Compassion in World Farming **Food Business**

How to develop an Antibiotic Stewardship Programme: A guide for corporates

INTRODUCTION

This document provides guidance on the steps required for food companies to develop an effective Antibiotic Stewardship Programme (ASP). An ASP provides a clear strategy to achieve responsible use of antibiotics in your supply chain, helping you as a company to take control of the process and ensure its effective implementation, to:

- reduce the unnecessary use of antibiotics
- eliminate/robustly regulate the use of human critical antibiotics[i]
- help prevent the development of antibiotic resistance

AN EFFECTIVE ASP IS REQUIRED TO PROTECT ANIMAL HEALTH AND WELFARE TODAY AND MAINTAIN THE EFFICACY OF OUR ANTIBIOTICS INTO THE FUTURE.

THE IMPORTANCE OF AN ANTIBIOTIC STEWARDSHIP PROGRAMME

An Antibiotic Stewardship Programme (ASP) refers to a strategy that is implemented in your supply chain to ensure more responsible use of antibiotics. The strategy includes four key pillars of activity, i. Stakeholder mapping and management, ii. Measurement and target setting, iii. Implementation and iv. Communication and evaluation.

Overuse of antibiotics in human medicine is partly responsible for the increase in antibiotic-resistant bacteria. However, for a range of bacteria, farm animal use contributes significantly, and for some infections it is the main source of resistance (Figure 1). This fact has been established via decades of research and is acknowledged by organisations such as the World Health Organisation and the European Food Safety Authority.

What are antimicrobials?

Antimicrobials are substances of natural, synthetic, or semi-synthetic origin, which at low concentration kills or inhibits the growth of microorganisms, but cause little or no damage to the host. Antimicrobials act against all types of microorganisms: bacteria (antibacterial), viruses (antiviral), fungi (antifungal) and protozoa (antiprotozoal).

By strict definition, the word "antibiotic" refers to substances produced by microorganisms that act against another microorganism. Thus, antibiotics do not include antimicrobial substances that are synthetic (sulfonamides and quinolones), or semisynthetic (methicillin and amoxicillin), or those which come from plants (quercetin and alkaloids) or animals (lysozyme). All antibiotics are antimicrobials, but not all antimicrobials are antibiotics. Since "antibacterials" are the largest and most widely known and studied class of antimicrobials, the terminology is used interchangeably. For ease of reference and consistency with other initiatives in the industry, we therefore refer to antibiotics throughout this guide, though the principles behind developing an effective programme can apply to all antimicrobials.[ii]

[i] A total ban is not always the best alternative because some important antibiotics for humans remain as a last line of defence for animals, and for some species, such as turkeys, where there is a smaller range of approved antibiotics

[ii] http://amrls.cvm.msu.edu/pharmacology/antimicrobials/antimicrobials-an-introduction

According to a survey performed in the UK by the National Office of Animal Health (NOAH 2015), consumer awareness about the misuse of antibiotics in farm animals grew from 68% in 2008 to 75% in 2014. However, there is still misunderstanding of the different types of usage of antibiotics (for example 71% of the consumers still believe that antibiotic usage for growth promotion is allowed in the EU [1]).

Media coverage is also driving public concern. The Alliance to Save Our Antibiotics was identified as one of the key factors raising awareness of how animal production systems are one of the key causes of the overuse of antibiotics and concomitant rise in bacterial resistance [2]. The Alliance provides useful information on the overarching problem of antibiotic resistance and its importance to human health[iii], and with others, highlights the business risk and case for investor action to reduce the use of antibiotics[iv].

Responsible use of antibiotics is a key element of the corporate responsibility for any company with farm animals in its supply chain. Neglect of this responsibility represents not only a gap in ethical practices but also a significant reputational risk. Conversely, implementing an effective ASP can bring a number of benefits: better animal health and welfare (as explored in Figure 2), closer relationships with your supply chain, and a positive story to tell to customers. The company's Antibiotic Stewardship Programme should be founded on current thinking and issues related to antibiotic use. The Programme should be guided by a clear overarching aim: to achieve responsible use of antibiotics, which should be underpinned by specific time bound targets for reduction in antibiotic use. The Programme and associated policies should enable the company to be clear about its plans and goals, the procedures adopted to achieve these, and should provide a solid foundation for clear communication and reporting in the future.

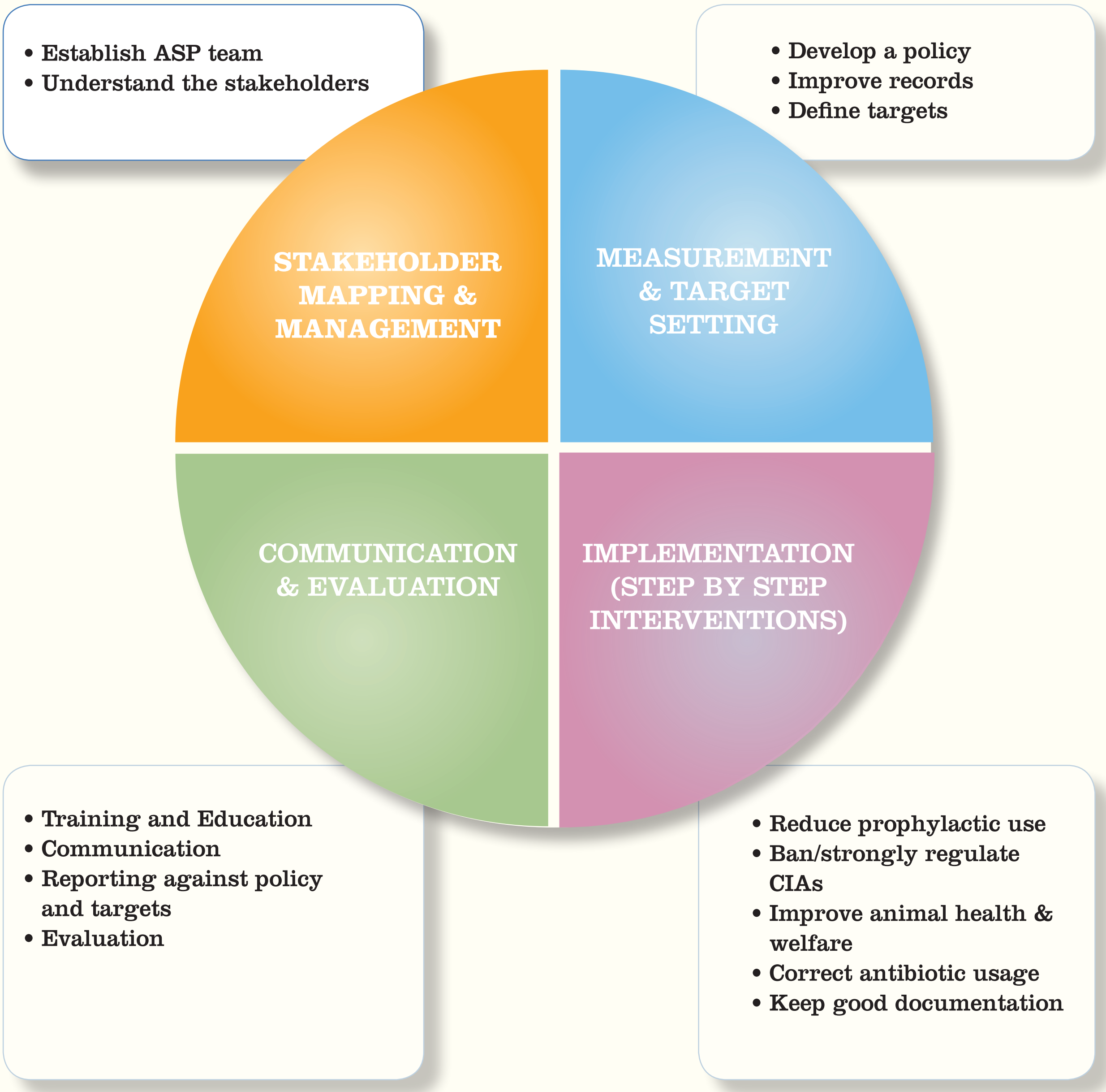
Figure 1 – Antibiotic resistance: How it spreads.

Handle antibiotics with care campaign (© WHO 2015, http://www.who.int/antimicrobial-resistance/en/)

[iii] http://www.saveourantibiotics.org/

[iv] Superbugs and Super Risks: The Investment Case for Action. A briefing for investors http://www.saveourantibiotics.org/media/1758/superbugs-and-super-risks-the-investment-case-for-action-briefing-november-2016.pdf

Figure 2 – Four key pillars of activity[v] to be addressed within an effective Antibiotic Stewardship Programme



[v] This document draws on a number of other models, specifically the Practical Guide to Antimicrobial Stewardship in Hospitals (2013)

1. STAKEHOLDER MAPPING AND MANAGEMENT

ESTABLISH AN ASP TEAM

i. Allocate people/resources to the programme

A team of suitably skilled people and sufficient resources – both financial and time-based resource – should be allocated by the head of the organisation to implement and evaluate the programme. A key component of the ASP is leadership on, and culture around, the issue of antibiotic use. This can be articulated as a common goal among different stakeholders: *'Responsible use of antibiotics'.*

ii. Ensure the team is multidisciplinary

The team members must possess the right power, expertise, credibility and leadership. These individuals need to convince the different stakeholders involved in the process (such as farmers, manufacturers and vets) of the added value of the programme. This team should be multidisciplinary so that different perspectives are taken into account and a pragmatic and flexible approach is adopted, ensuring achievement of the ASP goals.

iii. Identify clear lines of accountability to help drive change

There are a number of different people, groups and organisations that can and should be identified as accountable and responsible for driving change such as: assurance schemes, food buyers, vets and producers.

UNDERSTAND THE STAKEHOLDERS

Understanding or mapping all the stakeholders is a very useful exercise. Part of this assessment should involve assessing motivations and different characteristics such as language, potential barriers to change, as well as relationships that the food company has established with the various stakeholders.

i. Assess motivations

Understanding different stakeholders' motivations from the start is pivotal for the development and successful continuation of the ASP. A multidisciplinary team will help to provide some insight, but also promoting meetings with the different groups, or relevant people from the different groups of stakeholders, will contribute to a more precise view of their motivations. For example, convening a farmers meeting is a good first place to pose questions such as: 'What do you understand by responsible use of antibiotics?' and 'What would be the main drivers for reduction of the use of antibiotics in your farm?'

ii. Understand language, and barriers for the different stakeholders

What can be implemented will depend on local needs/issues, species-specific related issues, geography, available skills/expertise, and other resources. Explore the factors that need to be addressed in order to achieve a specific goal. For example: some retailers want antibiotic-free meat (see ANNEX 1) because of growing consumer demand [3], but farmers may not have the conditions, husbandry practices, or knowledge in which to rear healthy animals without the use of antibiotics; such barriers and expectations need to addressed.

iii. Assess nature of, and influence over, supplier relationships

A key consideration is the level of control the company has over its suppliers: does the company have direct contact with the farm or is the contact made through an intermediary? In the latter case, please see ANNEX 2, for suggested questionnaires to assess the approach towards antibiotic use. Recording antibiotic use will always happen at a farm level (see SECTION 2 – Measurement and Target Setting).

2. MEASUREMENT AND TARGET SETTING

DEVELOP A POLICY

The first step in addressing the issue of responsible antibiotic use in practice is to develop an overarching policy that clearly sets out the corporate aims, beliefs and ambitions. The policy should be publicly available.

An antibiotic policy should include:

i. A statement outlining why responsible use of antibiotics is important to the company

ii. An explanation of the core beliefs and key commitments of the company relating to antibiotics use in farm animals

iii. Further explanation of specific policies to address key issues. The scope (geography, product range, etc.) of each policy should be specified.

When developing a policy the objectives and how they are going to be achieved and measured should be agreed **by all the key stakeholders and communicated clearly.**

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IMPROVE RECORDS

"If you cannot measure it, you cannot improve it"
Lord Kelvin 1824-1907

i. Gather quantitative and qualitative information on antibiotics

Guidance on 'what' and 'how' to record regarding antibiotic usage has yet to be defined / standardised. In order to prepare yourself, you will need to consider the following factors:

1 **Quantity of antibiotic used versus quantity of antibiotic sold, for each class of antibiotic**: In the EU countries and some others, there is a legal requirement to report annually the quantity of antibiotics sold for farm animal production purposes. This data can have different levels of detail, but is usually not provided by livestock sector. However, data based on antibiotic sold may not be an accurate reflection of antibiotics used. Accurate recording of antibiotic use on farm therefore is the best method to obtain more precise usage data. This is usually in the form of mg active ingredient used per kg liveweight.

2 **Type of animal**: Type and quantity of antibiotic used is generally determined by the animal species (and motive for use). In order to report by livestock sector and set relevant targets for different species, it is important that antibiotic used is recorded and analysed by type of animal.

3 **Live weight and number of animals**: In order to be able to calculate and compare results, information about the total weight, number of animals and average weight of animals in the supply needs to be collected (at farm level or chain level for a food company). More accurate data can be obtained if use is recorded by production stage, for example sows versus meat pigs, dairy cows versus calves. This is usually in the form of mg active ingredient per kg liveweight or per animal. The other unit commonly used that relates to live weight is the 'Population Correction Unit' (PCU). PCU takes into account the animal population as well as the estimated weight of each particular animal at the time of treatment with antibiotics

4 **Animal years**: Animals have varying lifespans depending on their production use, for example a dairy cow may have a commercial lifespan of 4-5 years compared to a broiler chicken of 35 days. In order to accommodate for differing lifespans a standard unit 'animal years' is adopted, and is the cumulative number of days that an animal is alive in one year, so the dairy cow has an animal year of 1 compared to 0.1 in the broiler chicken (35/365)[vi]

[vi] http://www.autoriteitdiergeneesmiddelen.nl/Userfiles/Eng%20rapport%20AB%20gebruik%202015/def-engels-rapportage-ab-gebruik- 2015.pdf).

5 **Motive for use**: It is important to understand why antibiotics are being used, for example 10 mg of Penicillin per treatment cycle per animal used for respiratory disease in cattle. This will allow you to identify and address specific problems, and to assess whether your strategies are working.

6 **Type and method of use**: Ideally, antibiotic use should be classified by type of use – preventive (prophylactic or metaphylactic) or for treatment of clinical disease. The route of administration (water, feed, injection, topical) may help distinguish this, for example administration in water and feed is commonly related to preventive treatments, and the motive for use may be able to distinguish prophylactic from metaphylactic.


© iStock

This information must be recorded robustly on farm, then collected and analysed at both the individual farm and company level. If the company does not have direct contact with the farms in their supply, a suggested supplier questionnaire is given in APPENDIX 2, this will give a reasonable perception of the level of control suppliers have regarding the use of antibiotics.

The European Medicines Agency (EMA) is the organisation appointed to develop the general principles that should apply when collecting antibiotic use data at a national level. This data is relevant when comparing usage levels in the supply chain with the national levels of antibiotic usage. The EMA has recommended three units for reporting national use: mg/kg, DDDvet/kg DCDvet/kg.[viii] To calculate these units the data referred above is necessary. For more information, please see EMA's guidance notes.[ix]

ii. Identify and use an appropriate data collection tool

The level of data recording varies by species, country and farm (even when producing the same species/ product). There are different in-country strategies and regulations to record national levels of use of antibiotics but the majority of them are underpinned by collection tools developed by the national organisations for the different species. A good example is the newly developed tool by AHBD Pork: electronic medicine book for pigs (eMB-Pigs)[x]. This tool offers an easy way for farmers to record antibiotic use at the farm level and a straightforward means of gathering the data and conducting analysis at a central level (e.g. at corporate level).

If there is no such option in the country the business operates, then a basic tool may need to be developed, such as a simple excel sheet, where farmers record antibiotics used according to the process described in the previous subsection. Another option would be to use existing software on farm. The key rule is that any data collection tool/requirement is kept user friendly, so it is actively adopted by the range of people responsible for the ASP.

iii. Standardise recording

Whatever information is collected and whatever tool is chosen, it is crucial to keep the collection of data standardised (i.e. the same information is collected, in a compatible format, with the same or very similar tools). This will allow the company to have a central database for ease of analysis.

If different collection systems already exist, then the ASP team will need to either agree a common system and oversee its implementation, or find a solution to centralise the information and gather/analyse data in the most intuitive way possible.

Note: Precise records of antibiotic administration can also help to ensure the company is compliant with the legislation requirements for withdrawal periods. Food businesses should be fully informed of national legislation in place for controlling residues in meat and milk and if necessary implement an internal audit for antibiotic residue on animal products.

DEFINE TARGETS

Targets, either absolute or on a year-on-year basis, are a very important feature of any ASP. They provide a focus for action, and are important to give context when reporting results, and are a key feature for communicating both publicly, and internally on the ASP. Targets should be specific

[viii] http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2015/06/WC500188890.pdf)
[ix] http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2017/03/WC500224492.pdf)
[x] https://emb-pigs.ahdb.org.uk/

and measurable and have an associated timeframe for delivery.

These targets should focus on addressing the most pressing problems related to the use of antibiotics in animals. These are outlined in Section 3: Implementation, and include the use of critically important antibiotics to human medicine as well as veterinary medicine, the prophylactic use of antibiotics and as their use as growth promoters, and the quantity of antibiotics used. Targets should be published with reference to any specific cases in which exceptions may occur.

Examples of targets for reduction:

- McDonald's has set a number of global targets, such as 'Prohibit the use of antimicrobials in food animals that are by WHO definition "critically important" to human medicine, and not presently approved for veterinary use'[xi].
- Friesland Campina has adopted the national target of 50% reduction of the level of use in 2009[xii]. In 2015 this target was achieved. They now have further goals to reduce the use of antibiotics, mainly focusing on better health and welfare, such as increasing the culling age and reduction of the prevalence of mastitis.

There are also other national levels examples, such as:

a. Denmark: Set a 10% target reduction for the pig industry by 2020 and a 20% reduction for the cattle industry by 2018. These reduction targets were based on an already low antibiotic usage: Compared to all EU countries, Denmark has the eighth lowest use, only surpassed by countries with significantly lower animal production[xiii].

b. United Kingdom: The British approach is more generic, being 50mg/kg PCU the target set for every livestock sector by 2018[xiv]. Each livestock sector are anticipated to set their own species-relevant targets towards the end of 2017.

When setting targets, a food company should refer to:

i. **Existing internal information**: If the company already monitors some of the antibiotic usage in its supply chain, this should help inform the setting of both quantitative and qualitative targets tailored to their situation.

ii. **Existing guidelines**: Different organisations and countries provide guidelines with qualitative as well as quantitative information. A good example of target setting is the British Poultry Council Antibiotic Stewardship Report (refer to Case Study 1).

iii. **Best practice advice**: This field is constantly evolving and companies should check for the latest guidance. from health and regulatory bodies

[xi] https://corporate.mcdonalds.com/content/dam/sites/corp/nfl/pdf/McDonalds-Global-Vision-for-Antimicrobial-Stewardship-in-Food.pdf

[xii] https://www.duurzamezuivelketen.nl/resources/uploads/2017/12/sectorrapportage-2015.pdf) - Dutch only

[xiii] http://www.food.dtu.dk/-/media/Institutter/Foedevareinstituttet/Publikationer/Pub-2016/Report-DANMAP-2015.ashx?la=da - pages 16 and 17)

[xiv] https://www.gov.uk/government/news/uk-on-track-to-cut-antibiotic-use-in-animals-as-total-sales-drop-9)Institutter/Foedevareinstituttet/Publikationer/Pub-

3. IMPLEMENTATION

STEP-BY-STEP INTERVENTIONS

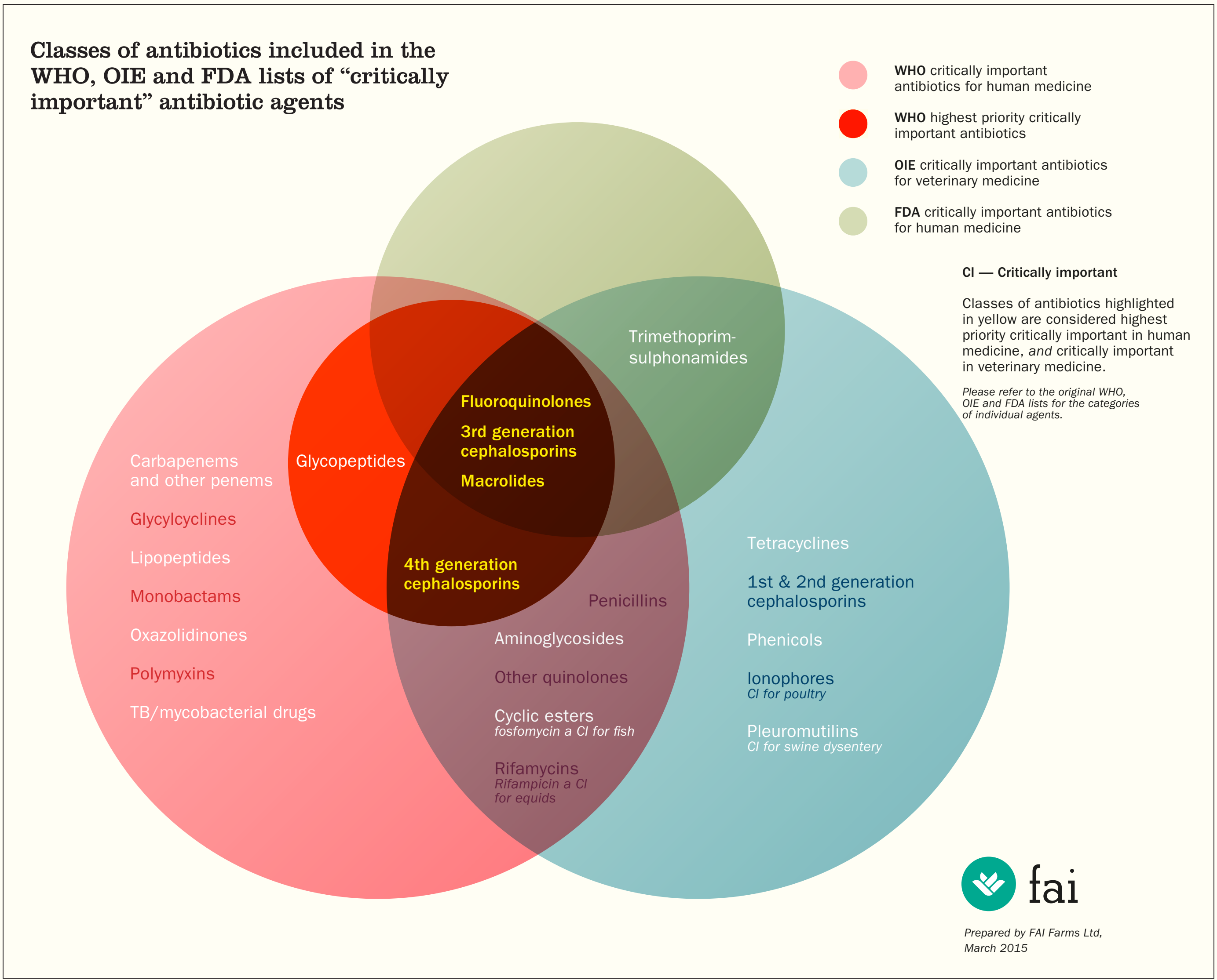
A number of key steps are common to almost every published set of guidelines on responsible use of antibiotics. Specific interventions should include:

i. Prohibit and/or robustly regulate the use of critically-important antibiotics

There are several classifications identifying critically-important antibiotics for humans and animals (WHO, OIE and FDA) (Figure 3)[xv].

The classifications overlap for three classes of antibiotics: fluoroquinolones, third- and fourth-generation cephalosporins and long-acting macrolides. Action on these classes must therefore be made a priority to address. Addressing the other classes is also important in the overarching ASP, since it should deal with the responsible use of antibiotics in general, not just the critically important ones. The relative importance of the other classes varies within different species.

Figure 3 – Diagram showing the overlapping of the three main antibiotic importance classifications (WHO, OIE and FDA)



[xv] There are some classes of antibiotics that are only allowed for use in humans. These antibiotics should never be used in any animal at any point of the supply chain.

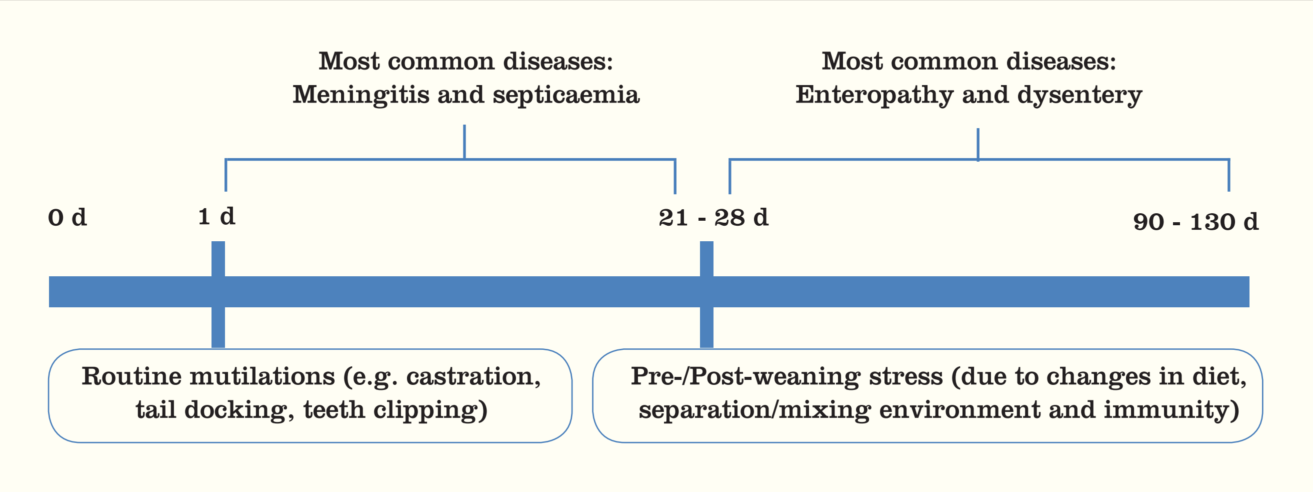
ii. Reduction of prophylactic use:

Antibiotics are given prophylactically (i.e. routine, preventative) when there is a perceived risk of infection, even if clinical signs are not present. This risk is usually due to a less favourable environment (e.g. high stocking density) or to a stressful period/ incidence in the production cycle (e.g. weaning). To minimise the preventive use of antibiotics these different risk periods and possible stressors, should be identified by species, production systems and husbandry practices (Table 1). A more specific example is given in Figure 4, outlining risk periods during pig rearing, such as mutilations, where the presence of an open wound increases the risk of infection which is minimised by the use of topical or systemic antibiotics.

Table 1 – Main issues related to antibiotic use in some of the key farmed species

Dairy cows	Dry cow therapy is often performed with prophylactic use of antibiotics as well as with critically important antibiotics (CIAs), to prevent mastitis during the dry period
Rabbits	Prophylactic use of antibiotics (mainly tetracycline) is an intrinsic characteristic of intensive caged systems, to prevent gastrointestinal and respiratory diseases.
Broilers	Major prophylactic use of CIAs such as cephalosporin and fluoroquinolones, to prevent gastrointestinal and respiratory diseases.
Fish	Major quantities of antibiotics are used to prevent emergent bacterial diseases such as Vibriosis and infections by *Aeromonas* spp. Assurance schemes such as organic ones regulate this use.

Figure 4 – Example of high risk periods for prophylactic use of antibiotics during meat pig rearing

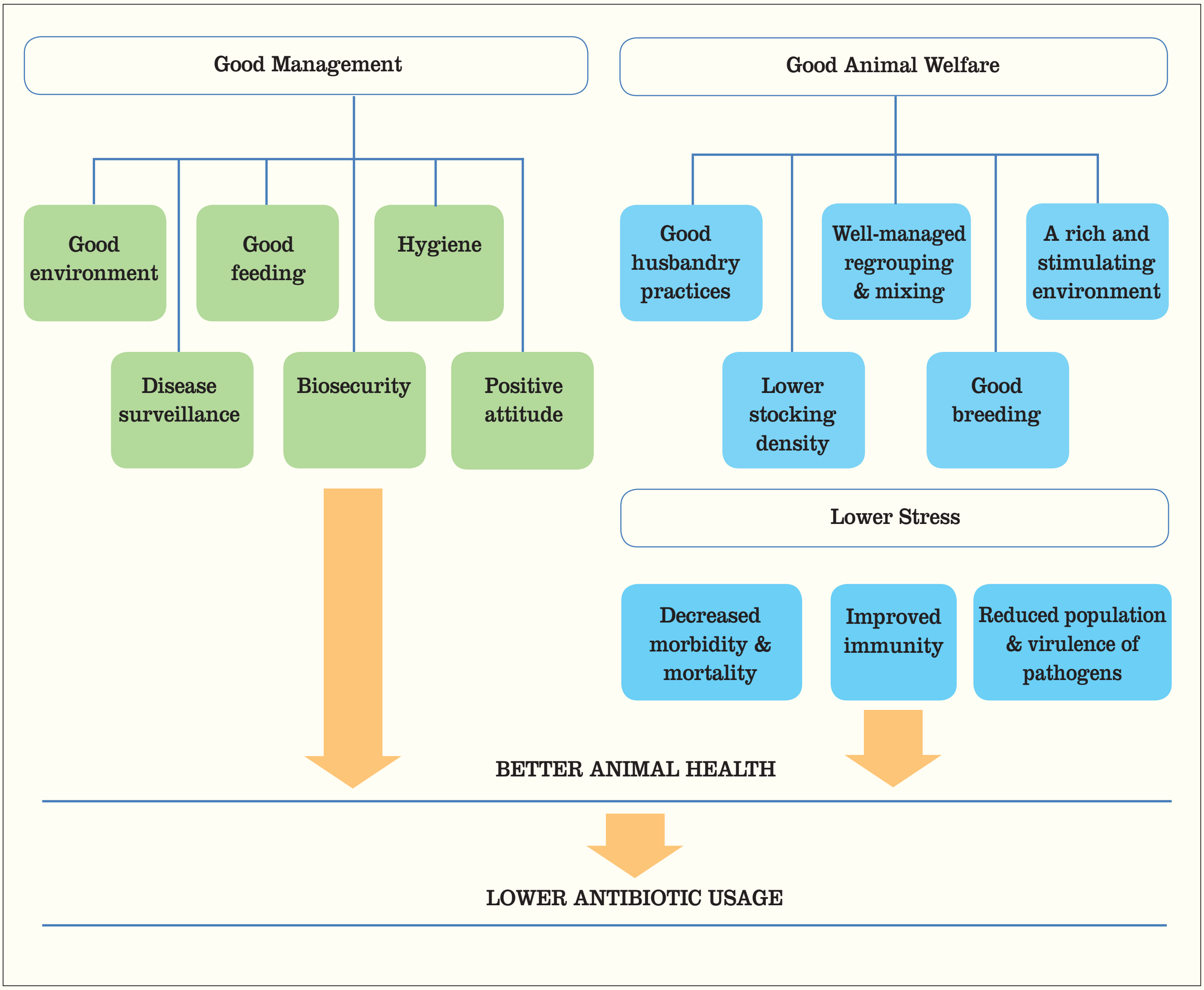


iii. Improve animal health through good management and good animal welfare standards.

The recent European One Health Action Plan against AMR recognises animal husbandry practices and animal welfare as two key areas to invest for reduction of AMR[xvi]. There are several guidelines on how to improve animal health (e.g. RUMA, BVA, NOAH). Although animal care or animal welfare are referenced frequently, the relationship between good animal welfare, good health and lower use of antibiotics is rarely elaborated (Figure 5). In this section we provide scientific evidence as well as practical interventions to improve animal welfare thereby lowering the use of antibiotics.

[xvi] https://health.ec.europa.eu/system/files/2020-01/amr_2017_action-plan_0.pdf)

Figure 5 – Schematic illustration of approaches to reduce antibiotic usage through improved management and animal welfare



Improvements to animal welfare on farm can be achieved by reducing and/or eliminating the main risk factors or stressors experienced by the animals. Examples of stressors include **social isolation** (e.g. individual housing of dairy calves, sow stalls), **regrouping and mixing** animals (e.g. group formation at weaning in piglets, mixing of sows after weaning or insemination), **high stocking densities or low space allowance** (e.g. animals reared at high stocking densities have a higher probability to be contaminated with pathogens from other animals in the pen), **selection for high productivity** (breeding) (hyperprolific sows; fast growing broilers (Figure 6), high yielding dairy cows) and **routine mutilations** (as explained in the previous section).

Different components of the farm animal's immune system may be affected by higher levels of stress [4]–[6]. For example, dairy cows with higher cortisol levels are more susceptible to infectious challenge due to a lowering of the peripheral number of blood lymphocytes [7]. There is some evidence that pigs with low coping abilities are more likely to have a lowered immune response when housed in a **barren environment** than in a pen with straw for enrichment [8].

The presence of stressors and consequently higher levels of stress also lead to higher antibiotic use due to higher morbidity rates, poorer immune systems and higher risk of disease spread.

Main risk factors or stressors:

a. **Social isolation**

Isolating social animals negatively affects their emotional state and is reflected in their behaviour and their ability to cope with immunity challenges such as pathogens, for example:

- Calves that are temporarily separated from pen-mates show signs of stress including increased vocalisation, immobility and reduced exploration [9]; additionally, the frequency of *Salmonella* shedding increases when calves experience social isolation [10].

- Pigs when partially or completely isolated show increased attempts to escape and less playful behaviour [11]. In addition, social deprivation in early life (piglets separated from the sow) negatively impacts the future stress response of the piglets, via reducing the binding capabilities of the stress-hormone receptors [12], whilst pigs with a higher social rank showed less susceptibility to Aujeszky's disease [13].

- In beef cattle, a combination of maternal separation, transportation and weaning, leads to greater susceptibility to a secondary bacterial challenge [14].

- Confinement is also a type of social isolation, as well as a stressor in itself due to the inability to perform natural behaviours. When comparing the quantity and percentage of leucocytes and neutrophils between sows in stalls and sows in group housing, Karlen and colleagues (2007) found a higher percentage of neutrophils and a lower number and percentage of lymphocytes in sows in stalls in late gestation, suggesting immune dysfunction. Furthermore, sows in the group housing showed better immunological status on the basis of lymphocyte proliferation, proving to have a higher immune competency.

There are rewarding properties to social contact with conspecifics, which benefit the welfare of an individual, as reviewed by Rault [16], who concluded *"This aspect [social contact] might constitute one of the foundations for welfare researchers to leap from the absence of negative welfare to the provision of positive welfare and emotional experiences"*.

b. **Regrouping and mixing**

Regrouping and mixing farm animals can lead to high levels of stress [6], [17] and aggression, since most farmed species have a complex social hierarchy that once formed usually remains stable [18]–[19].

- In pigs, barrows (castrated males) show a reduced response to vaccination when mixed with unfamiliar conspecifics and a higher temperature when exposed to pathogenic microorganisms [6]. Regrouping piglets also led to significantly higher faecal concentrations of *Salmonella* and higher *Salmonella* invasion of the tonsils and lymph nodes [20].

c. **High stocking densities**

Insufficient space to live and to create functional areas, such as separate feeding/drinking, resting, and activity zones is common place in intensive agriculture. This can lead to aggression and high stress levels if animals are unable to retreat or avoid aggression from others – [21], as well as increased competition for resources and resting places leading to increased stress levels [22]. Lack of space can cause a general disturbance in behaviour patterns such as feeding [23]–[25], and resting times [26]–[27], and can be associated with poor immune function, such as:

- Pigs housed at higher stocking densities had a decreased antibody response to an antigenic challenge compared to pigs housed at lower densities [28]–[29].

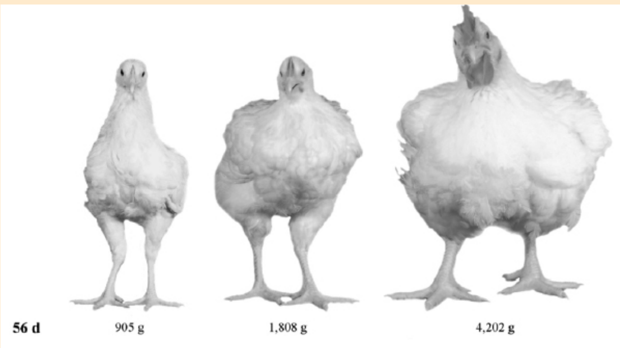
- In calves stocking density was one of the extrinsic risk factors identified for respiratory disease [30]–[31].

d. **Genetic selection for high growth rate, milk yield and egg production**

Genetic selection for higher production rates such as growth rate in broiler chickens, has a range of negative impacts, particularly on the animal's immune response which has been negatively correlated with the selection for higher body weight in a shorter period of time [32]. Specific examples of this negative impact are:

- In turkeys during natural outbreaks of Erysipelas, *Pasteurella multocida* and Newcastle disease, those bred for higher body weight were more susceptible to disease challenge and subsequently had a higher mortality rate [33]–[34].
- Broiler breeds from 2001 were found to have a weaker immune response to viral challenges and four times higher rate of mortality at 42 days of age, when compared with genetic lines from 1957 [35].

Figure 6 - Zuidhof *et al.* (2014)



From 1957 to 2005 growth rate increased by >400% with 50% reduction in the Feed Conversion Ratio. Such genetic progress has led to a multitude of unintended consequences, such as lethargy, cardiovascular disease, poor walking ability, altered immune function and meat quality issues.

The impact on the immune response can also pose a threat to human health safety, not only because animals are more prone to be carriers of foodborne disease pathogens, but also because the pathogens themselves can become more aggressive (increased virulence and capability of spreading) in the presence of stress related hormones:

- The permeability to microorganisms of the gastrointestinal tract and the virulence and multiplication rate of its microbial populations, increased when in the presence of catecholamines (which includes the stress related hormone norepinephrine) [36].
- In laying hens exposed to stress, there is evidence of higher risk of contamination of the eggs with *Campylobacter* as well as in broilers where there is an increased vulnerability to *Campylobacter* and *Salmonella* in stressful situations [37].
- *Salmonella* exposure to norepinephrine (a hormone and neurotransmitter produced in stress situations) prior to incubation in pigs led to higher invasiveness and more widespread dissemination within the tissues [38] and enhanced motility of the microorganism [39].

Research has proven in different ways the importance of high animal welfare for a lower and more responsible antibiotic use.
To put this in practice there are some practical strategies for higher welfare measures to adopt for a more responsible use of antibiotics:

- Group housing (even if just in pairs)
- Lower stocking density
- Area(s) for retreat
- Environment enrichment
- Increased feeding space and feeding availability
- Increased lying space
- Early mixing

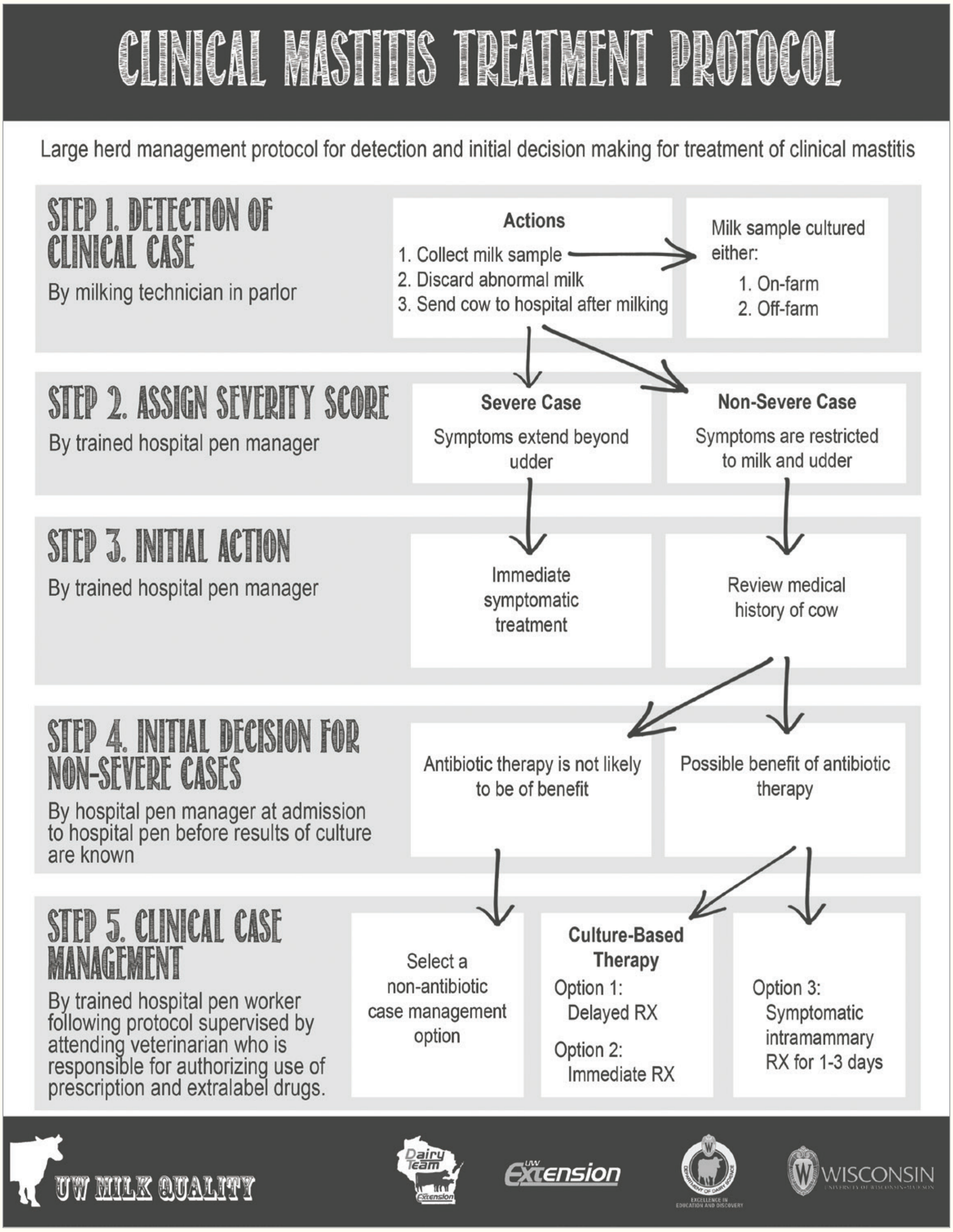
For more information on these practical solutions, please go to:
http://www.compassioninfoodbusiness.com/resources/

iv. Correct identification of need, selection and administration of antibiotics

The need for an antibiotic should always be assessed whenever there is a presence of clinical signs. Once a situation is identified as requiring an antibiotic, a careful selection of its type avoids unnecessary exposure of the bacteria to antibiotics that do not have an effect on them. Likewise, choosing the correct route of administration as well as calculating the right dose, helps not only to make sure the antibiotic has an effect on the pathogens, but that it reaches a sufficient concentration to tackle the bacteria effectively.

A good example of this process is the treatment of clinical mastitis in dairy cows. In some farms, only 50% of the mild to moderate cases of mastitis require antibiotic treatment [40], so it is important to identify the right procedure whenever a clinical case appears. The Milk Quality Group from the University of Wisconsin has developed several resources on how to responsibly apply antibiotics in clinical mastitis cases, featuring very comprehensive diagrams such as the one in Figure 7.

Figure 7 – Decision diagram of clinical mastitis treatment protocol. UW Milk Quality Group[xvii]

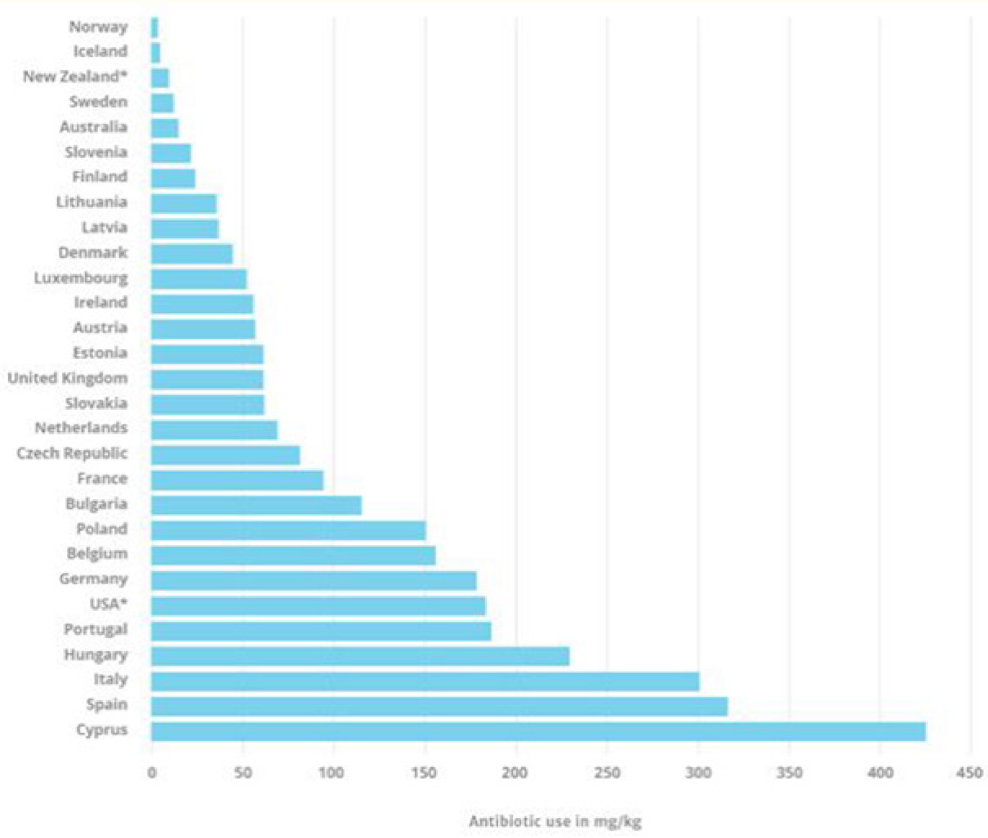


Finally to achieve the correct identification, selection and administration of the different stakeholders in the process need to be educated (e.g. milking technicians, farmer, veterinarian). The British Veterinary Association has resources available to help implement these measures (https://www.bva.co.uk/News-campaigns-and-policy/Policy/Medicines/Antimicrobials/)

[xvii] https://milkquality.wisc.edu/

Figure 8 – Example of an infographic supplied by the BVA to help farmers implement measures for a more responsible use of antibiotics at the farm

Figure 9 – Amount of antibiotics used per kilogram in food producing animals in EU countries. Source: AMR Review 2015



v. Keep accurate records of antibiotic use

As highlighted in the 'Improve records' section, there are 3 fundamental steps for good recording of antibiotic use:

- Gather quantitative and qualitative data regarding antibiotic use
- Standardise methods for data collection
- Identify and utilise an appropriate data collection and analysis tool (e.g. information by country on antibiotic use – Figure 9).

4. EDUCATION & EVALUATION

TRAINING AND EDUCATION

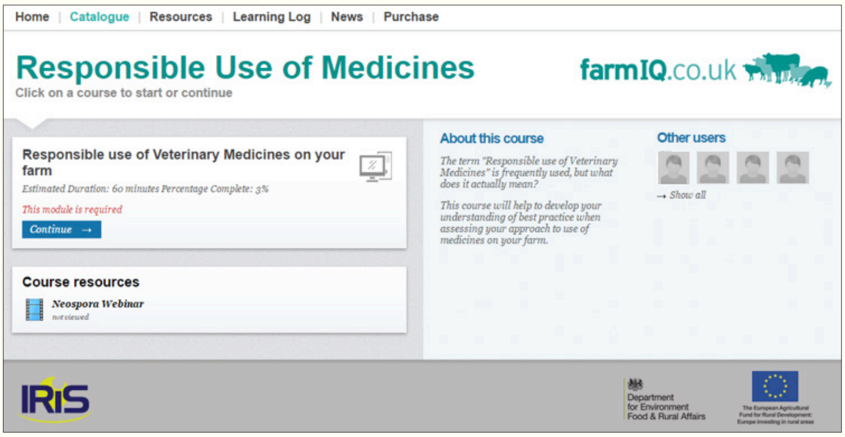
Education is a key component in any Antibiotic Stewardship Programme, and should be tailored for a range of audiences: producers, manufacturers, retailers, food service and even the public. Increasing people's knowledge of how antibiotics work, how they should be used, and how misuse can lead to resistance and less effective treatments, leads to empowerment, ownership, support and compliance with the ASP.

Make a list of target audiences and tailor knowledge transfer to suit their different backgrounds, for example:

- Farmers
- Vets
- Technical teams
- Animal welfare personnel
- Customers/consumers

Training and education can be passive, such as developing/uploading antibiotic usage guidelines, or active such as participation in workshops. Figure 10 illustrates a good example of a free on-line course designed to help people working with cattle to have a better understanding of best practice in responsible use of antibiotics and is available at www.farmiq.co.uk

Figure 10 – Screen grab taken from online course on responsible use of medicines by farmIQ (www.farmiq.co.uk), 2016



Training could also feature new methods of learning such as applications for smart phones. When aimed at the end users of antibiotics (farmers and vets) the final goal should always be to change mind-sets and behaviours concerning antibiotic use.

COMMUNICATION

Communication is core to the ASP. Communication needs to be clear and simple and provide the end receiver with a clear vision and understanding of the benefits of the policy. Communication needs to happen both within and beyond your organisation, and include the opportunity for two-way dialogue.

i. At an internal level

In order for the ASP to succeed, your company will need to communicate with all the stakeholders involved, and facilitate and improve communication links between them. For example, by promoting better two-way communication between farmer and vet; the vet can establish themselves as a champion of the ASP and the farmer can feedback on any issues related to the uptake of the veterinary advice; both can discuss solutions and agree effective ways forward.

ii. At an external level

Overall consumer trust levels in the available information related to antibiotics has grown [1], but food companies are not the primary source consumers trust to get information about animal production [41]. There are some specific practices which consumers broadly agree would improve their trust in the source of information (The centre for food integrity, 2014):

1. Better labelling of key production and nutritional information
2. Public tours of farms and/or food production facilities
3. Honest answers to queries about food production on the company's website.

Clarity is also an important feature when communicating results. A recent study conducted in the UK from the Wellcome Trust[xviii] showed that most people, if they had heard of antibiotic resistance at all, thought that it was their body which becomes resistant to antibiotics, rather than the bacteria that cause drug-resistant infections.

One way of addressing consumers with clarity and increasing trust is by having an active Antibiotic Stewardship Programme and a clear public policy on responsible use of antibiotics.

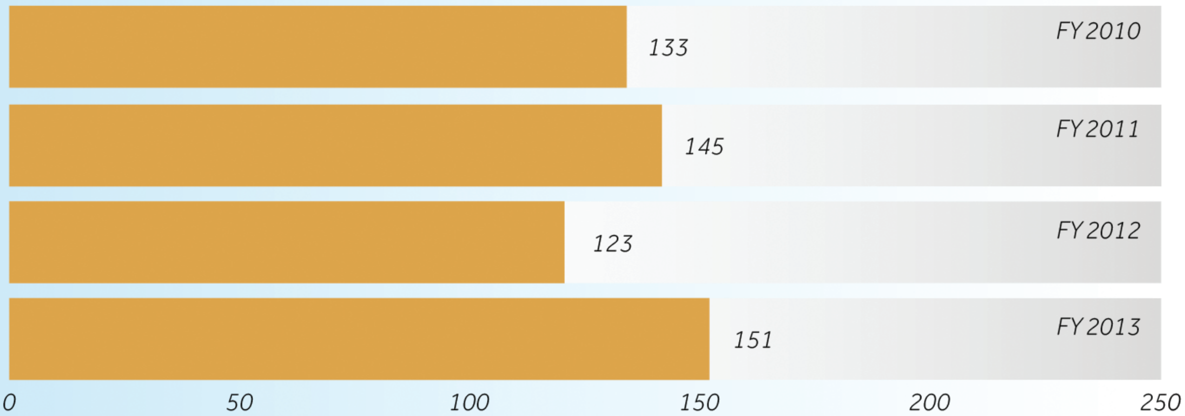
Figure 11 – Smithfield Foods (WH Group) reporting on antibiotic use. Case study highlighted in the 2014 Business Benchmarking Report

Smithfield Foods (part of WH Group)[23]

Smithfield Foods began reporting on antibiotics usage in 2007. Today, the company reports being the only major US hog producer to provide this information. For fiscal 2013, Smithfield refined its metrics to provide a more meaningful, accurate measurement. Prior data were based purely on quantities of feed-grade antibiotic products purchased each year. These products, which are bought pre-mixed, contain active ingredients (the antibiotic itself) and inactive ingredients (such as roughage and minerals), both of which, it states, vary widely depending on the manufacturer.

Smithfield's new metric is based on the total active ingredient given to the pigs through feed as well as via water and injections. For fiscal 2013, the total was 151 milligrams per pound, compared to 123 milligrams per pound for fiscal 2012.

Smithfield Foods - *Antibiotics used (milligrams per pound)*



All values reported by fiscal year. Accurate totals are not available for fiscal 2009 due to the acquisition of Premium Standard Farms during that time frame.

Content based on published material by Smithfields Foods. See http://www.smithfieldcommitments.com/core-reporting-areas/animal-care/antibiotics-use/antibiotics-reporting/

xviii https://wellcome.ac.uk/press-release/antibiotic-resistance-poorly-communicated-and-widely-misunderstood-uk-public

REPORTING AGAINST POLICY AND TARGETS

Having a policy increases greatly the transparency of a company, and it should always be a dynamic statement with annual reporting including year on year progress. An example of this reporting is the Smithfield Foods (WH Group) case highlighted by the 2014 Business Benchmarking Report[xix] (Figure 11). Reporting against policy and targets should ideally occur annually; if this is not practicable every other year is advisable.

In the Smithfield Foods example above, transparency may be considered good, but the levels of antibiotic use are still high. For example, reported national use in the pig industry in Denmark and Netherlands are 48 mg/kg and 47mg/kg. This illustrates the need not just for reporting, but to evaluate antibiotic use against set targets.

Reporting should include declaration of key achievements and progress made towards targets, with an explanation of the results and planned next steps. Measures of progress and targets can be related to both processes (e.g. developed a antibiotic monitoring tool or launched a research project) and outcomes (e.g. achieved 25% reduction in active ingredient of x antibiotic administered per live weight).

Case studies

To aid the development of the company's plan, and to demonstrate that ASPs are commercially viable and already implemented in different sectors of the industry, here are three examples of some Case Studies:

1-British poultry sector in the lead - British Poultry Council antibiotic Stewardship
2-Antibiotic stewardship in the UK dairy sector - Langford Veterinary Clinic - Langford Farm Animal Practice, University of Bristol
3-Swedish retail members Antibiotic Stewardship

EVALUATION

Internal evaluation against plans should be based on the policy and targets, and be as critical and honest as possible. Effective solutions should be amplified and ineffective or less effective measures should be revised and in some cases dropped. The evaluation can also aid reporting, helping to clarify, for example, cases where the results were not expected. The most important outcome of this evaluation is the capability of acting where the plan is not working and therefore improving it. The industry was able to meet its targets of specific percentages of reduction of the different antibiotic classes. Examples of such actions can be found in the British Poultry Council Antibiotic Stewardship case study[xx].

These actions have already proven to be very effective allowing substantial reduction of the CIA such as fluoroquinolones and macrolides. It also allowed to stop the preventive use of antibiotics and the ban of Colistin use across the poultry sector.

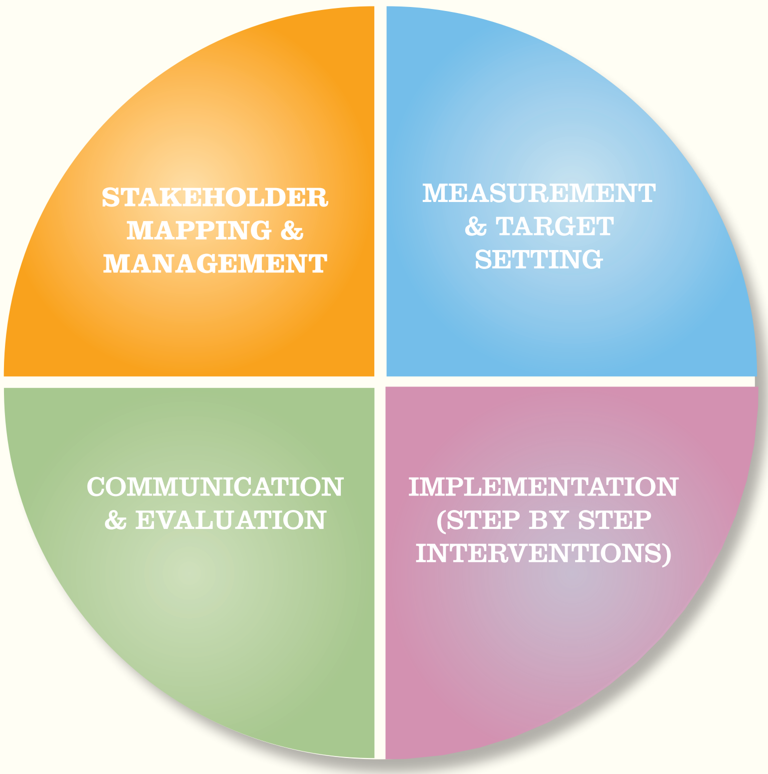
[xix] https://www.bbfaw.com/media/1057/bbfaw-methodology-report-2014.pdf
[xx] https://www.compassioninfoodbusiness.com/resources/

CONCLUSION

It is important for any food company to be as transparent as possible concerning the use of antibiotics. This may look like a colossal task, and even scary, but it is impossible to escape the ever increasing awareness of the antibiotic problem and the part played by livestock production.

With an effective Antibiotic Stewardship Programme, a company is able to act, report, evaluate and improve its responsible use of antibiotics, based on solid data, meeting societal demands with transparency.

Figure 12 – Four pillars for an effective ASP



Messages to take home

1 - Establish your team and understand your stakeholders

2 - Develop a policy, record and set specific targets

3 - Implement practical interventions, including improvements in the living conditions and holistic welfare of farm animals

4 - Train, educate and communicate your policies and practices to internal and external stakeholders

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GLOSSARY OF TERMS

Antimicrobial drug: According to the WHO definition: "Any substance of natural, synthetic, or semisynthetic origin which at low concentrations kills or inhibits the growth of microorganisms but causes little or no host damage. This definition includes antimicrobials, but excludes anticoccidials, disinfectants and antiseptics, metals such as zinc, and other compounds such as natural oils."

Antibiotic: An antimicrobial that kills or inhibits bacteria.

Antimicrobial resistance (AMR): Antimicrobial resistance (AMR) is resistance of a microorganism to an antimicrobial drug that was originally effective for treatment of infections caused by it.

Veterinarian: According to OIE's definition, "Veterinarian refers to a person with appropriate education, registration or licensed by the relevant veterinary statutory body of a country to practice veterinary medicine/ science in that country".

Critically important antibiotics (CIA): The World Health Organisation (WHO) has developed and applied criteria to rank antimicrobials (which include antibiotics) according to their relative importance in human medicine2. The list is designed to help guide usage in farm animals and thus preserve the effectiveness of currently available antimicrobials. The antimicrobials are classified into three groups: critically important, highly important, and important. Critically important antibiotics include cephalosporins and fluoroquinolones; one example of the latter is ciprofloxacin, relied on as a firstline treatment for severe *Salmonella* and *Campylobacter* infections in adults.

Categories of antibiotic use:

There are four broad categories of antibiotic use on farm:

1. Therapeutic – Giving a treatment when clinical disease is identified.

2. Metaphylatic – Giving treatment to a group of animals when some are showing signs of illness.

3. Prophylactic – Giving a treatment in anticipation of a disease. On-farm this is often to a group of animals when there is a perceived risk of infection.

4. Growth promotion – Giving antibiotics to improve the growth rates of animals. At low doses of particular antibiotics, food conversion rates improve, most likely due to changing the composition of gut microflora, which enables animals to grow faster using less feed. This practice is banned in the EU but widely practised outside Europe.

Stocking density: Number of animals per m^2. Different species, ages, groups of production or even production systems, have different space requirements. It is considered that the stocking density it is too high when an animal is not given enough space to lay down comfortably, turn around, have space to exercise and express its natural behaviours. Compassion in World Farming advocates the allometric curve as the method to use to accurately calculate the space requirements for each species.

Fast growing breeds: These breeds of animals have been genetically selected to grow at a higher speed than the normal standard for that breed. This fast development usually brings severe consequences to the health of the animal, for example, poor bone structure, that leads to poor animal welfare due to the pain and limitations associated with that.

Environmental pathogens: Environmental pathogens are microorganisms that are usually present in the environment of the farms, and can be harmful to animals living in that environment if the right conditions (such as lower immunity of the animals, higher number of microorganisms in the environment, etc) are established.

Mixing and regrouping: Different moments in the production cycle of animals that require those animals either to change from their original group to a new group of animals (regrouping) or for two or more groups of animals to be mixed in a same pen (mixing).

Mortality: Number of animals that die in a given time period, divided by the total number of animals in the same unit (farm, pen, age group, etc.) in the same time period.

Morbidity: Number of animals that express clinical signs of illness in a given time period, divided by the total number of animals in the same unit (farm, pen, age group, etc.) in the same time period.

Virulence of a pathogen: Level of capacity of the pathogen to infect the host. The level of virulence of the same type of microorganism may vary in different conditions.

Microbial population: Number of microorganisms present in a given area (e.g. 1000 Ecoli/ml)

Mutilation: A painful procedure that interferes with the bone structure or sensitive tissues of an animal. These procedures, often performed without adequate pain relief, may be done to prevent abnormal or unwanted behaviours (e.g. tail biting in pigs, injurious pecking in laying hens), to improve meat quality (e.g. castration), or to ease handling (e.g. dehorning).

Routine mutilations: The mutilation of all animals done at herd/flock level rather than individual level. Procedures carried out in a preventive manner before a problem occurs and without trying to identify the underlying issues (such as inappropriate housing, feeding, handling) making the mutilation necessary.

Weaning stress: Piglet stress associated with the separation from the mother with the goal to end the lactation period.

National Office of Animal Health (NOAH): National office that represents the UK animal medicine industry: its aim is to promote the benefits of safe, effective, quality medicines for the health and welfare of all animals.

Responsible Use of Medicines in Animals (RUMA): Independent non-profit group involving organisations that represent all stages of the food chain from 'farm to fork' that was established to promote the highest standards of food safety, animal health and animal welfare in the British livestock industry.

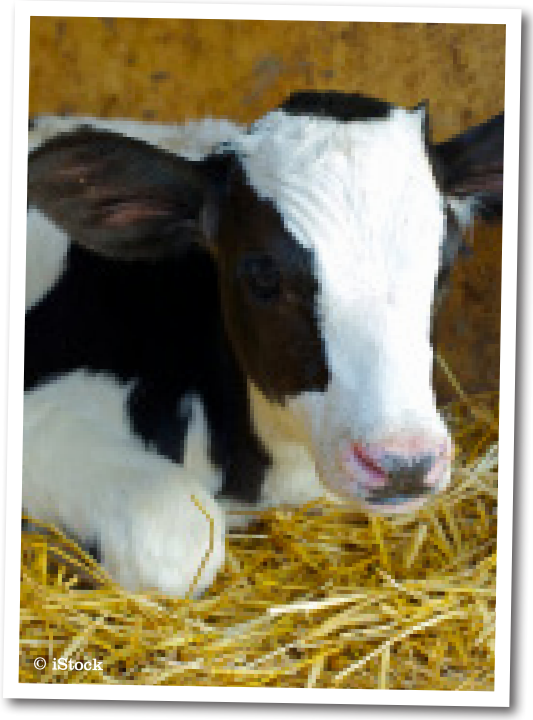
Food and Agriculture Organization (FAO): Agency of the United Nations whose aims are to eradicate hunger, food insecurity and malnutrition; the elimination of poverty and the driving forward of economic and social progress for all; and, the sustainable management and utilisation of natural resources, including land, water, air, climate and genetic resources for the benefit of present and future generations.

World Health Organization (WHO): Specialised agency of the United Nations of which the primary role is to direct international health within the United Nations' system and to lead partners in global health responses.

Food and Drug Administration (FDA): Federal Agency of the United States Department of Health and Human Services responsible for protecting and promoting public health through the control and supervision of food safety, tobacco products, dietary supplements, prescription and over-the-counter pharmaceutical drugs (medications), vaccines, biopharmaceuticals, blood transfusions, medical devices, electromagnetic radiation emitting devices (ERED), cosmetics, animal foods & feed and veterinary products.

World Organisation for Animal Health (OIE): Intergovernmental organisation coordinating, supporting and promoting animal disease control of which the main objective is to control epizootic diseases and thus to prevent their spread.

European Medicines Agency (EMA): European Union agency responsible for the protection of public and animal health through the scientific evaluation and supervision of medicines.



ANNEX 1

ANTIBIOTIC-FREE ANIMAL PRODUCTS

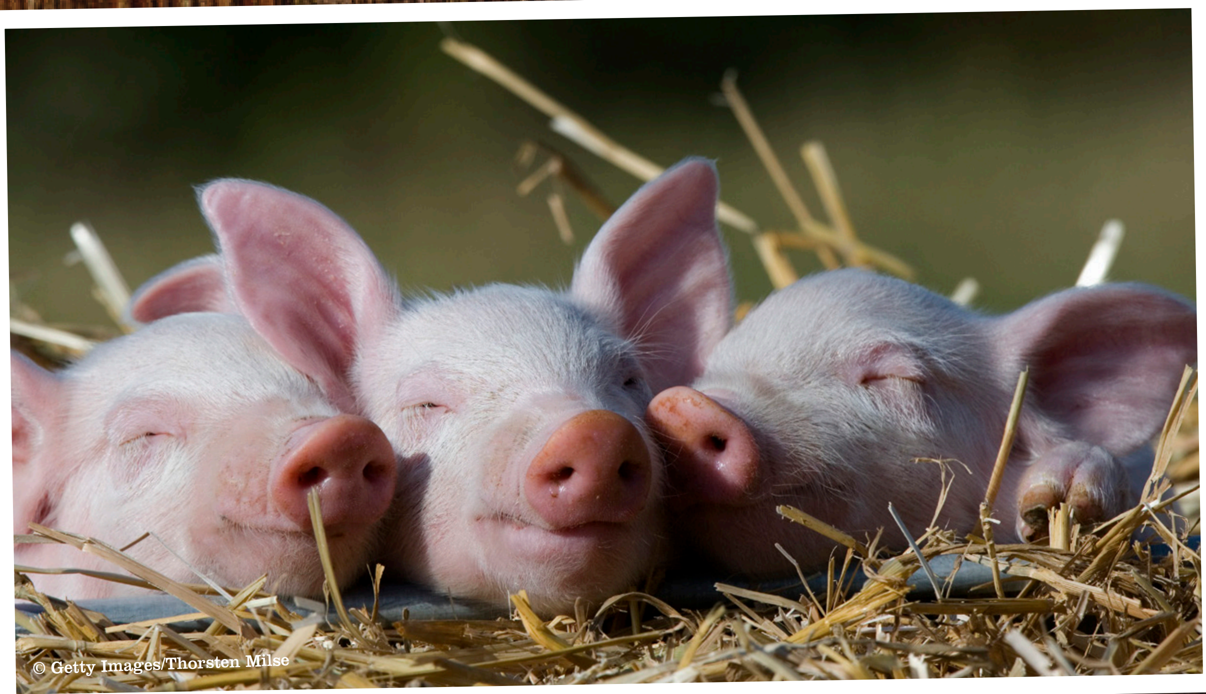
There is a growing trend over the past few years, particularly in the United States, for companies to sell 'antibiotic-free meat'. This label indicates that the meat has come from animals that were not subject to antibiotic treatments at any point in their life. However, there is a range of interpretations which may apply to just part of an animal's life cycle, a proportion of the supply chain, or be limited only to therapeutic use.

'No human antibiotics' is a similar label that some companies have adopted. In this case, food businesses are dealing specifically with the use of - and resistance to - antibiotics in animals that are also used in humans.

Whilst it is clear that the overuse of antibiotics in farming must be addressed, to enable a significant reduction in antibiotics the fundamental features of intensive systems must also be addressed. Simply stopping the routine use of antibiotics without also changing the animals' environment could increase the risk of sickness and have a negative impact on animal welfare. In some systems or species, it may also be the case that fewer antibiotics are compensated for with alternative 'props' such as a heavy vaccination regime and/or use of prebiotics and probiotics, which do not fundamentally address the conditions in which the animals live.

In accordance with an 'antibiotic-free' label, animals that receive therapeutic treatment of antibiotics (in response to a disease episode) are removed from the antibiotic-free supply chain. This runs the risk of sick animals not being treated in a timely fashion. Therapeutic antibiotic treatment is an important component of maintaining good animal welfare. Stopping or delaying therapeutic treatments could cause significant suffering and greatly compromise the welfare of sick animals, who should receive treatment when they need it.

Whilst 'antibiotic-free' is easily understood and appealing to the consumer, it is not an easy solution and an 'antibiotic-free' approach should only be undertaken responsibly and with due consideration for the conditions in which the animals are reared.



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ANNEX 2

SUPPLIER QUESTIONNAIRE

When not in direct contact with the farms that supply animal products to your business, you can provide a questionnaire for your suppliers to complete to help you assess if they are practising responsible use of antibiotics on farm. The questionnaire can be split into a general section followed by a species-specific section adapted for the most commonly used antibiotics for that species; antibiotic use in routine husbandry procedures, such as routine mutilations or dry cow therapy, and during high risk periods. The example overleaf is for broiler chickens.

General questions

If any antibiotics are in use for any purpose, please complete all of the following questions:

Is any prophylactic treatment practised (i.e. giving antibiotics in anticipation of disease)?

Please state Yes/No.

Is any metaphylactic treatment practised (i.e. giving antibiotics to a group of animals when only some are showing signs of illness)?

Please state Yes/No.

Is all treatment therapeutic (i.e. giving antibiotics only to animals showing signs of illness)?

Please state Yes/No.

Please confirm that antibiotics are only used under the direction of a veterinary surgeon and that withdrawal times are adhered to.

Please state Yes/No.

Is the quantity of antibiotic used recorded? If yes, please specify the methodology. If no, please specify the reason for not recording.

Is there any off-label use?

Please state Yes/No.

Antibiotic use in broilers

Are any antibiotics used for any purpose? Including growth promoters and the use of coccidiostats to manage coccidia parasites (even if these are ionophores that are not used in human medicine)

Please state Yes/No.

If yes are any of the highest priority WHO critically important antibioticsin human health in use?

These are: 3rd and 4th Generation Cephalosporins, Macrolides, Fluoroquinolones and Glycopeptides.

If yes please list any: 3rd and 4th Generation Cephalosporins used e.g. Cefovecin, Cefquinome and Ceftiofur.

If yes please list any: Macrolides used e.g. Gamithromycin, Kitasamycin, Tilmicosin, Tulathromycin, and Tylosin.

If yes please list any: Fluoroquinolones used e.g. Danofloxacin, Difloxacin, Enrofloxacin, Marbofloxacin and Orbifloxacin.

If yes please list any: Glycopeptides used e.g. Avoparcin.

Please confirm that records of antibiotic use (duration, route used) are maintained for individual or the smallest possible group of animals which include the quantities of antibiotics administered.

Please state Yes/No.

Please provide further details on the above as necessary.

Please detail how antibiotic residue levels are monitored to ensure that they are within legal limits.

If in excess of legal limits, please confirm how the stock is controlled to ensure that it does not enter the company's supply chain?

Are there any plans to reduce antibiotic usage or to exclude any antibiotics?

Please state Yes/No.

Please detail the level of reduction and timescales.

COMPASSION in world farming **Food Business**

How to develop an Antibiotic Stewardship Programme: A guide for corporates

Compassion in World Farming

Compassion is recognised as the leading international farm animal welfare charity. It was founded in 1967 by Peter Roberts, a British dairy farmer who became concerned about the development of intensive factory farming.

For more information visit ciwf.org

Food Business Programme

Compassion in World Farming's Food Business team works in partnership with leading manufacturers, food service businesses and supermarket retailers that have the ability to positively impact large numbers of animals in their supply chains.

We believe in collaboration and a solutions-led approach, developingrelationships that are based on trust, mutual benefit and reward for progress.

For more information visit compassioninfoodbusiness.com

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