



**REPORT OF THE MEETING OF THE OIE AD HOC GROUP ON PRIORITISATION OF DISEASES  
FOR WHICH VACCINES COULD REDUCE ANTIMICROBIAL USE IN CATTLE, SHEEP, AND GOATS<sup>1</sup>**  
**Paris, 7 -9 May 2018**

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## **1. Opening**

The OIE *ad hoc* Group on Prioritisation of Diseases for which Vaccines could reduce Antimicrobial Use in cattle, sheep, and goats met from 7 to 9 May 2018 at the OIE Headquarters in Paris, France.

Dr Matthew Stone, Deputy Director General International Standards and Science of the OIE, welcomed the participants and introduced the OIE, its mission, its standard setting and animal health reporting activities, and its approach to providing scientific advice. He commented on the growing OIE efforts toward increasing transparency in the animal health situation globally, also through the development of guidelines and recommendations on priority areas for Veterinary Services at the international level.

Dr Stone reaffirmed the OIE position that antimicrobials are essential tools for protecting and maintaining animal health and welfare when used responsibly and prudently, and that the use of antimicrobials for growth promotion is to be avoided, as it is contrary to the principle of prudent use.

Dr Stone highlighted the growing importance of combatting antimicrobial resistance (AMR) and the OIE contribution to the international efforts to fight it, also in the framework of the Global Action Plan on AMR. He explained that the work is mainly distributed on two pillars, the development of a monitoring and evaluation framework, for which the OIE is refining, with its Tripartite partners, the WHO and the FAO, a set of indicators to be used at the global level to support Members in establishing their national action plans, and the development of a stewardship framework, addressing research and development (R&D), prudent use and access. As part of its standard setting mandate, the OIE established standards for the Harmonisation of national antimicrobial resistance surveillance and monitoring programmes and for the Monitoring of the quantities and usage patterns of antimicrobial agents used in food-producing animals in its Terrestrial Animal Health Code, which were recently revised and will be proposed for adoption at the upcoming General Session in May 2018, together with the updated OIE List of Agents of Veterinary Importance. An OIE *ad hoc* Group on AMR, which was formed in 2000, and has met periodically since that time, has overseen the development and revision of these standards and recommendations.

The second OIE annual report on the use of antimicrobial agents intended for use in animals was published in 2017. Dr Stone commented that the number of Members engaged with the data collection is increasing, and that the report offered several reporting options for Members, allowing quantitative reporting of antimicrobial use. Another important element of the OIE AMR activities was the training of the OIE National Focal Points for Veterinary Products, which are provided to build capacities and knowledge, including on the market authorisation process and to drive Focal Point engagement in the national action plans.

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<sup>1</sup> Note: This ad hoc Group report reflects the views of its members and may not necessarily reflect the views of the OIE. This report should be read in conjunction with the September 2017 report of the Scientific Commission for Animal Diseases because this report provides its considerations and comments. It is available at: <http://www.oie.int/en/international-standard-setting/specialists-commissions-groups/scientific-commission-reports/meetings-reports/>

Dr Stone informed the Group that the OIE is involved in the activities of the STAR-IDAZ International Research Consortium, a forum of public and private R&D programme owners/managers aiming to coordinate research on animal health at global level, for which it co-hosts the Secretariat. This collaboration would facilitate the uptake of the Group recommendations by research funders, ensuring impact. Similarly, the collaboration with GALVmed would support the picking up on the recommendations to develop specific vaccination which suits their mandate.

## **2. Appointment of chairperson and rapporteurs, and adoption of the agenda**

The Group appointed Dr Cyril Gay as the chairperson of the meeting and Professor David Jordan agreed to act as rapporteur.

The Agenda, which was adopted without changes, and the List of Participants are presented in [Appendices I and II](#) of this report, respectively.

## **3. Background to the meeting**

Dr Elisabeth Erlacher-Vindel, Head of the Science and New Technologies Department, provided background information on the reasons for convening the *ad hoc* Group. To address requests from several Countries and organisations for information on where to target research to reduce the use of antimicrobials in animals, in 2015 the OIE convened a first *ad hoc* Group aiming to identify priority diseases in chickens, swine and fish. The current Group represented a follow up on this approach, to identify priority diseases for cattle, sheep, and goats.

Dr Erlacher-Vindel explained the rationale and work performed by the first *ad hoc* Group and presented the process that was followed for agreeing on the tables for reporting and for ranking priorities. She suggested that the new Group might want to consider improving the definition of categorisation of research priorities.

Dr Erlacher-Vindel highlighted that the work of these *ad hoc* Groups is part of the provision of scientific advice activities of the OIE and is not directly related to its standard-setting activities. She emphasised that the focus of the discussions should not be on vaccine development itself, but rather on the capacity of reducing the use of antimicrobial agents through vaccination. While it was recognised that other practices need to be also implemented to reduce antimicrobial use, only vaccination should be covered by the Group.

The participants introduced themselves to the Group and presented relevant background information from their specific fields of expertise.

## **4. Review and address the Terms of Reference for the *ad hoc* Group meeting**

The Group heard the background information presented by the participants and considered the draft Terms of Reference (ToR) (attached in [Appendix III](#) of this report).

The Group discussed considering water buffalo in the ToR. It was finally decided that, although water buffalo is an important species in some regions, for the time being this *ad hoc* Group should focus on *Bos taurus* and *Bos indicus* only, since these species are more globally farmed than other bovidae. The Group agreed that no inter-species prioritisation should be performed.

The Group proposed minor adjustment to the ToR for the meeting.

The Group noted that, while regional perspectives should be taken into consideration for some aspects, bacterial and non-bacterial diseases should be ranked based on their importance at global level. The ToR were amended accordingly.

The Group agreed that, while the cost of vaccine was important, it was more appropriate to refer to ‘barrier to adoption’, which encompasses cost-prohibition and also includes vaccine distribution. The ToR were amended accordingly.

The Group recognised that some vaccines have marginal benefit and are based on older technologies, and this can result in high use of antimicrobials. The availability of modern technologies and knowledge might be utilised to deliver enhanced vaccines, but would require significant investment in research and development.

The Group discussed on which particular stakeholders and interested parties should be considered as the target audience for the report. It was agreed that, in particular, public funders are a key stakeholder, and there were examples of uptakes of the recommendations of the first *ad hoc* Group by public funders. The Group noted that the report would also help public and private research and development institutions to prioritise their investment. Furthermore, the report would be a useful resource for national and international policy makers in animal health. It was pointed out that, especially for diseases that are not financially attractive targets for investments by pharmaceuticals companies (*e.g.* neglected diseases), donor support would be critical to ensure vaccine development.

The Group agreed that zoonotic agents that do not cause disease in animals, and thus do not directly lead to use of antimicrobial agents use in animals, were out of the scope of the current *ad hoc* Group.

## 5. Refine template and criteria for the ranking of diseases

The possibility of dividing the Group into two subgroups, one looking at cattle and the other one at small ruminants, was considered. The participants presented their expertise on the different species: since most experts had experience in several of the species covered by the ToR, it was agreed that it would be more effective to conduct the work with the Group as a whole.

The Group agreed that cattle, sheep, and goats were to be discussed separately.

The Group discussed about targeting dairy and meat cattle separately and agreed that this would create additional and unnecessary complexity to the tables. It was agreed that references would be made in the report if a specific priority applied to a specific subgroup only (*e.g.* if the identified priorities relate to dairy or meat animals, or to feedlot or grass-fed animals). This same principle was applied to sheep and goats.

The participants discussed the adoption of the template and guiding criteria for the ranking of diseases used by the *ad hoc* Group convened on this subject in 2015.

Although it was recognised that not all antimicrobial agents would have the same relevance from an antimicrobial resistance (AMR) viewpoint, the Group decided to highlight diseases for which the highest volumes of antimicrobials would be used, in the context of the rate of disease occurrence.

The Group noted that, in many cases, a reduction of use of antimicrobial agents in cattle, sheep, and goats could be achieved by effective vaccines against a viral or parasitic disease, since the clinical signs of infection with some of these pathogens are often similar to bacterial diseases, and bacterial infections can develop secondarily, thus necessitating antimicrobial agent therapy.

The Group agreed that the focus should be on identification of diseases where a new or improved vaccine would have the maximum effect on reducing the use of antimicrobial agents in cattle, sheep, and goats.

The Group discussed and agreed that the following criteria would be applied for ranking research priorities:

- High priority: The agent or the disease/syndrome results in a high use of antimicrobial agents and there are no readily available vaccines, or the vaccines are suboptimal in terms of efficacy or safety or practicality, or are cost-prohibitive.
- Medium priority: The agent or the disease/syndrome results in a medium use of antimicrobial agents and there are no readily available vaccines, or the vaccines are suboptimal in terms of efficacy or safety or practicality, or are cost-prohibitive.
- Low priority: The agent or the disease/syndrome results in a low use of antimicrobial agents, regardless of whether a vaccine is readily available and effective.

The Group ranked the vaccine research priorities for each syndrome/pathogen based firstly on the use of antimicrobial agents as above. The Group then adjusted this preliminary ranking based upon current vaccine availability and quality, and on the technical knowledge necessary to develop or improve vaccines to reduce antimicrobial use.

The Group decided to separate the diseases entailing high and medium use of antimicrobials from the ones which implies lower use by listing the diseases in two separate tables, with the latter ones noted in Appendices. This will help simplify the tables and better emphasise the priorities. Nevertheless, the Group highlighted that some diseases that are scored as having low use of antimicrobials at a global level, might still be a considered a high priority at a regional level.

The Group proposed that a focus for research should include studies to demonstrate that vaccine could reduce use of antimicrobial agents under field condition, as this information might serve to increase the uptake of existing vaccines that are underutilised.

It was noted that, in some cases, vaccines might exist but are not used due to lack of availability (*e.g.* problems linked to delivery system, registration, access). This problem is more common in some regions, where antimicrobial agents are more accessible to farmers than vaccines and where veterinarians and veterinary paraprofessionals guidance is lacking, ultimately leading to poor antimicrobial stewardship. Poor access to diagnostic services may also contribute to poor antimicrobial stewardship. In these circumstances, the culture of preventive vaccination often receives relatively little emphasis, and farmers primarily rely on therapeutic antimicrobial products. The Group agreed that, while it would be interesting to identify regional-specific barriers to adoption of vaccines leading to a reduction in the use of antimicrobial agents, this was out of the scope of the Group ToR.

It was noted that, for many pathogens, effective vaccines already exist. However, the degree, breadth, level of global distribution, consistency of supply, or duration of protection afforded was not optimal, thus providing a barrier to the uptake of the vaccine.

## **6. Rank diseases for the two focus areas**

### **6.1. Key principles adopted**

In order to facilitate identification of infections where new or improved vaccines would have the maximum potential to reduce antimicrobial use, a number of categories were investigated:

1. Identification of the most prevalent and important bacterial infections in cattle, sheep, and goats that are associated with high antimicrobial use.
2. Identification of common non-bacterial infections in cattle, sheep, and goats showing clinical signs that trigger empirical antimicrobial treatment (*e.g.* for diarrhoea) and which also result frequently in bacterial co-infection.
3. An assessment of antibiotic use in response to the syndromic indication or diagnosed disease. This was categorised as high, medium or low in the context of considered use compared with the total use of antimicrobial agents in that animal species.
4. The availability of a vaccine(s), and if available, their effectiveness.
5. The potential for a new or improved vaccine to reduce the need for antimicrobial treatment.

Also considered out of scope were autogenous vaccines, primarily because of lack of broad applicability across regions, registration variability and the absence of global efficacy data.

### **6.2. Limitations**

As a consequence of adopting the above criteria, it became evident that there were many data gaps. For example, key information such as a current list of all available vaccines that have marketing authorisation, amount of antimicrobials used for different infections, and the relative incidence of different infections worldwide are not available. In addition, since only a few scientific studies, if any, have investigated the use of antimicrobial agents related to viral diseases, relying solely on objective quantitative data was not feasible. Lastly, the large number of diseases assessed was such that it was not possible to perform a comprehensive bibliographic review.

Based on the above limitations, conclusions of the report are based on considerations weighted primarily on the participating experts' professional knowledge and advice.

Due to its global focus, regional and national differences could not be accommodated by this report. Nevertheless, the report provides a framework for regions and countries to adopt a similar process for prioritising diseases.

### 6.3. Cattle diseases

#### Respiratory

The bovine respiratory disease complex (BRD) is a multifactorial disease attracting high level of antimicrobial use in cattle, especially in feedlots. For vaccine development, a syndromic, multi-pathogen, approach would be preferable to address all animal health risks. The Group suggested that regulatory agencies' performance requirements for licensing of vaccines might not reflect how these vaccines subsequently perform in the field. The need for DIVA (Differentiating Infected from Vaccinated Animals) vaccines was discussed. However, BRD is primarily a production-limiting disease rather than a regulated disease for domestic or international trade. Thus, the experts agreed that incorporating DIVA functionality in vaccines for BRD would have a low relevance, and would be unlikely used to support decisions on domestic or international trade. Where evidence of compliance with vaccination is needed, other opportunities exist.

The major organisms involved are:

- a. *Mannheimia haemolytica*: Regarded as a primary pathogen and features a lack of cross protection among different strains;
- b. *Pasteurella multocida*: Regarded both as a primary and a secondary pathogen. It was recognised that the existing vaccines notably have marginal efficacy and there is a potential lack of cross protection among *P. multocida* field isolates;
- c. *Histophilus somni*: Regarded as an opportunistic pathogen, that is less common and for which it was difficult to know the efficacy of the available vaccines under field conditions;
- d. Bovine viral diarrhoea virus (BVDV): Considered by the group to be the viral pathogen that elicits the most significant use of antimicrobial agents in BRD;
- e. *Mycoplasma bovis*: The Group agreed that the role in BRD was lower than for other pathogens, and that although it was found with increasingly higher occurrence, its role as a causal agent in BRD was uncertain;
- f. Parainfluenza virus 3 (PI3), BHV-1 (IBR): Both these viruses were recognised as being lesser contributors to antimicrobial use, and existing vaccines are effective and safe. For IBR, DIVA vaccines have been shown to be useful for eradicating the disease in several countries of Europe;
- g. Bovine respiratory syncytial virus (BRSV): Adequate vaccines are available;
- h. Bovine coronavirus: Recognised as an emerging respiratory pathogen. While a vaccine is available, its efficacy is uncertain.

Apart from BRD, the Group considered another respiratory disease as within the scope, Contagious Bovine Pleuropneumonia (CBPP, *Mycoplasma mycoides subsp. mycoides*). CBPP is one of the most relevant diseases in Africa, where it entails high use of antimicrobial agents, which could lead to establishment of a carrier state. Vaccines have low efficacy, their access is limited to official control programmes, and have short duration of immunity and safety issues (residual virulence).

*Dictyocaulus viviparus* (lungworm) was also considered as relevant to cattle health, but the use of antimicrobials was not considered high enough to warrant including this pathogen in the list.

#### Mastitis

The main causal agents of cattle mastitis were considered: *Streptococcus agalactiae*, *Streptococcus uberis*, Coagulase negative *Staphylococci*, *Staphylococcus aureus*, *Escherichia coli*, and *Mycoplasma bovis*. The Group agreed that antimicrobial use for mastitis was higher in modern, intensive dairy production as compared to grass-based production. Most of these agents provoked high use of antimicrobials, with the exception of *E. coli*, and *M. bovis*. The Group agreed that it was common practice to treat the disease and select for less susceptible animals through culling practices, rather than

to prevent it through vaccination. The occurrence of multiple strains, the lack of cross-protection of available vaccines, and the difficulty of building a specific immune response at the site of infection were identified as a current difficulty. The Group recognised that other pathogens could provoke mastitis, but have a low impact on antimicrobial use, and thus were not discussed.

One hurdle associated with the development of mastitis vaccines for cattle is the broad coverage provided by the current dairy antimicrobial treatment strategies. Dry cow therapies provide control against a number of different contagious and environmental pathogens. From a herd perspective, development of a vaccine against individual pathogens will not eliminate the need for control of the other pathogens often found in infected cows. Development of combination vaccines that address the common mastitis pathogens would offset this issue, but represents a difficult technical challenge that would require a significant investment in research and development.

### Lameness

Lameness is a priority issue for the dairy sector, together with mastitis. The Group identified interdigital and digital dermatitis as the dominant lameness syndromes attracting antimicrobial use. *Fusobacterium necrophorum* is the main causal agent in cattle. It provokes significant use of antimicrobials, and vaccines are not globally available. *Trueperella pyogenes* and *Treponema spp.* were also discussed. While both these agents are often present in lame cows, their role as causative agents for lameness needs further investigation.

### Enteric

Enteric diseases are an important cause of antimicrobial use, especially in feedlot systems. *Fusobacterium necrophorum* entails high use of antimicrobials, especially in feedlots, arising from acidosis. No vaccines are labelled for enteric disease/acidosis/liver abscesses; and off-label use of *F. necrophorum* vaccines designed for other diseases provides limited efficacy.

*Salmonella enterica* is a notable zoonotic disease involving antimicrobial resistance. The disease's greatest effects on animals are in dairy calves soon after birth, which are exposed to the challenge before the onset of immunity that might be derived from vaccination. *Salmonella spp.* vaccines are available to address the prevalent subspecies/serotypes in the various regions (e.g. *S. enterica* serotype Dublin, *S. enterica* serotype Newport, *S. enterica* serotype Typhimurium). These vaccines are generally used in herd programmes to control the level of *Salmonella spp.* bioburden within the vaccinated herd, leading to lower levels of *Salmonella spp.* exposure to the new animals entering in the herd. This then results in a lower level of the disease.

Enterotoxigenic *E. coli* provokes a high use of antimicrobials, especially in dairy farms. Effective vaccines do exist, but are not available in every region.

Bovine rotavirus and bovine coronavirus are also causal agents of neonatal diarrhoea in calves, which may be treated with antimicrobials because the cause of symptoms is frequently undifferentiated. Rotavirus infections, being more prevalent than coronavirus, are likely to attract higher use of antimicrobials. In both cases, effective vaccines exist, even if with limited geographic availability.

Johne's disease (*Mycobacterium avium subsp. paratuberculosis*) was judged to entail medium use of antimicrobials. The condition is often undiagnosed or misdiagnosed, and maybe mistaken for other forms of bacterial enteritis. Vaccine availability is geographically limited, and existing products present several drawbacks. The Group agreed that DIVA vaccines would provide advantages for disease management, trade and movement of animals.

*Cryptosporidium parvum* and *Eimeria spp.* were viewed to provoke medium use of antimicrobial agents, being higher in regions where syndromic treatment is provided without relying on diagnostics. Currently, no vaccines are available. In a similar manner, helminths were also considered as contributing to inappropriate antimicrobial use, and this is likely to vary between different regions, depending on the quality of veterinary services. The Group agreed to assign helminths-vaccine research as a high priority because of the additional advantage of reducing anthelmintic resistance. *Trueperella pyogenes* was considered out of scope, due to the low use of antimicrobials at a global level, and/or the availability of effective vaccines. BVDV was also excluded, since there was an acknowledgement that BVDV is no longer considered an important enteric pathogen.

### Systemic

The Group discussed several pathogens causing infections of a systemic nature:

- *P. multocida* (Haemorrhagic septicaemia): Provokes high use of antimicrobials, even though the existing vaccines appear effective. Thus, research into vaccine for this agent was not deemed a priority;
- *Leptospira spp.*: Entails medium use of antimicrobials, and the Group observed that regional differences in serovars act to limited vaccine availability and use;
- *Bacillus anthracis*: Prophylactic antimicrobial treatment in affected herds is performed in some regions, leading to medium antimicrobial use, even though effective vaccines are available.

### Reproductive

Metritis/endometritis syndrome associated with *T. pyogenes*, *E. coli*, and *F. necrophorum* was considered. The Group agreed that this syndrome entails high use of antimicrobials, and that existing vaccines are not registered for metritis.

### Cutaneous

The Group discussed about *Dermatophilus congolensis* (rain scald), which causes severe skin infections in cattle. This pathogen entails medium use of antimicrobials under certain climatic conditions, and no vaccines are available.

### Vector-borne

Vector-borne pathogens in cattle were considered. *Anaplasma marginale* was considered a major contributor to antimicrobial use; vaccines are effective but have limitations in availability and administration. *Ehrlichia ruminantium* (heartwater) is present in several regions, where it imposes high antimicrobial use. High use of antimicrobials and absence of vaccine for *Trypanosoma spp.* were noted, and major research challenges were identified for vaccine development for these pathogens. Theileriosis (due to *T. parva* and *T. annulata*, depending on the region) is a major issue in some regions, where it causes high use of antimicrobials. Nevertheless, the impact on antimicrobial use at global level is medium. Vaccines are available for some but not all of the main *Babesia spp.* causing disease in cattle (*B. bigemia*, *B. divergens*, *B. bovis*), which entails a medium use of antimicrobials.

The Group highlighted that, in some regions, antimicrobial use is associated with tick infestation to control tick-borne pathogens. Vaccines exist against some individual tick species (*i.e. Rhipicephalus microplus*); vaccines against multiple species of ticks could be a useful tool for reducing antimicrobial use.

The Group also discussed several transboundary diseases, *i.e. Mycobacterium bovis*, *Brucella abortus*, bluetongue virus, foot-and-mouth disease virus, lumpy skin disease virus, and *Coxiella burnetii*, and agreed that antimicrobial treatment was largely uncommon for these diseases. Several *Clostridium* species were considered also, but were not addressed further for the same reason. Nevertheless, in some regions antimicrobial treatment might be applied (due to lack of diagnosis), but without major impact on antimicrobial use at global level.

Pathogens/diseases which entail high and medium use of antimicrobial agents in cattle are reported in Table 1. Other relevant pathogens/diseases which entail low use of antimicrobials are reported in Appendix IV.

**Table 1: Pathogens/diseases which entail high and medium use of antimicrobial agents and for which vaccines would significantly reduce the need for antibiotic use in cattle**

Key syndrome / Disease	Primary pathogen(s)	Antimicrobial Use [High, Medium, Low]	Commercial vaccine exists* [Yes/No]	Major constraints to use of vaccine / vaccine development	Vaccine Research Priority [High, Medium, Low]
<b>Respiratory</b>	<i>Mannheimia haemolytica</i> (Bovine Respiratory Disease Complex, BRD)	High	Yes	<ul style="list-style-type: none"> <li>Timely delivery (time of vaccination in relation to natural challenge)</li> <li>Onset of immunity (one dose versus two doses)</li> <li>Differences in serotype</li> <li>Potential lack of cross-protection</li> <li>Leukotoxin content in some vaccines is not controlled</li> </ul>	High
	<i>Pasteurella multocida</i> (BRD)	High	Yes	<ul style="list-style-type: none"> <li>Timely delivery</li> <li>Marginal efficacy</li> <li>Potential lack of cross-protection</li> </ul>	High
	<i>Mycoplasma mycoides subsp. mycoides small colony</i> (Contagious Bovine Pleuropneumonia, CBPP)	High	Yes	<ul style="list-style-type: none"> <li>Marginal efficacy</li> <li>Short duration of immunity</li> <li>Safety (live vaccine with residual virulence)</li> <li>Access limited to official control programmes</li> </ul>	High
	<i>Histophilus somni</i> (BRD)	High	Yes	<ul style="list-style-type: none"> <li>Timely delivery</li> <li>Adverse reactions when used in large combinations</li> <li>Basic research needed on epidemiology and pathogenesis</li> </ul>	Medium
	Bovine Virus Diarrhoea Virus (BRD)	High	Yes	<ul style="list-style-type: none"> <li>Timely delivery</li> <li>Maternal antibody interference</li> <li>Not all vaccines protect against Type 1 and Type 2, and Hobi-like viruses</li> </ul>	Medium
	<i>Mycoplasma bovis</i> (BRD)	Medium	Yes	<ul style="list-style-type: none"> <li>Timely delivery</li> <li>Limited efficacy</li> <li>Vaccine not available in all countries</li> <li>More research needed on epidemiology and pathogenesis</li> <li>Lack of challenge model</li> <li>Co-infections</li> </ul>	High
<b>Mastitis</b>	<i>Streptococcus agalactiae</i>	High	Yes	<ul style="list-style-type: none"> <li>Marginal efficacy</li> <li>Strain variation</li> <li>Lack of cross-protection</li> <li>Multiple doses needed for efficacy</li> </ul>	High
	<i>Streptococcus uberis</i>	High	Yes	<ul style="list-style-type: none"> <li>Marginal efficacy</li> <li>Strain variation</li> <li>Lack of cross-protection</li> <li>Multiple doses needed for efficacy</li> </ul>	High
	Coagulase negative <i>Staphylococci</i>	High	Yes	<ul style="list-style-type: none"> <li>Marginal efficacy</li> <li>Strain variation</li> <li>Lack of cross-protection</li> <li>Multiple doses needed for efficacy</li> </ul>	High
	<i>Staphylococcus aureus</i>	High	Yes	<ul style="list-style-type: none"> <li>Marginal efficacy</li> <li>Strain variation</li> <li>Lack of cross-protection</li> <li>Multiple doses needed for efficacy</li> </ul>	High

Key syndrome / Disease	Primary pathogen(s)	Antimicrobial Use [High, Medium, Low]	Commercial vaccine exists* [Yes/No]	Major constraints to use of vaccine / vaccine development	Vaccine Research Priority [High, Medium, Low]
Lameness (interdigital and digital dermatitis)	<i>Fusobacterium necrophorum</i>	High	Yes	<ul style="list-style-type: none"> <li>• Cost prohibitive</li> <li>• Limited efficacy</li> <li>• Limited availability</li> </ul>	High
Enteric	<i>Fusobacterium necrophorum</i>	High	Yes	<ul style="list-style-type: none"> <li>• No products labelled for this application. When used off-label, limited efficacy for enteric diseases/acidosis/liver abscess</li> </ul>	High
	<i>Salmonella enterica subsp. enterica</i>	High	Yes	<ul style="list-style-type: none"> <li>• Predominant serotypes (e.g. Typhimurium, Dublin) vary between geographic regions</li> <li>• Lack of cross-protection between serotypes</li> <li>• In dairy calves, exposure precedes onset of active immunity following vaccination</li> <li>• Limited availability</li> </ul>	Medium
	Enterotoxigenic <i>Escherichia coli</i>	High	Yes	<ul style="list-style-type: none"> <li>• Effective vaccines available for predominant strains</li> </ul>	Low
	Rotavirus	High	Yes	<ul style="list-style-type: none"> <li>• Reasonable efficacy of vaccine</li> <li>• Limited geographic availability</li> </ul>	Low
	Helminth enteric parasites	Medium	No	<ul style="list-style-type: none"> <li>• Need research in vaccine technology for multi-cellular parasites</li> </ul>	High
	<i>Cryptosporidium parvum</i>	Medium	No	<ul style="list-style-type: none"> <li>• Research and development investment needed</li> </ul>	Medium
	<i>Mycobacterium avium subspecies paratuberculosis</i> (Johne's disease)	Medium	Yes	<ul style="list-style-type: none"> <li>• Existing vaccines have safety and performance issues (including potential cross reactions on TB test)</li> <li>• Require new vaccine technologies</li> <li>• Need DIVA vaccine</li> <li>• User safety</li> <li>• Injection site reactions from experimental vaccines</li> <li>• Limited distribution</li> </ul>	Medium
	<i>Eimeria spp.</i>	Medium	No	<ul style="list-style-type: none"> <li>• Research and development investment needed</li> </ul>	Medium
	Bovine coronavirus	Medium	Yes	<ul style="list-style-type: none"> <li>• Satisfactory efficacy of vaccines</li> <li>• Limited geographic availability</li> </ul>	Low
Systemic	<i>Pasteurella multocida</i> (haemorrhagic septicaemia)	High	Yes	<ul style="list-style-type: none"> <li>• Satisfactory vaccines, but issues with availability</li> </ul>	Low
	<i>Leptospira spp.</i>	Medium	Yes	<ul style="list-style-type: none"> <li>• Limited efficacy, due to regional differences in serovars</li> </ul>	Medium
	<i>Bacillus anthracis</i> (anthrax)	Medium	Yes	<ul style="list-style-type: none"> <li>• Effective vaccines available</li> </ul>	Low
Reproductive	<i>Trueperella pyogenes</i>	High	No	<ul style="list-style-type: none"> <li>• No vaccine labelled for metritis</li> </ul>	High
	<i>Fusobacterium spp.</i>	High	No	<ul style="list-style-type: none"> <li>• No vaccine labelled for metritis</li> </ul>	High
	<i>Escherichia coli</i>	High	No	<ul style="list-style-type: none"> <li>• No vaccine labelled for metritis</li> </ul>	High
Cutaneous	<i>Dermatophilus congolensis</i> (rain scald)	Medium	No	<ul style="list-style-type: none"> <li>• Lack of a challenge model</li> <li>• Difficult to grow the pathogen for vaccine production</li> </ul>	Medium

Key syndrome / Disease	Primary pathogen(s)	Antimicrobial Use [High, Medium, Low]	Commercial vaccine exists* [Yes/No]	Major constraints to use of vaccine / vaccine development	Vaccine Research Priority [High, Medium, Low]
Vector-borne	<i>Anaplasma marginale</i>	High	Yes	<ul style="list-style-type: none"> <li>Vaccine production based on live animal infection</li> <li>Limited availability</li> <li>Difficult administration</li> <li>Adequate efficacy</li> </ul>	High
	<i>Ehrlichia ruminantium</i> (heartwater)	High	Yes	<ul style="list-style-type: none"> <li>Low production capacity</li> <li>Lack of strain specificity</li> <li>Vaccine production based on live animal infection</li> <li>Limited availability</li> <li>Difficult administration</li> <li>Adequate efficacy</li> </ul>	High
	<i>Trypanosoma spp.</i>	High	No	<ul style="list-style-type: none"> <li>Antigenic variation for African Animal Trypanosomosis (AAT)</li> </ul>	High
	Bluetongue virus	Medium	Yes	<ul style="list-style-type: none"> <li>Strain specific vaccine</li> <li>Partial cross-protection</li> <li>Potential reversion to virulence for live attenuated vaccines</li> <li>Caution for use in pregnant animals</li> </ul>	High
	<i>Babesia spp.</i>	Medium	Yes	<ul style="list-style-type: none"> <li>Vaccines not available for all species</li> <li>Low production capacity</li> <li>Vaccine production based on live animal</li> <li>Limited availability</li> <li>Difficult administration</li> <li>Adequate efficacy</li> </ul>	Medium
	<i>Theileria parva</i>	Medium	Yes	<ul style="list-style-type: none"> <li>Infection and treatment method (ITM) vaccine</li> <li>Adequate efficacy</li> <li>Difficult administration</li> <li>Residual virulence</li> <li>Limited availability</li> <li>Cost</li> </ul>	Medium
	<i>Theileria annulata</i>	Medium	Yes	<ul style="list-style-type: none"> <li>Cold chain required</li> <li>Low production capacity</li> <li>Limited availability</li> </ul>	Medium
	Ticks	Medium	Yes	<ul style="list-style-type: none"> <li>Limited species coverage</li> <li>Vaccine only available in limited countries</li> </ul>	Medium

\* does not cover autogenous vaccines

#### 6.4. Sheep Diseases

##### Respiratory

Ovine respiratory disease is a multifactorial disease attracting a high level of antimicrobial use in sheep, especially in grain-fed systems. *M. haemolytica* (regarded as a primary pathogen) and *P. multocida* (regarded as a primary or secondary pathogen) are the main agents involved, and attract a high use of antimicrobials. Most of the existing vaccines target both agents, but have marginal efficacy. *Mycoplasma ovipneumoniae* can also play an important role in the syndrome. In contrast to cattle, viral agents (*i.e.* PI3) were considered as lesser contributors.

The virus causing peste des petits ruminants (PPR) was considered. While PPR is a systemic disease, respiratory complications are one of the major clinical signs and thus antimicrobial agents are used. Vaccines are effective and safe. The experts highlighted that there was a relatively low use of vaccines in some endemic countries when there is low compliance with official programmes. DIVA and combination vaccines are available. Despite the impact of the disease, the Group agreed that its relevance in terms of research priority for development of vaccine to reduce antimicrobial use would be low.

## Mastitis

*Mycoplasma agalactiae*, one of the causal agents of classical contagious agalactia (an OIE listed disease), was considered. The disease is present in several regions and is becoming more widespread. While vaccines are available, the disease provokes medium antimicrobial use.

The main causal agents of sheep mastitis were considered to be *M. haemolytica*, Coagulase-negative *Staphylococci*, and *Staphylococcus aureus*. The Group agreed that antimicrobial use for this syndrome was generally medium in sheep, depending on the farming practices (*i.e.* higher in intensive production). Unlike cattle, vaccines for these causes of mastitis do exist and are effective. However, their uptake is low due to lack of awareness of vaccine options. While the Group recognised that there are other pathogens that could provoke mastitis in sheep, they have low impact on antimicrobial use, and so were not considered further.

## Lameness

Lameness is a priority issue for sheep production, and provokes significant use of antimicrobial agents. Ovine virulent footrot (*Dichelobacter nodosus*) was discussed: commercial multi-strain vaccines provide short duration and offer poor cross-serotype protection. However, farm-specific vaccines customised to one or two serogroups that are present, although expensive, provide highly effective immune response and can cure infected sheep. Research is underway to overcome interference resulting in short duration immunity induced by multi-strain vaccines, by developing a common-antigen vaccine. No vaccine is available for *F. necrophorum* (foot scald, foot abscess), provoking high use of antimicrobials. Vaccines exist for *Trueperella pyogenes* (foot scald), and *Corynebacterium pseudotuberculosis* (foot abscess), but have limited efficacy. Nevertheless, these diseases have less impact on antimicrobial use as compared to footrot.

## Enteric

Enterotoxigenic *E. coli* provoke high use of antimicrobials, especially for young sheep. Effective vaccines exist but appear to receive little use, since antimicrobials are convenient and used on a syndromic basis. Johne's disease (*M. avium subsp. paratuberculosis*) entails medium use of antimicrobials on account of it being mistaken for other forms of bacterial enteritis. Existing vaccines have user-safety issues and can provoke adverse reactions at the site of injection. The Group agreed that DIVA vaccines would perhaps assist in disease management and trade and movements of vaccinated animals. *Cryptosporidium parvum* and *Eimeria spp.* provoke medium use of antimicrobial agents. Helminths entail low use of antimicrobials, and were thus not considered by the Group. Unlike cattle, *F. necrophorum* and *S. enterica* entails lower use of antimicrobials, due to lower occurrence of disease due to these agents. Reasonably effective vaccines exist for rotavirus and *Clostridium perfringens*, which provoke low antimicrobials use.

## Systemic

Ovine caseous lymphadenitis (*Corynebacterium pseudotuberculosis*) was considered the only systemic disease for which antimicrobial use in sheep was high at a global level. While vaccines are available, their efficacy is variable.

Several other pathogens, for which a medium consumption of antimicrobials was identified, were considered (*i.e.* *Bibersteinia trehalosi*, *Pasteurella multocida*, *Campylobacter jejuni*, *Chlamydophila spp.*, and Sheep pox virus). Other pathogens (*i.e.* *C. burnetii*, *Salmonella abortusovis*, and *Brucella ovis*) were considered by the Group, and it was decided that they had a low priority due to the relatively low impact on antimicrobial use at global level.

## Vector-borne

Vector-borne pathogens in sheep were considered. *Ehrlichia ruminantium* (heartwater) is present in several regions, where it is believed to attract high antimicrobial use.

Bluetongue virus (BTV) was discussed. Antimicrobial agents are used early in bluetongue outbreaks, especially in countries where the viruses are endemic and a firm diagnosis of the cause of sickness is delayed. Current vaccination control is complicated by the diverse nature of BTV and the potential that

vaccines containing the relevant strains are not available in the country at the time of the outbreak. A cross-protective vaccine covering the full range of serotypes would help minimise antimicrobial use, but is technically challenging.

The impact of *Anaplasma phagocytophilum*, *Theileria spp.* of small ruminants, *Trypanosoma spp.*, and *Babesia spp.* on antimicrobial use was considered not significant, and these pathogens were not further discussed.

Reproductive syndromes were discussed by the Group, and it was agreed that none of the pathogens entailed sufficiently high antimicrobial use at a global level as to be further considered.

Pathogens/diseases which entail high and medium use of antimicrobial agents in sheep are reported in Table 2. Other relevant pathogens/diseases which entail low use of antimicrobials are report in [Appendix V](#).

**Table 2: Pathogens/diseases which entail high and medium use of antimicrobial agents and for which vaccines would significantly reduce the need for antibiotic use in sheep**

Key syndrome / Disease	Primary pathogen(s)	Antimicrobial Use [High, Medium, Low]	Commercial vaccine exists* [Yes/No]	Major constraints to use of vaccine / vaccine development	Vaccine Research Priority [High, Medium, Low]
<b>Respiratory</b>	<i>Mannheimia haemolytica</i>	High	Yes	<ul style="list-style-type: none"> <li>Timely delivery</li> <li>Onset of immunity (one dose versus two doses)</li> <li>Differences in serotype</li> <li>Potential lack of cross-protection between serotypes</li> <li>Leukotoxoid content in some vaccines is not controlled</li> </ul>	High
	<i>Pasteurella multocida</i>	High	Yes	<ul style="list-style-type: none"> <li>Timely delivery</li> <li>Marginal efficacy</li> <li>Potential lack of cross-protection</li> </ul>	High
	<i>Mycoplasma ovipneumoniae</i>	High	No	<ul style="list-style-type: none"> <li>Limited efficacy</li> <li>Lack of cross protection</li> </ul>	High
	Peste des petits ruminants virus	High	Yes	<ul style="list-style-type: none"> <li>Effective and safe vaccines available</li> <li>Need combination vaccines with other respiratory pathogens</li> <li>Relatively low use of vaccine in some endemic countries when official programmes have low compliance</li> <li>DIVA vaccines needed</li> </ul>	Low
<b>Mastitis</b>	<i>Mycoplasma agalactiae</i> (contagious agalactia)	Medium	Yes	<ul style="list-style-type: none"> <li>Live attenuated vaccine efficacious, inactivated vaccine suboptimal</li> <li>Potential reversion to virulence</li> <li>Notifiable disease</li> </ul>	Medium
	<i>Mannheimia haemolytica</i>	Medium	Yes	<ul style="list-style-type: none"> <li>Effective vaccine available</li> <li>Low demand for vaccine</li> <li>Lack of awareness</li> </ul>	Low
	Coagulase negative <i>Staphylococci</i>	Medium	Yes	<ul style="list-style-type: none"> <li>Effective vaccine available</li> <li>Strain variation</li> <li>Lack of cross-protection</li> <li>Multiple doses needed for efficacy</li> </ul>	Low
	<i>Staphylococcus aureus</i>	Medium	Yes	<ul style="list-style-type: none"> <li>Effective vaccine available</li> <li>Strain variation</li> <li>Lack of cross-protection</li> <li>Multiple doses needed for efficacy</li> </ul>	Low

Key syndrome / Disease	Primary pathogen(s)	Antimicrobial Use [High, Medium, Low]	Commercial vaccine exists* [Yes/No]	Major constraints to use of vaccine / vaccine development	Vaccine Research Priority [High, Medium, Low]
<b>Lameness</b>	<i>Dichelobacter nodosus</i> (ovine virulent footrot)	High	Yes	<ul style="list-style-type: none"> <li>Short duration of immunity</li> <li>No cross-serotype protection</li> <li>Vaccine antigen interference in large combination vaccines</li> <li>Cost prohibitive farm-specific mono-valent and bi-valent vaccines</li> <li>Vaccine only available in limited countries</li> </ul>	High
	<i>Fusobacterium necrophorum</i> (foot scald)	High	No	<ul style="list-style-type: none"> <li>Limited efficacy of experimental vaccines</li> </ul>	High
	<i>Trueperella pyogenes</i> (foot abscess)	Medium	Yes	<ul style="list-style-type: none"> <li>Limited efficacy</li> </ul>	Medium
	<i>Corynebacterium pseudotuberculosis</i> (foot abscess)	Medium	Yes	<ul style="list-style-type: none"> <li>Limited efficacy</li> </ul>	Medium
<b>Enteric</b>	Enterotoxigenic <i>Escherichia coli</i>	High	Yes	<ul style="list-style-type: none"> <li>Effective vaccines available for predominant strains</li> </ul>	Low
	<i>Mycobacterium avium</i> subspecies <i>paratuberculosis</i> (Johne's disease)	Medium	Yes	<ul style="list-style-type: none"> <li>Need DIVA vaccine</li> <li>User safety</li> <li>Injection site reactions</li> </ul>	Medium
	<i>Cryptosporidium parvum</i>	Medium	No	<ul style="list-style-type: none"> <li>Research and development investment needed</li> </ul>	Medium
	<i>Eimeria</i> spp.	Medium	No	<ul style="list-style-type: none"> <li>Research and development investment needed</li> </ul>	Medium
<b>Systemic</b>	<i>Corynebacterium pseudotuberculosis</i> , <i>C. spp.</i>	High	Yes	<ul style="list-style-type: none"> <li>Vaccines available, but variable efficacy</li> </ul>	Medium
	<i>Bibersteinia trehalosi</i>	Medium	Yes	<ul style="list-style-type: none"> <li>Lack of cross protection</li> </ul>	Medium
	<i>Pasteurella multocida</i> (haemorrhagic septicaemia)	Medium	Yes	<ul style="list-style-type: none"> <li>Limited availability</li> <li>Satisfactory efficacy</li> </ul>	Medium
	<i>Campylobacter jejuni</i>	Medium	Yes	<ul style="list-style-type: none"> <li>Limited efficacy</li> <li>Limited availability</li> </ul>	Medium
	<i>Chlamydophila</i> spp.	Medium	Yes	<ul style="list-style-type: none"> <li>Satisfactory efficacy</li> <li>Caution for use in pregnant animals</li> <li>Vaccine covers <i>C. abortus</i></li> </ul>	Low
	Sheep Pox Virus	Medium	Yes	<ul style="list-style-type: none"> <li>Satisfactory efficacy in sheep</li> </ul>	Low
<b>Vector-borne</b>	<i>Ehrlichia ruminantium</i> (heartwater)	High	Yes	<ul style="list-style-type: none"> <li>Low production capacity</li> <li>Lack of strain specificity</li> <li>Vaccine production based on live animal infection</li> <li>Limited availability</li> <li>Difficult administration</li> <li>Adequate efficacy</li> </ul>	High
	Bluetongue virus	Medium	Yes	<ul style="list-style-type: none"> <li>Strain specific vaccine</li> <li>Partial cross-protection</li> <li>Potential reversion to virulence for live attenuated vaccines</li> <li>Caution for use in pregnant animals</li> </ul>	High

\* does not cover autogenous vaccines

## 6.5. Goat Diseases

### Respiratory

Caprine respiratory disease is a multifactorial disease resulting in high level of antimicrobial use. *M. haemolytica* (regarded as a primary pathogen) and *P. multocida* (regarded as a primary or secondary pathogen) are the main agents involved, and these attract high use of antimicrobials. Most of the vaccines target both agents, but are limited in availability and/or efficacy. There is maybe some variation in breed resistance to *M. haemolytica*, occurring in some regions. Similar to sheep, viral agents (*i.e.* PI3) were considered as lesser contributors to disease occurrence in goats.

Contagious Caprine Pleuropneumonia (caused by *Mycoplasma capricolum subsp. capripneumoniae*) was discussed as important cause of respiratory disease in some regions, and as provoking high use of antimicrobials. While vaccines are generally considered as efficacious, there are issues of suboptimal potency, efficacy and supply. Other small-ruminant *Mycoplasma* species complicate the epidemiology of the disease.

Peste des petits ruminants virus causes systemic disease in goats, but respiratory complications are a major feature and cases might be treated with antimicrobials. While vaccines are effective and safe, there is relatively low use of vaccines in some endemic regions, where official programmes have low compliance. DIVA and combination vaccines are available.

### Mastitis

The main causal agents of goat mastitis were considered: *M. agalactiae*, *Mycoplasma mycoides subsp. capri*, *Mycoplasma capricolum*, *Mycoplasma putrefaciens*, *M. haemolytica*, Coagulase negative *Staphylococci*, and *S. aureus*. The Group agreed that antimicrobial use for this syndrome was generally medium in goats, depending on the farming practices (higher in intensive production). Except for mycoplasmas, vaccines are mostly available and effective, but the uptake is low due to lack of awareness of vaccine options. Although antimicrobial use is medium for mycoplasmas, therapy has low effectiveness and could lead to establishment of carrier status. While the Group recognised that there are other pathogens that could provoke mastitis in goats, they have low impact on antimicrobial use, and were not discussed further.

### Lameness

Lameness is a priority issue for goat production, provoking significant use of antimicrobial agents. Vaccines for virulent footrot (*D. nodosus*) for goats are not available, and sheep vaccine causes severe reactions when administered to goats. No vaccine is also available for *F. necrophorum*, which is the only pathogen entailing high antimicrobial use. As for sheep, vaccines exist for *T. pyogenes* (foot scald, foot abscess) and *C. pseudotuberculosis* (foot abscess) but present efficacy limitations. However, these pathogens have a lower impact on antimicrobial use as compared to footrot.

### Enteric

Enteric diseases of goats were considered. This syndrome was not recognised as being a major cause of antimicrobial use in goats. *Eimeria spp.* provoke medium use of antimicrobial agents. Johne's disease (*M. avium subsp. paratuberculosis*) entails low use of antimicrobials. Helminths entail low use of antimicrobials, and were therefore not considered.

### Systemic

Similar to sheep, *Corynebacterium pseudotuberculosis* was considered the only systemic pathogen for which high antimicrobial use occurs for goats. Suboptimal efficacy of the available vaccines was recognised as an issue in this species. Several other pathogens, attracting medium consumption of antimicrobials, were considered (*i.e.* *B. trehalosi*, *C. jejuni*, *Chlamydophila spp.*, and Goat pox virus). In the case of *C. burnetii*, low antimicrobial use excluded it from further consideration.

### Vector-borne

Vector-borne pathogens in goats were considered. Only *Ehrlichia. ruminantium* (heartwater) was considered as having a significant impact on antimicrobial use.

Reproductive syndromes were discussed by the Group. It was agreed that none of the pathogens entailed antimicrobial use high enough at a global level as to be further considered.

Pathogens/diseases which entail high and medium use of antimicrobial agents in goats are reported in Table 3. Other relevant pathogens/diseases which entail low use of antimicrobials are report in [Appendix VI](#).

**Table 3: Pathogens/diseases which entail high and medium use of antimicrobial agents and for which vaccines would significantly reduce the need for antibiotic use in goats**

Key syndrome / Disease	Primary pathogen(s)	Antimicrobial Use [High, Medium, Low]	Commercial vaccine exists* [Yes/No]	Major constraints to use of vaccine / vaccine development	Vaccine Research Priority [High, Medium, Low]
Respiratory	<i>Mannheimia haemolytica</i>	High	Yes	<ul style="list-style-type: none"> <li>Timely delivery</li> <li>Onset of immunity (one dose versus two doses)</li> <li>Differences in serotype</li> <li>Potential lack of cross-protection</li> <li>Leukotoxoid content in some vaccines is not controlled</li> </ul>	High
	<i>Pasteurella multocida</i>	High	Yes	<ul style="list-style-type: none"> <li>Timely delivery</li> <li>Marginal efficacy</li> <li>Potential lack of cross-protection</li> </ul>	High
	<i>Mycoplasma capricolum subsp. capripneumoniae</i> (Contagious caprine pleuropneumonia, CCPP)	High	Yes	<ul style="list-style-type: none"> <li>Suboptimal production process (low yield)</li> <li>Vaccine is efficacious, but issues of suboptimal potency</li> <li>Other small ruminant <i>Mycoplasma spp.</i> complicate epidemiology</li> </ul>	High
	Peste des Petits Ruminants Virus (PPR)	High	Yes	<ul style="list-style-type: none"> <li>Effective and safe vaccines available</li> <li>Need combination vaccines with other respiratory pathogens</li> <li>Relatively low use of vaccine in some endemic countries, when official programmes have low compliance</li> <li>DIVA vaccine needed</li> </ul>	Low
Mastitis	<i>Mycoplasma agalactiae</i>	Medium	Yes	<ul style="list-style-type: none"> <li>Live attenuated vaccine efficacious, inactivated vaccine suboptimal</li> <li>Potential reversion to virulence</li> <li>Notifiable disease</li> <li>Carrier animals</li> </ul>	Medium
	<i>Mycoplasma mycoides subsp. capri</i>	Medium	No	<ul style="list-style-type: none"> <li>Limited efficacy of experimental vaccines</li> </ul>	Medium
	<i>Mycoplasma capricolum</i>	Medium	No	<ul style="list-style-type: none"> <li>Limited efficacy of experimental vaccines</li> </ul>	Medium
	<i>Mycoplasma putrefaciens</i>	Medium	No	<ul style="list-style-type: none"> <li>Limited efficacy of experimental vaccines</li> </ul>	Medium
	<i>Mannheimia haemolytica</i>	Medium	Yes	<ul style="list-style-type: none"> <li>Effective vaccine available</li> <li>Low demand for vaccine</li> <li>Lack of awareness</li> </ul>	Low
	Coagulase negative <i>Staphylococci</i>	Medium	Yes	<ul style="list-style-type: none"> <li>Effective vaccine available</li> <li>Strain variation</li> <li>Lack of cross-protection</li> <li>Multiple doses needed for efficacy</li> </ul>	Low
	<i>Staphylococcus aureus</i>	Medium	Yes	<ul style="list-style-type: none"> <li>Effective vaccine available</li> <li>Strain variation</li> <li>Lack of cross-protection</li> <li>Multiple doses needed for efficacy</li> </ul>	Low

Key syndrome / Disease	Primary pathogen(s)	Antimicrobial Use [High, Medium, Low]	Commercial vaccine exists* [Yes/No]	Major constraints to use of vaccine / vaccine development	Vaccine Research Priority [High, Medium, Low]
<b>Lameness</b>	<i>Fusobacterium necrophorum</i> (foot scald)	High	No	• Limited efficacy of experimental vaccines	High
	<i>Dichelobacter nodosus</i> (virulent footrot)	Medium	No	• Severe reactions to sheep vaccine	High
	<i>Trueperella pyogenes</i> (foot abscess)	Medium	Yes	• Limited efficacy	Medium
	<i>Corynebacterium pseudotuberculosis</i> (foot abscess)	Medium	Yes	• Limited efficacy	Medium
<b>Enteric</b>	<i>Eimeria spp.</i>	Medium	No	• Research and development investment needed	Medium
<b>Systemic</b>	<i>Corynebacterium pseudotuberculosis</i> , <i>C. spp.</i>	High	Yes	• Vaccines available, but variable efficacy	Medium
	<i>Bibersteinia trehalosi</i>	Medium	Yes	• Lack of cross protection	Medium
	<i>Campylobacter jejuni</i>	Medium	Yes	• Limited efficacy • Limited availability	Medium
	<i>Chlamydophila spp.</i>	Medium	Yes	• Satisfactory efficacy • Caution for use in pregnant animals • Vaccine covers <i>C. abortus</i>	Low
	Goat pox virus	Medium	Yes	• Satisfactory efficacy in goats	Low
<b>Vector-borne</b>	<i>Ehrlichia ruminantium</i> (heartwater)	High	Yes	• Low production capacity • Lack of strain specificity • Vaccine production based on live animal infection • Limited availability • Difficult administration • Adequate efficacy	High

\* does not cover autogenous vaccines

## 7. Agree on an overall priority list of animal diseases where availability of vaccines could reduce the use of antimicrobials taking into account technical and financial constraints to vaccine usage

The Group emphasised that there was a fundamental need for significant investment to use cutting-edge technologies to address the significant gaps in the available vaccines needed to address antimicrobial resistance.

It was also recognised that Public-Private-Partnerships would be essential to bridge researchers and vaccine manufacturers to achieve the above goal.

The Group agreed that effective vaccines for the diseases listed in Tables 1-3 could substantially reduce the use of antimicrobial agents in cattle, sheep, and goats. It was acknowledged that notable scientific and technical hurdles exist. However, an overarching investment in vaccine research could have a significant impact, particularly if the research addressed the following seven gaps (not listed in order of priority):

1. Efficacy consistent with control needs;
2. Maternal antibody interference;
3. Cross-protection or inclusion of relevant strains in vaccine formulations;
4. Occurrence of immunological interference in multivalent vaccines;
5. Induction of mucosal immunity for respiratory, enteric and mastitis pathogens;

6. Duration of immunity;
7. Onset of immunity.

## **8. Any other issues**

The Group recommended that communication of the outcomes of the Group should be pursued apart from the publication of the final report.

The Group suggested the report be distributed for consideration to funders of research, global animal health research organisations (*e.g.*, STAR-IDAZ IRC), and that global vaccine research networks be supported to pool resources and expertise to address gaps for each of the priority diseases listed in Tables 1-3.

It was acknowledged that in some regions, even if vaccines are available, the lack of defined vaccination programme makes the uptake of such tools limited.

## **9. Finalisation and endorsement of the draft report**

The Group adopted the report.

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.../Appendices

**AD HOC GROUP ON PRIORITISATION OF DISEASES  
FOR WHICH VACCINES COULD REDUCE ANTIMICROBIAL USE IN CATTLE, SHEEP, AND GOATS  
Paris, 7 – 9 May 2018**

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**Agenda**

1. Opening
2. Appointment of chairperson and rapporteurs
3. Background of the meeting
4. Review and address the Terms of reference for the *ad hoc* Group meeting
5. Refine template and criteria for the ranking of diseases
6. Rank diseases for the two focus areas
  - a. Cattle diseases
  - b. Sheep and goat diseases
7. Agree overall priority list of animal diseases where availability of vaccines could reduce the use of antimicrobials taking into account technical and financial constraints to vaccine usage
8. Any other issues
9. Finalisation and endorsement of the draft report

**AD HOC GROUP ON PRIORITISATION OF DISEASES**  
**FOR WHICH VACCINES COULD REDUCE ANTIMICROBIAL USE IN CATTLE, SHEEP, AND GOATS**  
**Paris, 7 – 9 May 2018**

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**AD HOC GROUP ON PRIORITISATION OF DISEASES  
FOR WHICH VACCINES COULD REDUCE ANTIMICROBIAL USE IN CATTLE, SHEEP, AND GOATS  
Paris, 7 – 9 May 2018**

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**Terms of Reference**

**Background**

To address the threat of antimicrobial resistance, the WHO with the support of the OIE and FAO drafted a Global Action Plan on Antimicrobial Resistance. In the development of this plan, the use of vaccines to prevent diseases and to reduce the prevalence of infections was considered as being one of the possible options to reduce the use of antimicrobial agents at the global level.

The OIE convened, in 2015, an *ad hoc* Group to provide guidance on the prioritisation of diseases for which the use of already available and new vaccines could reduce antimicrobial use in animals, as well as to make recommendations for targeted research programmes for improved and new vaccines. The *ad hoc* Group focussed its activities on chickens, swine and fish. To complete this work, the OIE has agreed to convene a second *ad hoc* Group to prioritise diseases for which vaccines could reduce antimicrobial use in domestic ruminants (cattle, sheep, and goats).

**Purpose**

The *ad hoc* Group will provide guidance on prioritisation of diseases for which the use of already available and new vaccines could reduce antimicrobial use in domestic ruminants (cattle, sheep, and goats).

**Terms of Reference**

1. Consider diseases for which the availability and use of appropriate vaccines could reduce antimicrobial use in domestic ruminants (cattle, sheep, and goats).
2. Rank bacterial and non-bacterial diseases in domestic ruminants (cattle, sheep, and goats) by animal group, which cause the highest use of antimicrobials in the animal species concerned.
3. Refine the ranking by considering relevant factors impacting vaccine development, effectiveness or implementation of vaccination (examples could include but are not limited to the feasibility to develop vaccines, factors affecting the effectiveness of vaccines, such as number of implicated pathogens/strains, specific host immune reactions, general immune status related factors, or other factors that might reduce implementation of vaccination, such as current vaccine costs).

**Expected output of the *ad hoc* Group**

The development of a list of ranked priority diseases to guide research on vaccine development or improvement for domestic ruminants (cattle, sheep, and goats) with the overall aim of decreasing the use of antimicrobial agents at the global level.

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**Table 1 - Appendix. Pathogens/diseases which entail low use of antimicrobial agents and for which vaccines would reduce the need for antibiotic use in cattle**

Key syndrome / Disease	Primary pathogen(s)	Antimicrobial Use [High, Medium, Low]	Commercial * vaccine exists [Yes/No]	Major constraints to use of vaccine / vaccine development	Vaccine Research Priority [High, Medium, Low]
<b>Respiratory</b>	Parainfluenza-3 virus (Bovine Respiratory Disease Complex, BRD)	Low	Yes	<ul style="list-style-type: none"> <li>Adequate efficacy, relative to the impact of the disease</li> </ul>	Low
	Bovine Herpesvirus-1 / Infectious Bovine Rhinotracheitis (IBR) virus (BRD)	Low	Yes	<ul style="list-style-type: none"> <li>Adequate efficacy and safety</li> <li>DIVA vaccine available</li> <li>Eradicated from some countries in Europe</li> </ul>	Low
	Bovine Respiratory Syncytial Virus (BRD)	Low	Yes	<ul style="list-style-type: none"> <li>Adequate efficacy and safety relative to the impact of the disease – sufficient to prevent secondary bacterial infection</li> </ul>	Low
	Bovine Coronavirus (BRD)	Low	Yes	<ul style="list-style-type: none"> <li>Emerging respiratory pathogen</li> <li>Originally developed for enteric disease. Efficacy not fully established for BRD</li> <li>More research needed on epidemiology and pathogenesis</li> </ul>	Low
	<i>Dictyocaulus viviparus</i>	Low	Yes	<ul style="list-style-type: none"> <li>Live irradiated larvae</li> </ul>	Low
<b>Mastitis</b>	<i>Escherichia coli</i>	Low	Yes	<ul style="list-style-type: none"> <li>Marginal efficacy</li> <li>Multiple doses needed for efficacy</li> </ul>	Low
	<i>Mycoplasma bovis</i>	Low	No	<ul style="list-style-type: none"> <li>Vaccines for respiratory disease available, but not effective for mastitis</li> </ul>	Low
<b>Lameness (interdigital and digital dermatitis)</b>	<i>Trueperella pyogenes</i>	Low	No	<ul style="list-style-type: none"> <li>Uncertain role of organism in disease and production loss</li> <li>Limited efficacy (experimental vaccines)</li> </ul>	Low
	<i>Treponema spp.</i>	Low	No	<ul style="list-style-type: none"> <li>Uncertain role of organism in disease and production loss</li> <li>Limited efficacy (experimental vaccines)</li> </ul>	Low
<b>Enteric</b>	<i>Clostridium perfringens</i>	Low	Yes	<ul style="list-style-type: none"> <li>Vaccines have satisfactory efficacy</li> </ul>	Low

\* does not cover autogenous vaccines

**Table 2 - Appendix Pathogens/diseases which entail low use of antimicrobial agents and for which vaccines would reduce the need for antibiotic use in sheep**

Key syndrome / Disease	Primary pathogen(s)	Antimicrobial Use [High, Medium, Low]	Commercial vaccine exists* [Yes/No]	Major constraints to use of vaccine / vaccine development	Vaccine Research Priority [High, Medium, Low]
<b>Respiratory</b>	Parainfluenza-3 virus	Low	Yes	<ul style="list-style-type: none"> <li>Adequate efficacy relative to the impact of the disease</li> </ul>	Low
<b>Enteric</b>	<i>Fusobacterium necrophorum</i>	Low	No	<ul style="list-style-type: none"> <li>Vaccine available for footrot, but not labelled for this application</li> </ul>	Low
	<i>Salmonella enterica subsp. enterica</i>	Low	Yes	<ul style="list-style-type: none"> <li>Effective vaccines available but low use, due to low prevalence of disease</li> <li>Dominant serotypes vary between geographic regions</li> <li>Lack of cross-protection</li> <li>Limited availability</li> </ul>	Low
	<i>Clostridium perfringens</i>	Low	Yes	<ul style="list-style-type: none"> <li>Vaccines have satisfactory efficacy</li> </ul>	Low
	Rotavirus	Low	Yes	<ul style="list-style-type: none"> <li>Reasonable efficacy of vaccine</li> <li>Limited geographic availability*</li> </ul>	Low
<b>Systemic</b>	<i>Coxiella burnetii</i>	Low	Yes	<ul style="list-style-type: none"> <li>Available in few countries</li> <li>Satisfactory efficacy</li> <li>Cost prohibitive</li> </ul>	Low
	<i>Salmonella abortusovis</i>	Low	No	<ul style="list-style-type: none"> <li>Disease present in few countries</li> </ul>	Low
	<i>Brucella ovis</i>	Low	Yes	<ul style="list-style-type: none"> <li>Satisfactory efficacy</li> <li>Caution in use for older animals that will test positive</li> </ul>	Low

\* does not cover autogenous vaccines

**Table 3 - Appendix Pathogens/diseases which entail low use of antimicrobial agents and for which vaccines would reduce the need for antibiotic use in goats**

Key syndrome / Disease	Primary pathogen(s)	Antimicrobial Use [High, Medium, Low]	Commercial * vaccine exists [Yes/No]	Major constraints to use of vaccine / vaccine development	Vaccine Research Priority [High, Medium, Low]
<b>Respiratory</b>	Parainfluenza-3 virus	Low	Yes	<ul style="list-style-type: none"> <li>• Adequate efficacy, relative to the impact of the disease</li> </ul>	Low
<b>Enteric</b>	<i>Mycobacterium avium subspecies paratuberculosis</i> (Johne's disease)	Low	Yes	<ul style="list-style-type: none"> <li>• Vaccination may interfere with diagnostic tests for Johne's disease</li> <li>• Strong reaction with <i>Mycobacterium spp.</i></li> </ul>	Low
<b>Systemic</b>	<i>Coxiella burnetii</i>	Low	Yes	<ul style="list-style-type: none"> <li>• Available in few countries</li> <li>• Satisfactory efficacy</li> <li>• Cost prohibitive</li> </ul>	Low

\* does not cover autogenous vaccines

