic remedies registered for both human and veterinary use. However, only veterinarians are allowed to rededicate human homeopathic products for the use of food-producing animals. On the other hand, there are some complex remedies (with indication) registered for veterinary use which can also be administered by the farmer without a veterinary prescription.

4.2 Legislation concerning the use of phytotherapy

In general, the EU legislation on medicinal products for veterinary use (Directive 2001/82/EC) applies to all substances administered to animals to treat or prevent disease, including phytotherapeutic remedies. Directive 2001/82/EC also pronounce that veterinary medicinal products for food-producing animals require prescription, although Directive 2006/130/EC allows the omission of prescript if the product can be confirmed as very safe and without side effects for the users, animals, consumer, environment etc. Another restriction for treatment of food producing animals is that all administered substances are to meet a maximum residual (MRL) standard in accordance with Regulation 37/2010/EC. At the date of publication around 70 plants and botanical extracts are included in the list.

Manufacturers of medicinal products can apply for either central approval by the European Medicinal Agency (EMA) or national approval by the national medicinal agencies. Such approval

requires a full medicinal registration procedure with documentation on product safety, quality, and pharmacological tests as well as clinical trials. However, the pre-clinical and clinical trials may be omitted if detailed references to published scientific literature can demonstrate that the product constituents are in well-established medicinal use (WEU) with an acceptable level of efficacy and safety. At the time this report was compiled no phytotherapeutic remedies for animals had been centrally approved as veterinary medicinal products by the EMA. The total number of veterinary herbal remedies the various member states of the European Union have approved and the extent to which they require veterinary prescription could not be ascertained by the authors of this report.

Via the homepages and contact with national medicinal agencies in Europe the authors found that the availability of approved products varied greatly. Sweden, Finland, Latvia, Iceland, Austria and Estonia currently have no approved veterinary herbal medicinal products. In the United Kingdom (UK), nine veterinary herbal medicinal products are approved; all are sold over the counter (i.e. do not require a prescription) and are only approved for use in companion animals. In the UK and Sweden, all herbal medicines for animals are treated as veterinary medicinal products according to directive 2001/82/EC. In Germany, all purely herbal veterinary medicinal products on the market for food-producing species are for traditional use, registered according to Sections 39b and 39c resp. Section 109a German Drug Act (last amended 2014). This means that they have undergone a simplified registration procedure (similar to the process for human traditional herbal medicinal products described in Directive 2004/24/EC) and as such they may be sold over-the-counter. However, while it is not considered *lege artis* for veterinarians in Sweden to prescribe phytotherapeutic remedies (not being listed as evidence based medicine), veterinarians in Germany seem to use these types of products frequently.

Many products are available to the farmer without a veterinary prescription. They are often sold as feed additives for healthy animals which enhance the immune system, support growth and stabilize the intestinal microbiota. Remedies are also available for the farmer over the internet. Moreover, in some areas farmers employ products they have made themselves. At the time of writing this report, it was recognised that there is a substantial ‘grey area’ in the regulatory status of many herbal products. For many products available on the internet the form in which they are approved is not clear (as feed additive, medicinal product or if at all).

5 Factual findings

5.1 Use of homeopathy in farm practice

In light of the worldwide spread of antibiotic resistance, various alternative therapies beyond antibiotics have been investigated over the last few decades, including vaccines, probiotics, phage therapy, and phytotherapy. In comparison to these approaches, the role of homeopathy is only minor in the overall context. However, homeopathy can be fairly important in some European countries while virtually non-existent in others. Furthermore, it is highly relevant internationally for the organic sector in most countries. Due to the individualised approach of classical homeopathy, homeopathic products are expected to be primarily used for the treatment of individual diseased animals rather than for groups. Correspondingly, homeopathy is used far more often in dairy than in pig or poultry production. In the case of group treatment in pig and poultry production, combined homeopathic products are used in favour of single ingredients. This approach is often used in livestock production when information about symptoms and the modalities of every single animal is lacking or when the aim is prevention.

On-farm assessment and questionnaires were conducted to gain a better understanding of the current use of homeopathic remedies on organic dairy farms in Germany, France and Spain. The results displayed considerable heterogeneity in the use of homeopathic remedies on the farms inside and between countries. The on-farm assessment of existing conditions for homeopathic treatment often revealed poor hygiene and preventive management. Separate sick pens were rarely available. Early detection measurements (e.g. body condition scoring, foremilk samples, udder palpation, the California mastitis test, measurement of body temperature, etc.) were rarely performed and - if implemented - seldom documented. Thus, structural and non-structural pre-existing conditions on the test farms were often far from being appropriate for the early detection of disease in animals and to ensure a target-oriented treatment procedure. (For further details see Deliverable D4.2.)

Questionnaires from the farms revealed that there were no uniform treatment procedures for homeopathy, neither for anamnesis or diagnosis nor for selection and application of the homeopathic remedy. Each farmer seems to have developed his/her own homeopathic treatment strategy; regardless of the principles of homeopathy. Moreover, the homeopathic experts found that most farmers only had a poor level of awareness of the principles of homeopathy. In many cases, farmers were acting illegally by making use of homeopathic products not approved for food-producing animals without having a veterinarian rededicate these products for animal use following the cascade principle. The assessment of treatment success was mainly only performed visually by the farmers, increasing the risks that partial recovery or subclinical diseases could be overlooked, resulting in relapse or chronic disease. Finally, it was revealed that homeopathic treatment and the outcomes were either rarely or even never documented. Therefore, no information about the homeopathic substances applied and the healing rates for food-producing animals receiving homeopathic treatments were available. The results indicate that homeopathic *lege-artis* treatment of diseased food-producing animals is invariably not present. This self-referential approach (and often inappropriate use of homeopathy by farmers) clearly increases the risk of poor therapeutic success and extended suffering in diseased animals.

A questionnaire answered by veterinarians who were members of the International Association for Veterinary Homeopathy (IAVH) revealed that in most European countries, veterinarians' employment of homeopathic remedies on sick animals is very limited. In a few countries (Austria, Germany, France) treatment is somewhat more common. Half of the respondents stated that they use homeopathy in more than 30% of their treatments. In countries where homeopathy is more commonly used, the respondents saw a relatively good outlook for the education and training of veterinarians in homeopathy. (For further detail see Deliverable D 4.4.)

In most countries, the use of homeopathy on farm animals without veterinarians was estimated to be far higher than the proportion of farm animals who were being homeopathically treated by veterinarians. In an Irish study from 2006, four out of the six studied organic dairy herds used homeopathic products; and homeopathy was the first choice in 59.9% of the 232 cases in the study (O'Mahony & Healy, 2006). Thus, a considerable number of unrecorded treatments conducted by non-veterinary practitioners and farmers can be assumed. Moreover, the quality of information received from the respondents differed considerably between countries. The results indicate that the expertise in homeopathy and the use of homeopathy in European Countries by veterinarians and non-veterinarians are highly heterogeneous.

5.2 Use of phytotherapy in farm practice

Deliverable D9.4 provides an overview of the current use of phytotherapeutic remedies on pig and poultry farms in France, Germany, The Netherlands and Spain. A questionnaire was therefore

developed and addressed to veterinarians or feed advisors using phytotherapy to assess the context and the surrounding conditions in which these remedies are used in poultry and pig farming practice. The results of the survey illustrate considerable heterogeneity in the use of phytotherapeutic products. A detailed anamnesis and diagnosis was not always performed, which is not surprising as these products were often applied by the farmer and/or feed adviser without veterinary supervision. Plant compounds generally came in the form of essential oils while the length of administration and indications were quite heterogeneous. Treatment data were seldom recorded. Formal knowledge might often be insufficient, as even those who have already used phytotherapeutic products had little or no proper education on this matter. There was thus a lack of essential requirements for the target-oriented and effective use of phytotherapeutic products.

Many products are available to the farmer without a veterinary prescription. They are often sold as feed additives for administration to healthy animals to enhance the immune system, support growth as well as stabilizing the intestinal microbiota. However, these additives lack any transparency, especially regarding the criteria for their production and the proof of efficacy when used in farm practice. Remedies are also available for the farmer over the Internet. Moreover, homemade products produced by the farmer are also frequently used in some areas. A substantial 'grey zone' was recognised in the regulatory status of many herbal products. For many products available on the internet it is not clear in which form they are approved (as feed additive, medicinal product or at all).

A recent study on organic dairy farms in Sweden, France, Spain and Germany showed that more than 60% of the farmers interviewed from Germany and France made use of phytotherapy, 5% of the clinical cases were treated with phytotherapy in Spain, while no Swedish farmers used this kind of remedies. (For further detail see Deliverable D4.2). In Switzerland it was reported that conventional farmers also have knowledge of herbal remedies and frequently use them (Disler et al., 2014). This indicates that factors like local tradition, knowledge and farm structure may be more important than whether the production method is organic or conventional.

5.3 Use of antibiotics in farm practice

In the case of infectious bacterial diseases, antibacterial drugs have been seen as the first and often only intervention option for individual or group treatment and control of infections to prevent further spread for decades. However, they have also been used as a production tool to prevent or suppress infections in at risk populations living under suboptimal conditions and/or to increase weight gain or improve feed efficiency. There are large differences in the quantity and type of antibiotics used between farms and between countries/regions in the European Union (EMA, 2015). Drivers of antibiotic use in livestock production are complex; e.g. prevalence and incidence of disease, perception of health problems, presence or absence of regulatory systems, availability and price of remedies, cost of preventive measures, tradition and last but not least individual perception.

The fifth European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) report presents data on the sales of veterinary antimicrobial agents from 26 EU/EEA countries in 2013, provided at package level according to a standardised protocol and template. Overall, treatment for pigs, cattle, poultry and sheep/goats accounted for 34 %, 32 %, 13 % and 12 %, respectively, of the population correction unit in the 26 countries (EMA, 2015). Aggregated together for all 26 countries, the sales (mg/PCU) of premixes accounted for 38.2 % of the overall sales, while 33.7 % were oral powders, 19.6 % were oral solutions, 7.6 % were injectable preparations, 0.6 % were intramammaries and 0.3 % were oral pastes, bolus and intrauterine preparations. The of premix and oral powders varied considerably between the countries, which could be attributed to whether the farmers in the country administered medicated feedstuff from a feed mill in the case of premix or whether group treatment

constituted an oral powder as feed top-dressing at the farm. It could also be influenced by the distribution of the animal species, as group medication is mostly used in poultry and pigs, and e.g. less for sheep or goats. Also, the products available and national policies for feed medication can have an influence. Although a small proportion of the oral powders and oral solutions are for treatment of one individual animal or a limited number of animals, the sales figures for these pharmaceutical forms can reasonably be recorded as group treatment, including groups in one pen/house.

6 Economic considerations

Options and limitations in the use of alternative remedies to reduce the use of antibiotic are not reflected comprehensively without taking into account economic considerations. This applies to both conventional and alternative treatments. How the possible financial impacts of previous strategies and measures and of considered changes are viewed influences how possible tools and methods are classified (Jansen & Lam, 2012; Richert et al., 2013). The readiness to implement curative and preventive measures rely to a high degree on the argument that considerable improvements can be achieved via these investments (Jansen et al., 2009). Furthermore, the individual versus herd level perspective matters a lot in terms of risk and level of expected investment. The individual focus places all the investment (time, effort, money, management) on the individual animal; therefore the returns on that investment must be produced by that animal (Slenning, 2001). In contrast, preventive measures places the investment on the entire flock, so the return hoped for is carried by the whole flock. Also, the farm specific treatment strategy is directed at the whole herd and the unit of interest becomes the group and not the individual. Spreading the responsibility for paying back the investment to more than one animal reduces the risk that the debt will not be met. However, focussing economic calculations on the herd level is detrimental to individual animals that suffer from the impacts of disease and are in need of immediate and appropriate treatment.

Simulation scenarios were analysed with normative simulation models to gain insight into the importance of when treatment started, transmission rates, and cure rates for various infectious diseases in pig and broiler production. This was in order to quantify financial effects of different treatments and diagnostics. For further details see Deliverable 9.5. The results revealed that at medium to fast transmission rates for parasitic infections, treatments with a high cure rate had a significantly higher income rate per treatment than those with a low cure rate. For a bacterial infection at a slow transmission late, intermediate and early start of treatment, income differed significantly. Also under medium and fast transmission rates for all treatments, income differed significantly. The simulations of a bacterial infection indicate that mortality is an important factor on fattening pig farms. The increase in mortality for infected animals from 2.2% to 4% caused labour income to be negative in many scenarios of the simulations. The results demonstrate the importance of early diagnosis and effective infection treatment to avert the occurrence of high mortality disease in fattening pigs. Thus, a management strategy that enables the early detection of symptoms of disease within the herd and is able to realise high cure rates can increase labour income. The scenarios emphasise the financial potential when implementing improved animal health management. Nevertheless, the financial options of an improved animal health management have to be assessed in the context of the farm system involved.

When striving for a balance between effort expended and possible benefits in preventing disease, the farm management has to struggle with a lot of uncertainties amongst others: the development of disease, the effectiveness of different measures and their cost-benefit-relationship. Furthermore, the question arises which interests are given the highest priorities? When an individual animals shows

signs of health problems, the farmer has to evaluate whether the symptoms might be only temporary and the animal might be able to cure itself via an immune response. This would naturally also save the farmer expenditures. On the other hand, a delayed in the commencement of diagnostic and treatment measures impairs the success of therapy; the fact that the animal cannot cope with the invaders will cause extended suffering. Thus, delayed action during the first stages of a disease enhances the risk of possible negative side effects for the farm animals. Although group treatment with broad-spectrum antibiotics seems to imply less effort and cost than the separation of single animals at the first sign of disease and initiating a comprehensive diagnostic procedure and preventive measures, this group treatment could well contribute to the development of antibiotic resistance and thus aggravate the food safety issue.

This means that animal health surveillance can play a critical role in the process of disease mitigation, prevention, and the use of medicinal products. It could provide essential information to help policymakers make decisions about interventions, such as the use of antibiotics or vaccination of diseased animals to protect human and animal health, and to promote animal welfare (Häsler & Howe, 2012). Key features of this surveillance are the systematic collection, collation, analysis and interpretation of animal health data (prevalence of selected productions diseases), and communicating the resultant information to those with the authority to react on it. While the scientific usefulness of surveillance is widely accepted, its economic value to society still needs to be evaluated. For optimal efficiency, the combined cost of surveillance and intervention for mitigation of a given disease should be minimized, typically expressed as a reduction in prevalence or incidence. The economic objective should be to maximise the margin of net benefit to society (gross benefit) minus the expenditures on surveillance and intervention (resource costs). It is the value of losses avoided relative to the costs of surveillance and intervention that matters for animal health policy.

7 Intermediate conclusion

From the previous results of the IMPRO-project and the background information provided, different critical points for addressing the crucial question whether alternative treatments have potential to replace the use of antibiotics are: efficacy of remedies, effectiveness of treatment, medical indication, side effects on the issue of AHW.

- Efficacy of homeopathic and phytotherapeutic products have been documented in comparably few RCTs. As these studies are lacking any reproducibility, a general statement on efficacy cannot be validated but require the implementation of numerous RCTs under modified experimental conditions.
- Additionally, it is not possible to provide evidence on the effectiveness of homeopathic and phytotherapeutic treatments in farm practice due to a lack of a verifiable documentation on the incidence of diseases, the use of remedies, and the evaluation of therapeutic success. The effectiveness of any given treatment is largely context-related and thus cannot be generalised. The administration of alternative remedies in livestock production seems to be highly heterogeneous and self-referential using the suppositions, expectations and estimations of those using them, either veterinarians, non-veterinarians or farmers.
- While the sales figures for the pharmaceutical types of antibiotics show that these to a very high percentage (> 90%) used for group treatment, classical homeopathy is directed towards the individual sick animal’s specific symptoms. In contrast, the use of combined homeopathic remedies and the use of phytotherapy is seen both in individualised treatment strategies as well as in metaphylactic and prophylactic medical application in groups.

- Due to the high uncertainties regarding the success of therapy with homeopathic and phytotherapeutic products, alternative treatment strategies are at risk to extend the suffering of diseased animals while compromising AHW.
- Animals which suffer from infectious diseases are the cause of pathogens spreading through the herd and further introduce contaminated food products into the food chain. Thus, unsuccessful treatments increase the risk to food safety.

In summary, homeopathic and phytotherapeutic products only provide very limited options for replacing the use of antibiotics in the future. The use of homeopathy is mainly restricted to the treatment of individuals and seldom used for group treatment in poultry and pig production where most antibiotics are used given via oral application. Thus, homeopathy cannot be seen as a relevant alternative or as a replacement for antibiotics. This applies also to the actual use of phytotherapy which seems to be more favoured as a prophylaxis and supportive tool (feed additive) rather than a single medicinal product that is responsible alone for therapeutic success. Insufficient information about the ingredients together with inappropriate diagnostic procedures and monitoring of treatment success (as well as limited expertise on the farm level) are questioning the therapeutic effect when using homeopathic and/or phytotherapeutic products. In such cases where antibiotics actually are replaced in this way, there are several requirements which are still to get to be fulfilled. Amongst others, it should be ensured that where infectious diseases are present, a reliable diagnosis is made, an appropriate remedy be selected, and the effectiveness of therapeutic measures is assessed and documented. This requires expertise that laypeople commonly cannot provide. The use of homeopathy and phytotherapy should thus be left in the hands of skilled professionals to prevent farm animals from suffering due to improper treatment.

Facing a high risk of extended suffering for diseased animals due to unsuccessful treatment and in face of the prevalence of PDs in livestock production, it seems to be reasonable that discouraging the use of alternative remedies for food producing animals might be an option worth considering. However, a ban of alternative remedies is not seen as an appropriate means to solving the current challenges in livestock production for several reasons:

- There is no reason to exclude that alternative medicinal products are effective. Efficacy has been shown in several RCTs, however, without on-going studies under modified conditions.
- A ban on alternative products in food producing animals cannot work as long as these products are still available on the market for use with non-food animals and for humans. E.g., although homeopathic products meant for use in humans but designated for food producing animals have to be dedicated by a veterinarian this law is obviously widely circumvented in farm practice.
- The current legislation encourages the avoidance of allopathic treatments in organic livestock production if alternatives are available and prescribes a doubling of the withdrawal time for milk and meat compared with conventional herds (see Annex). The US regulations even define any animal treated with antimicrobials as being non-organic for the rest of its life (USDA, 2011). Consequently, the use of antimicrobials in organic herds has a severe impact on the fate of the treated animal. A ban of alternative treatments would further increase the risk that many farm animals might not be treated at all. This might provoke further discussions whether no treatment is worse than an inefficient treatment. However, such a debate might further distract the attention from other, more relevant obstacles that impede improvements of the animal health and welfare status. While the focus is placed on the issue of treatment, the awareness is often not focussing simultaneously on safeguarding a clear and evidence based reduction in the prevalence of production diseases.
- While alternative products may not be applied to a certain standard in farm practice, it is also questionable whether conventional medicine, e.g. antibiotics, is always used in practice

successfully and according to the guidelines on 'The prudent use of antibiotics in veterinary medicine' in farm practice as the Federation of Veterinarians of Europe (2014) recommend. E.g., studies indicate that farms rarely investigate diagnostic tests to detect the pathogen responsible.

- Many consumers concerned about the development and spread of antibiotic resistance are in favour of animal products being labelled as produced without the use of antibiotics while making use of alternative remedies. While these wishes widely ignore the issue of AHW and the risk of contaminating food with zoonotic pathogens, a ban of alternative treatments would not help address the concerns about the use of antibiotics.

As remedies are means to an end, the focus should not be placed on the means alone but on the question of how to achieve the end by making use of the most appropriate and effective tools and methods while minimising negative side effects. An acceptable cost-benefit relationship or relevant incentives or penalties are needed at the same time, ensuring that farmers are willing to implement means appropriately in order to get closer to the end of healthy farm animals.

8 Various options for improving therapeutic success

While the treatment of diseased animals should focus on the recovery from health disorders, the basic causes of disease should be rectified and possible negative side effects for the animals should be minimised. In the case of infectious diseases, therapeutic measures safeguard the organism from losing the battle against invaders and cut short suffering. Here, antibiotics are a powerful tool, but they have negative side effects. However, in face of the complex, interacting processes, there is generally more than one way of dealing with the challenges. None of the options can always claim to be the best solution. Indeed, the efficacy of options depends greatly on the context in which they are implemented. A holistic approach is required to improve levels of AHW while reducing the use of antibiotics in food producing animals.

8.1 Improving farm animals' immune strength

The best alternative to the use of remedies is to strengthen the immune system of farm animals. The development of the immune system in vertebrates is the evolutionary answer to any life-threatening or chronically debilitating microbial pathogens that may threaten an organism. The immune system of animals is directly involved in host defence against infectious organisms and in developing tolerance to sources of non-threatening antigens (Savelkoul, 2014). Because of the capacity of the immune system to adapt to the farm specific situation, it represents the most effective and efficient defence which the farm animals can use to control bacterial infections. This applies both for commensals that are normally present and suddenly turn into pathogens and for secondary invaders. Moreover, a well-functioning immune system prevents or at least drastically reduces the multiplication and spread of zoonotic germs which is very relevant for the food safety issue. Impaired immune function can be associated with increased susceptibility to infectious agents and simultaneously increased severity of infections necessitating the use of remedies and reducing the chance of therapeutic success. For various reasons, the farm animals' immune system is not always capable of dealing with pathogens appropriately. E.g., malnutrition and specific nutrient deficiencies impair immune function and increase susceptibility to infection. Large variations when facing germ pressure, often due to high stock density and/or an inappropriate hygiene regime and experiences with pathogens in earlier life stages account for the variations observed in immune function. Correspondingly, the immune system is often overwhelmed by manifold stressors and/or the resources which are required to cope with the respective situations may not be available.

8.2 Optimising treatment strategies

While the emphasis should always be on prevention and control of new infections in herds, some new infections are inevitable. Farm animals can get sick even under good living conditions, although less so than otherwise. It is therefore important to have an effective and cohesive strategy for spotting and dealing with symptoms, which all members of the management team are familiar with and are able to execute quickly and effectively. Above all, obtaining decent cure rates in farm practice relies on early detection of diseases and early intervention. E.g., fore-milking is one essential mastitis-detection tool, which is sadly often overlooked on some dairy farms in favour of time saving. Identifying mastitis solely on the basis of clinical changes to the udder and reduction in yield is arguably responsible for a significant proportion of mastitis cases re-occurring (Maxwell et al., 2015).

When it comes to treatment, the most effective medicinal product should be used as soon as possible, at the right dose and for the full course until the animals have at least to some degree recovered. However, appropriate treatment depends on a comprehensive and thorough diagnosis, which requires expertise and takes time and thus is not always undertaken (Barkema et al., 2006). A prolonged period of treatment, adjunctive treatment with anti-inflammatory drugs and palliative measures such application of heat, hygiene regulations, adequate nutrient supply and optimised climatic conditions are further factors well known for ensuring the success of therapy. Last but not least, separating diseased animals from the group is very important for the recovering process but even more key in preventing the spread of pathogens and contamination of other animals in the herd. Due to the fact that isolating diseased animals from the group is very time consuming and the provision of separate sick bays is expensive, group treatment with antimicrobials has become the most convenient and cheapest farm practice. It follows logically that group treatment via oral administration is responsible for more than 90% of the antimicrobials used in farm practice (EMA, 2015).

Furthermore, it should be considered that there are different definitions of a state of cure, with several ways of assessing the outcome of treatment. These include the resolution of clinical signs as perceived by the farmer, the indirect assessment using post-treatment indicators, and the gold-standard approach using serial bacterial culture. The obtaining of a bacteriological cure has been shown to depend on the pathogen present, case severity, variation in immune response among farm animals, efficacy of the treatment protocol and how rapidly treatment is initiated (Hillerton & Kliem, 2002). Routinely monitoring cure rates (clinical and sub clinical) and submission of a representative sample of clinical cases for bacteriology are the most relevant ways of gaining an overview and finding the best options for farm specific situations. Ultimately, using treatment protocols and documentation the results of follow-up checks should ensure the responsible use of remedies on the farm. These protocols should be a part of herd-health plans and should be reviewed regularly, providing an opportunity to examine the farm's health data and the success of any treatment strategies, take into account any changing patterns, and ensure that the suggested protocols are appropriately and effectively executed.

8.3 Improving biosecurity and reducing production diseases

From an AHW perspective, farm animals should be kept under appropriate living conditions and provided with appropriate resources (in terms of nutrients, room to execute their behavioural patterns, shelter from compromising climatic conditions and pathogens, etc.) which enable them to adapt to their specific living conditions without disturbance or disease development. Next to enhancing the power of the immune system and improving the treatment strategies, tightening biosecurity is one of the best alternatives to intervention using antimicrobials. Interest in biosecurity

as a holistic tool for improving the total health status of the herd which considers clinical and subclinical diseases potentially present has only grown recently. Results invariably show that despite the well-known importance of biosecurity, there is poor implementation of many biosecurity measures and ample room for improvement (Dewulf, 2014).

9 Barriers to therapeutic success

Implementing the most appropriate and most successful treatment strategy for curing diseased animals is anything but a self-driven process. This could only happen if ensuring a high health level in food producing animals were given the highest priority in farm practice. However to be able to survive in the business, farmers have to strive for the appropriate return of investment while faced with a generally global competition. This competition is becoming increasingly ruinous due to a continual drop in prices. Thus, the cost-benefit-relationship is one of the most important decisions about when and how to treat diseased farm animals. Unfortunately, neither the costs nor the benefits can be assessed easily, particularly in the very specific situation when the symptoms of disease become manifest. The battle between the capacity of the immune system on the one hand and the pathogens' capacity to multiply and spread on the other hand is characterised by very dynamic processes; it is very difficult to predict the outcome. Moreover, considerable uncertainty exists about how effective some treatments are, which don't help improving whether treatment will ensure therapeutic success. On the farm level, a wide range of diagnostic tools, preventive measures, medicinal products, and pro- and metaphylactic treatment strategies exist. Assessing which measures might prevent the almost unforeseeable development of disease requires comprehensive expertise and availability of data. The degree of germ pressure or how weak an immune system may be cannot be assessed and tested. In addition, impacts often become obvious an extended time delay. Thus - without comprehensive efforts - prognostic validity may be poor. The retrospective search for possible causes of diseases may also not succeed. This explains the large variation in therapeutic success and in the prevalence and incidence of production diseases between farms.

How the work level involved in diagnostic, treatment or post-treatment procedures is estimated depends not least on the perspectives involved. This is particularly true for alternative medicinal products. Thus, questions concerning the use of alternative products and the problems resulting cannot be answered or solved by only focussing on single aspects but can be addressed with a comprehensive study of pros and cons of various options weighed against different priorities.

While the negative side effects of the production cost squeeze and the predominant use of antimicrobial drugs in livestock production become more and more obvious, so does the need to find alternative options. Due to the high level of complexity, it is not be surprising that controversial debates have arisen between different stakeholders (and even within animal science) about the best solutions. While alternatives always challenge the predominant approaches, it is the duty of applied science to identify the most convincing and evidence-based arguments in the context in which remedies act. This duty is complicated by the fact that animal science has failed to clearly identify and define the areas of uncertainty in livestock production so far. Weighing heavier though is the fact that many lay people (particularly consumers and to some degree farmers) are more and more attracted to what many scientists despise. This controversial development cannot be ignored, especially when consumers are clients and veterinarians are service providers whereas farmers are both, depending on the stakeholders they are dealing with.

9.1 Veterinarian's perspective

The profession of veterinarians is aimed at treating animals successfully, contributing to a decrease in the prevalence of production diseases and associated suffering. Good antimicrobial stewardship seeks to select the most appropriate drug, at the correct dose, route and duration of treatment, to provide a positive clinical outcome while having minimum impact on the emergence of antimicrobial resistance. However, veterinarians are not authorized to treat farm animals in ways they might believe to be most effective. As service providers, they must follow the considerations and decisions of their farmer clients regarding: when diseased animals should be treated, which treatment method should be preferably used, and how much expenditures the veterinarian is allowed to invest. Veterinarians act both as practitioners in emergency cases and as advisors, offering information and support to the farmer in gaining a decision about the most appropriate treatment thus trying to strike a balance between the interests of the farmer and his own interests. Additionally, they are also requested to take into account the interests of the farm animals regarding easing suffering and the interests of consumers with respect to food safety issues. Veterinarians compete with other advisors and practitioners for the farmers' favour. Veterinarians might claim to provide the best expertise but they are also the ones with the highest bill. The treatment is governed by what farmers believe is the best cost-benefit relationship and return of investments which will emerge from the various offers and strategies. Farmers influence the prescribing practice in food animals as farmers can easily move their business between practices. Thus, veterinarians are captured in various conflicts. They cannot ignore the specific attitudes and beliefs of their clients without compromising their own income. An increasing number of farmers seem to want their animals to be treated by their local veterinary practitioner using alternative medicine. Even so, the number of farmers interested might not be enough, their readiness to pay adequately for labour too low and the belief of the veterinarian in the effectiveness of this treatment strategy limited. At the same time, farmers often try to apply homeopathic products themselves or ask a non-veterinary practitioner to use cheap homeopathic treatment. These and other reasons, seen separately or in combination, are significant enough to prevent veterinarians from investing time and money to become a specialist in homeopathy. (For further details see Deliverable 4.2.)

9.2 Farmers' perspective

As owners of the farm animals, farmers bear the main responsibility for their well-being. Apart from being responsible for organising an adequate nutrient supply and appropriate housing and hygienic conditions, the farm animals' 'carers' are the first who perceive if farm animals' behaviour deteriorated and when signs of clinical and subclinical diseases emerge. They evaluate whether signs indicate the need for immediate or delayed actions. They decide which animals should be treated or not and when, and whether diseased animals are separated or not. They also decide which veterinarian is consulted if at all, and last but not least: to what degree external professionals are allowed to invest time and money in curing the diseased animals. This question is related to both alternative and conventional treatment.

On the other hand, preventive measures can be very expensive in terms of investments and labour time, while the use of antimicrobial drugs often appears the less expensive option. Antibiotics are often used as a cheap production tool providing advantages for those who use these tools to the expense of the negative side effects that are related to an overuse of antibiotics. Continuously increasing amounts of last resort antimicrobials used over the last decades in livestock production indicate the benefits these drugs have provided to increase cost efficiency. This situation contrasts with the general expectation in society that prophylactic and metaphylactic use of antimicrobials should not be used as a substitute for good housing, comprehensive hygiene and management practices. This way of thinking, however, ignores the fact of a severe competitiveness between

livestock farms on a global base for the lowest productions costs. Many farmers struggle a great deal to prevent bankruptcy and often fail to be successful.

Many farmers feel prompted by the wishes of many consumers to reduce the use of antibiotics in food-producing animals. The farmers who wish for their animals to be treated with alternative remedies are confronted with the fact that there are only a few veterinarians with expertise in homeopathy or phytotherapy, with numbers varying considerably between regions. Many farmers feel they are not being taken seriously enough by veterinarians in their wish for support during the homeopathic treatment and thus seek support from non-veterinary practitioners or treat by themselves. The latter is facilitated by the ready availability of homeopathic products - either from pharmacies or the internet - and by the many training opportunities offered to lay people by farmer organisations. There is no European or national legislation that prohibits farmers and non-veterinarians making use of homeopathic products, except for *Colchicine* and *Aristolochia*. Although forbidden, these drugs have been found in the stable pharmacies of 11 out of 64 organic dairy farms visited (see Deliverable 4.2). Another conflict with the law is the fact that many farmers use homeopathic products dedicated to humans although only veterinarians are allowed to make use of those drugs for food producing animals. However, farmers are often reluctant to consult the vet because of the additional costs. In organic livestock production, a loss of its organic status and the associated products occurs, where more than three antimicrobial treatments are given to the same animal within one year or more than one course of treatment if their productive lifecycle is less than one year, resulting in financial loss to the farmer. Therefore, the consultation of a vet and the use of conventional products are often bypassed. Obviously, options to reduce production costs by homeopathic treatments (e.g., self-medication, low costs for remedies, no withdrawal period, etc.) seem to play an important role for farmers.

There are reasons to assume that diseased animals are not always treated appropriately if at all. In many cases, treatments might be retarded in the hope of self-curing processes or because of conflicting areas in face of limited availabilities of time in the day-to day practice or because of a low priority in the ranking order of urgencies. Thus, alternative treatment strategies have to be considered not only as an alternative to the treatment with chemically-synthesised remedies but also as an alternative to non-treatment. Instead of doing nothing at all in the case of diseased animals, it might seem appropriate to many farmers to give it at least a try with homeopathic and/or phytotherapeutic products. Some farmers may claim to have gathered their own knowledge and experience on how to deal with diseased animals. However, most of the 64 organic dairy farmers asked during a farm visit were not aware of the principles of homeopathy and did not have appropriate expertise in anamnesis, diagnosis, decision about the value of and method of treatment, selection of remedies, use of remedies, specific cases of treatment, and monitoring treatment success (Deliverable 4.2).

To implement a successful treatment strategy, thorough documentation is needed. However, farmers are often very reluctant to do so because they are afraid that they might criminally implement themselves with these documents when stable pharmacies are inspected by official veterinarians. While the EC-Regulation on organic agriculture claims that the farmer should strive for immediate and successful treatment to prevent the extended suffering of diseased animals and prescribes the documentation of treatments (see Annex), there is insufficient or level of monitoring which would force farmers to both follow the rules and organic principles to maintain a high level of animal health. Due to a lack of control, farmers cannot be accused of improper use of medicinal products and do not have to face the risk of any penalties if they do not treat immediately and successfully.

9.3 Market situation

When consumers are asked about their wishes regarding animal products, they often state that animals should be kept in housing conditions appropriate to the animals' health and welfare; they should be able to comfortably pursue natural behaviours; and additionally, antibiotic use should be reduced to a minimum to prevent residues and the development of antibiotic resistance (Yiridoe et al., 2005; Magkos et al., 2006; Aertsens et al., 2009; Martelli, 2009). Increasing levels of antimicrobial resistance in human and veterinary medicine have raised concerns about overprescribing and the indiscriminate use of antimicrobials (Guardabassi, 2014). Trends can be summarised as a high societal pressure on livestock producers and on the actors in the food supply chain to use antibiotics responsibly in order to regain consumer's trust (Aumüller, 2014). Use of antibiotics in food-producing animals is being scrutinised due to the treatment and prophylaxis of large numbers of animals, and the perceived risk from the zoonotic transfer of resistant pathogens from animals to humans. Many consumers therefore favour first, avoiding antibiotics or second, using alternative remedies in farm practice. As various questionnaires reveal, this is particularly wished by the consumers of organic products (Sundrum, 2014). Retailers are fully aware of consumers' wishes and often advertise their products accordingly. When retailers promote particular aspects of products, they generally do not forget to emphasise that the products' added value can be easily attained by paying a small premium.

The organic market does currently not distinguish between products from healthy animals and those which have suffered during their lifetime from clinical and subclinical diseases. By offering the same price for different animal health standards, the market favours farming strategies which go for minimum expenditure on preventive and therapeutic measures. On the other hand, farmers who strive for a high level of AHW and therapeutic success are facing a higher amount of work without being honoured by premium prices. While farmers can only be expected to implement appropriate measures for disease prevention and treatment if the work necessary is rewarded adequately, the market does not provide incentives for farmers willing to improve disease prevention and treatment and does not punish failures to meet a high AHW level. Thus, market conditions can be blamed for supporting unfair competition which is carried out to the cost of the farm animals.

In general, the public think that antibiotics are used more often in conventionally-produced meat, eggs and milk than in animal-friendly varieties and believe that antibiotics are least used in organic production (Meeusen et al., 2014). When asked, only consumers who bought organic products were prepared to pay more for an antibiotic-free product. On the other hand, information about the use of antibiotics in organic livestock production is scarce. An investigation into the use of antibiotics on fattening pigs in Denmark showed that the conventional herds consumed three times as much as the organic herds (Hegelund et al., 2006). A study in Switzerland revealed that bacteria in milk from organic dairy cows with mastitis exhibited the same degree of antibiotic resistance as found previously on conventional farms (Busato et al., 2000). In a Norwegian study on udder health and antibiotic resistance on conventional and organic farms, resistant pathogens were isolated from sub-clinically infected quarters in 48.5 % of the cases in conventional herds and 46.5 % in organic herds (Garmo et al., 2010). From the results of a comprehensive review, Smith-Spangler et al. (2012) concluded that the literature published shows little evidence that organic foods are significantly safer than conventional foods. According to the authors, consumption of organic foods may reduce exposure to antibiotic-resistant bacteria. Bacterial contamination of retail chicken and pork was common but unrelated to the method of farming. However, the isolating of bacteria resistant to 3 or more antibiotics was more likely in conventional than in organic chicken and pork.

Although the EC-Regulations on organic livestock productions provide a good framework for dealing with diseased animals and on how to ensure the appropriate use of remedies (for further details see the extract of the EC Regulations in the Annex), a high prevalence of production diseases in organic livestock production indicates that many organic farmers are not able to ensure a high animal health status (For further details see Deliverable D2.5). Obviously, there is a fundamental conflict between the wishes of consumers regarding a high AHW status and the difficulties many farmers have in keeping animals healthy and in establishing a successful treatment strategy in the case of illness. The reasons behind this conflict are manifold. However, we learn from the previous situation in organic livestock production that it is not sufficient to provide better housing conditions and prescribe regulations on how to deal with diseased farm animals.

Consumers are neither fully aware nor be expected to fully understand the complex processes and the trade-offs arising between different aims, values and interests in livestock production. For many consumers (especially those who buy organic food), the use of antibiotics in the production process is a matter of concern. However, they are not able to overlook possible conflicts between the use of antibiotics, economic implications, prevalence of production diseases and the issue of food safety. Farms where preventive and therapeutic measures fail to sustain an adequate level of AHW risk the multiplication and increased spread of zoonotic pathogens into the food chain. Britain's Food Standard Agency (2015) recently revealed that nearly three-quarters of fresh chicken in super-markets and butchers was contaminated with the food-poisoning bug *Campylobacter*. Simultaneously, the issue of AHW can be jeopardised due to high prevalence of production diseases and prolonged suffering due to unsuccessful treatment strategies.

10 Animal health management in need of orientation

Animal health management encompasses a number of different topics. The issue of treatment and use of conventional and/or alternative remedies often play a subordinate role. Various remedies are used to treat farm animals. These animals vary greatly in their symptoms, their ability to adapt to intrinsic and extrinsic stressors and to react to the treatment applied. At the first onset of symptoms various remedies are administered within different time intervals, in different dosages and with greatly differing levels of expertise in selecting the appropriate remedy for the particular animal and specific farm situation. Moreover, treatments are accompanied by different (and often insufficient) follow-up checks. There is much scope for improving accuracy in the documentation of therapeutic success. The complexity of interactions between the numerous intrinsic and extrinsic variables involved in the development of diseases (and correspondingly in the recovery from disease) suggests that the effectiveness of alternative and conventional treatments cannot be reduced to single factors, but depends greatly on the context in which treatments take place. From the AHW perspective, each treatment should rely on the best method of achieving therapeutic success. However, treatment approaches are often undertaken with a biased perspective of the by each of the various stakeholders involved. According to the results of an on-farm assessment (see Deliverable D4.2), farmers and veterinarians seem to be rather self-referential in their way of thinking and acting in the case of illness. In the first place, they seem to pursue their own way of thinking of what might be appropriate or not and thus illustrate their own lack of clear external reference values which need to be present for the implementation of a generally acceptable treatment strategy.

In the case of clinical control trials, the efficacy of a new drug is evaluated by comparing the results obtained in an experimental group with those of a control group treated with conventional drugs. Where the new drug achieves significantly higher cure rates than the control treatment, it is generally accepted as being sufficiently efficacious independently of the achieved level of cure rate.

Due to a lack of reliable documentation and thus a lack of comparable data, the reference value to which the outcomes of each new treatment is compared is an estimation from the decision makers' (generally the farmer and/or the veterinarian) head. Thus, benchmark data on the effectiveness of on-farm treatments are seldom available or valid. Decisions about the effort required for the diagnostic procedure, the time and duration of interventions, the selection of the remedies used and the follow-up checks are based on the decision maker's personal experience. This means each decision about the treatment of diseased farm animals is based on self-referential judgements, whereas proper considerations of possible trade-offs are often neglected.

From the perspective of the public interest and concerns, it is important that farmers understand the significance of the prudent use of remedies and treatment strategies, not just to counteract the loss of effectiveness in antibiotics due to antimicrobial resistance but also to avoid the extended suffering of the farm animals due to unsuccessful therapy and possible public health hazards. Perhaps one of the main obstacles in promoting successful treatment and the prudent use of remedies is that AHW is still not perceived as a major problem area in the food producing sector. Responsible use of antimicrobials is a synonym for reducing the use of antimicrobials for many, for others it is equivalent to making use of alternative products, while the issue of AHW seems to be widely ignored. First and foremost, it takes a specific level of knowledge to be able to shift from a widely-used applicable and relatively cheap option to a much more complex, often more expensive and not always fail safe approach: tightening biosecurity on the farm level, improving hygiene, housing conditions and climate control, enhancing the power of the immune system, and early separation of diseased animals from the group.

By contrast, it is easy to claim that prophylactic and metaphylactic use of antimicrobials should not be used as a substitute for good housing, hygiene and management practices. However, is it actually possible to consider more options with higher costs than before? Of course, this only works when there is (societal translated into political) pressure to leave old practices behind and above all incentives to develop and implement new intervention strategies. 'Using remedies as little as possible and as much as necessary' (FitzGerald, 2014) might be a general guideline; however, it gives rise to more questions than answers. While remedies are primarily a means to an end, the question arises: who is defining the end? When do ends justify negative side effects at the expense of other stakeholders? Who is able to assess and decide what is possible? Which parameters do they use? What is necessary where there are conflicting areas? Both therapeutic success as well as the negative side effects of treatments are influenced to a high degree by context. What might be effective in the one context is not necessarily the first appropriate option in another farm situation. What might look efficient from one person's perspective (e.g. farmers aiming at low production costs) may, however, be in conflict with other stakeholders' objectives.

In livestock production, treatments are practiced very heterogeneously between farms. This makes it nearly impossible to predict the outcome of a treatment either with homeopathic, phytotherapeutic or conventional products. Therapeutic success and level of PDs are the outcome of the farm specific interactions between intrinsic variables within the farm animals and extrinsic variables from the living conditions. The prevalence of production diseases indicates how far the animals' ability to adapt and cope with changing conditions in their environment is overstressed. Reducing intrinsic and extrinsic stressors would support farm animals in coping with their living conditions and in increasing therapeutic success. However, this requires an appropriate risk management and the use of various resources. Conflicts in the allocation of resources are often resolved at the expense of farm animals and their well-being (Rauw, 2009; Sundrum, 2015). The resource allocation problems which emerge from the conflicts cannot be solved by only relying on farmers' motivation and education but require regulatory measures at a higher level.

A high prevalence of production diseases indicates a high number of farm animals in need of appropriate treatment and concerns the issue of animal welfare directly. General agreement is expected at the conclusion that disease prevention would be the best way of meeting the demands of the common interest and the different concerns about public health. However, prevention is costly and will only be implemented when mandatory for all farmers; so that investors in preventive measures do not face disadvantages from their market competitors who achieve competitive advantages using lower production costs bur neglect proper preventive measures and appropriate treatment standards. This is all at the expense of the common good.

Therapeutic success and prevalence of production diseases are the outcome of very complex processes within each farm system. They develop highly heterogeneously and thus cannot be grasped or thought through by stakeholders who are only able to consider their own interests. In face of the trade-offs between different interests, the education of veterinarians, farmers and other animal owners will not be enough to ensure recognised societal ownership of both problems and solutions. Trade-offs and conflicting aims have to be worked out at the farm level. A first step in ensuring good stewardship has already been taken by monitoring and regulating the use of remedies. Setting baseline levels for use of antimicrobials, penalising farmers and veterinarians who continually exceed these levels, and/or removing the vets' ability to sell antimicrobials so there is not profit component, have already been introduced in some European Union countries. For instance, in the Netherlands it was possible to reduce the use of antibiotics by about 58% over a period of 5 years following a target defined by the government (van Beers-Schreurs, 2014). However, such approaches have their problems; for example, monitoring daily doses could encourage total cessation of antibacterial use or stopping as soon as an animal appears to be improving rather than finishing the course. As is the case in organic livestock production, it will also encourage the use of alternative treatment strategies. Thus, the previous regulations really do risk increasing problems in AHW rather than solving them.

Organic livestock production has developed as an economically successful alternative to conventional production. It is often characterised by the drive for higher levels of AHW through the implementation and certification of enhanced minimum standards (Sundrum, 2014). However, the high prevalences of production diseases in organic livestock farming generally differ little from those in conventional production indicating that the approach of enhanced minimum standards failed to provide improved animal health management. Independently of the species, enhanced minimum standards and a preference for alternative treatment cannot claim to have been successful in contributing to lower prevalence of production diseases and higher treatment success (Tuyttens et al., 2008; Sundrum et al., 2010; Alban et al., 2015). Obviously, more work is needed than just avoiding overcrowding and providing tailored options for animals to live out their natural behaviour in improved housing. A main barrier is in the fact that the EC Regulations (see extract in the Annex) do not address the trade-offs between different objectives and also have ample room for (mis-)interpretation of the guidelines and the priorities each farmer ought to set. Thus, the EC Regulations are not able to prevent unfair competition and inappropriate treatment and should thus be reworked. From a superordinate perspective, legal conditions which ensure fair competition between organic farmers and support achieving an acceptable low level of production diseases are also seen as the best strategy to improve therapeutic success. While nothing can be gained by further increasing minimum standards (see D5.5.), there is need for orientation on a meta-level to prevent conflicts between different aims being dealt with at the expense of AHW. Neither remedies nor treatment strategies are an end in themselves but a means to an end. As such, they should be assessed according to how well they meet their purpose. If the success rate of therapy are not evaluated (as is generally the case in farm practice), treatment strategies are at high risk of becoming merely symbolic; the pretence of action without sufficient evidence of effectiveness.

The complexity based on the interactions between highly variable intrinsic and extrinsic factors cannot be studied with an inductive approach but should be supplemented with an output oriented (deductive) approach and an iterative process between top down and bottom up derivations. Output orientation should starting with the monitoring of production diseases on the farm level. The results from each farm over a defined time span can be averaged. The mean values gained provide orientation for all farms participating using bench-marking. The options for such a procedure in organic dairy production were outlined in Deliverable D2.5 in further detail. With regular monitoring, it is possible to focus on farm situations which deviate considerably from the median and to proceed with further in-depth investigations on the reduction of stressors while simultaneously administering the most appropriate treatment strategy which supports healing and prevents extended suffering in diseased farm animals. While farmers are in need for orientation on the objectives that should be achieved from outside the production system, it should be left to the farm management to decide which means and intervention strategies are best for the farm's specific situation as long as they support the management to reach the targets defined. Correspondingly, a farm centric and *equifinal* approach should be implemented to deal with the complexity of the interconnected factors within the farm system. For further detail see Deliverable 5.5. While the complexity cannot be grasped by studying single factors and their impacts, the outcomes of the complex processes within the farm system have to be assessed regarding the degree to which target values (e.g., prevalence levels of production diseases) are achieved as part of the whole farm system's output. If a thorough documentation of diseases, treatment measures and therapeutic success took place, treatment strategies could be assessed retrospectively with regard to how much they ensure a high therapeutic success and a low level of production diseases.

To overcome the self-referential estimations in animal health management and the resulting unilateral decisions, a target oriented approach is required. In view of the fact that both food safety and AHW are common goods, it should not be left to single farmers to decide what level of production diseases and degree of therapeutic success is acceptable. Moreover, it is highly unethical that the farmers who try to reduce their production costs at the expense of the common good gain a competitive advantage through receiving the same price for their products, although there are varying significant negative side effects on common goods due to the farm practices. Correspondingly, the development and promotion of regulatory measures for the monitoring of production disease and the success of treatment needs to be set up in a way that veterinarians and farmers cannot circumvent the process of documentation.

11 Final conclusions

In the controversial debate on the use of remedies (either homeopathic, phytotherapeutic or antimicrobial products), the focus is often narrowed to comparisons between the products while the 'ends' to which these products are 'the corresponding means' are often not properly considered or even completely ignored. This relates to the question whether the ends, particularly therapeutic success, can be practically achieved on the farm as well as whether (and to what degree) negative side effects occur that might be linked to the use of specific products. Although the discussion is highly influenced by societal and political motives, the debate should be kept focused and should be evidence-based as far as possible. However, due to a lack of farm level evaluations, and thus a lack of valid data, it is very hard to meet these demands. Due to the fact that farmers are not obliged to do proper follow-up checks or to assess whether treatment strategies are effective for the farm specific situation, estimations are based primarily on clues gathered from various investigations and on the general results of numerous scientific studies. Based on the detailed reflections about the use of alternative and conventional remedies from various perspectives, it is concluded that treating

food producing animals with alternative as well as with conventional remedies leaves ample room for improvement. Within the IMPRO project comprehensive studies on the issue of alternative treatments have been conducted in Workpackage 4 and 9. In this report, the main results and key statements of the Workpackages have been extracted and placed in a broader context. The results and the further reflections have emerged the following conclusions:

1. Reviews revealed a high degree of uncertainty concerning the efficacy of homeopathic and phytotherapeutic products. The results of the previous RCTs have not so far been reproduced and thus cannot be generalised. The small number of data available displays only limited potential alternative treatments may have regarding their contribution to the successful treatment of diseased farm animals.
2. Some studies conclude potential, but it was not possible to draw firm conclusions due to limitations in the study design. Not even one scientific study was repeated under comparable conditions. Consequently, the use of homeopathy and phytotherapy lacks any reproducibility and cannot claim to have sufficient prognostic validity where therapeutic efficacy is concerned.
3. Therapeutic success does not just depend on the efficacy of a remedy under standardised conditions but is also based on the effectiveness of a remedy used under heterogeneous on-farm conditions. Effectiveness comes into question without the consistent implementation of *lege-artis* procedure, including early perception of symptoms, detailed diagnosis of the susceptive disease, removal of the main causes, selection of the appropriate remedies, progress follow-up check and documentation of the therapeutic success rate. Our investigations revealed that *lege artis* procedure for the use of alternative products was rarely implemented on the visited farms. Remedies were mainly bought without consultation of a veterinarian. A thorough diagnostic was rarely performed, while follow-up checks of treatment outcome, documentation, and expertise of users about the products and the principles of homeopathy were poor.
4. While the use of alternative products is supported by National legislation in some European countries, it has declined in others. Although a simplified registration procedure does not require the verification of the efficacy of alternative products, the number of alternative remedies, registered for use in food-producing animals, is limited. Manufacturers often show no interest in the registration of herbal remedies due to high costs and low profits without being able to protect the composition of their products against competitors.
5. Apart from the uncertainties regarding their effectiveness, differences in the mode of action (e.g. individualised approach of homeopathy) make alternative treatments largely unsuitable for replacing antibiotics in group treatment, which represent more than 90% of the antibiotics used in food producing animals.
6. There is real reason to conclude that poor rates of therapeutic success are often associated with extended suffering of the diseased animals and thus jeopardises AHW. Reducing the use of antibiotics without accompanying measures - particularly the monitoring of PD prevalence - is expected to encourage the use of alternative remedies. However, as the current report reveals, alternative remedies (homeopathy and phytotherapy) are far from providing a consistent approach. Thus, switching from antibiotics to homeopathy or phytotherapy might increase the prevailing problems for AHW rather than solving them.
7. Following a *lege-artis* treatment procedure for disease symptoms is seen as an essential requirement for improving therapeutic success of remedies. This, however, requires additional manpower and costs which often contradict with the farm management's general objectives of reducing effort and production costs. Farmers neither face benefits when they achieve a high level of therapeutic success and a low prevalence of production disease nor do they face penalties if they deviate considerably from the average. The trade-offs are highly variable and difficult to assess. (This issue has been addressed in Deliverable 5.3). While retailers do not

offer adequate incentives and do not cover the additional costs necessary for improved therapeutic success rates, the farmers should not be left alone in dealing with the trade-offs.

8. In the case of infectious diseases, non-treatment, alternative treatment or administration of antimicrobial products for individual animals or via group treatments (metaphylaxis) are different options, associated with quite different levels of work and cost. On the other hand, the different treatment strategies (while varying in their therapeutic success rates) have different negative side effects. These might either affect farmers' income or cause the extended suffering of diseased animals if treatment were to be unsuccessful.
9. Pressure on production costs caused by current market conditions are a main driving force in reducing effort and cost of animal health management on many farms at the expense of implementing improved disease prevention measures, improved therapeutic success rates, and a substantial decrease in the prevalence of production diseases.
10. Without economic incentives for successful and reliable animal health management and penalties for the excessive impairment of common goods, the current market conditions support unfair competition between farmers to the cost of the farm animals.

In this report, the main question was whether alternative treatment strategies provide options that are not open for conventional strategies or whether the expectations of their effectiveness are excessively optimistic and unrealistic. Due to the fact that remedies are means to an end and therapeutic effects are highly context-dependent, statements with respect to an appropriate use of alternative remedies cannot be reduced to the properties of the medicinal product alone. In fact, their use should be assessed according to the purpose and the degree to which targets are achieved. Nevertheless, it has been finally concluded that alternative treatments are at a real risk of leading hopes in the wrong direction if not properly rectified.

12 Recommendations

The following recommendations are put forward:

- Concerning research on homeopathic and phytotherapeutic therapy, further clinical trials with a study design of high scientific quality should be implemented and repeated as well as studies that control the effectiveness of remedies at farm level. Correspondingly, appropriate funding should be provided and collaboration in research should be strengthened.
- The therapeutic success in connection with the use of traditional and alternative remedies should always be in focus. This requires the development of legal and economic frameworks to support the implementation of a *lege-artis* treatment procedure, including the verification of therapy outcome and a target-oriented documentation.
- Improvements of education and training with regard to the therapeutic success on the farm level under heterogeneous conditions are necessary to consider the context-dependent effects.
- Centralized registration of alternative remedies on a European level should be considered.
- In the case of phytotherapy, knowledge on active ingredients within the products and appropriate dosage as well as compatibility with other ingredients should be ensured.
- Based on our results, the preference for homeopathy and phytotherapy by Art. 24 (EC 889/2008) is in question. It is recommended to implement mandatory follow-up checks and documentation of treatments on farm level to improve animal health and welfare. To ensure the availability of expertise needed, the main responsibility for the therapeutic use of homeopathy/ phytotherapy should be assigned to a veterinarian.
- The degree of therapeutic success and the consequences for AHW should not be left to individual farmers' discretion. According to the general objectives in Regulation (EC) No. 178/2002, the responsibility for food safety and animal health has been transferred to the primary producers and the people who process food. This implies that primary producers have to ensure that they achieve certain standards by implementing self-checks. This does not currently include the use of remedies and the aim of keeping production diseases low.
- Regulation bodies should define mandatory target values for AHW. Apart from the regulations concerning the use of antibiotics and the monitoring procedure for zoonotic pathogens, the monitoring of selected production diseases is seen as urgently necessary in overcoming the subjective assessments of farmers when it comes to judging the outcome of treatments. Recommendations have been developed by the IMPRO project (see Deliverable D5.5).

13 Glossary

- **Active ingredient:** Any ingredient/s present in the product, that is/are intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease or to affect the structure and function of the body.
- **Allopathy:** is a term coined in the 19th century by Samuel Hahnemann, the founder of homeopathy, as a synonym for mainstream medicine and is nowadays used to describe conventional chemical-synthesized medicine or non-homeopathic treatment.
- **Antimicrobial substance:** A naturally occurring, semi-synthetic or synthetic substance that exhibits antimicrobial activity (kill or inhibit the growth of micro-organisms) at concentrations attainable in vivo. Antiparasitics and substances classed as disinfectants or antiseptics are excluded from this definition (OIE 2011).
- **Botanical Medicine:** Also called Herbal Medicine or Phytotherapy. Refers to using whole plants or plant parts (seeds, berries, roots, leaves, bark, or flowers) for medicinal purposes. Used in this re-view to include all types of remedies derived from plants regardless of level of processing and ex-traction process.
- **Evidence based medicine:** emphasizes the use of evidence from well designed and conducted research in medicine decision-making. The term was originally used to describe an approach to teaching the practice of medicine and improving decisions by individual physicians. In 1972, Archie Cochrane published “Effectiveness and Efficiency”, which described the lack of controlled trials supporting many practices that had previously been assumed to be effective. The term "evidence-based medicine", as it is currently used, has two main tributaries. Chronologically, the first is the insistence on explicit evaluation of evidence of effectiveness when issuing clinical practice guidelines and other population-level policies. The second is the introduction of epidemiological methods into medical education and individual patient-level decision-making.
- **Feed additive:** Feed additives are products used in animal nutrition for purposes of improving the quality of feed and the quality of food from animal origin, or to improve the animals’ performance and health, e.g. providing enhanced digestibility of the feed materials. Feed additives may not be put on the market unless authorization has been given following a scientific evaluation demonstrating that the additive has no harmful effects, on human and animal health and on the environment (2011/25/EU).
- **Herbal medicine/Herbalism:** also called botanical medicine, phytomedicine or phytotherapy. Re-fers to using a plant's seeds, berries, roots, leaves, bark, or flowers for medicinal purposes. Herbal-ism has a long tradition of use outside of conventional medicine and is commonly associated with several traditional treatment philosophies like for example Ayuruvedic treatments, Chinese traditional medicine and Japanese Kampo.
- **Herbal medicinal product:** any medicinal product, exclusively containing as active ingredients one or more herbal substances or one or more herbal preparations, or one or more such herbal sub-stances in combination with one or more such herbal preparations (Directive 2001/83/EC).
- **Homeopathy:** is a system of alternative medicine created in 1796 by Samuel Hahnemann, based on his doctrine of “like cures like”, according to which a substance that causes the symptoms of a disease in healthy individuals will cure similar symptoms in sick individuals (“Simile-Rule”). The remedies are used in a diluted form according to the potentiation procedure described in the homeopathic pharmacopoeia. Ingredients for homeopathy can be of herbal, mineral or animal origin.
- **Homeopathic dilution:** also known as potency of a homeopathic remedy and produced by a process known as “potentization” or "dynamization". The potency defines to which extent the original substance or mother tincture is diluted with alcohol or distilled water and then vigorously shaken in a process called "succussion". Two groups of potencies are used in homeopathic

remedies: “D” for decimal, means a dilution by a factor of 10 and “C” for centesimal for diluting a substance by a factor of 100 at each stage. Hahnemann advocated 30C dilutions for most purposes (Hahnemann S (1921), The Organon of the Healing Art (6th ed.), aphorism 128).

- ***Lege artis:*** means according to the law of the medical art or state of the art. It denotes that a certain intervention or procedure is performed in a best known way.
- **Metaphylaxis:** refers to a use in still clinically healthy but likely to be infected due to close contact with diseased animals (EMA 2012).
- **Placebo:** is a remedy or medical treatment, that imitates another remedy, but without any active ingredients compared with the tested remedy. Sometimes animals given a placebo treatment will have as actual improvement in a medical condition, a phenomenon commonly called the placebo effect. The explanation for this could be conditioning of the animals, methods of administration may be important (unspecific immune responses) as well as the owner, that is willing to invest time and efforts to observe and treat his animals with more attention.
- **Prophylaxis:** Preventive use of remedies or vaccines without an extraordinary high risk to get infected, e.g. after surgery, dry-cow-treatment or to eliminate or minimize the possible infection.
- **Phytogenic feed additive** (PFA)**:** Often also called phytobiotics or botanical supplement. Commonly de-fined as plant-derived compounds incorporated into diets to improve productivity of livestock through amelioration of feed properties, promotion of the animals’ production performance, and improving the quality of food derived from those animals.
- **Phytotherapy:** Sometimes considered synonym to Herbal medicine, Botanical medicine. However, the term is also used to separate the practice of traditional botanical medicine from the science based practice where pharmacological tests and clinical trials are used to standardise the content of active substances or marker compounds in plant-derived medications used to treat disease.
- **Premix:** A uniform mixture of one or more micro-ingredients with diluent and /or carrier. They are used to facilitate uniform dispersion of micro-ingredients in a larger mix**.**
- **Prophylaxis:** Preventive use of remedies or vaccines without an extraordinary high risk to get in-fected, e.g. after surgery, dry-cow-treatment or to eliminate or minimize the possible infection.
- **RCT – Randomized Controlled Trials:** is a specific type of scientific experiment and the gold standard for a clinical trial. RCTs are often used to test the efficacy or effectiveness of various types of medical intervention within a patient population. Randomization means that study subjects before the intervention to be studied begins are randomly allocated to receive one or other of the alternative treatments. After randomization, the two (or more) groups of subjects are followed in exactly the same way, except for the different treatments. The most important purpose of proper randomization is to minimize allocation bias and balancing known and unknown prognostic factors in the assignment of treatments. Additionally control groups are included in Randomized-Controlled-Trials to minimize the effects of variables other than the single independent variable. This increases the reliability of the results, often through a comparison between control measurements and the other measurements. Control-Groups like a group treated with a placebo, a conventional drug or without a treatment are performed parallel to the experimental group (e.g. treated with a homeopathic drug).
- **Withdrawal period**: Time required after administration of a drug to a food-producing animas needed to assure that the pharmaceutical residues in food (meat, milk, and eggs) is below a determined maximum residue limit (MRL).

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Annex

Council Regulation (EC) No. 834/2007 and Commission Regulation (EC) No 889/2008 on organic agriculture

The **Council Regulation (EC) No. 834/2007** on organic agriculture prescribes in Article 14 (b):

i) Personnel keeping animals shall possess the necessary basic knowledge and skills as regards the health and the welfare needs of the animals;

viii) Any suffering, including mutilation, shall be kept to a minimum during the entire life of the animal, including at the time of slaughter;

and in Article 14 (e): with regard to disease prevention and veterinary treatment:

(i) Disease prevention shall be based on breed and strain selection, husbandry management practices, high quality feed and exercise, appropriate stocking density and adequate and appropriate housing maintained in hygienic conditions;

(ii) Disease shall be treated immediately to avoid suffering to the animal; chemically synthesised allopathic veterinary medicinal products including antibiotics may be used where necessary and under strict conditions, when the use of phytotherapeutic, homeopathic and other products is inappropriate. In particular restrictions with respect to courses of treatment and withdrawal periods shall be defined.

The **Commission Regulation (EC) No 889/2008** claims in Article 24 (Veterinary treatment):

(1) Where despite preventive measures to ensure animal health as laid down in Article 14(1)(e)(i) of Regulation (EC) No 834/ 2007 animals become sick or injured they shall be treated immediately, if necessary in isolation and in suitable housing.

(2) Phytotherapeutic, homeopathic products, trace elements and products listed in Annex V, part 3 and in Annex VI, part 1.1. shall be used in preference to chemically-synthesized allopathic veterinary treatment or antibiotics, provided that their therapeutic effect is effective for the species of animal, and the condition for which the treatment is intended.

(3) If treatment is essential to avoid suffering or distress of the animal, chemically-synthesised allopathic veterinary medicinal products or antibiotics may be used under the responsibility of a veterinarian.

(4) With the exception of vaccinations, treatments for parasites and compulsory eradication schemes where an animal or group of animals receive more than three courses of treatments with chemically-synthesised allopathic veterinary medicinal products or antibiotics within 12 months, or more than one course of treatment if their productive lifecycle is less than one year, the livestock concerned, or produce derived from them, may not be sold as organic products, and the livestock shall undergo the conversion periods laid down in Article 38(1). Records of documented evidence of the occurrence of such circumstances shall be kept for the control body or control authority.

(5) The withdrawal period between the last administration of an allopathic veterinary medicinal product to an animal under normal conditions of use, and the production of organically produced foodstuffs from such animals, is to be twice the legal withdrawal period.