UNIVERSIDADE DE LISBOA

Faculdade de Medicina Veterinária

THE ECONOMIC IMPACT AND CONTROL MEASURES OF BOVINE RESPIRATORY DISEASE – A QUALITATIVE APPROACH

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“Um navio aportado está seguro, mas não é para isso que os navios são feitos.”

“A ship in harbor is safe, but that is not what ships are built for.”

Grace Hopper

“Cai sete vezes, levanta-te oito.”

Provérbio Japonês

“Fall seven times, stand up eight.”

Japanese Proverb

The Economic Impact and Control Measures of Bovine Respiratory Disease – A Qualitative Approach

Abstract

Bovine Respiratory Syncytial Virus (BRSV) is a well-known cattle virus, and a key intervenient in the genesis of Bovine Respiratory Disease (BRD). Given its importance, the development of a DIVA vaccine has been established as one of the objectives of a European research project named SAPHIR. BRD is one of the most widespread and costly cattle diseases worldwide but, despite the recognition of its relevance and the substantial investments made in control expenditures, there is still a considerable lack of knowledge concerning its actual economic impact in the dairy and meat cattle value chain. With the objective of collecting primary data concerning epidemiology, presence of risk factors, production losses and expenditures in BRD prevention and treatment on Portuguese farms, two questionnaires were developed and implemented using a convenience sample of five dairy and five meat farms. This case study led to the conclusion that, despite being present in the majority of the farms surveyed, there seems to be an over-all lack of data concerning the quantification of BRD's economic impacts in primary production, regardless of their recognition and considerable expenditures on medical and prophylactical tools. As proposed, the case study allowed for the identification of gaps concerning BRD and its management, with future work needing to be focused on obtaining a deeper knowledge regarding the meat cattle value chain, evaluating the existence of detailed treatment and vaccination records at farm level, as well as accurate disease prevalence and incidence, and quantification of existing production losses. Considerable control expenditures were also seen in a case study conducted by researchers from the Royal Veterinary College under the SAPHIR project. Despite their presence at farm level, it seems rather difficult to establish a direct correlation between risk factors and disease presence and magnitude. This finding reflects the complex multifactorial nature of BRD, and was transversal to both studies.

Key words: Bovine Respiratory Syncytial Virus; Bovine Respiratory Disease; cattle; economic impact.

O Impacto Económico e Medidas de Controlo da Doença Respiratória Bovina – Uma Abordagem Qualitativa

Resumo

O Vírus Respiratório Sincicial Bovino (BRSV) é um dos vírus bovinos de maior relevo, e um interveniente chave na génese da Doença Respiratória Bovina (DRB). Dada a sua importância, o desenvolvimento de uma vacina DIVA foi estabelecido como um dos objetivos de um projeto de investigação Europeu denominado SAPHIR. A DRB é uma das mais difundidas e dispendiosas doenças dos bovinos mas, apesar do reconhecimento da sua relevância e de substanciais investimentos visando o seu controlo, existe ainda uma considerável falta de conhecimento no que toca ao seu impacto económico concreto na cadeia de valor de bovinos de leite e carne. Com o objetivo de recolher dados acerca da epidemiologia, presença de fatores de risco, perdas produtivas e despesas em termos de prevenção e tratamento da DRB em explorações Portuguesas, dois questionários foram desenvolvidos e implementados numa amostra de conveniência constituída por cinco explorações de bovinos de leite e cinco explorações de bovinos de carne. Este estudo de caso permitiu concluir que, embora a DRB esteja presente na maioria das explorações inquiridas há, de forma generalizada, uma falta de informação no que toca à quantificação dos seus impactos económicos na produção primária, apesar do seu reconhecimento e de despesas consideráveis em ferramentas médicas e profiláticas. Como fora proposto, este estudo de caso permitiu identificar lacunas no que toca à DRB e seu maneio, com trabalho futuro a dever focar-se no aprofundamento do conhecimento relativamente à cadeia de valor da carne bovina, averiguação de existência de registos detalhados de tratamento e vacinações nas explorações, valores precisos de prevalência e incidência da doença e quantificação das perdas produtivas existentes. Despesas consideráveis no controlo da DRB foram igualmente observadas num estudo de caso conduzido por investigadores do Royal Veterinary College ao abrigo do projeto SAPHIR. Apesar da sua presença ao nível das explorações, revela-se bastante difícil estabelecer uma correlação direta entre fatores de risco e a presença e magnitude da doença. Este resultado reflete a natureza complexa e multifatorial da DRB, tendo sido transversal a ambos os estudos.

Palavras-Chave: Vírus Respiratório Sincicial Bovino; Doença Respiratória Bovina; gado bovino; impacto económico.

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Abbreviations and Symbols List

AI	Artificial Insemination
ADG	Average Daily Gain
BCoV	Bovine Coronavirus
BHV-1	Bovine Herpesvirus Type 1
PI_3V	Bovine Parainfluenza-3 Virus
BRD	Bovine Respiratory Disease
BRSV	Bovine Respiratory Syncytial Virus
BVDV	Bovine Viral Diarrhoea Virus
BAL	Bronchoalveolar Lavage
CFR	Case Fatality Rate
ºC	Degree Celsius
DIVA	Differentiating Infected from Vaccinated Animals
$	Dollar
ELISA(s)	Enzyme-Linked Immunosorbent Assay(s)
€	Euro
EU	European Union
FMV-ULisboa	Faculdade de Medicina Veterinária - Universidade de Lisboa
FCR	Feed Conversion Ratio
Ha	Hectares
HRSV	Human Respiratory Syncytial Virus
IgA	Immunoglobulin A
IgE	Immunoglobulin E
IgG	Immunoglobulin G
IgM	Immunoglobulin M
IBR	Infectious Bovine Rhinotracheitis
ISO	International Organization of Standardization
Kg	Kilogram
NSAID(s)	Nonsteroidal Anti-Inflammatory Drug(s)
NUTS	Nomenclature of Territorial Units for Statistics
PCR	Polymerase Chain Reaction
£	Pound
Lb	Pound-mass
®	Registered Trademark
RT-PCR	Reverse Transcription Polymerase Chain Reaction
RNA	Ribonucleic Acid
RVC	Royal Veterinary College
SID	*semel in die*
SCC	Somatic Cell Count
m^2	Square meters
SAPHIR	Strengthening Animal Production and Health through the Immune Response
SARA	Subacute Ruminal Acidosis
UK	United Kingdom

INTRODUCTION

Bovine Respiratory Syncytial Virus (BRSV) is one of the most well-known viruses of cattle, being endemic in most countries, and a causal agent of disease in both dairy and meat herds. Despite its ability to cause disease *per se*, its most important role is as the main viral agent of the scourge that is Bovine Respiratory Disease (BRD). BRD is one of the most studied cattle health problems worldwide, with considerable investments being made towards the minimization of its negative impacts on production. However, and despite the abundant documented knowledge of BRD, this disease continues to be one of the biggest challenges faced by the sector. The multifactorial nature of BRD, with several pathogens, environmental and management risk factors may help explain this fact, in addition to the increased intensification of bovine production, which makes it even more difficult to achieve an effective control. Much emphasis has been put on pharmacological control of this disease, with new molecules being released both in terms of antimicrobials and vaccines. Concerning vaccines, their beneficial effect on BRD prevention, if included in a holistic disease approach, is unquestionable. However, and especially considering BRSV, their field efficacy is far from consensual, and there is still margin for further development. Due to this fact, and as a reflection of this virus's importance in the establishment of respiratory disease in cattle, the development of a marked BRSV vaccine has been included as one of the goals of a European research project named SAPHIR, which stands for "Strengthening Animal Production and Health through the Immune Response". The project is still at an early phase, and one of its multidisciplinary foundations is the economic evaluation of the impacts BRSV has on bovine production, as well as the assessment of already existent BRSV-control methods. The Royal Veterinary College (RVC) in London is an active participant in this task and, during the author`s internship at the RVC from January to March of 2016, it was possible to collaborate on a literature review concerning the subject, which was afterwards approved by a panel of experts and whose preliminary results are presented on Annex I. The initial part of this internship, undertaken at the Faculdade de Medicina Veterinária - Universidade de Lisboa (FMV-ULisboa) in Lisbon also encompassed a literature review about BRSV and its impacts, with special focus on its reality in Portugal. The information available proved to be very scarce, despite some data pointing towards a significant BRSV prevalence in Portuguese dairy and meat bovine herds, as well as to the use of vaccines against the virus[1].

[1] Given this paucity of information concerning not just the economic impact of BRSV but of BRD as a whole, a review article of the subject was compiled in a paper submitted to the Revista Portuguesa de Ciências Veterinárias in early 2016.

Given the complex interaction BRSV has with all the other infectious and non-infectious factors involved in the aetiology of BRD, it proves very difficult to attribute specific economic impacts to BRSV alone, and therefore this work proposes to present its economic impact in the context of BRD. It should be noticed that estimating the economic impact of a certain disease is the pillar to evaluate the benefits that can potentially arise from its control, and serves to justify investments such as vaccines, like what is being done under the SAPHIR project. Therefore, the structure of this thesis will be as follows:

- A review of the current knowledge concerning BRSV, followed by its contextualization in BRD and a review of the different forms BRD can assume on both the dairy and the meat sectors;
- A brief description of cattle populations, production data, number and dimension of holdings, as well as dairy and veal/beef production systems in Portugal and the UK was considered pertinent, especially since some risk factors concerning BRD are practically indissociable from intrinsic aspects of certain production systems;
- The importance and implications of economics in the study of animal disease and its control is discussed afterwards, followed by the compilation of production losses and expenditures due to the presence of BRD in the dairy and meat sectors, culminating in a model that presents the impact of BRD on the dairy and meat bovine production chains, as well as data required for the quantification of this impact;
- With the objective of collecting primary data concerning the presence and economic impacts BRD has on Portuguese dairy and meat herds, two questionnaires were developed and implemented in a small sample of farms. The methodology for their development, as well as main results, are presented in Chapter VI;
- In the final chapter, besides drawing out some conclusions about the present work, we also look at what can be done in the future towards BRD's control, with focus on some aspects concerning BRSV.

CHAPTER I: Bovine Respiratory Syncytial Virus Infection

1.1. The Virus

BRSV is a virus belonging to the *Paramyxoviridae* family and *Pneumovirus* genus, and has been recognized as an important agent of respiratory disease in both beef and dairy cattle since its discovery in Switzerland in 1970 (Schreiber et al., 2000; Alm, Koskinen, Vahtiala & Andersson, 2009; Sarmiento-Silva, Nakamura-Lopez & Vaughan, 2012). It is acknowledged as an important causal agent of respiratory disease in dairy calves, nursing beef calves and feedlot calves, but its relevance extends to adult cattle as well (Baker, Ellis & Clark 1997; Hägglund, 2005). As with other syncytial viruses, its name derives from the characteristic cytopathic effect observed both *in vivo* and *in vitro*, the formation of syncytium, multinucleated cells derived from the fusion of various cells (Baker et al., 1997).

BRSV is a negative sense, single-stranded RNA enveloped virus, with the viral genome encoding for 11 proteins: the large attachment glycoprotein (G), the fusion protein (F), the small hydrophobic protein (SH), the matrix protein (M), the nucleoprotein (N), the phosphoprotein (P), the RNA polymerase (L), the M2-1 and M2-2 proteins, and two non-structural proteins, NS1 and NS2 (Taylor, 2008; Guzman & Taylor, 2015). The F and G proteins seem to be the most relevant in the development of protective immunity, since neutralizing antibodies are mainly directed at these two proteins (Nettleton et al., 2003; Blodörn, 2015). BRSV exhibits limited genetic variation, especially concerning the F protein, which stands in favour of cattle vaccination. Furthermore, the lipid envelope makes the virus frail outside the host, and sensible to common detergents (Hägglund & Valarcher, 2015). The virus is very closely related to Human Respiratory Syncytial Virus (HRSV), with similarities in terms of epidemiology and pathogenesis allowing the use of calf models infected by BRSV in studies concerning HRSV. Reversely, the study of the human virus has provided valuable information concerning the disease in bovine populations. There are also similar syncytial viruses that affect other animal populations, like ovines and caprines (Baker, 1991; Baker et al., 1997; Valarcher & Taylor, 2007; Gershwin, 2012; Stilwell, 2013).

Apart from being a primary disease agent, BRSV can predispose to secondary bacterial infections by *Mannheimia haemolytica*, *Pasteurella multocida*, *Histophilus somni* and *Mycoplasma bovis*, culminating in the development of BRD (Valarcher & Taylor, 2007; Klem, Tollersrud, Osterås & Stokstad, 2014; Sacco, McGill, Pillatzki, Palmer & Ackermann, 2014;). Reported values point to up to 40% of viral infections being complicated by secondary bacterial infections (Klem, Kjæstad, Kummen, Holen & Stokstad, 2016). In fact, BRSV has been acknowledged as the main viral component of BRD, mainly due to its high seroprevalence but also to the strong association between viral infection and the development of respiratory disease (Larsen, Tegtmeier & Pedersen, 2001; Blodörn et al., 2015).

1.2. Epidemiology

BRSV is a ubiquitous virus, having been isolated in bovine herds in Europe, America and Asia with seroprevalences that range between 30% and 100% both in dairy farms and in beef herds, and it is considered an endemic agent in many countries. The described levels of morbidity range from 60% to 80% having been reported, in some outbreaks, mortality rates that reach 20-30%, especially when there are other concomitant viral and bacterial infections (Valarcher & Taylor, 2007; Sacco et al., 2014; Blodörn, 2015; Hägglund & Valarcher, 2015). The reported high morbidity levels seem to be due to the rapid spread of the virus within infected herds, which leads to high viral herd prevalence (Klem et al., 2013). Truthfully, it is believed that the majority of cattle populations will be affected by this virus at some point (Woolums, 2010).

The variation in the seroprevalences registered is usually due to the type and age of animals sampled (Hägglund & Valarcher, 2015). It is more difficult to evaluate the frequency of BRSV infections in adult cattle, given the usually high seroprevalence registered in these animals when performing a point prevalence study (Valarcher & Taylor, 2007), and the fact that acquired antibodies are detectable for several years, even in the absence of reinfection (Ohlson, Emanuelson, Tråvén & Alenius, 2010).

The clinical manifestation of disease due to BRSV may vary between herds, depending on the level of viral circulation within the herd. In populations in which the virus is generally present, or in which vaccination programmes are implemented, it is expected that only younger animals develop clinical signs, with calves between one and six months of age being the most affected, and with infection being known to occur even in the presence of maternal antibodies. On the contrary, clinical signs can be transversal to all of the herd when the virus is introduced in previously naïve populations (Valarcher & Taylor, 2007; Woolums, 2010; Stilwell, 2013; Sacco et al., 2014; Hägglund & Valarcher, 2015). In these cases, morbidity levels may reach 100% and studies suggest that adult cattle, especially high production first and second parity cows, pregnant and newly calved cows are in fact more severely affected than other categories of animals within the farm (Raaperi, Bougeard, Aleksejev, Orro & Viltrop, 2012; Hägglund & Valarcher, 2015). Other factors involved in disease expression are concomitant infections with other viruses, environmental factors and stressors such as transportation, gestation, lactation and nutrition (Elvander, 1996).

Regardless of the fact that infection can occur despite the presence of maternal antibodies, and that even seropositive calves may suffer reinfection, antibodies seem to provide at least partial protection, given that both incidence and severity of disease seem to be inversely related to maternal antibody titres (Larsen et al., 2001).

There are several risk factors identified as predisposing to BRSV infection, such as environmental causes like temperature fluctuations, dusty environments, inadequate building ventilation and high humidity levels, as well as stressors related to general management, like weaning, transportation, handling and mixing of animals from different sources. Larger herds, with higher population densities, are also more prone to infection, given the increased contact between animals and increased circulation of farm personnel. Farms located in areas where animal exchanges are common and dual purpose farms also present a higher risk (Raaperi et al., 2012; Sarmiento-Silva et al., 2012; Klem et al., 2013; Sacco et al., 2014; Hägglund & Valarcher, 2015;). Bidokhti, Tråvén, Fall, Emanuelson and Alenius (2009), upon studying the antibody prevalence to BRSV in organic versus conventional farms concluded that organic herds had lower seroprevalences, which could be due to the stricter management practices adopted in these farms, such as closely regulated trading of animals between farms, as well as the implemented quarantine period. Production type seems to also be relevant in the epidemiology of BRSV infections, which have been shown to have increased in parallel with the concomitant intensification of cattle production.

In temperate regions, BRSV outbreaks occur mainly during autumn and winter, but may also occur in the summer (Valarcher & Taylor, 2007; Blodörn, 2015). Infections in winter seem to lead to higher rates of seropositive animals within the herd, though. This may be due to the fact that infectious pressure is higher during the cold months, in which animals are more frequently housed, with high densities and inadequate levels of ventilation and humidity predisposing to infection (Klem et al., 2013).

There is yet no consensus concerning the introduction and maintenance mechanisms of BRSV in cattle populations, with theories of asymptomatic carriers, re-infections and viral mutations, as well as both direct and indirect transmission routes having been proposed (Stilwell, 2013; Blodörn et al., 2015). Despite the fact that cattle are the natural viral host, it is not discarded that other species may play a role in its epidemiology. These may include ovines and caprines, but also species like camelids or bison (Valarcher & Taylor, 2007). It is often theorized that BRSV may lead to persistent infected cattle, which may aid the virus in surviving during the summer, being reactivated and leading to new outbreaks of disease even in herds not subjected to reinfection, but this theory remains yet to be fully clarified (Van der Poel, Kramps, Middel, Van Oirschot & Brand, 1993; Hägglund & Valarcher, 2015).

Viral transmission occurs by direct contact between infected animals and by aerosols, (Valarcher & Taylor, 2007). Airborne transmission, however, doesn't seem to be very effective, as concluded by several authors. Ohlson et al. (2010) found that in Sweden there were seronegative farms in the midst of areas were BRSV prevalences were very high. Sarmiento-Silva et al. (2012) also consider airborne transmission between herds to be of less importance, strengthening the importance of introduction of infected animals into the herd instead. Indirect transmission, either through humans or fomites is considered of major importance in the epidemiology of BRSV. This may be supported by the occurrence of outbreaks in closed herds or in herds in which outbreaks occur shortly after a visit by animal professionals. In fact, not providing boots for visitors was concluded in one study to augment the risk of BRSV infection (Ohlson et al. 2010). The probability of indirect transmission is directly related to viral load and level of fomite contamination, and also to the existence of contact with vulnerable animals (Hägglund & Valarcher, 2015).

There is some data supporting a possible difference in predisposition to BRSV infection concerning different breeds, indicating that American Red breeds and the Blanc Bleu Belge may be less resistant to the virus. Another study points to a more severe disease manifestation in Holstein-Angus crossbred calves compared to pure Holstein calves (Baker et al., 1997).

1.2.1. BRSV Prevalences in Portugal and in the UK

There isn't an abundant amount of information published concerning the prevalence of BRSV in Portuguese cattle, especially in recent years. The results found in some studies aiming to evaluate the virus seroprevalence in Portuguese herds are presented on Table 1, and demonstrate the expressiveness of the virus in both dairy and meat herds.

Table 1: Reported BRSV prevalences in mainland Portugal between 2003 and 2007

Year	Region	Authors	Data Collected	Main Findings
2003	Entre Douro e Minho	Segalab, S.A. (unpublished data)*	• 124 dairy farms (10% random selection from a total of 1208 dairy farms); • Animals tested were older than six months and preferably not vaccinated; • BRSV seroprevalence was evaluated with an Indirect ELISA kit in a total of 1055 samples.	• Seroprevalence in non-vaccinated animals = 77%; • Seroprevalence in rearing calves = 57.9%; • Seroprevalence in heifers = 78%; • Seroprevalence in cows = 91.1%; • Only seven farms were classified as negative for BRSV; • 93.7% of farms were classified as suspected of BRSV infection.
2003	Alentejo	Mariano, Vilhena & Saloio (unpublished data)*	Three studied regions: • Litoral Alentejano (34 meat herds and 288 animals tested); • Monforte (25 meat herds and 429 animals tested); • Montemor-o-Novo (five dairy farms with 188 animals tested and 29 meat	BRSV Seroprevalence per region: • Litoral Alentejano = 64.2% • Monforte = 47.6% • Montemor-o-Novo= 58.9%; • Of the 93 tested farms, only 12 were declared BRSV-negative (four in the Litoral Alentejano, five

			• herds with 440 animals tested); • BRSV seroprevalence was evaluated with the indirect ELISA method.	in Monforte and three in Montemor-o-Novo).
2007	Ribatejo	Stilwell et al.	• Eight herds belonging to the same farm, in an extensive production system; • 136 cows (not vaccinated against respiratory viruses) and 73 male calves were tested; • Mertolenga, Preta and Cruzada breeds; • BRSV seroprevalence evaluated with an Indirect ELISA kit.	• BRSV seroprevalence in adult cows = 50.7% Seroprevalence by breed: Mertolenga = 36.2% Preta = 58% Cruzada = 63.5%; • BRSV seroprevalence in calves at weaning = 10% Cruzada breed calves had a 2.048 higher probability of being BRSV-positive than Preta breed calves (p<0.05).

Table 1: Reported BRSV prevalences in Portugal between 2003 and 2007 (continuation)
*Source: Stilwell, G. (2016), personal communication.

The prevalence of BRSV in UK dairy and meat herds has been studied by several authors throughout the last decades, and some major findings can be reported (Table 2).

Table 2: Reported BRSV prevalences in the UK between 1980 and 2014

Year	Country	Authors	Data Collected	Main Findings
1980	England	Stott et al.	• Virological survey from 1972 to 1975; • 1540 beef-rearing calves; • 1143 nasopharyngeal swabs performed for viral culture; • 1069 sera analyzed, with antibodies titrated in microneutralization tests.	• BRSV was detected in 78 samples from a total of 540 viral detections; • 58.1% of BRSV infections were diagnosed during outbreaks of disease; • 73% of BRSV infections were detected during the winter months; • By the age of 9 months, BRSV had been diagnosed in 70% of calves.
1998	England and Wales	Paton et al.	• 341 dairy herds; • Samples collected from July to December 1996; • ELISA testing for antibody detection in bulk tank milk.	• 100% of the herds tested were positive for BRSV antibodies (however, the vaccination status against BRSV was unknown).
2010	Scotland	Hotchkiss et al.	• Cross-sectional study; • 68 farms (33 beef and 35 dairy); • 637 calves; • Deep nasal swabs with real time RT-PCR for RNA viral detection.	• Four calves from two farms were positive for BRSV (two calves were from dairy farms and the other two were from beef herds).
2012	Scotland	Thonur et al.	• 541 clinical samples from respiratory or abortion material;	• BRSV was detected in 28 samples (5.18%).

			• Samples were tested with a multiplex real time RT-PCR.	• Positive samples included nasal swabs and lung and tracheal samples.
2014	Ireland	O'Neill, Mooney, Connaghan, Furphy & Graham	• Retrospective study; • Calves ≤3 months from dairy and suckler herds; • 1364 BRD submissions; • PCR testing.	• BRSV was the 2nd most commonly detected virus, and was found in 51.2% of all multiviral detections; • BRSV was detected most commonly between November and February.

Table 2: Reported BRSV prevalences in the UK between 1980 and 2014 (continuation)

1.3. Signs and Pathology

The viral incubation period ranges between two and five days. Clinical signs are usually seen seven to ten days after a stressful event such as transport, but may be seen up to 30 days or more after arrival at destination. The disease developed may be asymptomatic, restricted to the upper areas of the respiratory tree or also involve the lower respiratory tract (Valarcher & Taylor, 2007; Sacco et al., 2014). There are several reasons that justify differences in the severity of disease manifestation, which include: virulence of viral isolates, levels of maternal antibodies, concomitant infections with other pathogens, management practices and environmental conditions (Baker et al., 1997).

The impairment of the upper respiratory tract manifests itself by the presence of cough accompanied by nasal and ocular seromucous discharge, which becomes mucopurulent in the presence of concomitant bacterial infection. Affected animals may exhibit depression, anorexia, milk production decrease, hyperthermia, tachypnea and abdominal breathing. Thoracic auscultation may reveal areas with an increased vesicular murmur, crackles and wheezes, caused by phenomena of bronchopneumonia or bronchiolitis. However, the absence of abnormal sounds is a common finding in this pneumonia, even in the presence of intense dyspnea (Valarcher & Taylor, 2007; Stilwell, 2013). In previously naïve herds, the infection leads to an increase in rectal temperature in two days after exposure and, in three to four days, there is usually a peak in rectal temperature, which reaches values above 40º Celsius (Stilwell, 2013).

Animals in great respiratory distress are usually found exhibiting an orthopneic posture manifested by open mouth breathing, lowered head and stretched neck, as well as sialorrhea, and may sometimes develop pneumothorax, pneumomediastinum or pneumopericardium. In some cases, it is possible to observe the presence of subcutaneous emphysema in the cervical, scapular or perineal areas (Valarcher & Taylor, 2007; Sacco et al., 2014), which is caused by the rupture of alveoli and consequent migration of free air through the mediastinum (Baker et al., 1997).

At necropsy, the most consistent pathological finding of BRSV infection is a cranioventral bronchointerstitial pneumonia, associated with severe bronchiolitis (Baker et al., 1997). The craniovental lung lobes usually show areas of atelectasis and consolidation, sometimes paired with visible mucopurulent discharge in the bronchus and small bronchi. On the other hand, the caudodorsal lobes frequently show signs of emphysema and edema. In case of secondary bacterial infections, usually with a cranioventral distribution, the lung parenchyma is usually more distended and consolidated (Baker et al., 1997; Valarcher & Taylor, 2007; Sacco et al., 2014). Microscopic lesions in the cranioventral lobes show evidence of proliferative and exudative bronchiolitis with concomitant alveolar collapse, degeneration and necrosis of both ciliated and non-ciliated epithelium, syncytia formation, type II pneumocyte hyperplasia and exudative or proliferative alveolitis. The airway lumen is usually obstructed by neutrophils, macrophages and desquamated epithelial cells, with eosinophils sometimes found both in the lumen and lamina propria of the respiratory tract (Valarcher & Taylor, 2007; Sacco et al., 2014). It should be noted that even though BRSV may be identified as the aetiological agent, necropsies performed at later stages of disease might only reveal the presence of secondary bacteria, and therefore it is important to aim for an early infection diagnosis (Hägglund, 2005).

Reinfections with BRSV usually result in mild disease, with slight pyrexia, dyspnea and, albeit less frequently, cough, or even in subclinical disease, a probable consequence of the development of active immunity following primary infection. Vaccinated herds may also experience sporadic cases of subclinical disease (Baker et al., 1997; Stilwell, 2013).

1.4. BRSV Pathogenesis

Before addressing the pathogenesis of BRSV infection, it is perhaps worth mentioning the peculiarities of the bovine respiratory tract, which can act both as predisposing and aggravating factors for the development of respiratory disease in these animals.

The particular susceptibility of the bovine respiratory tree to disease is due to the following features: bovines have a small respiratory capacity in comparison to their metabolic needs, the bronchial tree also being very narrow; the interalveolar septa are very thick and almost inelastic, which impairs recovery after inflammatory processes; the air speed through the mucociliary apparatus is about 50% slower than in other species of similar size; their rather high respiratory rate aids in aerosol transportation; they usually have a low count of alveolar macrophages and also demonstrate a high susceptibility to infections by *M. haemolytica* (Stilwell, 2013).

Upon infection, the virus replicates predominantly in the superficial layer of the respiratory ciliated epithelium, but can also replicate in type II pneumocytes (Valarcher & Taylor, 2007; Taylor, 2008). After initial colonization of the nasal cavity epithelium, BRSV extends to the lower respiratory tree, affecting the trachea, bronchi, bronchioles and ultimately reaches the alveoli (Blodörn, 2015).

The virus causes a disruption of the ciliated respiratory epithelium by direct lesion of the mucociliary escalator, which affects the clearance of bacterial agents from the lungs, apart from being responsible for the destruction of alveolar macrophages, further undermining respiratory tract defenses (Baker, 1991; Larsen et al., 2001; Stilwell, 2013). This is usually accompanied by the induction of several pro-inflammatory chemokines and cytokines, which recruit cells like neutrophils, macrophages and lymphocytes to the respiratory tract (Taylor, 2008). The direct tissue damage instigated by the virus, added by ventilation and clearance impairment, clear the way for secondary bacterial infections (Blodörn, 2015; Hägglund & Valarcher, 2015).

Resulting disease severity is not always directly connected to the viral load, however, being suggested that the host's inflammatory response is accountable for a significant portion of the clinical manifestation and pathogenesis of the infection (Gershwin, 2012; Sacco et al., 2014; Blodörn, 2015), leading to the production of Immunoglobulin E (IgE), which is accountable for the mediation of allergic phenomena and anaphylactic reactions (Woolums, 2010). It has been demonstrated that, when in the presence of anti-BRSV IgE, developed disease is more severe (Gershwin, 2012). Even though the virus exhibits cytopathic effects in tissue culture, cytopathic effects following *in vitro* infection of bovine epithelial cells are much reduced, or even nonexistent. This also adds to the theory that the host response to BRSV infection plays a key role in its pathogenesis (Valarcher & Taylor, 2007).

Due to this apparently hypersensitive reaction, BRSV-induced disease is sometimes described as biphasic, with the first stage of disease being characterized by a short period of uncomplicated respiratory disease, which is then followed by a second stage of extreme respiratory distress, corresponding to the hypersensitive reaction. The time interval between these two stages may vary between days and weeks and this form of the disease, even though not being a regular outcome, is usually fatal (Baker, 1991; Stilwell, 2013). Despite the fact that there is currently no consensual justification for the development of this response, it is admitted that factors like the simultaneous presence of other disease agents or allergen particles, as well as genetic predispositions, may play a role (Woolums, 2010).

1.5. Diagnosis

The diagnosis of BRSV infections can be performed using both direct and indirect methods. The first allow the detection of the virus itself, its antigens or its RNA, while the second aim at detecting specific antibodies against the virus (Blodörn, 2015). The differential diagnosis with bacterial pneumonias is mostly based on clinical presentation: in viral pneumonias, there are no toxemia phenomena and the animals are usually in an alert and active state, contrary to what happens in bacterial pneumonias. The differential diagnosis with other respiratory viruses may also be useful.

In Infectious Bovine Rhinotracheitis (IBR), caused by Bovine Herpesvirus Type 1 (BHV-1), for instance, there are usually signs of conjunctivitis and lesions on the nasal mucosa (Stilwell, 2013).

1.5.1. Direct Methods for BRSV Diagnosis

Viral isolation of BRSV is a problematic technique, due both to its extreme lability as well as the fact that inoculation in cellular cultures is not always feasible (Stilwell, 2013; Blodörn, 2015). Therefore, techniques for antigen or viral RNA detection may be preferable. These include immunofluorescent staining in histological sections and antigen Enzyme-Linked Immunosorbent Assays (ELISAs), which can be used to detect BRSV antigens in body fluids. The Polymerase Chain Reaction (PCR) method allows the detection of viral RNA in bronchoalveolar lavage (BAL) fluid up to 13 days following experimental infection in calves (Blodörn, 2015). Given the frequent co-infection of the respiratory tract by different viruses, multiplex PCR is a useful diagnostic tool, since it allows for the simultaneous diagnosis of these viruses, contributing to a more cost-effective diagnosis (Thonur et al., 2012).

Viral replication is detectable from two to three days post infection, continuing up to seven to ten days post infection. In the early stages of clinical disease, tissue samples from typical BRSV lesions in the cranioventral lung lobes are often the best to use in viral detection (Sacco et al., 2014).

Cytology, performed either from samples collected during BAL or during necropsy, has great weight as a diagnostic tool, allowing the identification of inclusion bodies and the characteristic syncytial cells. These cells can be found free in the bronchial lumen, in the bronchial epithelium or in the alveolar walls and lumen (Valarcher & Taylor, 2007; Stilwell, 2013).

1.5.2. Indirect Methods for BRSV Diagnosis

The execution of paired serum analysis with the purpose of detecting seroconversion phenomena or significant raise in anti-BRSV antibody titres is widely used (Blodörn, 2015). A four-time increase in antibody titers 15 days after the establishment of clinical disease is quite consistent with BRSV infection. However, when interpreting the serology, one must consider the virus ubiquity and inclusion in many of the commercialized vaccines, as well as the presence of maternal antibodies in young animals (Stilwell, 2013). Antibody titres may be determined using virus neutralization assays or the ELISA technique (Blodörn, 2015). Of the range of ELISA tests available, the indirect ELISA is perhaps the most frequently used. It should be noted that this test is merely qualitative, serving to differentiate between positive and negative herds (Klem et al., 2014).

Antibody levels in bulk tank milk have been used to assess the BRSV status of dairy herds. However, bulk tank milk serology may have a limited use as a diagnostic tool concerning BRSV infections, given that antibody levels can remain high for several years even in the absence of reinfection. It has been found that antibodies against BRSV can be detected in the serum of adult cattle for at least two years post infection. Given this fact, assessment of herd status based on serology from young animals or milk samples from primiparous cows may be preferable than performing bulk tank milk tests (Klem et al., 2014). However, there appears to be a good correlation between serum and milk antibodies levels, and the use of milk samples may be a more convenient screening method for potential health control programmes in dairy herds (Ohlson, Blanco-Penedo & Fall, 2014). Bulk tank milk testing is considered to be a financially attractive and effective method for disease monitoring, having been used in disease eradication programmes as well as epidemiological studies. The fact that it can be used in all lactation stages and that it doesn't seem to be affected by the presence of subclinical mastitis are some of its advantages (Williams & Winden, 2014).

Upon primary infection of seronegative calves, IgM and IgA may be present from day eight to ten post infection and can be detected ranging from two to four weeks, while IgG_1 can persist up to at least four months and IgG_2 probably persisting after that period (Larsen et al., 2001; Blodörn, 2015). On the contrary, infection of calves with circulating maternal antibodies doesn't promote relevant changes in serum antibody titres, with the exception of a feeble IgM and IgA responses. As for adult cattle, IgG_1 antibodies are known to persist for at least three years post infection. Selective serological tests (such as ELISAs) aimed specifically at the detection of IgA, IgM and IgG antibodies may help in the establishment of the occurrence of an outbreak of disease, taking into account the persistence of each of those classes of antibodies (Blodörn, 2015).

1.6. Treatment

There is no specific treatment against viral infection. Treatment is merely symptomatic, or aimed at controlling the secondary bacterial infections through the use of antimicrobials.

Glucocorticoids like dexamethasone or nonsteroidal anti-inflammatory drugs (NSAIDs) can be used to control the inflammatory phenomena associated with the infection (Stilwell, 2013). Glucocorticoid treatment can be a useful option in cattle suffering from severe dyspnea. In weaned beef calves, a standardized treatment with dexamethasone (10 mg, SID) for two days has been recommended. NSAIDs will have the advantage of not being immunosuppressive when compared to glucocorticoids. In a study, flunixin meglumine was shown to reduce body temperature of affected calves (Baker et al., 1997). Bronchodilators like atropine and diuretics for pulmonary edema can also be useful, while the use of antimicrobials should be reserved only to cases in which there is a suspicion of bacterial infection (Stilwell, 2013). In addition to the use of medical tools, affected animals should be put under sheltered conditions, with availability of food and water. Dehydration and electrolyte imbalances should be corrected recurring to oral or intravenous fluid therapy (Baker et al., 1997).

1.7. Prevention and Control

BRSV control measures revolve mainly around management practices that aim at reducing viral circulation, as well as vaccination programmes. Despite the weight put on vaccination, there is still little consensus about its efficacy, and field studies concerning this subject are scarce (Glass, Baxter, Leach & Jann, 2012). In order to obtain maximum efficacy, vaccination programmes need to be combined with correct management and biosecurity measures, in a more holistic approach towards BRSV control (Hägglund & Valarcher, 2015).

1.7.1. Biosecurity and Management Practices

Even though the importance of biosecurity practices is widely recognized, the fact that there is still much to understand about BRSV's epidemiology makes it difficult to define specific measures aiming at controlling the virus. The reliance on biosecurity practices is highly dependable on the type of farm. It is more likely to be successful in farms that implement correct quarantine procedures when introducing new animals and that purchase animals with a known negative BRSV-status, or that do not buy animals at all, than in farms in which comingling animals from a variety of different sources is a common practice (Hägglund & Valarcher, 2015).

Despite its usual association with vaccination programmes, biosecurity practices can be used as a single preventive measure, which comes with both advantages and disadvantages. The non-use of vaccines avoids the introduction of pathogens into the herd, also minimizing immune-induced pathology and saving the costs of the vaccines themselves. It also allows for a viable serological monitoring of virus spreading. On the other hand, having a completely susceptible population comes with the risk of, in case of virus introduction, gargantuan levels of morbidity and mortality transversal to the entire herd, since the virus is likely to cause more severe and rapid establishment of disease in naïve herds (Hägglund & Valarcher, 2015). The risk of severe disease in naïve herds is an argument often used in favour of not aiming for BRSV eradication (Blodörn, 2015).

Management practices such as reducing animal density, grouping animals of similar age, prompt isolation of sick animals, good building ventilation and correct hygiene of materials such as buckets and nipples as well as facilities like maternity pens and calf-rearing installations, associated with timing in the administration of good quality colostrum, dry bedding, correct analgesia during procedures like dehorning or castration and reduced transportation times, may also aid in disease prevention (Hägglund & Valarcher, 2015). Other practices include avoiding the introduction of new cattle into the herd or establishing a good quarantine period. For BRSV, two weeks seems to be a viable choice, considering the viral incubation period (Baker et al., 1997; Woolums, 2010).

1.7.2. Vaccination and Immunology

Vaccination against BRSV aims to protect naïve animals from clinical disease, as well as contribute to minimize viral transmission among and between herds (Blodörn, 2015). It can be used either as a continuous and seen as indispensable method or be reserved for situations when the risk of disease is higher. The categories of animals intended to be vaccinated are very important in the design of a vaccination scheme. In BRSV seronegative animals, or in calves in which maternal antibodies against the virus are no longer present (for example animals intended to be transported to fattening units at six-eight months of age), vaccines of parenteral administration seem to be effective during a temporary period of usually months, even though they require a booster dose (Hägglund & Valarcher, 2015).

In their study, Stilwell, Matos and Carolino, (2007) advise that, upon weaning at five to six months of age, suckler calves should be vaccinated against BRSV, as well as other key respiratory viruses like BHV-1, Bovine Viral Diarrhea Virus (BVDV) and Parainfluenza-3 Virus (PI_3V). An alternative to this could be to vaccinate the mothers around the time of birth, aiming for passive antibody transfer through the colostrum. However, it is known that maternal immunity against BRSV is of short duration, the authors stating a maximum of two months.

Calves that are going to be integrated in veal production or heifer rearing units usually need to be vaccinated at a very young age, given the high probability they will come in contact with the virus early in their lives. Concerning the fact that passive immunity against BRSV is at most occasions not ideal, active immunity of calves has a major role in disease prevention. Given the presence of maternal antibodies in these young calves, vaccination usually needs to be performed recurring to several boosts, which will of course come with additional costs (Stilwell et al., 2007; Hägglund & Valarcher, 2015). Despite providing some level of protection against BRSV infection at an early stage of life, maternal antibodies have a negative effect on the establishment and duration of the humoral immune response induced by vaccination, especially when inactivated vaccines are used. The duration of maternal antibodies against BRSV appears to be different between dairy and beef herds, with reported average values of 3.2 months in dairy herds and values around 6.1 months for suckler calves (Klem et al., 2013). The persistence of maternal antibodies may vary accordingly to different factors, such as: nutritional status of both the mother and the young, serological antibody titres in the pre-partum cow, quantity and quality of colostrum ingested by the calf during the first 24 hours after birth and the infectious agent considered (Stilwell et al., 2007; Blodörn et al., 2015).

Maternal antibodies, however, do not seem to impair the cellular immune response. It is known that protection against BRSV is dependent on both the humoral and the cellular immune systems, with antibodies having a role in combating the launch of infection and cells like cytotoxic T cells being indispensable in the clearance of previously established infections in the respiratory tract. Calves without serum antibodies but with circulating BRSV-specific T cells seem to develop stronger humoral and cellular responses when challenged than calves lacking these cells (Blodörn, 2015). Cellular immunity may be strengthened by vaccination (Stilwell et al., 2007).

Despite the general use of vaccines against BRSV, its efficacy is still controversial, with different levels of protection reported, as well as some disease enhancement phenomena in calves, and there is therefore a need for improvement in that field. There are some difficulties in the development and appliance of vaccines in young calves, namely: the necessity to vaccinate animals whose immune system is still immature, the interference with maternal antibodies and the successful establishment of an effective and long lasting immune response (Larsen et al., 2001; Sacco et al., 2014). The fact that experimental infection does not usually lead to clinical disease with the same magnitude as natural infection is also an obstacle in the evaluation of BRSV vaccines (Baker et al., 1997; Patel & Didlick, 2004).

There are currently several vaccines available against the virus, both attenuated and killed, but very little has been published concerning their efficacy in calves with maternally derived antibodies (Patel & Didlick, 2004). These vaccines are mainly polyvalent, BRSV being associated with other respiratory viruses (Stilwell, 2013), but there are monovalent vaccines against the virus as well. Under field conditions, and especially in feedlot systems, the identification of the specific viral agents involved in an outbreak of respiratory disease is sometimes not feasible, and therefore the use of polyvalent vaccines is usually favored (Stilwell, Matos, Carolino & Lima, 2008).

The mucosal route of administration, recurring to live vaccines, is known to be more resistant to the effects of the presence of maternal antibodies compared to the parenteral route, and can therefore be more effective in inducing protection in young calves (Larsen et al., 2001; Valarcher & Taylor, 2007). The intranasal administration of live BRSV vaccines has proven to be more efficient in reducing viral shed than parenterally administered vaccines (Vangeel et al., 2007), with the quickly triggered immunity development making them appropriate for use during disease outbreaks (Stilwell, 2013).

All vaccines currently available against BRSV don't allow the serological distinction between infected and vaccinated animals. Therefore, the production of marked vaccines, for example by deletion of non-essential viral genes, is one of the main goals of vaccine development against BRSV. By enabling the differentiation of infected from vaccinated animals, these so called DIVA vaccines facilitate the monitoring of viral transmission in areas where vaccination is practiced and also allow the monitoring of changes in vaccine efficacy and safety. DIVA vaccines come with the advantage that costs can be reduced by no longer needing isolation and trials of animals aiming for the study of vaccine induced immune responses, since these antibodies will be distinguishable from those induced by natural infection even under field conditions. They also allow for the serologic diagnosis of BRSV infections in previously vaccinated animals (Valarcher & Taylor, 2007; Blodörn, 2015; Hägglund & Valarcher, 2015).

1.8. Contextualization of BRSV Infection in Bovine Respiratory Disease

As mentioned above, BRSV may stand as the main viral aetiological BRD agent. Despite the knowledge of the virus's pathogenesis and nefarious effects, it is extremely difficult, if not nearly impossible, to assess the economic impact of the virus *per se*, given its inclusion in the multifactorial disease that is BRD. BRSV's primary action is often concealed, and it is known that the virus has a synergic association with other respiratory viruses and bacteria (Stilwell, 2013). Given this syndromic nature of BRD, it is often challenging to identify the specific pathogens responsible for disease development (Grissett, White & Larson, 2015). Therefore, it may be difficult to assess the individual weight of each infectious agent in the development of disease and concurrent production losses under field conditions. In fact, most large scale epidemiological studies researching production losses and economic impacts of BRD are commonly based on clinical diagnosis without specific aetiological agent diagnosis (Klem et al., 2016).

Taking that into account, emphasis will be put on the economic impact of BRD as a single entity in the cattle industry, with some particular aspects concerning specific impacts of the virus being brought to attention. Given the description of the impacts of BRD in the dairy and meat sectors presented ahead, a literature review of the subject is needed.

BRD is a multifactorial cattle disease, involving intricate interactions between infectious agents and environmental, management and host factors (Edwards, 2010; Grissett et al., 2015). It is one of the most extensively studied diseases in cattle, its research going back to the late 1800s (Taylor, Fulton, Lehenbauer, Step & Confer, 2010). However, in spite of all the investment done in BRD, it continues to have a negative impact on bovine production, mainly due to its complex aetiology (Edwards, 2010).

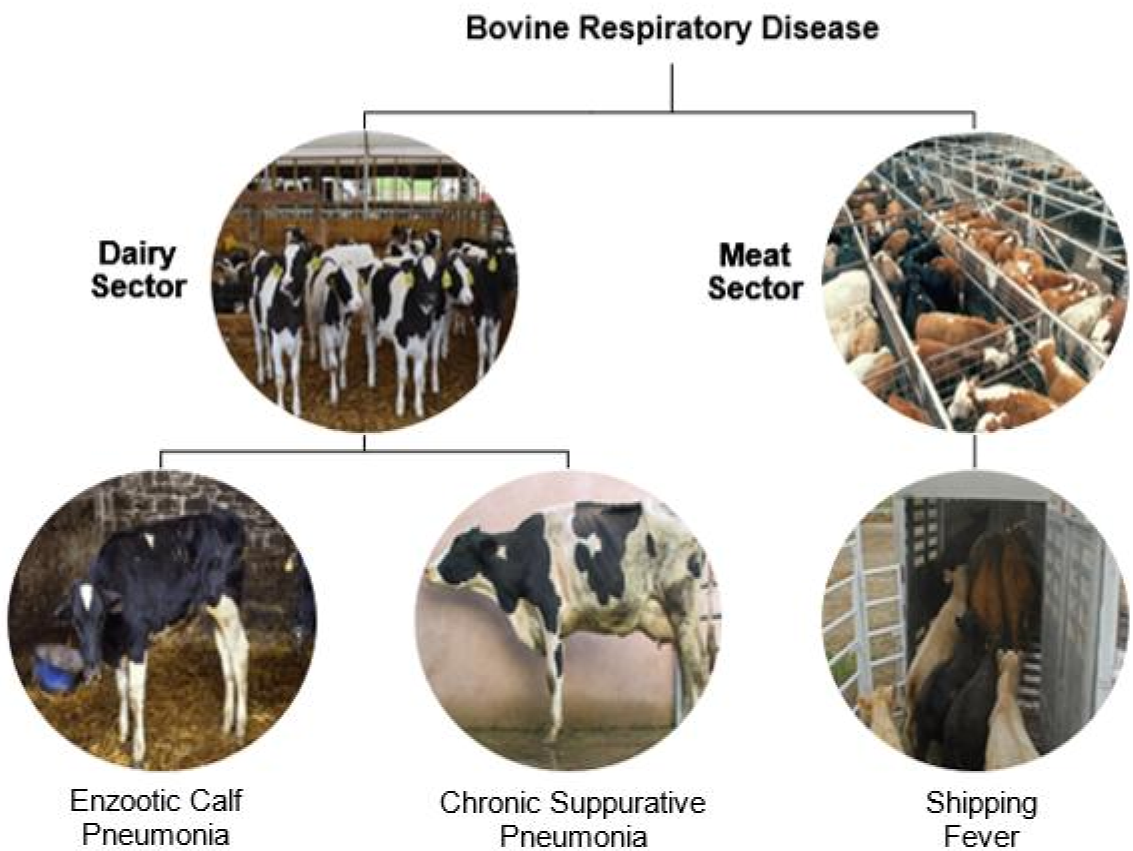
The most common viruses implicated in BRD are BRSV, BHV-1, PI_3V, BVDV and Bovine Coronavirus (BCoV), with *M. haemolytica*, *P. multocida*, *H. somni* and *M. bovis* standing as the main bacterial agents. Besides the capacity of viruses to cause primary disease, they usually act in synergy with bacteria, either in precursor or coexisting infections. By colonizing the upper respiratory tract, viruses compromise the host's immune system and allow the proliferation and colonization of the lower respiratory tract by bacterial agents, usually commensal of the bovine upper respiratory tract (Edwards, 2010; Taylor et al., 2010).

The establishment of disease is greatly aided by environmental factors such as poor ventilation, dusty environments, extreme temperature oscillations and humidity levels. Several management factors, such as high animal density, transport, commingling, pain caused by mutilations and weaning can also act as 'triggers' or 'stressors', compromising the immune system and predisposing to disease (Taylor et al., 2010; Stilwell, 2013). The importance of environmental and management factors in the development of BRD is greatly supported by the fact that investigators usually fail to replicate the common manifestations of disease in animals solely exposed to infectious agents (Taylor et al., 2010). It should be noted that the effects of these stressors may vary between animals, given that each animal will react to them differently depending on its physiological and psychological state when challenged, and also on the intensity and duration of the challenge. Therefore, it is expected that, in a group of animals affected, different patterns of disease will arise even in the presence of the same stressors (Hartigan, 2004).

The concept of stress has intensively been used in the discussion of BRD. In general, and despite a lack of clarity concerning practical conclusions on its management, it is assumed to be the major challenge to animal welfare, general health and desired productivity, especially in more intensified production systems. It should be noted that stress is an indispensable phenomenon in all animals, allowing them to deal with challenges to their homeostasis by releasing suitable levels of glucocorticoids, catecholamines and noradrenalin. Glucocorticoids and catecholamines inhibit some leucocyte, macrophage and lymphocyte functions while promoting a decrease in cytokines and inflammation mediators. However, the acute stress response also leads to an increased release of growth hormone and prolactin, enhancing the immune response. The problem arises with chronic stress, in which the combination of the immunosuppressive effects of glucocorticoids and catecholamines, combined with the decrease of growth hormone and prolactin renders the animal more susceptible to infectious diseases, particularly those that affect the respiratory and digestive systems (Hartigan, 2004).

Even though much emphasis has been put on its nefarious effects in feedlot cattle (Snowder, Van Vleck, Cundiff & Bennett, 2006; Schneider, Tait Jr, Busby & Reecy, 2009; Brooks et al., 2011, Stilwell, 2013), BRD also plays a major role in dairy systems, affecting young calves, replacement heifers and adult cows with equally heavy consequences (Gorden & Plummer, 2010; Stilwell, 2013). Given the different categories of animals affected, as well as different risk and management factors involved, BRD may be compartmentalized into distinct clinical entities, addressed by different names, which are presented in Figure 1, and then discussed[2].

Figure 1: Most common manifestations of BRD in the dairy and meat sectors



[2] Image Sources:
'Dairy Sector': http://agrinutrition.com/wp-content/uploads/2014/03/DSC_0809.jpg
'Meat Sector': http://img2.allposters.com/images/RHPOD/190-2897.jpg
'Enzootic Calf Pneumonia': http://www.farminguk.com/images/News/24828_1.jpg
'Chronic Suppurative Pneumonia': Scott, 2013
'Shipping Fever': http://www.agweb.com/assets/import/images/Jack-Harrison-160.jpg

2.1. Enzootic Calf Pneumonia

Pneumonia in dairy calves can occur both as an endemic disease and in outbreaks. The chronic endemic disease is the most common manifestation, which has led to the term ‘enzootic calf pneumonia’ (Ames, 1997). It predominately affects calves before six months of age, with a peak incidence between two and ten weeks of life. However, it can also affect older animals, up to one year of age (Campbell, 2015). It is mainly a problem of dairy bred calves, either reared for veal or beef or as dairy replacements (Andrews, 2004). In fact, BRD is a major concern in heifer rearing, giving its high incidence and short and long term negative effects on these animals (Stanton et al., 2010). In affected cattle, morbidity levels can be expected to reach 100% while mortality, though variable, may reach a 20% rate (Campbell, 2015). There are apparently some breed differences concerning calf susceptibility to BRD, with Friesian and Jersey calves being pointed as particularly susceptible (Andrews, 2004).

2.1.2. Aetiology

The aetiology of enzootic calf pneumonia is in all similar to the one described for the BRD complex, with interactions between infectious, management and environmental stressors, and usually being initiated by a primary viral infection (Campbell, 2015). All the bacteria involved in the BRD complex have been associated with cases of disease, especially *P. multocida* and *M. bovis*, as well as the viruses, with mostly BRSV but also BCoV having been identified as primary agents in outbreaks (Ames, 1997; Gorden & Plummer, 2010; Stilwell, 2013).

The main route of infection is by direct transmission via nasal secretion or droplets (Sivula, Ames, Marsh & Werdin, 1996). Housed animals are therefore at a higher risk for developing disease (Campbell, 2015). Enzootic calf pneumonia is commonly associated with low temperatures and/or sudden drops in environmental temperatures, as well as high humidity levels. The cold seems to be a risk factor for infection in the manner that it somehow damages the respiratory tree defense mechanisms, affecting macrophages, ciliated and mucus-secreting cells as well as impairing lung clearance. Low temperatures also encourage the animals to huddle, which facilitates pathogen spread (Andrews, 2004). The level of noxious gases, like ammonia, methane or carbon dioxide can rise due to poor ventilation and inadequate facility cleaning, contributing to the mucosal lining lesion and impairment of cellular defenses (Ames, 1997).

Other identified risk factors associated with the occurrence of calf enzootic pneumonia are birth from a first-calf heifer, presence of concurrent diseases like diarrhea and inadequate colostrum feeding. Studies show that newborn calves with failure of passive antibody transfer are at a higher risk for developing BRD, with failure of passive transfer also being reported to increase the severity of clinical signs (Ames, 1997; Van der Fels-Klerx, Martin, Nielen & Huirne, 2002b).

A seasonal pattern for BRD occurrence has been described, with high disease incidence during autumn and winter and, even though the correlation between weather conditions and the occurrence of disease is difficult to prove, it seems that this is intimately related to management practices like housing of the animals in close proximity (Andrews, 2004).

2.1.3. Clinical Signs and Diagnosis

Affected calves can present with a reduction in feed intake, cough, dull and sweaty coat, lowered head, pyrexia, mucoid or muco-purulent nasal and/or ocular discharge, tachypnea and dyspnea. Applying pressure on the upper trachea will elicit animals to cough. Upon thoracic auscultation, crackles and wheezes can be heard, but in bacterial infection where lung consolidation is present abnormal sounds can be practically non-existent (Ames, 1997; Andrews, 2004). Chronical cases are identified by a poor response to treatment or frequent relapses, cachectic state, loud and painful breathing, cough and intolerance to exercise. On the contrary, they rarely present with fever or nasal discharge (Stilwell, 2013).

Producers and veterinarians usually diagnose and institute treatment of sick cattle based on clinical presentation, rather than on specific aetiology (Van der Fels-Klerx et al., 2002b). Farm personnel's ability to detect clinical cases is then an important factor to take into account, and has been reported to have a sensitivity of little more than 50% and a specificity of 100%. The implementation of standardized screening systems on the farm, which evaluate signs of disease like rise in rectal temperature, cough, nasal/ocular discharge and ear position may serve as a useful tool to correctly diagnose BRD cases of different severities, determine the need for therapy as well as its protocol, and also monitor treatment efficacy (Gorden & Plummer, 2010). Apart from the use of a screening system, complementary tests like nasopharyngeal swabs, bronchoalveolar lavage, cytology and pathogen culture can also be used, as well as fluorescent antibody tests (Andrews, 2004; Gorden & Plummer, 2010).

Necropsies can also be a valuable diagnostic tool, but care should be taken not to choose chronically affected animals or animals subjected to failed treatments, since this can lead to the isolation of bacteria that may not be representative of the primary disease pathogens. Therefore, sacrificing an animal in the acute phase of disease can sometimes provide more reliable results. Apart from enabling identification of pathogens, necropsies also aid in the determination of nutrition deficiencies and, for example, in diagnosing cases of aspiration pneumonia, common in farms which make an incorrect use of esophageal feeders (Gorden & Plummer, 2010).

2.1.4. Treatment

Antimicrobials are used in the treatment of pulmonary bacterial infections. The antimicrobial used should have a broad spectrum and be bactericidal, and the choice of which molecule to use is usually an empirical one, based on previous cases on the farm. Long-acting preparations are always risky, given the difficulty of instituting another therapy in case of treatment failure. Depending on the antimicrobial and the animal's response, treatment should be continued for three to five days. Symptomatic treatment can also be necessary, and mainly includes the use of corticosteroids or NSAIDs. Corticosteroids seem to aid in the recovery of sick animals that are not responding to antimicrobial therapy alone and, apart from diminishing inflammation, they stimulate the animals' appetite, which will also aid in their recovery. NSAIDs also possess anti-pyretic and analgesic properties (Andrews, 2004). Auxiliary agents like bronchodilators, mucolytics and diuretics may also be used (Stilwell, 2013). Upon diagnosis, sick animals should be promptly removed from the group, given access to palatable food and water and kept in a comfortable and drought-free environment (Andrews, 2004; Stilwell, 2013).

2.1.5. Prevention and Control

Given the multifactorial nature of BRD, disease prevention needs to encompass a holistic approach, usually combining key management and biosecurity practices with vaccination programmes (Andrews, 2004). Management practices, especially of housed calves, are of critical importance, with proper housing, adequate ventilation and appropriate nursery care playing central roles. Cows should be vaccinated against respiratory disease agents three or four weeks before calving to maximize the presence of colostrum antibodies. Maternity pens should be kept clean and dry, and calves should be removed from them immediately after birth, to minimize pathogen exposure. Calf navel dipping should also be a standardized practice, since it aids in the control of disease in newborn calves, and has been shown to reduce the percentage of calves treated for respiratory disease (Bach & Ahedo, 2008; Gorden & Plummer, 2010). Neonatal calves should be fed good-quality colostrum in the first six hours after birth, and its quantity should correspond to 8-10% of their body weight. Delivery by nurse bottle or esophageal intubation usually results in adequate passive antibody transfer, as well as providing an assurance that the calf has received an ideal colostrum volume (Andrews, 2004; Gorden & Plummer, 2010; Campbell, 2015).

Single calf housing should be privileged, at least in the first stage of life (by EU legislation it is only permitted until eight weeks of age), and preferably in an outdoor environment (Gorden & Plummer, 2010; Campbell, 2015), having been concluded that heifers raised in outdoor hutches were less likely to be treated for pneumonia than those raised indoors (Van der Fels-Klerx et al., 2002b).

Single housing may also be adopted in an indoor system (Gorden & Plummer, 2010). The increasing awareness of animal welfare, as well as equipment like automatic and computerized milk-feeding systems, have led to an increase in group housing of unweaned calves. It is worth mentioning again that commingling calves, especially from different sources, housing young animals with older ones and maintaining groups of high density are among the strongest predisposing factors for BRD, facilitating the spread of pathogens amongst the group (Van der Fels-Klerx et al., 2002b; Andrews, 2004; Svensson & Liberg, 2006). However, studies suggest that keeping the groups limited to a maximum of 10 animals results in improved growth and less morbidity due to respiratory disease, provided each animal has at least 2.3 to 2.8 m^2 available (Svensson & Liberg, 2006; Gorden & Plummer, 2010).

Proper nutrition is also crucial in the prevention of calf pneumonia, since nutrient consumption by the immune system increases in the presence of infectious challenge. In pre-weaned calves, the type of milk provided seems to also influence the occurrence of respiratory disease. A study found that feeding of waste milk in detriment of milk replacements may increase the growth rate of calves. However, it is advised to pasteurize the milk before giving it to the calves, for this process effectively reduces the presence of pathogenic bacteria associated with respiratory disease in milk. It should be noted that this comes with the inherent cost of acquiring a pasteurizer, and also requires the frequent monitorization of the process (Gorden & Plummer, 2010).

Even though it is known that weaning is always a stressful and delicate period for calves, not much has been published on its best methodology towards reducing the risk of respiratory disease. When weaning coincides with removing the calves from individual hutches into group pens, some authors advise that these two procedures should be done one to two weeks apart, while other authors have found no difference in the incidence of respiratory disease between calves immediately grouped after weaning and calves that stayed individually housed a certain period of time post-weaning (Gorden & Plummer, 2010). Stressors associated with grouping calves encompass social, environmental and nutritional changes, as well as an increase in exposure to pathogens opposed to an immature immune system, and therefore this is always a time in which there is a high susceptibility to BRD (Stanton et al., 2010). Whatever the case, weaning and grouping of calves should always be a time for a systematic observation for detecting sings of respiratory disease, and therefore preventing the introduction of calves shedding pathogens into the group (Gorden & Plummer, 2010). An "all-in-all-out" management system should be implemented and used whenever each group is established and exits the barn (Campbell, 2015). When grouping of calves is adopted, they should also be vaccinated against respiratory disease ideally three to four weeks before grouping occurs. Vaccination at this age is usually complicated by the presence of circulating maternal antibodies (Campbell, 2015), as mentioned before. The most accepted way to overcome this problem is the administration of intranasal vaccines, which lead to the production of antibodies like Immunoglobulin A (IgA) on the mucosal surface and consequent neutralization of pathogens at this level (Gorden & Plummer, 2010; Stilwell, 2013). However, given the characteristics of the calves' immune system at this time, as well as the complexities of their management systems, effective vaccination programmes may be difficult to develop (Gorden & Plummer, 2010). Concerning BRSV, vaccination efficacy of young calves seems not to have consensual results between farms. This may be due to the type of vaccine used and the fact that the pathogens present in the vaccines may not be the ones causing disease on the farm. Thus, before embarking on the development of an effective vaccination programme, it is of vital importance to identify the respiratory pathogens responsible for the cases of enzootic pneumonia on the farm (Andrews, 2004).

Concerning animal density, it should be noted that it does not have a linear relationship with ventilation requirements. In fact, a tenfold increase in building ventilation is required to maintain the barn's air pathogen load when animal density doubles. This is especially problematic in naturally ventilated barns, or in barns with negative pressure ventilation. On the contrary, positive ventilation systems may aid in the improvement of barn ventilation (Gorden & Plummer, 2010).

Common management procedures such as disbudding and castration also appear to affect the development of disease (Andrews 2004). Both these procedures are stressful and painful, leading to increased plasma cortisol levels, which are known to have an immunosuppressive nature (Taylor et al., 2010). To minimize this, they should be performed in younger animals in detriment of older ones, and always under some sort of anesthesia and/or analgesia method, which include the use of a local anesthetic like lidocaine, that can be used alone or in combination with a NSAID (Anderson, 2009). The timing at which these procedures are implemented is also relevant, and executing them more than two weeks before weaning can be beneficial (Andrews, 2004).

When needed, contact of farm personnel with the animals should be performed from younger to older calves and, upon contact with older animals, personnel should undergo hands and clothing disinfection procedures before coming into contact with younger, more susceptible calves. Sick animals should be housed in separate facilities, away from healthy or immunocompromised animals such as young calves and peri-parturient cows, in order to prevent the spreading of disease. Besides physical separation, these facilities should be positioned so that the airflow does not move from sick animals towards healthy ones (Gorden & Plummer, 2010).

When new animals are introduced into the herd, quarantine practices should also be standardized, despite being often overlooked. These practices should ideally include protocols for disease testing, vaccination and feeding, as well as disinfection programmes for the facilities. When buying milking cows, care should be taken to milk these cows away from the resident herd. The quarantine period should encompass a minimum of 14 to 21 days (Gorden & Plummer, 2010).

2.2. Chronic Suppurative Pneumonia

BRD is not a very common disease in adult animals, especially when compared to conditions like mastitis, lameness and metabolic and reproductive disorders. The incidence of pneumonia in adult dairy cattle is low but allegedly growing, values of 3.3% having been reported in the United States but these are responsible for about 11% of the overall mortality in dairy farms (Gorden & Plummer, 2010), a value also stated in a study conducted in Scotland between 2008 and 2013 (Oliver, Mason & Howie, 2014), and that might indicate that response to therapy is very poor in these cases. This lack of response may be due to a failure of early disease recognition, but also to a recrudescence of latent cases of enzootic calf pneumonia. These recrudescent cases take the form of chronic suppurative pneumonias (Stilwell, 2013), the most common pulmonary disorder of individual adult cows (Dalgleish, 1991).

2.2.1. Aetiology

These pneumonias arise in the sequel of unsuccessful BRD diagnostics and/or treatments, and usually manifest following a challenge that compromises the animal's immune system, like calving and early lactation, transportation and BVDV infection. The immunosuppression phenomena results in the recrudescence of pulmonary abscesses from which bacteria like *Trueperella pyogenes* and *Fusobacterium necrophorum* can usually be isolated. This latent infection is maintained during the entire life of the animal, and can repeat itself at times in which the immune system is compromised, for instance, at each calving (Stilwell, 2013). It is known that at the time of parturition there is a decrease in lymphocyte and neutrophil function, which impairs the cow's immune system. Adding to this, phenomena of negative energy balance and diseases like ketosis and hypocalcemia in early lactation, as well as conditions like subacute ruminal acidosis (SARA) may also contribute to this impairment and therefore increase the susceptibility to BRD (Gorden & Plummer, 2010).

In the UK, between 2005 and 2015, *T. pyogenes* was the most common pathogen identified at the time of necropsy in 362 dairy cows that suffered from respiratory disease (Mason, 2015).

2.2.2. Clinical Signs and Diagnosis

Clinical signs include dullness, weight loss, tachypnea and dyspnea, orthopneic posture, purulent nasal discharge, anorexia, halitosis and cough. In addition, these animals usually have poor body scores, stubbly and lusterless hair coat and a history of weak milk production, features consistent with a chronic condition. The presence of thoracic pain may be denounced by elbow abduction and reluctance to move. Affected cows also have a history of respiratory disease as calves (Dalgleish, 1991; Andrews & Windsor, 2004; Stilwell, 2013). In prolonged or frequently relapsing cases, a state of *cor pulmonale* may develop, with dilation of the right heart chambers and generalized edemas (Stilwell, 2013).

Diagnosing this condition if often challenging, due to the fact that producers frequently institute treatments before the veterinarian is called and that other conditions like peritonitis, endocarditis, pericarditis, liver abscessation and metritis also present with a history of weight loss and poor milk production (Scott, 2013). Diagnosis is facilitated by the history of chronicity of respiratory disease in individual animals, accompanied by clinical signs of cough and thoracic pain (Andrews & Windsor, 2004). It should be noted that cows are normally afebrile, even in the absence of previous antimicrobial administration (Scott, 2013). Apart from previous history and clinical signs, blood tests can be performed in order to help diagnose this condition, and normally reveal leukocytosis, neutrophilia and increased fibrinogen as well as total protein count due to an increase in globulin levels. Pulmonary abscesses can be easily visualized by performing a thoracic ultrasound (Stilwell, 2013). At necropsy, lesions take the form of a bronchopneumonia, with pronounced consolidation of the cranioventral lung areas and presence of exudate in the bronchi and bronchioles. In severe cases there may be a total destruction of the alveolar tissue. The characteristic abscesses are usually found in the ventral lung border (Andrews & Windsor, 2004).

2.2.3. Treatment and Control

The success rate of these cases is very disappointing, even after prolonged treatments. Treating animals with procaine penicillin for over a month is indicated, but is recommended only for animals of high value, whose milk is not destined for human consumption, or if one is aiming for a recovery prior to slaughter (Stilwell, 2013). Given the probable recurrence, infected animals should be directed to slaughter at a convenient time. Controlling the disease involves culling affected animals and ensuring that all pneumonia cases in young animals are promptly diagnosed and treated (Andrews & Windsor, 2004).

2.2.4. Prevention

Given its aetiology, practices aiming for the prevention of chronic suppurative pneumonias are exactly the same indicated for respiratory disease in young calves, in addition to attempt to eradicate BVDV at the farm (Stilwell, 2013). A farm management assessment should also be performed to ensure that conditions like negative energy balance, ketosis, hypocalcemia or SARA are not playing a role as contributors to BRD at farm level (Gorden & Plummer, 2010).

2.3. Shipping Fever

Shipping fever is a form of BRD that usually develops after transportation, hence its designation. It is exceptionally frequent and nefarious in feedlots, where large groups of animals from different sources are assembled, usually after weaning and transport. In fact, many authors avow that this disease is the most common and economically relevant disease in these systems, accounting for significant production losses and being responsible for more than 70% of registered mortality cases (Snowder et al., 2006; Schneider et al., 2009, Brooks et al., 2011, Stilwell, 2013), despite the great amount of resources injected into the development of new vaccines, antimicrobial and anti-inflammatory agents (Edwards, 2010; Wolfger, Timsit, White & Orsel, 2015). The peak of morbidity is usually seen two to three weeks after transport and commingling, with the first 45 days after arrival being held as the higher risk period. Disease can manifest in as much as 50% of animals present (Urban-Chmiel & Grooms, 2012; Stilwell, 2013; Campbell, 2015), which are usually between 6 months and 2 years of age (Andrews, 2004b).

2.3.1. Aetiology

Shipping fever is also multifactorial in nature, with environmental and management stressors, with or without the presence of viral pathogens, compromising the host's immune response and enabling the colonization and proliferation of bacteria in the lungs (Andrews, 2004b; Campbell, 2015). It is accepted that, in feedlot systems, more than 90% of unvaccinated cattle may be seropositive to BRSV, as well as to BVDV and PI_3V, with a reported seroprevalence of 70% in adult females in cow-calf operations (Radostits, 2001). *M. haemolytica* and, less commonly, *P. multocida* and *H. somni* are the main bacterial agents involved (Campbell, 2015). Bovines are particularly susceptible to *M. haemolytica*'s leucotoxin, which promotes the destruction of alveolar macrophages and neutrophils and leads to a rapid and vast destruction of lung parenchyma and induction of toxemia (Stilwell, 2013). This bacterium is also known to be a primary agent of respiratory disease (Wildman et al., 2008).

Stressors involved in the development of shipping fever can be additive and synergic in their nature (Edwards, 2010), and include: recent weaning, transportation over long distances, passage through auction markets, commingling, execution of management procedures on arrival, pain due to mutilations, dusty environments and nutritional stress due to a sudden change to a high-energy diet upon introduction into the feedlot (Campbell, 2015). Transportation is acknowledged to be the main non-infectious risk factor (Taylor et al., 2010), and it is often associated with exhaustion, starvation, dehydration, overheating and exposure to exhaust fumes from the transporting vehicle (Campbell, 2015). In terms of breed susceptibility, there is a consistent notion that the Hereford breed is particularly susceptible to BRD, both in feedlots and in bull testing facilities (Hay et al., 2016).

Cattle arriving at the feedlot usually comes from different sources and geographical locations, and frequently will be of different breeds, weights and immune statuses. Therefore, it is important for each farm to have an adequate herd health programme, typically based on the type of cattle received and the level of risk for such animals to develop BRD, with cattle designated as 'high risk' obviously demanding bigger disease control costs, such as labour and medicines (Edwards, 2010).

2.3.2. Clinical Signs and Diagnosis

Shipping fever is usually a disease of sudden onset, with animals presenting with dullness, anorexia, pyrexia (40-41ºC), ocular and/or nasal discharges, dropped ears, dry muzzle, rough hair coat, tachypnea, dyspnea and cough, which tends to exacerbate with exercise. In advanced cases, they may also demonstrate marked abdominal breathing and an expiratory grunt (Andrews, 2004b; Edwards, 2010). Apart from visual detection, additional diagnostic methods can be used (Edwards, 2010). Samples like blood, nasal and nasopharyngeal swabs, tracheobronchial lavage and tissue samples collected during necropsy can all be used in the aetiological diagnosis, with laboratorial methods like culture, immunohistochemistry, ELISA testing and PCR assays being available (Urban-Chmiel & Grooms, 2012). Alterations in acute phase proteins like haptoglobin and fibrinogen have been associated with the presence of BRD both in field conditions and in controlled trials, increasing with inflammation and tissue damage, with haptoglobin being more strongly evidence-supported (Wolfger et al., 2015).

Detection of BRD in feedlot cattle usually relies upon the detection of clinical signs by farm personnel. This is less than accurate, given cattle's instinctive masking of clinical signs of sickness (Edwards, 2010), with farm personnel sensitivity for detecting BRD being about 60%. It should be noted that an early BRD diagnosis is vital for ensuring lower mortality levels and relapse cases (Wolfger et al., 2015).

Death usually derives from a state of toxaemia and anoxia. At necropsy, more than one-third of the lung parenchyma displays pronounced consolidation, especially the ventral areas of the apical and cardiac lobes. Some animals may present emphysema, with serofibrinous pleurisy and fibrinous pericarditis also being common findings, along with pronounced pleural effusion. In some cases, there is a peracute form of disease with sudden death without any previous signs (Andrews, 2004b). Besides serving as a method for determining diagnosis accuracy, lack of therapeutic response and tissue collection for the identification of pathogens, necropsy is also a valuable tool in the sense that it provides vital information which aids in the development of future health programmes, apart from serving as a way for the veterinarian to educate farm personnel on disease process and lesion identification (Edwards, 2010).

2.3.3. Treatment

Providing therapeutic treatment to sick cattle aims to minimize performance losses as well as reduce death loss and the development of chronic cases (Edwards, 2010). Treatment should be instituted as early as possible and animals usually start to recover within one to three days, with full recovery taking up four to seven days (Andrews, 2004b).

There are numerous molecules available for use against the main BRD bacteria, namely cephalosporins, tetracyclines, macrolides and quinolones. The election of a particular antimicrobial should be a judicious one, supported by frequent antimicrobial susceptibility testing on the farm, due to the risk of development of resistant bacterial strands (Stilwell, 2013). *Ante mortem* culture and antimicrobial sensitivity testing of acute untreated cases provide the most reliable information when aiming for aetiological diagnosis, bacterial susceptibility and antimicrobial dosage (Radostits, 2001). Mild cases, in which animals do not present with anorexia and whose temperature remains below 39.5ºC don't usually require medical treatment. On the other side, animals with higher body temperatures and signs of severe depression and respiratory distress are illegible for immediate antimicrobial therapy (Stilwell, 2013).

Anti-inflammatory medicines can also aid in the recovery of sick animals, but should be reserved to cases when there is notorious respiratory distress. Provision of adequate ventilation, controlled environmental temperature and good bedding can also be beneficial (Andrews, 2004b; Stilwell, 2013). Nutrition of sick cattle is also an important factor, given that there is usually a decrease in feed intake that can reach 50% or more, so care should be taken to provide a palatable and balanced diet to these animals (Edwards, 2010).

Evaluation of treatment response is indispensable in determining the effectiveness of instituted treatment protocols, and can be accomplished through analysis of morbidity and mortality records. The pressure put on the Veterinary sector concerning the use of antimicrobials on farm animals, considering the crescent phenomenon of antimicrobial resistance, demands a rigorous use of these drugs and serves as an impulse to shift the efforts into prevention practices (Edwards, 2010).

2.3.4. Prevention and Control

BRD control in feedlots should be included in a herd health programme, which will aim to minimize losses associated with morbidity and mortality while at the same time maximizing feed performance and carcass value. For this to be successful, the programme must seek to diminish pathogen exposure, stimulate the animals' immunity and manage the many risk factors associated with the development of BRD. Hygiene measures are vital, and include: frequent cleaning of hospital facilities, feed bunks and water troughs and separate use of equipment destined for manure management and deadstock, as well as equipment used in the manipulation of feed (Edwards, 2010).

There has been much emphasis on the use of medicines for BRD management, despite increasing knowledge of the multifactorial nature of the complex, with husbandry practices often being overlooked. It has long been recognized that at times of stressful procedures, like dehorning and castration, the rise of cortisol levels coincides with a decline in the animals' immune function, making them more susceptible to diseases like BRD. Therefore, improving the timing of such procedures, in addition to better infrastructure design and handling techniques, may lead to improved cattle health and performance while at the same time satisfy the growing demands for animal welfare (Edwards, 2010).

Rather than rely on practices like vaccination at the time of arrival at the feedlot, focus must be put at the cow-calf level with the development of a competent calf immune system through rigorous husbandry practices on the farm of origin, combined with vaccination and weaning programmes. If the development of effective immunity is not initialized before arrival at the feedlot, it may prove difficult to ensure protective levels of immunity prior to disease challenge (Edwards, 2010). The importance of ensuring sound nutrition also extends to vaccination effectiveness, since nutrient deficiency can depress the immune system and therefore impair the development of an effective immune response to vaccination (Sweiger & Nichols, 2010).

Upon arrival, cattle must be directed to a receiving pen with good bedding, clean source of water and fresh and palatable hay and feed, preferably distanced from hospital facilities in order to prevent pathogen exposure. Animals should be quickly assembled into groups while minimizing the mixing of cattle from different sources. Transportation times should be reduced at maximum and, when long distances are unavoidable, resting periods with access to feed and water should be provided. Other practices that help minimize stress in feedlots include: avoiding loud vocalization and whistling, reducing the use of electric pods and ensuring good footing to avoid slips and falls (Edwards, 2010; Campbell, 2015). Adaptation to high-energy diets should be gradual, preventing phenomena of acidosis and anorexia, which may also impair the animals' immune response (Campbell, 2015). The animals can also be introduced to the feedlot diet still in the farm of origin, which will facilitate the adaptation (Andrews, 2004b).

Many of the practices above mentioned are included in a concept known as preconditioning, which is presented next. The concept of metaphylaxis and the nuances of vaccinating feedlot cattle are introduced afterwards.

2.3.4.1. Preconditioning

Preconditioning is defined as a set of management practices implemented around the time of weaning that aim to optimize the calves' immune system, as well as their nutritional status, while minimizing stress. The practices included in these programmes vary, but the most conventional ones comprise vaccination against respiratory disease, as well as other diseases like clostridiosis, parasite control, castration, dehorning and training to use feed bunks and water tanks. In addition, calves are usually weaned at least three weeks prior to transport. There is no universal preconditioning programme, and the most adequate one will vary accordingly to different production systems or regions. The decision to implement such a programme is also an economic one, given that producers must weigh the cost of implementing the programme against the additional value that will be generated by the preconditioned calves (Mathis, Löest & Carter, 2008). It is generally accepted that preconditioning calves leads to a reduction in morbidity and mortality due to BRD, with reports of increased Average Daily Gain (ADG) and better Feed Conversion Ratios (FCR), combined with lower expenditures on medicines and labour, adding value to the entire beef production system. However, there is variation between programmes, and with inadequate data collection and analysis it has proved difficult to determine the economic profitability of these interventions. The economic benefits for the cow-calf producers and feedlot owners are regularly questioned (Mathis et al., 2008; Hilton & Olynk, 2010) and, in a majority of situations, a premium price is required to compensate producers for the costs of preconditioning programmes (Radostits, 2001). This indicates that benefits in terms of improved productivity are both difficult to observe and are insufficiently clear for a producer to make a decision. On the buyer side, benefits in terms of having animals being kept in better conditions with lower levels of disease has not led to a willingness to pay premiums. More research is needed concerning the true economic value of this practice for different cattle types, participants in the production chain, season and geographical location (Lalman & Mourer, 2001).

2.3.4.2. Metaphylaxis

Metaphylaxis is defined as the strategic mass medication of a group of animals in order to minimize or eliminate an expected outbreak of disease, and has been declared an efficient and cost-effective practice in controlling bacterial pathogens involved in BRD. It is most commonly implemented upon arrival at the feedlot, when stress and pathogen exposure are higher, and its objectives include: reduction of morbidity and mortality; improved performance and profit and improved facilities management by reducing hospital crowding (Radostits, 2001; Edwards, 2010). Metaphylactic and prophylactic uses of antimicrobials are not the same, and their differentiation is worth mentioning. Prophylaxis is the mass administration of antimicrobials to a group of animals at risk of experiencing disease but without any disease present, acting as a preventive measure. Metaphylaxis, on the other hand, is the strategic administration of antimicrobials to a group of animals in which both sick and apparently healthy animals coexist, acting as an early curative treatment at the start of an episode of disease before clinical expression starts to occur, therefore avoiding outbreaks. It can consequently be described as a disease-control measure (Bousquet-Mélou, 2010). Metaphylaxis with long-acting antimicrobials such as oxytetracycline, tilmicosin, florfenicol, gamithromycin or tulathromycin is a commonly adopted practice in order to prevent the development of BRD upon arrival at the feedlot, with robust results in morbidity and mortality reduction and improved rate of weight gain (Campbell, 2015). Drug selection concerning this practice is an economic decision, and must ponder the cost of the antimicrobial, expected reduction in morbidity and mortality, expected performance gain, and the sale cattle price (Edwards, 2010).

2.3.4.3. Vaccination

Vaccination protocols against the main pathogens causing BRD are usually incorporated in a herd health programme, and are designed to stimulate cattle's immunity upon arrival at the feedlot, as well as reducing and controlling BRD outbreaks (Edwards, 2010). A routine procedure often adopted is vaccinating animals upon arrival at the feedlot. However, given the peak of BRD incidence in the first weeks after arrival and the fact that immunity takes two to three weeks to develop, this may not be the most adequate vaccination timing. Therefore, vaccination should be performed two or three weeks before transport, with possible booster upon arrival (Edwards, 2010; Campbell, 2015). When calves are vaccinated upon arrival a booster dose within seven to twenty one days may be necessary, given the possibility that the first administration of the vaccine, coincident with the high level of stress and the weakened immune system, may not have been entirely successful in the establishment of an effective immune response (Edwards, 2010).

As seen, BRD manifests itself in distinct ways in the dairy and meat sectors, with different patterns of occurrence, risk factors and nuances in disease prevention that need to be taken into account when aiming for an effective disease control.

Given that BRD's impact is being looked at in two distinct locations, it was considered pertinent to provide a brief description of cattle populations, production data, number and dimension of holdings, as well as dairy and veal/beef production systems in Portugal and the UK, in an attempt to identify risk factors contributing to BRD's development associated with these production systems. This description can be found in the following chapter.

CHAPTER III: Dairy and Beef Production Sectors: an Overview

3.1. Dairy Cattle Population and Production Data: Europe, Portugal and the UK

In 2014, the number of dairy cows in European member states (EU 28) stood at approximately 23.56 million animals, with 234 thousand heads in Portugal and 1883 thousand heads in the UK (AHDB, 2015b; Eurostat, 2015). Total cow's milk production registered an increase of 3.8% compared to the previous year, standing at 159 641 thousand tonnes, with Portugal and the UK presenting values of 2000 and 15 088 thousand tonnes, respectively (Eurostat, 2015). The apparent yield for the EU 28 was of 6 777 kg per head in 2014, with yield values in Portugal (8554 kg per head) and in the UK (8013 kg per head) above this average (Eurostat, 2013; Eurostat 2015b). The UK stands as the third largest milk producer in the EU, after Germany and France, and it is the tenth largest milk producer in the world (Bate, 2016).

In terms of self-sufficiency rates in 2014, Portugal registered a value of 96.8% when it came to milk products and 110.5% in drinking milk, reflecting a surplus production (INE, 2015). These self-sufficiency rates have remained relatively stable when looking forward from 2011 (INE 2013; INE, 2014b). In the UK, milk production as a percentage of new supply registered a value of 102% in 2014, which reflected a surplus production, a trend also seen from 2011 onwards (DEFRA, 2015).

In 2013, there were 6431 dairy holdings in Portugal, accounting for 2.4% of the total specialized holdings in the country. Between 2009 and 2013, there was a reduction in the number of holdings with the disappearance of smaller farms in parallel with an increase in average herd size from 28.6 to 34.5, while the total number of animals dropped 1.6%. Most Portuguese regions, namely the North, Centre, Algarve and Autonomous Regions, have some of the lowest agricultural holdings dimensions, with less than 4.05 hectares. On opposite, holdings in Alentejo are of significant greater size, and more similar to the ones found in northern and central European countries (INE, 2014). In Portugal, dairy cattle are usually kept in housed systems, with cows kept in barns with rows of cubicles and a central corridor, while calves are many times housed individually. Housing is more common in the Entre Douro e Minho and Beira Litoral regions, where more intensive dairy production is focused (INE, 2011). A significantly different milk production system is seen in the Azores region, in which cows spend the majority of their time on grass, with the existence of few stabling and feed storage facilities (Amorim, Alves, Manaças & Miranda., n.d.).

As for the UK, between 1995 and 2014 the number of dairy producers fell from 35 741 to 13 815, which represents a reduction of 61% (Bate, 2016). Dairy holdings are scattered across the UK, but recent years there has been a shift of milk production towards the West and South West of England, as well as West Wales (The Dairy Site, 2010). Given the fact that many smaller herds have ceased to exist, the average dairy herd size in the UK has risen: in 2014, the average number of cows per herd was 133, which contrasts with 97 in 2004 and 75 in 1996 (Bate, 2016). Given the favourable climate for growing grass, most dairy farming systems in the UK are grass-based systems, in which cows graze during spring and summer and are housed for up to six months, usually from late autumn to the end of winter. However, the number of predominantly housed systems is growing. Given the harsh winters, typical extensive systems in which cows spend the majority of time outdoors, are not common in the UK (The Dairy Site, 2010).

3.2. Meat Cattle Population and Production Data: Europe, Portugal and the UK

Bovine meat derives mostly from breeds destined for meat production, but can also come from dairy cattle. In fact, veal is mainly produced from Holstein male calves, which are essentially a surplus of dairy production. The economic viability of this enterprise is related to the supply of healthy calves, good quality milk replacers at a competitive price, adequate labour, ideally inexpensive housing facilities and market demand (Radostits, 2001). Meat production for the year 2013 concerning the different categories of cattle is presented on Table 3.

Table 3: Production of beef and veal by class of bovine animals: EU 28, Portugal and the UK, 2013

2013 (000 tonnes of carcase weight)	Total	Calves and Young Cattle	Heifers	Cows	Steers	Bulls
EU 28	7 271.7 (100%)	1 008.5 (13.9%)	1 033.2 (14.2%)	2 140.1 (29.4%)	623.9 (8.58%)	2 465.9 (33.9%)
Portugal	84.1 (100%)	21.5 (25.6%)	9.8 (11.7%)	17.3 (20.6%)	0.6 (0.7%)	34.9 (41.5%)
UK	847.7 (100%)	4.1 (0.48%)	228.2 (26.9%)	176.9 (20.9%)	329.6 (38.9%)	108.8 (12.8%)

Source: Eurostat, 2015b

In 2013 the main class of bovine animals used in meat production in the EU 28 were bulls, a trend also seen in Portugal. On the contrary, in the UK the main contributing categories were steers and heifers, with a much smaller contribution of calves and young cattle when compared with Portugal and the EU 28. Between 2009 and 2014, EU's meat production from bulls and heifers decreased 7%, while veal production (animals under eight months old) and young animal production (between eight and twelve months old) increased by 4% (Eurostat, 2015c).

Portugal registered a self-sufficiency rate for bovine meat of 47.5% in 2014, in parallel with a 3.3% decrease in production and a 10.8% imports increase compared to the previous year. Bovine meat is the third most-consumed meat in the country, with 17.5 kg *per capita* reported in 2014 (INE, 2014b; INE, 2015). In 2014, compared to the previous year, bovine meat production registered a decrease of 11% in the UK (DEFRA, 2015), totalling 7.3 million tonnes, which accounted for 17%

of the total UK meat production (Eurostat, 2015c). In terms of consumption, beef and veal accounted for 1 149 thousand tonnes, with a *per capita* consumption of 17.8 kg. The UK self-sufficiency rate for 2014 stood at 76.4% (AHDB, 2015).

In 2013 there were 15 206 meat cattle holdings in Portugal, accounting for 5.8% of the total of specialized holdings in the country. Bovine production has its largest expression in the Alentejo region, which has an almost exclusive focus on meat production. The reduction in the number of bovine holdings seen in previous years resulted in a rise of average herd size, a trend particularly expressive in the Alentejo region which, in 2009, had an average herd size of 138.4 animals (INE, 2011). Suckler herds are predominantly kept in extensive production systems, with stabling being of minimal importance in the Alentejo and Azores regions (GPP, 2007; INE, 2011).

In terms of bovine meat production, two important phases must be considered: the cow-calf phase, with the production of calves until weaning, and the fattening and finishing phase (Rodrigues, 1997; GPP, 2007). Concerning the cow-calf phase, Portuguese autochthonous breeds are usually privileged, either in purebred breeding or in cross breed with breeds specialized in meat production, with the whole descendancy being in this case destined for slaughter. Nucleus of purebred animals are kept for selection and as herd replacements (Rodrigues, 1997). In the Alentejo and Beira Baixa regions, there are essentially two calving seasons: a traditional one, in the summer (from August to October), and a second one in winter (from January to March). Calf weaning is usually implemented at around six months of age. Contrary to what happens in the southern regions, meat herds in the centre and northern regions don't have a particular calving season, with calving occurring throughout the year. However, given the usually higher demand seen during summer, slaughters tend to be more concentrated in this season. Production systems in these regions are mostly focused in the production and slaughter of female calves around six-eight months of age, at the time of weaning, with male calves being slaughtered from ten months of age until, in some cases, eighteen months of age (Rodrigues, 1997).

The fattening and finishing phase aims for the production of animals – deriving from either meat or dairy herds – destined to be slaughtered for meat production (Rodrigues, 1997; GPP, 2007). Given the different calving seasons and growth patterns, distinct systems can be adopted in this phase. Intensive systems, which are based predominantly in the Entre Douro e Minho, Ribatejo, Oeste and Beira Litoral regions, are the ideal ones for fattening animals that come from dairy herds or that are the result of crossbreeds from autochthonous breeds and specialized meat breeds. This system is the heavier in terms of animal densities, efficiency of production and feed inputs, and animals are slaughtered between 12 and 18 months of age (Rodrigues, 1997; GPP, 2007). In semi-intensive and more extensive systems, animals are slaughtered between 18 to 30 months and above three years of age, respectively. Given the predominant use of natural or sown pastures, with forages being used when supplementation is needed, animals experience a slower growth in these systems (Rodrigues, 1997), mainly found in the Alentejo region (GPP, 2007). The autochthonous breeds are not so efficient in these cases, which privilege crossbreedings like the ones between the Alentejana or Mertolenga Portuguese breeds and the Charolais breed (Rodrigues, 1997).

In 2013, there were 60 737 meat cattle holdings in the UK, with an average herd size of 29.25 heads (AHDB, 2015). Beef production systems in the UK derive from both suckler and dairy herds, contributing to the industry at nearly equal proportions. The systems differ at farm level, with some producers specializing in breeding or rearing certain types of animals. Generally, there are three main categories of cattle reared and marketed: breeding animals, namely the reproductive herd at the cow-calf level; ‘store’ animals and ‘finished’ animals. ‘Store” animals are animals that are destined to be slaughtered for meat production, but haven’t yet reached the optimum body condition to meet the market’s preferences, while ‘finished’ animals are fully ready for slaughter (EBLEX, 2009).

Given the short productive life of current dairy cows (approximately three lactations), most young female calves are reared as dairy herd replacements. Around 20% of dairy cows are inseminated with semen from a beef breed male, in order to produce offspring destined to the meat industry. The female offspring is finished for beef in forage based systems at about 20-30 months. As for the males, they are usually castrated and finished on a multiplicity of systems, frequently changing ownership in the process, and being slaughtered at about 24-30 months. Pure dairy-bred male calves, usually from Holstein and Holstein-Friesian breeds, are often reared and finished in groups destined for veal production. The UK market for veal is small but growing, both in terms of internal consumption and intra-community transfer. Male dairy calves can also be retained as bulls and intensively finished on a diet consisting mainly of cereals until 14-16 months (EBLEX 2009; AHDB, 2015c). As for steers, they are generally finished in 18 or 24 months systems. Autumn-born calves are usually reared and finished indoors, while late spring-born and summer-born calves are usually housed over the winter and can either be finished at grass or indoors (AHDB, 2015c). Concerning the suckler herd, which is mainly concentrated in the North and West of England, the majority of male suckled calves is castrated and sold as stores between 6 to 12 months of age, for finishing by specialized finishers at 18 to 24 months. Some producers choose to keep suckler males entire and finish them intensively on a cereal-based diet, to be slaughtered before 16 months of age. This is a highly specialized enterprise, with the need for higher inputs and a more difficult management. The advantages of this practice include the fact that bulls tend to have better feed conversion rates and produce leaner carcases with higher yield of edible meat in a shorter time than steers (EBLEX, 2009; AHDB, 2015c). Cattle can be purchased at various stages, but the most common practice is the purchase of weaned calves in autumn or stores at 10-11 months in the following spring (HCC, 2014). It should be noted that these stores may also change ownership a number of times before final finishing and slaughter (EBLEX, 2009).

A great portion of suckler herds is self-replacing, and therefore female calves will be reared as replacement breeding animals. Those unfit to do so are also destined for the meat industry, being finished on a forage diet at about 20-30 months (EBLEX, 2009).

From the description of dairy and beef production systems both in Portugal and in the UK, a few conclusions can be drawn in terms of BRD occurrence and susceptibility:

- The decrease in the number of cattle holdings seen in both locations has led to an increase in average herd size and animal density per farm. In parallel, the traditional housed systems for mainland Portuguese dairy cattle, a growing trend in the UK as well, carries an additional risk of BRD development – particularly of Enzootic Calf Pneumonia and Chronic Suppurative Pneumonia – when in comparison to more extensive systems;
- The complexity of the meat cattle value chains in both Portugal and the UK can likewise help explain why BRD – especially in the form of Shipping Fever – is such a massive problem in the sector, particularly considering the fattening and finishing phase. This complexity, with animals from a plenitude of origins being commingled and subjected to practices like castration, passage through auction markets and ownership changing, usually under prolonged transport times, leads to a BRD susceptibility that is intrinsic to the production chain. The increased intensification of meat production also presents an obstacle towards an effective BRD control, since it usually leads to heavier animal densities, especially when considering indoor systems;
- When looking at consumer's trends in terms of meat preferences, 2013 data reveals that veal accounts for about 25% of the total bovine meat production in Portugal and, despite lower values, the veal market is also growing in the UK. Therefore, Enzootic Calf Pneumonia in veal production systems is also something that must be taken into account in both countries;
- Suckler herds are usually kept in more extensive systems, in which the pressure of known BRD stressors is considerably lighter, a fact that might explain the lesser importance of this disease upon this type of production.

All things considered, it is understandable that BRD, despite the efforts that have been put on its control, still acts as a negative input in both dairy and meat production, both in Portugal and in the UK. Therefore, its impacts on the cattle value chain are worth mentioning. Their distinction, however, may be clarified by a concise review of the economics of animal disease and respective control strategies, presented on Chapter IV.

The importance of production animals to human societies has been acknowledged for a long time. Livestock production results in a series of outputs, like meat, milk and traction power, as well as still being a form of social status and investment in many societies. As a reflection of this importance, animal health policies are constantly being developed, and are far from immutable, changing alongside society (Rushton, Thornton & Otte, 1999; Rushton, 2013). The intensification of livestock systems has led to the establishment of diseases and disease-complexes that usually are of endemic nature and manifest themselves mainly through decreases in productivity (Martin, Meek & Willeberg, 1987), which is the efficiency of conversion of inputs into outputs, expressed as the rate of output divided by the rate of input (Rushton et al., 1999; Otte & Chilonda, 2000). Modern livestock farming is becoming increasingly competitive, therefore, controlling and minimizing the costs of production, in parallel with improving animal health, is vital for an efficient and successful production (Christy & Thirunavukkarasu, 2006).

The common knowledge that livestock disease has a substantial economic impact in both developed and developing countries has led to several attempts to estimate the true economic impact of disease, as well as assess the costs and benefits of disease control strategies (Bennett, 2003). Indeed, in the EU, the demand for economic analysis concerning disease prevention and control has been rising (Pinior, Köfer & Rubel, 2014). Determining the optimal control level of animal disease recurring to economic analysis is an intricate task due to several reasons, which include the diversity of diseases affecting animals, both in terms of agents, epidemiology and nature of occurrence, as well as differences concerning disease prevention, treatment and response (Rushton, 2009).

Before further approach to the use of economics when it comes to animal disease, a simple definition of economics is timely. Economics, contrary to popular belief, is not a science that deals solely with monetary units. That is indeed a very limited view of economics, since currency and financial analysis are only some of the elements contemplated in an economic analysis. The main objective of economics is to aid in making rational choices concerning the allocation of resources which are, in their very nature, scarce. Economic decisions at farm-level, for instance, are usually focused on the allocation of resources like land, capital and labour, amongst different uses. Animal health economics, a relatively recent discipline, aims to provide information destined to support the decision-making process concerning animal health management (McInerney, Howe & Schepers, 1992; Dijkhuizen, Huirne & Jalvingh, 1995; Marsh, 1999; Otte & Chilonda, 2000).

Initially, the approach on the economics of animal disease followed one of two paths: gross estimates of the cost due to a particular disease, often obscure in their calculation, in which the final result would be a considerable financial sum, with the notion that the higher the sum, the higher the economic importance of the disease in question; or benefit-cost analysis, in which the costs of a certain disease control programme were balanced against the benefits expected by the introduction of that same programme. If the benefits were equal or greater than the costs, that is, if the benefit/cost ratio was equal or greater than one, then the implementation of the programme would be economically viable. However, both these approaches seem to be flawed in the way that they fail to provide guidance concerning the allocation of resources towards animal disease and its control (McInerney et al., 1992).

Given this fact, McInerney and others (1992), developed a framework for the economic analysis of livestock disease which, since then, has been used and adapted by other experts. Firstly, the terminology concerning economic concepts should be defined, namely in terms of losses (L) and expenditures (E). The sum of these two economic effects may be defined as the total cost of an animal disease (C) and, as simplified by the authors, be presented as C = L+E. A loss represents a reduction of output, either because a certain benefit is taken away or because a potential benefit was not obtained. The identification and quantification of many losses in livestock production due to the presence of disease is rather facilitated by the fact that most livestock products have an associated market price, which tends to reflect their economic value.

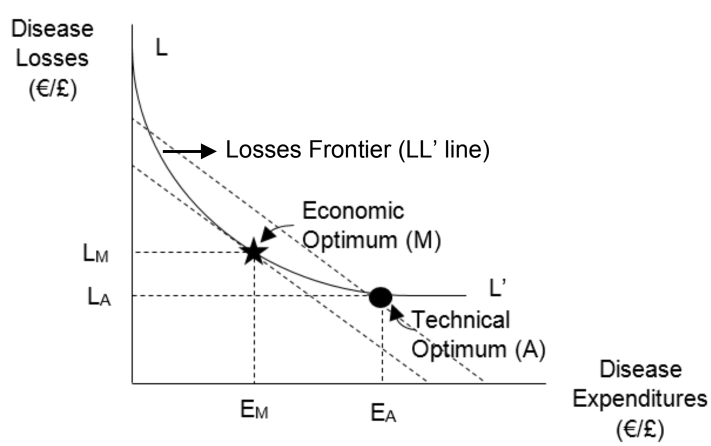
There are, however, certain key-elements that should be included in an economic analysis which do not have a market price, being therefore difficult to quantify. These are referred to as 'intangibles', and include the following examples: consumers' confidence in a given animal product, which will influence their willingness to purchase that product, and a reduction of the well-being of farmers and farm personnel due to the presence of disease, which is also applicable with people for whom animals have a strong cultural meaning (Henriques, Carvalho, Branco & Bettencourt, 2004). The importance of including intangibles in an economic analysis of animal disease is also quite evident when considering zoonosis. Even if, financially, a disease control programme doesn't seem viable, the priority of securing public health will most likely lead to the adoption of the programme, if there is no better alternative.

Considering expenditures, these represent the extra inputs/resources that have to be allocated to livestock production due to the presence of disease. Expenditures may take one of two forms: expenditures on treatment, which constitute an *ex post* disease response, in which resources are used in order to moderate the impact of the already present disease; and expenditures on control, which constitutes an *ex ante* response to disease, in which resources are allocated in an attempt to prevent the occurrence of disease. The relationship between these two types of expenditures can be a substitute one, in which a producer may choose to focus on one or the other or, most often, they can be complementary used. Not all expenditures concerning disease prevention and control are easily identifiable and seen as such, mostly because they have routinely been incorporated into common farm-management practices, such as housing conditions, environmental control and hygiene procedures (McInerney et al., 1992).

Adapting this framework, Bennett (2003) established the 'direct' costs of an animal disease as C = (L+R)+T+P, in which the total cost of disease (C) is the sum of output losses (L) due to the disease, non-veterinary expenditures such as increased feed and labour (R), expenditures on treatment (T) and expenditures on disease prevention (P). As for the 'indirect' costs of animal disease, the author mentions its impact on human health, animal welfare and on international trade, but does not include them in his study.

The determination of this so called 'cost' is not a simple one. The cost of disease can either be determined from the standpoint of the producer, comprising the private cost of disease, or from a societal point of view, comprising the public cost of disease. While the first may be simpler to calculate, the second provides a wider range of impact assessment, since it includes losses that affect other sectors of production apart from the primary sector, like product quality impairments, as well as state expenditures on public veterinary services, amongst other factors (McInerney et al., 1992). Given that the cost of disease seems to result from the sum of losses and expenditures, these two concepts are therefore inversely related, that is, if expenditures on treatment and control increase, the result should be a reduction in experienced losses. There are consequently numerous combinations of these two concepts, and it is an economic task to evaluate which of these combinations minimizes the total economic cost of disease. This conceptual relationship was defined by McInerney and others (1992) as the 'Loss-Expenditure Frontier', which is presented in Figure 2 in a simplified form.

Figure 2: The Loss-Expenditure Frontier (adapted from McInerney et al. 1992)



Upon analyzing the figure, it can be seen that if no expenditure is used in disease control, disease losses will be at their peak (L). From this point, increasing expenditures on treatment and prevention will lead to a reduction in experienced losses. The LL' line represents the 'frontier', that is, the minimal level of output loss that can be experienced at each level of expenditure. Points above the line signify an inefficient use of resources on disease control, given that those expenditures could be leading to a lower value of experienced losses, represented by a point on the LL' line. This type of model illustrates the notion that the economic benefit due to disease control can be calculated by taking into account the expected reduction in disease-induced losses, which corresponds to a certain level of expenditure on its control (Rushton, 2009).

The relationship between losses and expenditures follows the law of diminishing returns, that is, for each additional euro/pound spent in controlling disease, the additional return in terms of reduced losses will be progressively smaller, until it reaches a point in which additional expenditures will be irrational from an economic point of view, since they will not lead to additional reductions in losses. This point can be named the 'technical optimum' (A), and from there on, the loss-expenditure frontier becomes horizontal. It should be noticed that, should eradication be achieved, the curve would be shown to intersect the horizontal axis at a given expenditure level. However, in many cases, eradicating a disease at the individual farm level is hardly rational from an economic point of view, or even from a technical point of view, and the curve will likely take the presented form (McInerney et al., 1992; Marsh, 1999).

The relationship between losses and expenditures due to BRD, for instance, will likely take the form presented above, and the economic analysis of this disease would culminate in the ideal combination of expenditures on controlling the disease and the level of losses acceptable. This ideal combination is called the 'economic optimum' (M), and corresponds to the point on the LL' line in which an additional euro/pound spent on disease control is returned as another euro/pound as reduced losses, that is, when the value of expenditure is such that the extra economic benefits from controlling the disease (taking the form of reduced losses) equal the extra control costs (McInerney et al., 1992; Rushton, 2009).

From this, two vital conclusions can be drawn: firstly, more important than the cost of disease *per se* is the overall avoidable costs that arise from disease control and that, at the economic optimum, these avoidable costs are minimized; secondly, the economic optimum implies that there will always be an accepted cost due to the presence of disease, which can be presented as the sum of (L_M+E_M) (McInerney et al., 1992). The economic optimum is not a static concept, but a dynamic one, being influenced by advances in terms of disease-control methods and changes in consumer demand, as well as the price of inputs and outputs involved in the production process, and should therefore be under constant reassessment. For example, if the economic value of a certain livestock species increases, greater benefits can be obtained from investing in the control of diseases that affect that species (Otte & Chilonda, 2000; Rushton, 2009).

Another way of looking at animal disease is its influence on three basic concepts: people, products and resources. People are the engine of economic activity, since they are the demanders of livestock products and make decisions towards its purchase. The products correspond to the outputs of livestock production, and are either goods or services that aim to satisfy people's needs. As for the resources, they are the primary factors and services used to make the products, being the starting point of animal production. Disease acts as a negative input in the production chain, and can affect all three of its concepts: it can impair the process of transforming resources into products, leading to a reduction in output and/or to an increase of resources used, and it might also generate suspicion and distrust on consumers, which will likely lead to a drop in consumption (Dijkhuizen et al., 1995). It can then be concluded that disease impact, as well as the impact of its control, stretches throughout the production chain, from the farm to various processing and retailing intermediaries, before ultimately reaching the consumer (Marsh, 1999).

Determining the effects disease has on livestock production is an intricate task, given that these effects: are not always perceptible; are influenced by environmental and management factors; have a temporal dimension, which complicates their determination at different time frames; and often occur due to a combination of several diseases (Dijkhuizen et al., 1995).

A standardized method to evaluate the direct costs associated with 30 endemic diseases in the UK has been proposed by Bennett (2003), which involved: identifying the populations and production systems at risk, as well as the annual incidence of each disease on these populations; identifying and valuating the effects of each disease on the production systems; estimating the value of the direct losses due to disease on livestock production; and identification and estimation of the expenditures on treatment and control measures. A similar list of requirements for a thorough economic evaluation of animal disease control policies has been proposed by Otte and Chillonda (2000). These requirements include full knowledge of the disease and its occurrence, effects on the production process and those that extend beyond the process, as well as identification and benefit versus cost assessment of control measures.

As mentioned, economic analysis also serves as a vital tool in the evaluation of disease control programmes, which are in constant development (for example, when introducing new vaccines). Disease control means that a certain degree of disease will be seen as acceptable, and efforts will be made to reduce the prevalence of existent infections and the incidence of new ones, while at the same time minimizing production losses due to clinical disease (Radostits, 2001). Upon development, and prior to implementation, it is imperative to consider both the costs and the benefits of the programme, which will need to be weighed against each other. As proposed by Henriques et al. (2004), and to facilitate its assessment, costs can be divided into non-medical prevention costs and direct and indirect costs. The independent approach to non-medical preventive measures serves the purpose of highlighting its crucial importance in the success of the programme (Figure 3).

Figure 3: Costs of a disease-control programme (adapted from Henriques et al., 2004)

Costs of a Disease-Control Programme		
Non-Medical Prevention Costs	**Direct Costs**	**Indirect Costs**
Daily monitoring of animals; Control and restriction of animal movement; Infrastructures and handling for isolation and quarantine; Implementation and constant update of a record system.	Labour; Transport*; Infrastructures; Equipment; Sanitary culling*; Vaccines*; Sampling and diagnostic tests*; Medicines*. * = *variable costs*	Externalities; Impairment of reproductive selection programs due to sanitary culling; Loss of genetic heritage in breeds at risk of extinction due to sanitary culling.

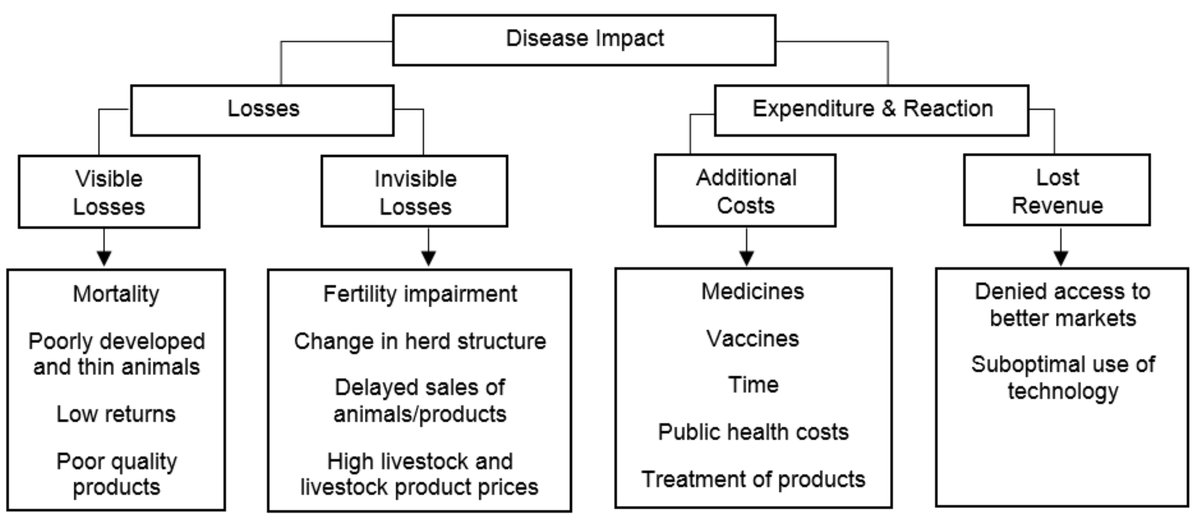
The direct costs of implementing a disease-control programme are usually easier to estimate than the benefits, and include both variable and fixed costs (Henriques et al., 2004). Variable costs are those specific of the developed programme, and therefore will vary accordingly to the level of programme activity. As for fixed costs like land, capital, labour, infrastructures and equipment, they usually do not vary over the period of analysis (Rushton, 2013). The existence of fixed or start-up costs, always present, creates a so called control threshold that needs to be surpassed by benefits as they are generated before covering the costs of the programme (Rushton, 2009).
Considering the indirect costs of a disease control programme, a concept worth mentioning is that of ‘externality’. Externalities can be defined as the consequence of a certain economic action experienced by unrelated third parties, and may be positive or negative if that consequence is beneficial or harmful, respectively. An example of a positive externality is the implementation of a vaccination protocol on an individual farm: by vaccinating their animals, producers can decrease the risk of infection spread to neighboring farms. Disease can also act as a negative externality, for example by increasing the risk of infection on neighboring farms or by contributing to environmental pollution due to residues of products used in disease treatment and control (Henriques et al., 2004).
The total costs of each programme are highly dependable on the disease itself, the country in which it is to be applied, the existent infrastructures and Veterinary services, production systems and size and scattering of livestock herds (Henriques et al., 2004).

As for the benefits, their assessment is usually more complex to determine, given that it demands a comparison between the costs attributable to disease with and without the programme

(Henriques et al., 2004). Benefits derived from animal disease control may be of different categories, as presented by Martin et al. (1987): benefits that are easily quantifiable, for example an increase in milk production; benefits not so easily quantifiable due to unclear or inaccurate market values or because the consequences of disease control are uncertain, for example the influence on the export price of beef, and, lastly, those benefits that fall under the intangibles category. By comparing different productivity measures between diseased and healthy animals, the loss of production efficiency due to the presence of disease can be estimated or, reversely, the expected production gains due to disease control can be assessed (Marsh, 1999). Upon evaluating the benefits derived from the implementation of the programme, and given their importance, externalities and intangible benefits should also be taken into account. These include: greater animal product quality and offer; access to new markets and improvement of trading relationships; growth of income and employment for Veterinary Medicine professionals; higher investment in livestock production due to less susceptibility to disease and a strong confidence-built relationship between farmers and veterinarians (Henriques et al., 2004).
When the benefits of the programme are finally determined, they are weighed against the costs of implementation and, if they surpass them, the programme is considered viable (Henriques et al., 2004). The costs and benefits of controlling a certain livestock disease may not always be easy to ascertain, however, either because there is a lack of information or because the collection of such information proves to be unviable from an economic perspective (Rushton, 2009).

A more recent framework for livestock disease-impact assessment further disaggregates the impacts of animal disease, and it is presented on Figure 4.

Figure 4: Compartmentalized disease impact on a livestock system



Sources: adapted from Rushton et al. (1999) and Rushton (2016)

Underlined by McInerney's definition of losses and expenditures, Rushton et al. (1999) developed a framework that illustrates the elements necessary for livestock disease impact assessment. The main division of this framework is the differentiation between losses due to the presence of disease, that is, the impact caused by the disease and its consequent health impairments, and expenditures that originate from human reaction to the presence of disease. Concerning losses, the authors also propose a division between visible losses, as in those losses that are directly and clearly perceived by the producer, and invisible losses, which have a tendency not to be so easily perceived in the short term. As for expenditures, disease-control measures in terms of treatment and prevention take the form of additional costs. Lost revenue corresponds to the opportunities lost due to the presence of disease, or even due to the risk of disease occurrence. This can translate into denied-access to markets, or to the inability of producers to use more productive breeds or more technically advanced technologies.

Upon considering the decision-making process in animal health economics, it is important to distinguish between the different levels of intervention, namely: farm level, regional level and both national and international level, given that the economic analysis in each of these will have distinct requirements and complexities. The simplest analysis occurs at farm level, where the main concern is to evaluate how disease affects herd productivity, as well as the costs of instituting a disease-control programme. At regional level the analysis will be more complex and, given its larger magnitude, there will most likely be a certain degree of uncertainty, and therefore might be useful to incorporate the probability of several outcomes into the analysis. Considering the larger scale of intervention, the positive influence of a disease control programme on the quantity of output produced should also be evaluated, given that there might be a deflation in the price of animal products due to an increased offer. If this happens, a transfer of benefits occurs from the producers, who will only retain a portion of what they invested, to the consumers, who will assimilate a significant proportion of these benefits through lower prices. The most complex form of analysis will be the one performed on national and international level, and the elements that need to be taken into account will be more numerous. Market restrictions and opportunities, as well as externalities, are of significant importance when performing a national economic analysis of disease and its control. An additional source of complexity will be the likelier inclusion of intangibles in the analysis (Morris, 1999).

There are several methods that can be used in the economic assessment of animal disease and its control, both at the farm/individual level and at national level, and the choice of one in detriment of others will depend on several factors, including: the problem's nature; the intricacy of the system involved; the availability of data and resources; and the use to which it will be put to (Otte & Chilonda, 2000). Some of the most widespread methods are summarized on Table 4.

Table 4: Economic methods for the evaluation of animal disease and its control

Economic Method	Intervention Level	Method Description
Gross Margin Analysis and Enterprise Budgets	Farm level	Used to evaluate an enterprise's economic viability. Gross margin is defined by the total revenue minus variable costs, with fixed costs not included in the analysis. The results are presented as output per standard unit (livestock units, acres, hectares, for example). An enterprise budget is calculated by subtracting fixed costs from the gross margin, allowing for the determination of profit from a given enterprise. Both these methods are useful for comparison of different enterprises and when evaluating the productivity of a specific enterprise, when the goal is profit maximization.
Partial Budgeting	Farm level	Describes the economic consequences of introducing a change in farm procedures (like a new vaccine or medicine), in the form of increase/decrease in net farm income. Requires four basic items to be evaluated and quantified: new costs plus revenue foregone, the 'costs', and costs saved plus new revenue, the 'benefits'. If the sum of benefits is greater than the sum of costs, adopting the change is advantageous for the farm. There is no incorporation of uncertainty or risk, and fixed costs are usually not included.
Decision Analysis	Farm level	More appropriate when there is uncertainty involved in the occurrence of disease, or concerning the different outcomes of events. It identifies all the available courses of action, and incorporates the notion of risk and attitude towards risk into the analysis. Three elements are considered: the alternatives available for the decision maker, the probability of occurrence of chance events and the financial value of the different outcomes. The expected value of an outcome is calculated by multiplying the probability by the value of the outcome. The analysis can be performed in the form of pay-off tables or decision trees, with these having the advantage of explicitly presenting the chronology of events.
Simulation Models	Farm level	Their objective is to simulate the dynamic and risk features of disease within livestock systems, in an abstract representation of reality. These models are computer-based, and built essentially for prediction purposes. This method is usually more time-consuming and expensive when compared to the others used at farm level.
Cost-Benefit Analysis	Sector, National and International level	Allows for the comparison of costs and benefits of a given enterprise that extends beyond a one-year period, given the inclusion of the concept of time value of money. This allows for the evaluation of a farm change over the course of several years, requiring not just the identification of costs and benefits, but also the time at which they occur. Discounting (conversion of future monetary values into present values) allows for the comparison of costs and benefits occurring at different times. This comparison is done recurring to three criteria: net present value, benefit-cost ratio and internal rate of return. It is held as the most useful method in analyzing costs and benefits of long-term disease control programmes at regional/national level.
Cost-Effectiveness Analysis	All levels	It helps determining how the desired result can be obtained at a minimum cost, taking into account both quantifiable and intangible benefits of a disease control programme. It is also useful when

		comparing control strategies with similar losses. It can be used *per se* or in hybridization with a cost-benefit analysis.
Mathematical Programming Methods	Sector, National and International level	The objective is to maximize an objective function. This method allows for the inclusion of several objectives and decision-making criteria accordingly to the interests of all stakeholders, aiming for a compromise solution. Their application requires a certain resourcefulness.
Economic Surplus	Sector, National and International level	Aims at quantifying the impacts of a change in the supply-curve of a given commodity and the resulting economic surplus, considering both consumers and producers of that commodity. This is based on the premise that that said change will alter the supply of that commodity, which will then have an effect on its price.

Table 4: Economic methods for the evaluation of animal disease and its control (continuation)
Sources: Adapted from Martin et al. (1987), Rushton et al. (1999) and Otte & Chilonda (2000)

Apart from intervention level, it is also of vital importance to contemplate the pattern of disease occurrence upon the choice of an analytical method. Endemic diseases, that occur in the vast majority of livestock herds in a given region or country and act as a negative production impact on a yearly basis, usually require only a gross margin and partial budgeting analysis at herd level, and a cost-benefit one at regional or national level. Partial budgeting is also useful in retrospective studies of disease outbreaks. Decision analysis is usually better suited when considering sporadic diseases that affect a limited amount of herds each year, given the necessity to include the probability of an outbreak into the analysis. For epidemic diseases, usually absent or present at a very low level due to a tight control, decision analysis also seems to be the most appropriate method, for the same reason (Martin et al., 1987; Morris, 1999; Rushton et al., 1999). Despite the different degrees of complexity and requirements, the biggest constraint in the use of these methods for the economic analysis of animal disease impact and control seems to be the lack of solid data, both in terms of financial accounting and production records, as well as its organization into a format that suits the analysis (Marsh, 1999; Rushton et al., 1999).

As seen, the economic assessment of animal disease is a multidisciplinary task, with key contributors from heterogeneous areas. There is also a role for the veterinarian professional other than their clinical skills, with this practitioner acting as a provider of information concerning disease occurrence, losses due to disease at various production stages and the availability and costs of control measures (Otte & Chilonda, 2000).

The economic impact of BRD on the bovine sector, under the form of losses and expenditures, will now be described in Chapter V.

CHAPTER V: The Economic Impacts of BRD on the Bovine Sector

For a more compartmentalized and practical understanding of the BRD impacts on the bovine sector, these will be differentiated between losses and expenditures, following the terminology proposed by McInerney and others (1992) detailed in the previous chapter. Concerning losses, and given that there are considerable differences between the dairy and meat bovine sectors, these will be approached independently in each sector.

5.1. Economic Impacts of BRD on the Dairy Sector – Losses

5.1.1. Daily Gain and Slaughter Weights

Enzootic calf pneumonia is shown to negatively affect the growth rate of dairy calves reared for veal and beef. In the presence of lung lesions at slaughter, cross-bred dairy and beef calves have shown reductions in ADG which, consequently, led to lower carcase weights at slaughter, with a loss of about 4.3 kg when compared to carcases without lung lesions (Ames, 1997). Pure dairy bred animals with pneumonic lesions at slaughter were estimated to have suffered a 7.2% reduction in ADG due to respiratory disease (Andrews, 2004).

5.1.2. Failure to Reach Growth Targets

Contrary to what happens in lactating cows, whose individual performance is daily measured in terms of milk yield, performance monitoring of dairy heifers is many times neglected (Bach & Ahedo, 2008). The growth rate of female dairy calves destined to become herd replacements is a determinant factor for age at first calving, also correlating to future milk production (Virtala, Mechor, Gröhn & Erb, 1996). A retarded growth rate, as seen in cases of enzootic calf pneumonia, can be expected to reduce lifetime milk and calf production and manifest itself as a greater age at first calving and increased probability of culling (Sivula et al, 1996).

Upon studying the effect of calfhood diseases on the growth of female dairy calves, Virtala and others (1996) concluded that pneumonia led to a reduction of weight gain of 3.8 kg during the first trimester of life. In a similar study, Donovan, Dohoo, Montgomery and Bennett (1998) reported that pneumonia in Holstein dairy replacement calves slowed growth during the first semester of life, so that these animals would need an additional 13 to 15 days to reach the same weight as healthy calves. In this study, with approximately five days of treatment required, the authors predicted a depression of 10.6 kg in 180 day weight gain. When it came to affected heifers, they would be expected to suffer a 3.2 kg reduction in growth by the time they reached 14 months, which translates to an additional 4.4 days to reach the same body weight of healthy herdmates. Another study concluded that, by 14 months of age, heifers that suffered from BRD were about

30 kg lighter than healthy herdmates, with some animals weighing 54 kg less (Van Der Fels-Klerx et al, 2002b). In a commercial dairy heifer rearing operation in Zaragoza heifers that suffered from respiratory disease left the operation at 675 days of age - compared to 669 days for healthy heifers - 624 kg (less 3 kg than healthy heifers) and had an average daily gain on 881 g/day, compared to 890 g/day reported for healthy heifers (Bach & Ahedo, 2008).

5.1.3. Mortality

When evaluating mortality costs due to a given disease, apart from the number of dead animals, it is also of importance to ascertain mortality distribution between the different categories of animals in the farm, since their economic value will be different and given the fact that mortality rates will probably vary between these categories (Henriques et al., 2004). Dairy farmers tend to underestimate calf mortality rates, a reflection of the lesser importance they attribute to calf disease. In developed countries, and under good management conditions, perinatal mortality (during the first 24 hours) should range between 1% and 3%, neonatal mortality (from 24 hours to 28 days) should be around 3% and older calf mortality (from 29 days to 182 days) should not go beyond 1%. The registered annual mortality for calves up to one month of age should ideally be inferior to 3-5% (Radostits, 2001).

BRD is held as the second most common cause of death in preweaned dairy calves, and the main cause of death in weaned dairy cattle (Gorden & Plummer, 2010; Love et al., 2016). Studies conducted on dairy farms point to pneumonia being responsible for up to 20 to 50% of all mortality cases. In addition, female calves treated for pneumonia in the first trimester of life had a 2.45 higher probability of dying before first calving (Ames, 1997). Upon evaluating the impact of dairy calf pneumonia, Ames (1997) also described mortality rates due to the disease that varied from 1.8% to 4.2%. Sivula and others (1996), reported mortality rates of 7.6% in dairy replacement calves, with pneumonia being accountable for about 30% of all occurring deaths. When mortality losses are very significant, dairy producers will be forced to raise the totality of surviving heifers and therefore will be unable to cull for selective herd improvement (Radostits, 2001).

BRD in dairy heifers may increase mortality by up to six times directly after the disease episode, and also increase the risk of mortality in later stages of life. Episodes of severe pneumonia in calves younger than three months were shown to increase mortality levels by nearly 20%, with affected animals having a 6.5 times higher mortality risk than healthy herdmates (Van Der Fels-Klerx et al, 2002b). Concerning mortality in older animals, mortality rates for severe cases of chronic suppurative pneumonia may be as high as 95% (NADIS, 2015).

5.1.4. Culling

At an annual basis, about 25% to 35% of cows in a dairy herd are culled (Radostits, 2001). In the UK, the annual culling rate in dairy herds revolves around 22% to 25% (Sherwin, 2015).
Dairy calves with episodes of respiratory disease have been shown to present a higher risk of culling in comparison with healthy herdmates (Sivula et al., 1996). This is also valid for cows treated as adults (Ames, 1997). The culling rate due to pneumonia has been reported to be of 3.6% (Andrews, 2004). It should be noted that precocious culling of dairy heifers may have a significant negative impact on the dairy enterprise, given that replacement heifers represent a major economic investment and are held as the second biggest financial input in the sector, preceded only by feed costs (Ames, 1997).

5.1.5. Fertility

The negative impact of BRSV infection upon bull fertility has been evaluated in both dairy and beef bulls. Bull fertility is a vital factor for the success of a dairy enterprise, since a single bull is used to breed a large number of cows, especially considering the widespread use of Artificial Insemination (AI) technology (Kathiravan, Kalatharan, Karthikeya, Rengarajan & Kadirvel, 2011). Semen quality used to breed cows either by AI or natural service is one of the factors that affect the conception rate (Johnson, 1997). Upon studying the effect of acute BRSV infection with concurrent respiratory disease in 79 dairy bulls in a reproductive station in Finland, Alm and others (2009) concluded that the seropositive bulls had poorer semen morphology and only 74.1% of normal spermatozoa, compared with 81.2% observed in seronegative bulls, which was statistically significant. Also significant was the effect on field fertility, with the 60-day non-return rates being 75.2% and 76.8% for BRSV seropositive and seronegative bulls, respectively.

5.1.6. Somatic Cell Count

Somatic Cell Count (SCC) is an important tool in the measurement of milk quality and a reflection of the mammary gland health status, being a key component of both national and international milk quality regulation. High SCC values are associated with reductions in milk yield and changes in milk quality (More, Clegg, Lynch & O'Grady, 2013). A level of SCC of 400 000 cells/mL, the maximum threshold allowed by European legislation, may correspond to a daily 2.61 kg of milk lost per cow (Rodrigues, Guimarães & Oliveira, 2012). Furthermore, high SCCs impair cheese production due to a reduction in curd firmness, increased fat and casein loss and diminished sensory quality, also reducing the shelf life of pasteurized liquid milk (More et al., 2013).
In Portugal, the main milk buyers and processors have different scales of prices paid to the producer depending on certain SCC thresholds, favoring and therefore incentivizing low SCC

levels (Rodrigues et al., 2012). This is also a common practice in the UK, with producers being financially rewarded for low levels of SCC and penalized for higher ones (AHDB, 2016). Therefore, the absence of bonification combined with the reduction in milk production due to high SCC levels can also present a negative impact on dairy farm's profitability (Rodrigues et al, 2012).

Upon studying BRSV's prevalence in bulk tank milk in Swedish dairy farms, Ohlson et al. (2010) estimated that prevalence to be of 79%. The authors also concluded that positive farms had higher SCC levels when compared to negative farms. Mean SCC levels for positive herds were estimated at 218 000 cells/mL, in opposition to 163 000 cells/mL estimated in negative herds. Another Swedish study reported a significant increase in SCC of 12 000 cells/mL for cows in herds suffering from BRSV outbreaks compared to cows from BRSV-free herds (Beaudeau, Ohlson & Emanuelson, 2010).

5.1.7 Milk Yield

There have been some reports of decreases in milk yield particularly due to BRSV infection. Since 1988 severe outbreaks of the virus have been known to occur in Swedish dairy herds, mainly naïve herds located in more isolated areas and that had a recent history of purchasing animals. During these outbreaks, milk production was reported to be reduced in 20% to 60% during one to two weeks post-infection (Elvander, 1996). In a BRSV outbreak that occurred in 1994-1995 in Norwegian dairy farms, the average daily milk loss was estimated to be of 0.7 kg of milk per cow in the seven days following a herd outbreak (Norström, Edge & Jarp, 2001). Recently infected herds in Sweden suffered a significant reduction in milk yield of 0.57 kg per day, and this reduction reached 0.91 kg per day in farms suffering from outbreaks of BRSV-induced disease (Beaudeau et al., 2010).

The impact of undifferentiated BRD on milk yield has also been studied, with this syndrome being perceived to decrease first lactation yield by 150 kg, with values ranging from 40 to 250 kg of milk (Van Der Fels-Klerx, Saatkamp, Verhoeff & Dijkhuizen, 2002). Decreased revenues due to losses in milk yield were also amongst the main negative effects of BRD in a study conducted by Demir and Bozukluhan (2012). In cases of chronic suppurative pneumonia, milk production has been reported to only reach 25% to 50% of expected yield (Scott, 2013).

5.1.8. Age at First Calving

Replacement heifers represent a major long-term investment in dairy enterprises, with no financial return until inclusion in the milking herd. Indeed, heifers generally became profitable only after their second lactation (Bach & Ahedo, 2008; Cooke, Cheng, Bourne & Wathes 2013). Age at first calving has a great weight on the total heifer-cost in more intensive systems, mainly because the efficiency of nutrient use and age are inversely related. Feed costs represent about 50% of the total cost of rearing (Bach & Ahedo, 2008). The number of calves needed to be reared as replacement animals is highly dependable on herd management and health, but approximately 30% of a milking herd is usually replaced on a yearly basis (Radostits, 2001).

It is known that one of the key objectives of dairy heifer rearing is ensuring an economically efficient growth so that calving occurs at an age and body weight at which lifetime milk production and profitability will be maximized, while also minimizing the probability of dystocia and post-calving metabolic diseases. For the Holstein breed, the ideal calving age has been reported to be around 24 to 25 months, with a target heifer weight at calving around 515 to 600 kg (Donovan et al, 1998; Bach & Ahedo, 2008). The earlier first calving is achieved, the shorter the unproductive life of that heifer will be, the lower the required number of replacement heifers will be, and rearing costs can be reduced due to decreased feed, labour and building costs (Bach & Ahedo, 2008; Cooke et al., 2013). In fact, reducing age at first calving from 25 to 24 months has been reported to come with a 4.3% decrease in replacement costs. Even though this reduction may have a detrimental effect on first lactation yield, aiming for a first calving age below 26 months seems to be economically viable, with biggest profits being attained with a 23-24 months goal (Cooke et al., 2013). Some authors have estimated that a daily loss of $1 to $3 can occur for each day beyond the goal of 24 months of age at first calving. This loss takes into account feed costs, veterinary-related costs, housing, labour and opportunity costs, amongst others (Ames, 1997). Similarly, Keown and Kononoff (2006), predicted a $30 monthly loss for each month without calving beyond the 24 months-goal. Following Keown's and Kononoff's study, Rodrigues and others (2012) estimated that, for each month beyond the 24 month-calving goal and for a milk price of 0.32€ per litre, producers would lose 31.03€.

Female heifers with poor growth rates, as those who suffered from respiratory disease as calves, tend to have a delayed age at first calving (Ames, 1997), as well as an increased probability of dystocia (Van Der Fels-Klerx et al, 2002b). The average first-calving age for heifers that suffered from BRD within the first 90 days of life has been reported to be delayed by three months in comparison to health herdmates. Concerning calving, heifers with history of BRD have been shown to have a 2.4 times higher probability of dystocia, due to the impairment BRD has on growth (Van Der Fels-Klerx et al, 2002b).

5.2. The Economic Impacts of BRD on the Meat Sector – Losses

5.2.1. Average Daily Gain, Slaughter Weights and Growth Targets

The significance of expenditures on treatment and prevention of BRD in feedlots is heavy, but may be surpassed by the economic impact this syndrome has on reduced performance and consequent less economic returns. However, given the inherent difficulty of evaluating these more 'hidden' performance losses, they are often overlooked despite their economic weight (Radostits, 2001; Williams & Green, 2007). ADG assessment acts as a general efficiency measurement and, given that feedlot animals are generally kept and evaluated in terms of productivity on a group basis, can be calculated as:

$$\text{ADG} = \frac{\text{Total weight gain by the group (kg, lb)} \div \text{Number of animals}}{\text{Days on feed}}$$

Beef cattle suffering from BRD were shown to have gained 3% less weight when compared to healthy herdmates, while at the same time their feeding costs were 18.5% higher (Griffin, 1997). Gardner, Dolezal, Bryant, Owens & Smith (1999) reported that steers treated for BRD presented a 4% lower ADG than non-treated steers (3.24 vs 3.36 lb/day), which resulted in 16.5% lower carcase weights for the treated steers. In addition, weight gain was reduced by 14.8 lb/day for each day a steer required medical treatment. Studies seem to support that the detrimental effects BRD has on ADG tends to be more significant when more than one episode of treatment is needed (Radostits, 2001). Williams and Green (2007) concluded that beef cattle whose lungs showed signs of pleurisy and consolidation had experienced significant reductions in ADG of up to 202 grams per day. Snowder and others (2006) concluded that feedlot calves diagnosed with BRD had statistically significant lower ADGs than healthy calves (0.95 kg/day versus 0.99 kg/day, respectively), while Schneider et al. (2009) reported decreases in ADG that ranged between 0.07 and 0.37 kg/day in steers suffering from BRD, which weighted about 11 kg less at slaughter than healthy ones. Despite the harmful effect BRD seems to have on ADG and slaughter weights, Brooks et al. (2011) concluded that feedlot heifers that were treated for BRD a total of three times, as well as heifers chronically affected, could reach slaughter weights and carcase characteristics similar to those reported for healthy heifers. However, that would demand a period of compensatory growth, with increased feed and housing costs, which would therefore result in poorer returns obtained from those animals.

Subclinical disease, reported in several studies concerning beef cattle, is also a grave and insidious consequence of BRD. If up to 20% of all growing calves may present ante-mortem signs of respiratory disease, up to 37% may present lung lesions at slaughter. Such lesions might decrease ADG by more than 0.2 kg/day and cost the producer around £30 to £80 per animal (Statham, 2013). In a previous study, Griffin (1997) reported a statistically significant difference of 0.225 pounds in ADG between cattle with and without lung lesions at slaughter, and concluded that animals with lung lesions at slaughter outnumbered those that had been previously diagnosed with BRD. Similarly, Gardner et al. (1999) concluded that cattle without lung lesions had heaviest final live weights as a result of 12% (3.48 vs 3.08 lb) greater ADG than cattle with lesions. The authors also noticed that about 37% of the steers taken as healthy had lung lesions at slaughter. Other study found that, for a 35% of a total of 469 feedlot animals treated for BRD, 68% of untreated cattle had lung lesions at slaughter. Upon evaluating these animals' feeding performance, cattle with lung lesions had experienced reductions in ADG of about 0.17 pounds per day (Edwards, 2010). Stilwell et al. (2013) found that in a sample of 166 Holstein-Friesian feedlot calves, 51 presented lung lesions at slaughter. From these, 59% had never been diagnosed with BRD, but presented lower ADG during growth.

Given the relevance of subclinical disease, analyzing the presence of BRD in feedlots could be enhanced by combining treatment records with records of lung lesions at slaughter. This feedback, provided it reaches the producers, may help them adjust their management practices in order to reduce the presence of BRD and its nefarious effects on their animals (Williams & Green, 2007).

Klem et al. (2016), investigated the impact of a BRSV outbreak in a Norwegian beef herd during the year 2011. The authors' capacity to attribute the negative impacts of the respiratory disease that affected the animals mainly to BRSV, besides antigenic detection, serum antibody titration and necropsy findings, is due to the fact that Norway has successfully eradicated other primary viral agents of BRD, namely BHV-1 and BVDV, with *M. bovis* never having been detected in the country. However, the authors were unable to prove that the production losses registered were not also due to secondary bacterial infections, which once again adds to the problematic of BRD as a multifactorial disease. In this study, a proportion of 21% (56 in 265) of bulls required treatment, with these animals being younger that non-treated animals, with a mean age of 156 days in comparison to 255 days. Both medicated and non-medicated bulls suffered losses in body weight during the time of the outbreak, although the loss was higher in medicated bulls, with statistically significant values of 6% and 3%, respectively. Bulls with clinical signs of disease had a significant slower growth rate during the eight months study period. In addition, upon comparing growth rates of apparently healthy bulls during the outbreak and another group of bulls one year later, the apparently healthy group had in fact an inferior growth rate in 111 g/day, which led to an additional 23 days for these animals to reach target weights. The FCR, which represents the amount of feed consumed in order for an animal to experience an increase of 1kg of liveweight, was also impaired by 79 grams of weight gain per kilogram of consumed concentrate.

Given this growth impairment, animals affected by BRD may need an additional 14 days to reach breeding weights (AHDB, 2013). Apart from its importance in the rearing of replacement dairy heifers, the negative effect of BRD on growth targets is also extremely relevant in animals destined for meat production. Growth rates are one of the key profitability factors for meat cattle rearing, since they determine feed costs and slaughter weights (Klem et al., 2016).

5.2.2. Carcase Characteristics and Meat Quality

The method of pricing cattle accordingly to carcase characteristics has led to a reevaluation of the impact BRD, similarly to other diseases, has on feedlots. When cattle are sold primarily based on liveweight, disease impact can be calculated as death loss, treatment costs and decreased feed efficiency and liveweight. However, when carcase quality is taken into account, disease impact investigation must also focus on the ability of disease to affect not only carcase weight but its quantity and allocation of muscle, fat and water. The evidence that BRD has damaging effects on carcase characteristics such as weight, longissimus muscle area, marbling and tenderness is growing. These detrimental effects seem to be particularly evident in animals suffering from multiple or prolonged disease episodes (Larson, 2005).

Williams and Green (2007), upon studying associations between lung lesions at slaughter and ADG in beef bulls, concluded that there was a significant positive association between the number of lung lobes affected and lower prices paid per carcase, with carcases with more extensive lung damage being significantly more likely to receive lower conformation grades. As a result of lighter final live weights, steers treated for BRD have been reported to have 2% lighter carcasses in a study by Gardner et al. (1999), which corresponded to a difference of 16.5 pounds between medicated and non-medicated steers. In addition, carcases from non-medicated steers were fatter, both externally as well as internally, when compared to medicated steers and had slightly higher mean marbling scores. Schneider and others (2009) reported that cattle never treated for BRD had more desirable estimates for all studied carcass traits when compared to treated cattle, namely hot carcase weight, longissimus muscle area, subcutaneous fat thickness and marbling score, and that hot carcase weight and marbling score had an inverse relationship with the number of BRD treatments needed. This relationship between marbling and the number of BRD treatments was also concluded in a study by Holland and others (2010). The impairment of BRD on subcutaneous fat thickness was also reported in a study by Garcia, Thallman, Wheeler, Shackelford and Casas (2010). This impairment may lead to a reduction in meat quality, since moderate levels of subcutaneous fat seem to improve tenderness by reducing the extent of cold-induced myofibrillar toughening, as well as enhancing *postmortem* muscle autolysis. Subcutaneous fat acts as a thermic isolator, reducing the velocity of cooling and avoiding dehydration and darkening of meat, and therefore has also been concluded to have a positive influence on meat tenderness and palatability. The desirable level of subcutaneous fat thickness should be a minimum of 2.5 to 3 millimetres in order to avoid cold shortening (Jeremiah, 1996; Bridi & Constantino, 2009).

It should be noticed that the meat industry itself may not be the principal driver of production since it is the consumers, with their demands, that guide production towards the satisfaction of their needs (Edwards, 2010). Consumers' perception of meat quality is therefore a driving factor for the industry, since it directly impacts its profitability. However, this perception is complex, dynamic and therefore difficult to define and assess (Troy & Kerry, 2010). In fact, the very definition of 'quality' is a complex one. The International Organization of Standardization (ISO) created a generally accepted definition of the term, describing quality as "the totality of features and characteristics of a product or service that bear on its ability to satisfy stated or implied needs" (Becker, 2000). The perception of quality by the consumer can be divided into two components: perception of quality based on perceived intrinsic and extrinsic quality cues at the time of buying, forming quality expectations, and experienced quality, upon preparation and consumption of the product. The correlation between expected and experienced quality is what determines consumers' satisfaction with the product, as well as the probability of future purchases (Banović, Grunert, Barreira & Fontes 2009). In terms of intrinsic meat characteristics, they can be divided into four categories: characteristics related to nutritional value, like levels of protein, fat and carbohydrates; characteristics indicating meat processing quality, like pH values, colour, fatness and water-binding capacity; characteristics indicative of hygienic and toxicological quality, like pharmacological residues and microbacterial status; and characteristics related to sensory quality, like tenderness, juiciness, flavour and marbling (Becker, 2000).

On the opposite, extrinsic quality cues are not part of the physical product, and comprise brand/labeling, price, place of purchase and country of origin, for example (Becker, 2000). Indeed, quality labeling is an extrinsic quality cue that consumers may use as a decision tool upon buying meat. In Portugal, quality labeling in the beef sector has grown in the last ten years and, in 2009, accounted for about 3% of the total beef production. However, studies exploring Portuguese consumers' perception of beef quality are very scarce. In one of these studies, the authors concluded that brand was the main quality cue used by Portuguese consumers at the time of purchase, and that it was used by them as a predictor of intrinsic quality cues such as colouring and fat content (Banović et al., 2009). Indeed, other studies state that the importance of extrinsic meat characteristics as drivers of purchase has been a growing trend in Europe (Glitsch, 2000; Verbeke, Pérez-Cueto, Barcellos, Krystallis & Grunert, 2010). A study concerning UK consumers, however, reported that they relied more on intrinsic characteristics when evaluating beef healthiness, even though extrinsic cues also play a significant part in the decision-making process (Verbeke et al., 2010). At the time of purchase, colour and fat content are regarded by consumers as the main indicators of meat quality, highly influencing the buying decision. Fat tends to be perceived as a negative beef attribute, with its positive influence on tenderness, juiciness and flavour seldom being perceived by consumers (McIlveen & Buchanan, 2001).

The negative effect BRD has on beef marbling is reported in several studies. However, upon considering this impact on bovine meat production, care must be taken, and a few considerations are perhaps worth mentioning. The use of marbling as a quality indicator is not without difficulties, since many consumers are not familiar with the term, and find themselves in doubt about how helpful this characteristic is for the assessment of beef quality (Glitsch, 2000). Marbling may be defined as the visible fat present in the interfascicular spaces of the muscle, that is, the intramuscular fat. It has been shown to affect meat juiciness, tenderness and flavour, being positively directed to meat palatability. The conception that marbling is a key contributor to beef palatability is not a universal one, however. The relationship between these two concepts has been widely discussed, with reports of low correlation stating that marbling only accounted for 10 to 15% of the variance in palatability, despite nearly all of the organoleptic properties of beef appearing to be positively related with intramuscular fat levels (Jeremiah, 1996; Troy & Kerry, 2010).

In their study, Brunsø, Bredahl, Grunert and Scholderer (2005) concluded that fat content is a somewhat dysfunctional intrinsic cue upon purchase, since its connection to key quality dimensions like tenderness and flavour is not perceived by consumers, who desire simultaneous low fat meat and highly palatable meat. Therefore, consumers may misjudge the link between marbling and eating quality, contributing to the common phenomenon of low degree of correspondence between expected and experienced quality (McIlveen & Buchanan, 2001).

The importance of colour as a driver of beef purchase has been mentioned, and it is known that marbling, for instance, can alter the visual perception of colour-related quality. The very colour of fatty tissues may influence consumers' preferences, since they usually prefer white-coloured fat in opposition to more yellowish fat, which is frequently wrongly perceived as fat from old and malnourished animals. Fat-colour variations are usually due to type of feed and the biological ability to convert compounds like carotene to other almost colourless forms like vitamin A (Troy & Kerry, 2010).

Marbling degree is affected by several factors, including: breed, slaughter weight, feed regimen and growth rate. It usually varies from 0.5% to 8% (Troy & Kerry, 2010), and seems to be positively related with the level of subcutaneous fat (Jeremiah, 1996).

5.2.3. Mortality and Culling

Mortality levels in feedlot animals are also a concern when it comes to BRD. A study conducted in American feedlots concluded that the total percentage of feedlot deaths attributed to BRD went from 52.1% in 1994 to 61.5% in 1999 (Snowder et al., 2006). The fraction of mortality due to BRD varies accordingly to management practices, prevention measures and infectious agents involved. For instance, mortality levels are usually lower when in the presence of primordial viral infection, increasing to more expressive levels in the presence of bacterial infections. Breed seems to also be a factor influencing morbidity and mortality in feedlot animals, with higher mortality rates reported in Simmental and Holstein-Friesian feedlot calves (Urban-Chmiel & Grooms, 2012).

It is estimated that, in the UK, one in thirteen beef bred calves dies during the rearing phase, with mortality reaching its peak during the first semester of life. Pneumonia is held as the most common cause of death and poor performance in young cattle from weaning up to ten months of age (Statham, 2013). A study conducted in 12 beef farms in the UK during 1978 concluded that, out of a mortality rate of 5.9%, a proportion of 2.7% was due to pneumonia (Andrews, 2004). A similar mortality rate of 2.9% in feedlot calves was reported by Stilwell and others (2013), while in four outbreaks of respiratory disease in beef calves in England and Wales morbidity levels due to BRD reached 90%, with a reported mortality rate of 3.9% (ADAS UK Ltd, 2015). It is worth noticing that mortality, especially in later production stages like finishing, comes with heavy financial losses due to the amount of resources already invested, which will therefore have no return (AHDB, 2013).

Cattle affected by BRD also present a higher culling risk (AHDB, 2013). Culling rates due to BRD in feedlot enterprises have been reported to reach 3.6% (Andrews, 2004).

5.2.4. Fertility

Upon considering cow-calf production, reproduction and profitability are two indissociable concepts. While cow fertility is important on an individual basis, bull fertility's importance is transversal to the entire herd, since bulls will be used to breed a larger number of females. This is even more evident in herds possessing a single breeding bull (Hansen, 2006). Despite this fact, the influence of bull fertility in both dairy and beef herds is many times overlooked. It is proposed that 20% or more of unselected breeding bulls may in fact be classified as subfertile. Therefore, it is crucial that bull fertility is regularly monitored by physical examination and analysis of breeding records is performed as part of a herd fertility management programme (Penny, 2016). Bull fertility can be divided into several parameters, namely: semen morphology and motility, libido, body condition score, ability to copulate, scrotal circumference and freedom from reproductive diseases (Hansen, 2006). Efficient beef herd fertility should aim for a 95% pregnancy rate in a period of 9 to 10 weeks of mating period, with a percentage of 65% or more cows calving in the first 3 weeks of the succeeding calving period (Penny, 2016).

Besides its reported impact on dairy bulls' fertility, BRSV has also been held responsible for possible fertility impairment in beef-breed bulls, with a demonstrated association between the development of testicular fibrotic lesions and an outbreak of BRSV-induced disease in a group of bulls in Argentina. During this outbreak, around 70% of 240 bulls manifested respiratory disease with increased rectal temperature (above 40ºC), with 16 bulls dying due to pneumonia. Immunohistochemistry of lung tissue confirmed the presence of the virus, which was considered as the primary infectious agent of the outbreak. The authors concluded that the biggest impairment on spermatogenesis was during the active disease process that led to fibrosis, since bulls with testicular fibrosis had semen with up to 94% of morphologically normal spermatozoa. Despite the conclusion that large quantities of fibrous tissue would be expected to lead to a reduction in sperm production, this was not measured in the study (Barth et al., 2008).

5.3. The Economic Impacts of BRD on Bovine Production – Expenditures

Expenditures due to BRD can be divided into two categories: expenditures concerning treatment of sick animals as well as capital used to replace animals due to mortality and/or culling phenomena and, on the other hand, expenditures concerning disease prevention. Because the general treatment and prevention guidelines are common to all forms of BRD, expenditures concerning this syndrome will be approached together, with specific reference to one sector or the other as needed.

5.3.1. Expenditures on BRD Prevention

Given its multifactorial nature, successful BRD prevention results from a synergic relationship between management and biosecurity practices in addition to medical tools. These last ones are the easiest to quantify, and are many times (wrongly) seen as the miraculous solution for avoiding BRD and its heavy losses. Vaccination stands as the ultimate pillar of medical prophylaxis concerning BRD, and therefore special attention will be given to this practice.

Vaccinating production animals has become a common practice throughout the world, with the prevailing notion that vaccines are one of the foundations for disease control and eradication and therefore help ensure animal health, welfare and productivity. The assurance of vaccination success, however, is dependable on several factors, including correct route of administration, opportune timing and targeted animals (Cresswell, Brennan, Barkema & Wapenaar, 2014). Other management factors must not be forgotten, especially when considering multifactorial diseases like BRD. In fact, a very low level of success can be expected to arise from medical prophylaxis if environmental risk factors are not under control (Stilwell, 2013).

The decision to implement a vaccination programme on a farm, considering both which vaccines to use and which animals should be vaccinated, is not a straightforward one, requiring the inclusion of several factors into the decision-making process. Apart from the obvious financial costs, logistical factors and possible adverse effects should also be weighed against the potential benefits that can arise from vaccination. Understanding farmers' incentives and impediments towards vaccination is vital for any attempt to motivate vaccine use. The most obvious factors to take into account will be the costs incurred and the health and productive benefits derived from vaccination, but it has also been reported that intangibles such as worker's and farmer's satisfaction may also play a role in the decision-making process of implementing a vaccination programme (Cresswell et al., 2014; Rushton, 2015).

There are currently several available vaccines, both in Portugal and in the UK, against respiratory disease agents, many of which incorporate BRSV. It should be noted that there are other vaccines against respiratory agents, such as monovalent vaccines against BVDV and BHV-1/IBR, but since the focus of this thesis is on BRSV, focus in being put on vaccines directed against the virus. These vaccines, as well as their immunization protocols, are detailed on Annex III. The majority of BRSV vaccines is available both in Portugal and in the UK, with a few exceptions: Hiprabovis®4 and Hiprabovis®Balance are only available in Portugal; on the other hand, Rispoval®RS is only available in the UK. With the exception of Rispoval®RS, all of the other vaccines that grant protection against BRSV are polyvalent vaccines, in which the virus is associated with other respiratory viruses and, in one case, with *M. haemolytica*. There are both live and inactivated/killed vaccines against BRSV, mainly destined for parenteral administration. The intranasal vaccine, which protects against BRSV and PI_3V has, as mentioned, great utility in outbreaks as well as minimal interference with circulating maternal antibodies.

The decision to opt for live of inactivated vaccines has both advantages and disadvantages. Live vaccines possess the advantages of providing a strong and long-lasting immunity while requiring few inoculations, being able to be administered effectively by non-parental routes, not requiring the use of adjuvants and minimizing the possibility of hypersensitive phenomena. Their disadvantages include: systemic reaction due to mild disease, possible reversion to virulent state due to mutation or recombination of pathogen genome with a wild pathogen strain, possible perpetuation of the pathogen in the animal and its environment, induction of abortion in pregnant animals, limited shelf-life and stricter storage conditions. As for inactivated vaccines, they possess the advantages of being less likely to cause disease and being more stable on storage. Given their residual virulence, inactivated vaccines usually lead to a short-lived immune response, often requiring multiple doses and parenteral administration for full efficacy. The required use of adjuvants to increase antigenicity may lead to local reactions at vaccination site. These vaccines are also associated with hypersensitive phenomena due to antigenic modification or contamination (Radostits, 2001).

The final price per dose of a given vaccine results from the addition of two distinct components: development and manufacturing costs. Development costs are fixed costs, comprising investments in both pathogen-circulation knowledge and laboratory skill. Manufacturing costs are variable, reflecting production scale, and therefore by increasing the number of demanded doses, unitary costs may be reduced. Development costs are usually supported by public sector investments, while the private sector serves this purpose concerning variable costs. Also requiring consideration are vaccine delivery costs, which comprise factors like dose price, labour and equipment to administer the vaccine, storage and distribution of the vaccine, as well as monitoring actions post-vaccination (Rushton, 2015).

Considering the current use of the mentioned vaccines, there is not a considerable amount of data available and/or published in Portugal or in the UK. The unpublished study conducted in the Entre Douro e Minho Portuguese region in 2003, and mentioned in the section concerning BRSV prevalences in mainland Portugal, also evaluated vaccination practices against respiratory viruses in the region. In a sample of 124 dairy farms, the results were as followed: 65.3% (n=81) of the enquired farms had active vaccination programmes against, at least, one respiratory virus; 25% (n=31) had never vaccinated their animals against any respiratory virus while 9.7% (n=12) had vaccinated in the past but did not vaccinate at that time. Of the 81 farms that had active vaccination protocols, 63% (n=51) used a quadrivalent vaccine against BRSV, BHV-1, PI_3V and BVDV. Specifically considering vaccination against BRSV, in the 124 dairy farms the main findings were: 50% (n=62) had active vaccination programmes against the virus; 41.9% (n=52) did not vaccinate against the virus and 8.1% (n=10) had vaccinated in the past.

In the UK, Cresswell et al. (2014) developed a questionnaire directed at dairy and beef producers aiming to evaluate the use of cattle vaccines, which was distributed to UK farmers between September and November 2011. The percentage of respondents that vaccinated against respiratory diseases (excluding monovalent vaccines against BVDV and IBR) was 17% out of a total of 114 dairy farmers and 35% out of a total of 92 beef farmers. Out of the 17% that vaccinated their dairy herds, 10% used Rispoval®4, 4% used Bovipast®RSP and 3% used Rispoval®IntraNasal RS+PI_3. When it came to beef herds, 17% were vaccinated with Rispoval®4, 5% with Bovipast®RSP, 4% with Rispoval®IntraNasal RS+PI_3, 1% with Rispoval®RS and another 1% with Rispoval®3. The remaining 7% used a monovalent vaccine against *M. haemolytica* (2%) and a bivalent vaccine against PI_3V and BHV-1 (5%). The main drivers of vaccination were experienced losses due to disease and upon Veterinary advice. Other drivers included disease testing and monitoring, show/sales requirement and empirical use. The authors also concluded that, in 14% of cases, farmers were vaccinating their animals too early and, in two cases, the vaccines implied were against respiratory diseases. This may be an important factor to take into account when considering the efficacy of vaccines against BRSV, given the recurrent problem of interference with maternally derived antibodies and risk of vaccine failure. The Veterinarian practitioner seemed to be the main vaccine supplier in this study, as well as the preferred source of information for farmers upon the decision whether or not to vaccinate and which vaccines to use. In fact, acting as a medicine supplier seems to comprise a significant part of farm veterinary practices in the UK, being reported that about 55% of their total income derives from medicine sales (Cresswell et al., 2014).

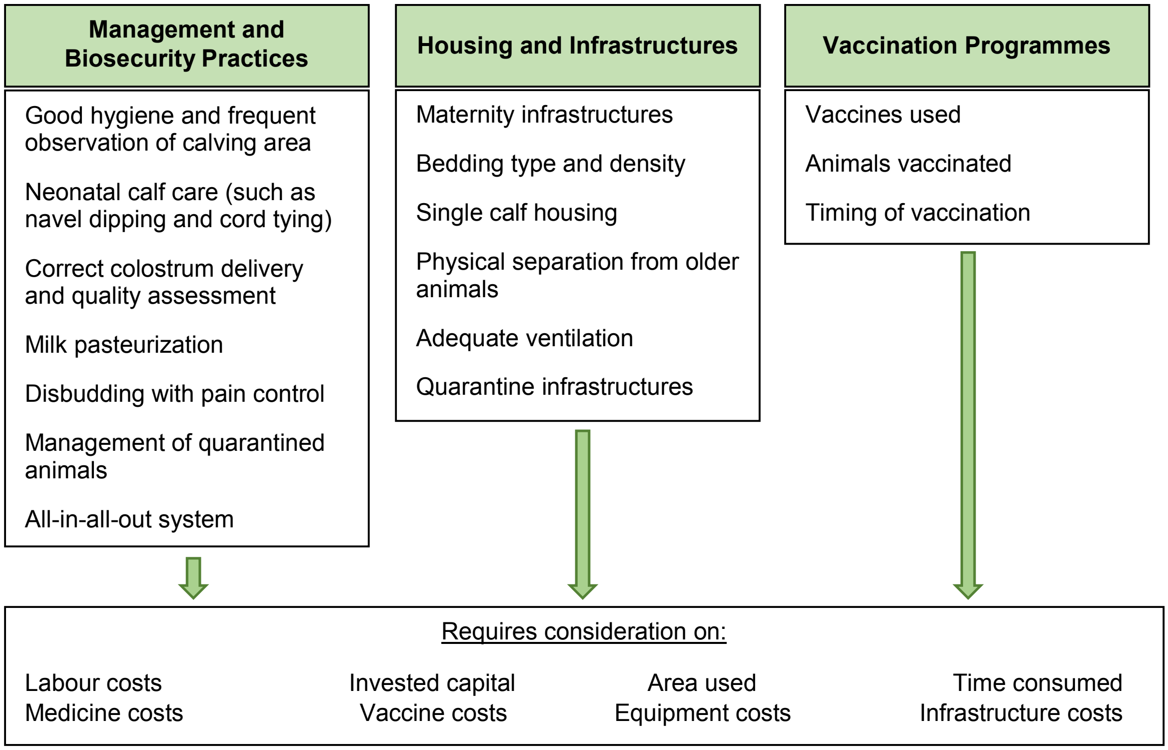
The fact that most available vaccines are polyvalent reflects the multiple infectious aetiology of BRD. However, the fact that there are not yet marked vaccines against BRSV, conjugated with the awareness that sometimes vaccination is implemented on an empirical basis, without knowledge of the real viral prevalence, proves to be an obstacle against the study of its seroprevalence and distribution in both dairy and meat herds, as well as its economic impact.

5.3.1.1. Dairy Calf Disease Control Programmes

Despite their importance in the dairy enterprise, poor attention has been given to calf health and production, in comparison to programmes of reproductive optimization and mastitis control, for instance. There is a tendency for change, however, with the increasing development of calf health management programmes that aim at controlling diseases such as enzootic calf pneumonia. These programmes have an inherent cost and, consequently, must also be contemplated in the economic assessment of BRD. The first step in their development is the establishment of a record-keeping system that provides information concerning: calf date births, dates of illness, diagnosis and instituted treatments, dates of deaths and necropsy findings, data on feeding, such as daily amount of milk and/or solid food consumed, as well as productive data like growth rates (Radostits, 2001). The collection and evaluation of this data will allow for both the estimation of losses and expenditures due to the disease as well as the benefits that may arise from disease prevention.

Concerning expenditures on the prevention of enzootic calf pneumonia, considerations on its costs are assembled on Figure 5.

Figure 5: Considerations on the costs of enzootic calf pneumonia prevention



BRD preventative practices in adult dairy cattle are very similar to those concerning calves, including proper nutrition, adequate vaccination protocols, biosecurity measures and correct ventilation. In addition, management measures must aim at minimizing the negative energy balance and phenomena such as ketosis, hypocalcemia or SARA (Gorden & Plummer, 2010).

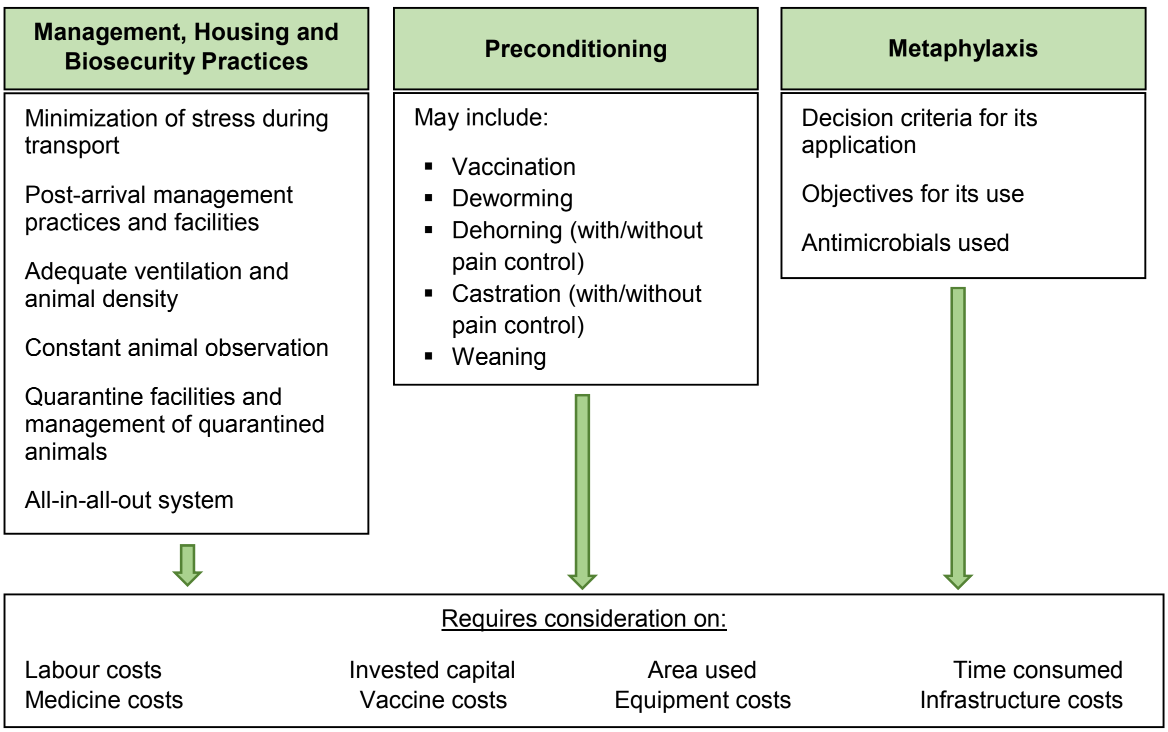
5.3.1.2 Feedlot Disease Control Programmes

The profitability of feedlot operations is highly dependable on two factors: cattle weight gaining and the improvement of carcase quality, so that there is an increase in the value per kilogram/pound of carcase. The biggest input in feedlot systems is feed, and therefore the cost of feed will be the main factor influencing the cost of growth and finishing of cattle. The economic viability of a feedlot system is also directly related to the time animals spend at the feedlot in order to achieve market demands: the longer it takes for the animal to reach target weight and carcase characteristics, the less economically efficient the system becomes (Radostits, 2001).

It is a common practice in feedlot systems to possess health management and production programmes, aiming at: maximizing feed performance and carcase value while minimizing time spent in the feedlot; minimize morbidity, mortality and culling rates; optimize expenditures concerning vaccine and metaphylactic use of antimicrobials, and ensuring personnel motivation and prompt detection and treatment of sick animals. The base of all this is a pragmatic and constantly updated record-keeping system (Radostits, 2001; Edwards, 2010).

Given its multifactoriality, a cost-effective BRD prevention programme at the feedlot level must focus not just on medical prophylaxis or metaphylaxis, but also on appropriate management and biosecurity practices, which will have inherent costs and therefore should be subjected to consideration. These measures are summarized on Figure 6.

Figure 6: Considerations on the costs of shipping fever prevention



It should be noted that an effective BRD prevention should start at the cow-calf level, with necessary expenditures considering vaccination of cows for antibody transfer through adequate colostrum feeding, farm biosecurity measures, parasite control, possible dietary supplementation and method of marketing cattle (Whittier, 2012).

In order to make economically viable decisions concerning BRD prevention, farmers need to achieve a better understanding concerning productive losses and risk factors associated with this disease, as well as the cost-effectiveness of available prevention measures (Van der Fels-Klerx et al., 2002b). The fact that little progress has been made in controlling BRD despite great advances concerning medical tools once again demonstrates that emphasis must also be put on the often neglected management and biosecurity practices in order to aim for a better, more economically advantageous control of BRD in both dairy and beef herds (Gorden & Plummer, 2010).

5.3.2. Expenditures on BRD Treatment

Treatment costs when it comes to BRD, as with any other disease, must take into account the medicines used, and their inherent cost, but also Veterinary services and farm labour required to treat and monitor sick animals, as well as possible existence of hospital-like facilities within the farm and equipment for sick-animal handling. Treatment costs may be easier to determine in acute situations rather than in chronical cases, in which the records available are, at best, imprecise, which will complicate the quantification of expenditures on treatment (Henriques et al., 2004).

As mentioned before, the main drug class used in the treatment of BRD are antimicrobials, directed at bacterial infections. The molecules available are numerous, both in Portugal and in the UK, and are summarized on Annex II. Despite belonging to different classes, all of the molecules indicated for the treatment of BRD have a suitable spectrum considering the bacteria involved, as well as being able to reach high levels in bronchial secretions and pulmonary tissues (Stilwell, 2013). The choice of a particular product must contemplate factors like antimicrobial susceptibility tests, previous cases on the farm and molecules successfully used. Another important thing to consider is the withdrawal period, in which animal products cannot be directed to human consumption.

Despite lack of scientific support, the combined use of several antimicrobials is frequently undertaken with the objective of maximizing treatment response. This is a rather illogical practice, given that most commonly used antimicrobials already have a wide spectrum of activity, even in mixed infections. This unjustifiable increase in treatment costs may also be counterproductive, given than some molecules may have antagonistic actions (Radostits, 2001). The unceasing use of antimicrobials aiming for BRD control is not without disadvantages. Apart from drug costs, there is also the risk of inefficiency and antimicrobial resistance, as well as not fully securing animal welfare, given that these drugs only control bacterial agents (Stilwell et al., 2008).

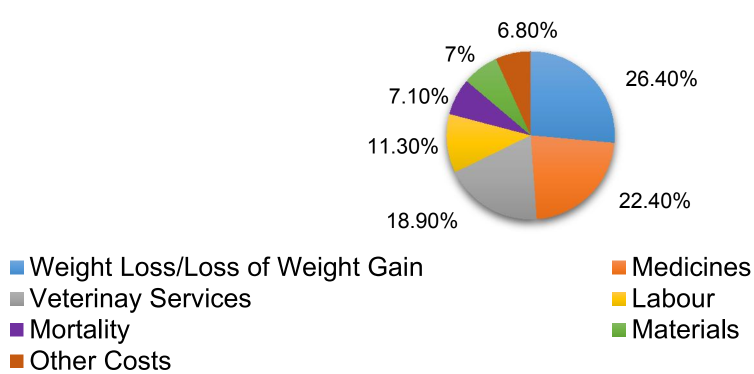
Anti-inflammatories are also commonly used in the treatment of BRD, paired with antimicrobials. Their judicious use is also required, not just because of their inherent financial cost but also because their use in non-adequate cases may even be harmful for animal recovery, since inflammation is a vital component of the healing process. They should therefore be reserved for situations in which there is notorious respiratory effort. There are several anti-inflammatory drugs approved for cattle use in Portugal and in the UK, namely: flunixin meglumine, dexamethasone, ketoprofen, meloxicam, carprofen, acetylsalicylic acid, tolfenamic acid and sodium salicylate, further detailed on Annex II.

Other medicines can be used besides antimicrobials and anti-inflammatories, with the obvious consequence of higher treatment costs. Furthermore, their utility and beneficial effects are still controversial. The main molecules available in Portugal and the UK are: adrenaline (a sympathomimetic agent), dihydrochlorothiazide (a diuretic agent) and bromhexine (a mucolytic agent), further detailed on Annex II.

Accordingly to Edwards (2010), a favorable first-treatment response should be around 80-85%. First-treatment responses above 90% may suggest the presence of a significant number of false positives, especially if this is paired with low case fatality rates, which is obviously not cost-effective (Radostits, 2001). The assessment of the efficacy of therapeutic response may be done through the combination of the Case Fatality Rate (CFR) and periodical evaluation of morbidity and mortality records. The BRD-CFR may be calculated by dividing the number of deaths due to BRD by the number of animals initially treated. An acceptable BRD-CFR rate should be between 6-10%, with accepted values of 15% in high risk cattle (Edwards, 2010).

The costs of calf pneumonia in both dairy and suckler herds were studied during outbreaks of this disease in twelve British farms (eight dairies and four suckler herds), during the winters of 1997-98 and 1998-99. Concerning dairy farms, calves suffering from pneumonia, and therefore included in the study, were either being reared as heifer replacements or destined for meat production. Upon aetiological diagnosis, with the use of nasopharyngeal swabs and paired serologies, it was observed that BRSV was the most commonly involved pathogen, being detected in four outbreaks, followed by *P. multocida* and PI_3V in two outbreaks, with *M. bovis* having been detected once. The generality of these dairy farms also had environmental and management risk factors for the development of calf pneumonia, namely: deficient ventilation, inadequate feeding, comingling of calves with different ages and inexistence of an all-in all-out system. An attempt was then made to quantify the total costs per ill calf, by summarizing a list of losses and expenditures due to the presence of calf pneumonia, even though the author did not differentiate these two categories. The proportions of the different contributors to the total cost, are summarized on Figure 7, adapted from Andrews (2000).

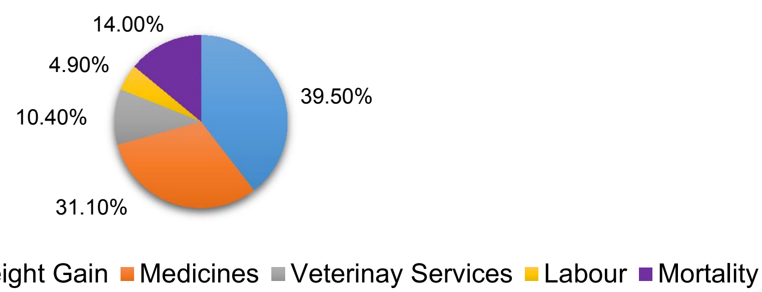
Figure 7: Proportion of the different contributors to the total cost of dairy calf pneumonia



In terms of treatment expenditures, medicines and veterinary services accounted for about 41% of the total estimated costs. The heaviest contributor to the total cost, however, seemed to be weight loss/loss of weight gain. Under the category 'Other Costs' were losses and expenditures registered after the studied period, and these included vaccines, rearing calves on other farms and additional deaths due to chronic pneumonias. Overall morbidity levels ranged from 41.7% to 90.5%, while mortality was observed in four farms, occurring in 1.5% of calves considered to be at risk of developing the disease, and 2.2% of those calves who were sick and treated. As for the financial cost of pneumonia, its value differed amongst farms, ranging from £8.59 to £78.74 per ill calf, with an overall average of £43.26. Considering the total cost of the outbreak on each of the eight farms, it varied from £85.92 to £2141.42. It should be noticed that the lowest cost was observed on the only farm that had an active vaccination programme, which included BRSV, PI_3V and IBR (Andrews, 2000).

In a similar way to what was done for dairy calves, Andrews (2000) also summarized a list of contributors to the total cost of suckler calf pneumonia in the rearing phase, including losses and expenditures due to the disease. The results are presented on Figure 8.

Figure 8: Proportion of the different contributors to the total cost of suckler calf pneumonia



In parallel with what was observed in dairy herds, weight loss/loss of weight gain and expenditures on medicines were the main contributors to the total pneumonia cost. However, pneumonia costs in suckler herds had considerable higher costs than in dairy herds. These higher costs were due to the fact that morbidity and mortality levels in suckler calves were significantly higher than in their dairy counterparts: morbidity in suckler calves ranged between 73.3% and 100%, with a mean of 90.3%, while mortality, observed in two farms, reached a 3.9% overall rate, with 4.3% of affected calves dying. Expenditures on medicines were more than 2.5 times higher in affected suckler herds when compared to dairy herds, with average values of £25.53 for suckler calves and £9.69 for dairy calves. The financial cost per suckler calf was therefore higher than what was observed in dairy calves, with an overall cost per ill calf of £82.10, ranging from £59.12 to £101.55. Considering the total cost of the outbreak on each of the four herds, it ranged between £1596.37 and £6499.50. Upon aetiological diagnosis, mixed bacterial growths were found and, in three of the four outbreaks, two or more viruses were associated with the presence of disease. Of these, BRSV was the most common, followed by PI_3V. Most affected animals were approximately six months old, already weaned, and were not vaccinated (Andrews, 2000).

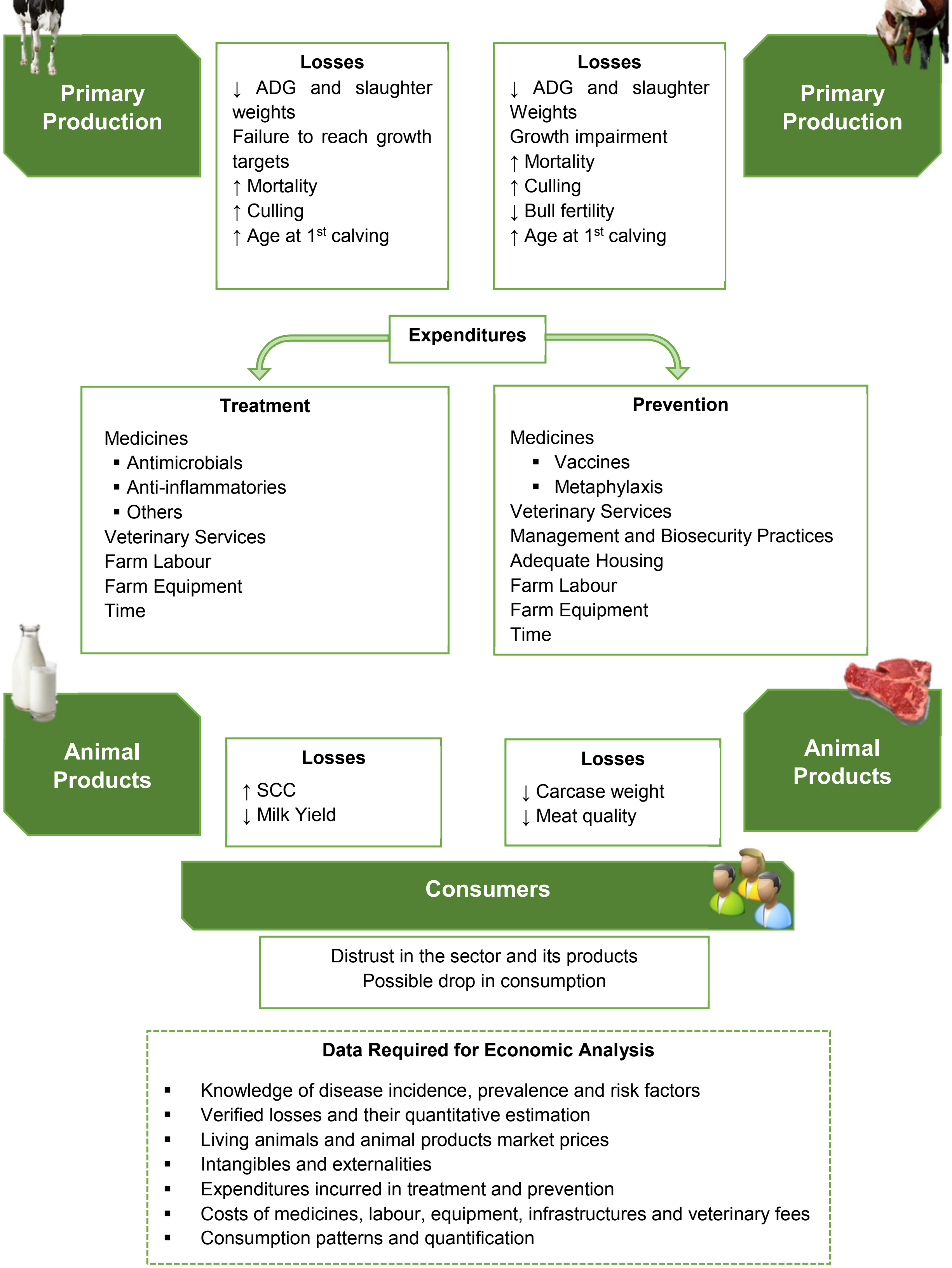
5.4. Summarization of BRD's Impacts on Bovine Production

BRD has, as seen, economic implications both in the dairy and in the meat sectors. The nefarious effects of this syndrome are heavily rooted on primary production, where expressive induced losses require equally large expenditures on prevention and control. However, despite these primary losses, the impact of BRD extends further ahead in the production chain, with both quantity and quality impairments concerning two of the main outputs of the sector, milk and meat. Another significant – but easily overlooked – aspect of this syndrome is the impact it has on the consumers. Despite not having zoonotic implications, BRD-induced disease will contribute to a depreciation of the sector's image in the eyes of the consumer through the reduction of animal welfare. This, conciliated with the knowledge of use of medical tools like antimicrobials in the worrying context of antimicrobial resistance may lead to a general distrust in the bovine production sector and consequent reduction in the consumption of its products.

In order to summarize the BRD impacts mentioned in this work on both bovine dairy and meat sectors, these were assembled in a model that differentiates between losses and expenditures, following the framework proposed by McInerney and others (1992). This model also illustrates the impact BRD has on the three main links of the animal production chain, namely: primary production, animal products and consumers. Taking all this information into account, attention is also brought to the requirements needed to perform an economic analysis of the impact BRD has on the bovine production sector.

This approach is illustrated on Figure 9.

Figure 9: The impacts of Bovine Respiratory Disease on bovine production – a model



6.1. Objectives

BRSV is, as seen, just one of the many infectious agents involved in BRD, in parallel with management and environmental factors, and therefore its economic impact *per se* is very difficult, if not impossible, to assess. Consequently, emphasis was put on disease manifestation and economic impact of BRD as a single entity on both the dairy and meat sectors, under the form of a literature review. Upon focusing on BRD's impact on Portuguese bovine herds, the results of this review lead to the conclusion that, to our knowledge, an attempt was never made to investigate such impact in Portugal, despite the existence of data pointing towards significant seroprevalences concerning respiratory viruses like BRSV, as well as vaccination practices.

Given this scarcity of available information concerning the assessment and quantification of the impact BRD has on Portuguese cattle populations, and similarly to what is being done in the UK under the SAPHIR project, two types of questionnaires were developed to identify the presence and impacts of this disease at farm level, through a case study, using a convenience sample of dairy and meat farms. The main objective was to gather primary data concerning epidemiology, presence of risk factors, production losses and expenditures in prevention and treatment of BRD on Portuguese farms with the purpose of assessing major research questions for future work.

6.2. Questionnaire Design and Sampling Method

Following the methodology proposed by Brancato et al. (2006) and Malhotra (2007), summarized on Annex IV, two questionnaires were developed in order to satisfy the proposed objective. The main source of information contributing to the conceptualization phase of questionnaire development was the literature review performed, which focused on the occurrence of BRD in the form of distinct clinical entities, namely: Enzootic Calf Pneumonia and Chronic Suppurative Pneumonia, with special relevance in the dairy sector, and Shipping Fever, highly damaging for the meat sector. This review revealed that, even though these entities share many resemblances, such as aetiological infectious agents and some treatment/prevention measures, there are also considerable differences amongst them, such as risk factors, and therefore the decision was made to elaborate two distinct questionnaires, one for each sector.

With the underlying knowledge of the syndromic nature of BRD, each questionnaire was compartmentalized into three distinct groups of questions, following a logical order:

- Group I: Farm Characterization – focuses on aspects like farm location, production type, breeds used, number of animals and their origin, as well as questions related to farm labour;

- Group II: Management Practices – aims at providing some insight concerning the presence of reported risk factors for the development of BRD. This group shows some variation between questionnaires, given the differences between risk factors contributing to the clinical entities that affect dairy and meat herds;
- Group III: Bovine Respiratory Disease at the Farm – focuses on the occurrence of BRD at farm level. The aim of this group is to collect primary data concerning both the epidemiology and the economic impact of BRD. Particularly considering the formulation of the economic impact questions, these were substantiated by the previously addressed frameworks proposed by McInerney and others (1992) and Bennett (2003), in which the cost of a given disease can be estimated as the sum of both experienced losses and incurred expenditures – in treatment and/or control. On a final note, it was considered pertinent to enquire farmers on whether or not they felt informed concerning this syndrome, as well as sources of information they use and/or consider appropriate when aiming for a deeper understanding of BRD, which is vital when targeting effective control and impact minimization of an economically important disease such as this one.

Upon design conclusion, the questionnaires were reviewed by an expert and slight alterations were made. This was followed by a field testing step, in which an assessment was made concerning the pertinence, phrasing and general appeal of the questionnaires, before entering the implementation phase and data collection. The full questionnaires may be found on Annexes V and VI. Due to some logistical and monetary constraints, the questionnaires were implemented only on a small number of farms (five dairy and five meat farms), using a convenience sample. The criterion used was the fact that those farms were geographically, timely and administratively accessible to the author, with willing owner participation. Despite the practicality of this method of sampling, one of its main flaws is that it is highly susceptible to bias. However, we do consider that this work may act as a pilot study, a basis for a more thorough, wide-ranging and significant attempt to estimate the impact of BRD on Portuguese herds in the future.

6.3. Statistical Analysis

The data obtained after the implementation of both questionnaires was treated recurring to the *Microsoft Office Excel 2013* and the *IBM SPSS Statistics 22* programs. All variables were initially coded before performing the statistical analysis.

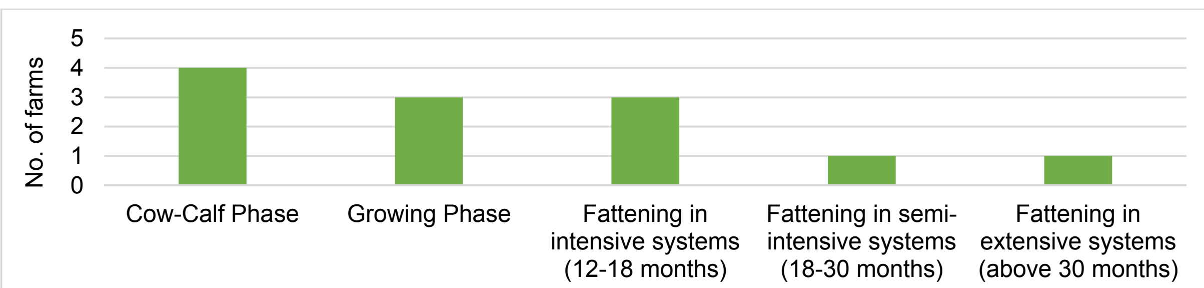
6.4. Results and Discussion

6.4.1. Sample Characterization

The five farms comprising the dairy sample were situated in distinct NUTS III regions, namely: Lezíria do Tejo (Chamusca, Benavente and Azambuja), Área Metropolitana de Lisboa (Sintra) and Península de Setúbal (Moita). In addition to milk production and rearing female calves as herd replacements, two farms also reared calves destined for veal production. The Holstein breed was used in pure line in three farms. As for the other two, both used the ProCross rotational crossbreed programme between the Holstein, Montbéliarde and Swedish Red breeds, with one of them also performing crossbreeds between the Holstein and Brown Suisse breeds.

The five farms comprising the meat farm sample were also located in different NUTS III regions: Lezíria do Tejo (Cartaxo/Santarém), Alentejo Central (Évora, two farms) and Península de Setúbal (Palmela, two farms). The existence of two distinct locations for one of the farms is due to the fact that production was divided between Cartaxo, which held the cow-calf and growing phases, and Santarém, in which the fattening phase was held. These farms were mainly characterized by the presence of the cow-calf phase (Graph 1), with one farm also finishing pure-breed Limousine males to sell as breeders.

Graph 1: Production phases present in meat farms



The cow-calf phase was generally held in more extensive systems, while the growing and fattening phases up to 30 months were held in predominantly intensive systems. The breeds used included the Alentejana, Limousine, Charolais, Salers, Brava, Mertolenga and Holstein in pure lines. Three farms also performed crossbreedings between some of those breeds.

The general characterization of the sampled farms in terms of size, number of animals, labour and productive/reproductive indicators is presented on Table 5.

Table 5: General characterization of dairy and meat farms (average values)

Average Values	Dairy Farms	Meat Farms*
Farm area (ha)	288	811
No. of animals per farm	1 147	2 217
No. of full-time workers per farm	19.4	4
Full-time labour cost (€/worker/year)	13 800	9 960
No. of family workers per farm	0	2.5
No. of part-time workers per farm	2	0
Part-time labour (hours/year)	1 000	0
Part-time labour cost (€/worker/year)	5 000	0
Milk production (L/cow/day)	32.3	n.a.
SCC (cells/mL)	264 200	n.a.
Milk total revenue (€/year)	1 557 654	n.a.
Meat cattle revenue	n.a.	
Average revenue (€/animal)		525
Total revenue (€/year)		90 000
€/Kg of liveweight		2.5
€/Kg of carcase		4
ADG (g/day)	n.a.	990
Calving interval (days)	389	391
Age at 1st calving (months)	24.3	34.3
Mortality rate (%)	8.6	14
Culling rate (%)	25.4	9
Fertility rate (%)	n.a.	90.6
Weaning rate (%)	n.a.	91.6
Calf rearing cost (€/calf/day)	1.7	No data
Fattening cost (€/animal/day)	No data	No data

* Data provided only by four respondents

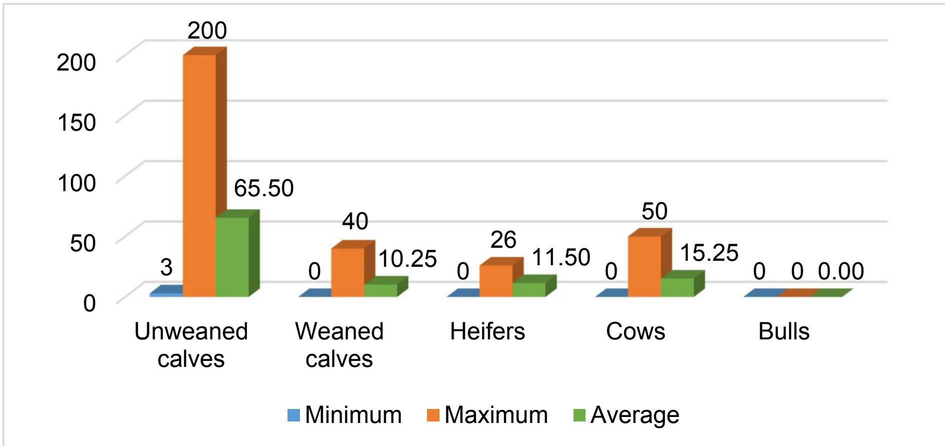
n.a. = not applicable

6.4.2. BRD Occurrence in Dairy and Meat Farms

After analyzing the primary data collected through the questionnaires, it was concluded that 80% of the enquired farms (four dairy and four meat farms) had experienced cases of BRD in the previous 12 months, with 410 sick animals in dairy farms and 415 in meat farms. Sick animals from dairy farms were predominately unweaned calves, with a total of 262 affected animals, and cows, with a total of 61 affected animals (Graph 2). These results are in accordance with literature reports, with Enzootic Calf Pneumonia being held as a major problem of calf rearing in dairy farms. There is a strong probability that affected cows were suffering from Chronic Suppurative

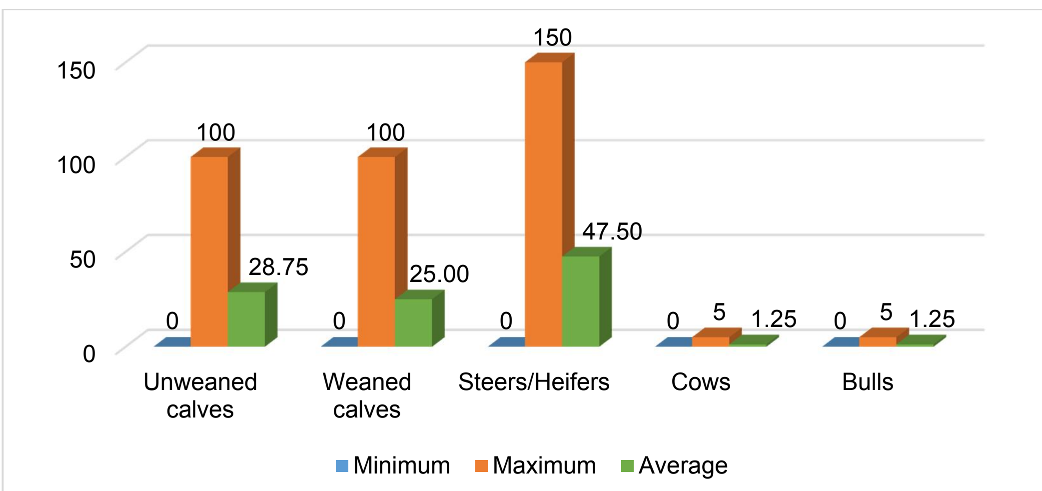
Pneumonia phenomena, given the fact that this is the most common respiratory disease in individual adult cows (Dalgleish, 1991), and that there seemed to be a history of pneumonia phenomena in female calf rearing in all farms with affected cows.

Graph 2: Number of sick animals in dairy farms by category



As for meat farms, steers and heifers in fattening systems were the main category affected by BRD, with a total of 190 affected animals (Graph 3).

Graph 3: Number of sick animals in meat farms by category



A large number of animals from meat farms were purchased from external sources and kept under predominantly intensive systems where BRD pressure, especially under the form of Shipping Fever, is higher. The number of cases in the two farms that kept animals in more extensive systems was much lower – with eight and seven unweaned sick calves. Contrarily, another farm stood out as being the one with the highest number of BRD cases in unweaned calves (n=100) and weaned calves (n=100). There is still a lack of information concerning BRD risk factors in nursing beef calves. Studies conducted in Canada and in the United States revealed that large herd size, occurrence of BRD in cows and diarrhea in calves, winter calving and introducing calves from external sources into the herd were positively associated with BRD occurrence and need for treatment. The Canadian study also concluded that herds in which cows were vaccinated against respiratory disease had a lower incidence of BRD in preweaned calves (Woolums et al., 2013). Weaning is considered a strong BRD risk factor in recently weaned suckler calves that undergo several stressful management changes at this phase, such as dietary change, moving from outdoor to indoor facilities, transportation and husbandry practices like dehorning and castration (Lorenz et al., 2011).

Considering this farm, which held the second largest meat herd, both unweaned and weaned calves were kept outdoors, with weaning being performed before six months of age, the lowest weaning age in sampled meat farms (in the other farms weaning was performed between six and seven months of age). The high number of cases in unweaned calves may be due to the fact that breeding cows were not vaccinated against respiratory disease, with vaccination being performed only in fattening animals between six and eight months old. The precocious weaning age, when in comparison to the other farms, may also be playing a role in the occurrence of BRD. Stilwell and others (2008), concluded that weaning age was significantly related to BRD's incidence in beef calves, with older calves being less likely to develop the disease. Also, given the fact that the farm possessed two breeding seasons, it would have been interesting to assess if there was a difference between calves born from each season and BRD's incidence, but such was not investigated. The majority of cases in weaned calves, on the other hand, was seen in purchased animals from multiples origins, which may be related to the fact that vaccination was only implemented in the first 48 hours post arrival, not enabling the development of an effective active immune response. It would also have been interesting to investigate if the farm had information concerning the history of purchased animals – for instance, if there was a difference in disease occurrence between animals purchased from auction markets and animals purchased directly from other farms -, as well as their herds of origin, namely in terms of BRD occurrence and vaccination practices, but such was not assessed in the questionnaire.

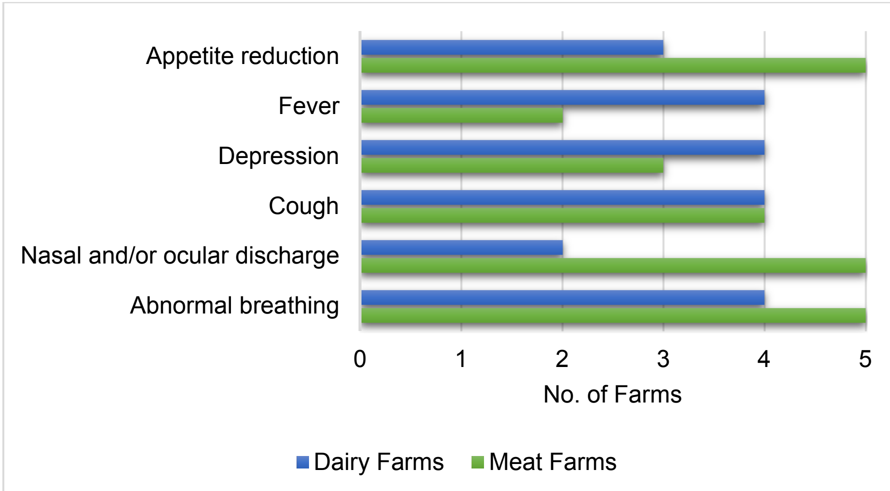
From the totality of farms, only 40% had estimated current BRD prevalences (Table 6), most of which being memory-based, a factor that may hamper the eventual calculation of BRD's impact at farm level.

Table 6: Current BRD prevalences at farm level

	Dairy Farms	**Meat Farms**
Reported BRD Prevalences	0% and 10% (mostly calves)	3% and 5%

In both groups of farms, BRD diagnosis was predominately based on clinical signs (Graph 4). In addition to the presented signs, drops in milk production and dull coat were also used in two farms as indicative signs of BRD.

Graph 4: Clinical signs used for BRD diagnosis in dairy and meat farms



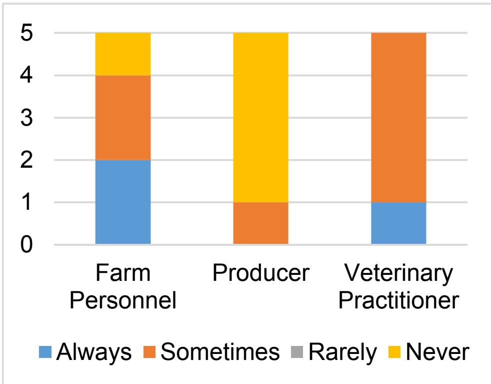
Apart from clinical signs, only 40% of farms resorted to other diagnosis methods (Table 7).

Table 7: Complementary diagnosis methods used in dairy and meat farms

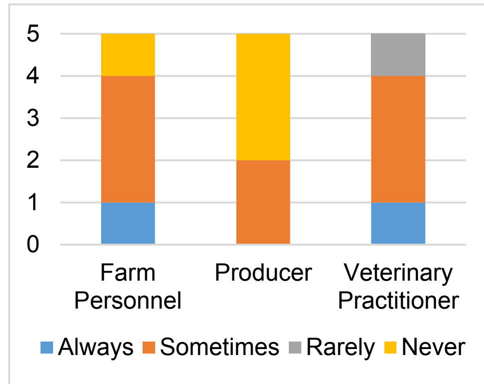
Dairy Farms	Meat Farms
Cardiothoracic auscultation (one farm)	Cardiothoracic auscultation (one farm)
Tracheal wash or bronchoalveolar lavage with sample collection (one farm)	Blood sample collection (one farm)

Diagnosis of clinical cases was performed by different intervenients, with farm personnel standing out as an important participant in both groups of farms (Graphs 5 and 6). However, farm personnel's sensitivity in detecting BRD clinical cases is reportedly of little more than 50% in dairy farms (Gorden & Plummer, 2010) and revolving around 60% in feedlots (Wolfger et al., 2015), which may indicate that a considerable number of cases is not being diagnosed. It is also worth mentioning that the report of the number of clinical cases was often memory-based, not due to consultation of existing records on the farm, and therefore we must take into account eventual under and over valorizations of their actual number.

Graph 5: Diagnosis performance on dairy farms



Graph 6: Diagnosis performance on meat farms

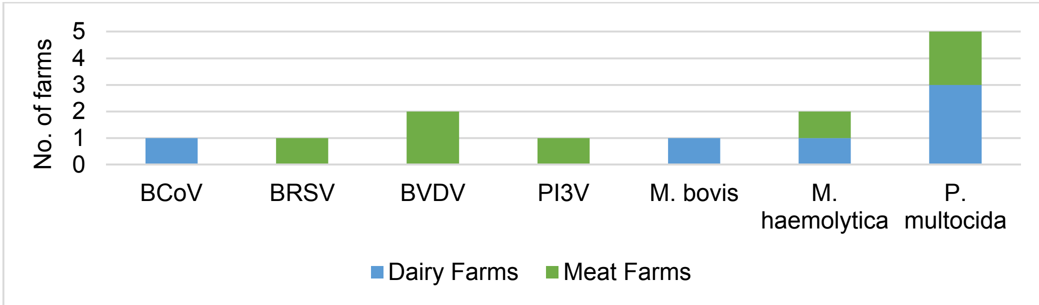


The fact that only 60% of analyzed farms (three dairy and three meat farms) performed isolation of sick animals may undermine disease control, given that isolation decreases the risk of disease spreading. This seems to be the case in dairy farms, in which the two of them not executing this practice were the ones with the highest number of clinical cases of BRD. The opposite was seen on meat farms that did not isolate sick animals, but it is worth mentioning that animals in these farms were kept in extensive systems, where infectious pressure is decreased.

Two meat farms had contacted the Veterinary practitioner particularly due to BRD occurrence in the previous 12 months, with a total of eight visits performed on one farm and a total of two on the other. When enquired about the costs of such visits, the first respondent declared that he did so in a contract for service regimen but did not disclose any values, while the second had no data available on the subject. In addition to the remaining three meat farms, none of the dairy farms had contacted a Veterinary Practitioner particularly due to BRD in the previous 12 months, which is due to the fact that these farms either had a full-time Veterinarian or that this practitioner performed routinely visits, usually once or twice a week, during which BRD cases would be addressed.

Infectious agents involved in BRD development had been identified in 60% of our sample (three dairy and three meat farms), with *P. multocida* being the most commonly identified agent (Graph 7).

Graph 7: Infectious BRD agents identified in dairy and meat farms

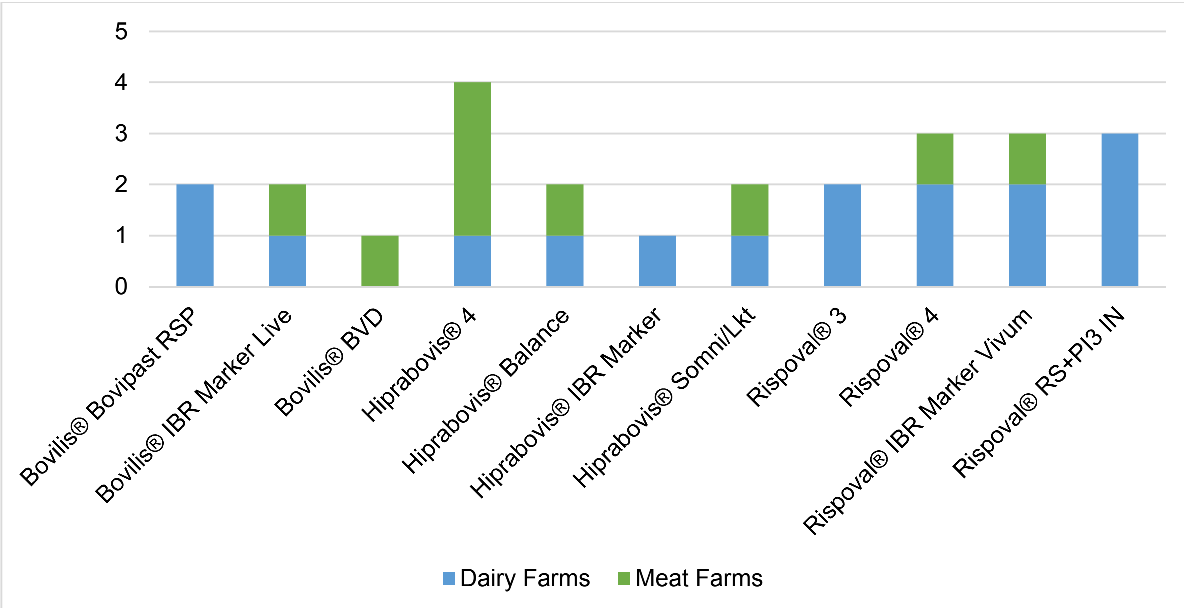


Of the three dairy farms that had identified bacterial agents, only one performed antimicrobial susceptibility tests. Neither of the two meat farms in which bacterial agents were identified had performed antimicrobial susceptibility tests. In addition, one of these farms was the only one reported to have had several cases of antimicrobial resistance in the past, but the respondent did not disclose the substances to which resistance was identified.

The presence of *P. multocida* in all dairy farms that had identified infectious agents, and in concurrence with BCoV in one farm, is in accordance with its importance in the genesis of Enzootic Calf Pneumonias. Similarly, the two meat farms in which this bacterium was found had had cases of pneumonia in suckler calves. Despite its previously reported high prevalences and significant role in the establishment of BRD, BRSV was only identified once. However, not all farms had performed aetiological diagnosis of BRD, and the ones that did so were not enquired about the methods used. It is known that the virus is extremely hard to isolate under laboratory conditions (Stilwell, 2013; Blodörn, 2015), and that necropsies performed at later stages of disease might only reveal the presence of secondary bacteria (Hägglund, 2005), therefore, we cannot exclude the current presence of the virus, as well as other agents, in our sample.

All farms had established vaccination protocols against BRD, which reflects the high importance put on this practice. Most vaccines used were common to both groups, with polyvalent vaccines widely present, and more than one vaccine was typically utilized per farm. The most commonly used vaccine was Hiprabovis® 4, used in 40% of the total sample, with 60% of dairy farms utilizing the Rispoval® RS+PI_3 IN vaccine (Graph 8). However, at least two respondents used this vaccine at an age inferior to manufacturer's minimum age of use, which might compromise the success of the vaccination protocol. Despite this fact, the two farms that did not use this vaccine had the highest number of BRD cases in the group. One dairy farm also used the vaccines Hiprabovis® Balance and Hiprabovis® Somni/Lkt in calves younger than minimum manufacturer's age of use, and this was the farm with the highest number of BRD cases within its group. All meat farms were administering vaccines accordingly to manufacturer's age of use. Monovalent marked vaccines against IBR were also often used, sometimes aberrantly in concomitancy with conventional, unmarked vaccines.

Graph 8: Vaccines used in dairy and meat farms



The number of animals vaccinated in the previous 12 months, as well as cost per dose of vaccine, were also analyzed. With the data collected, a spreadsheet was created recurring to the *Microsoft Office Excel 2013* program and expenditures on vaccination were calculated by multiplying the price per dose of vaccine by the number of doses used and by the number of animals vaccinated. (Table 8).

Table 8: Expenditures on vaccination in dairy and meat farms

		Dairy Farms	Meat Farms *
Average no. of vaccinated animals**		610.4 (53.2%)	1 698 (76.6%)
Vaccination cost per animal (€)			
	Average	11.3	9.7
	Range	7.5 – 16.4	7.5 – 11.7
Total Expenditure on Vaccination (€)			
	Average	6 897.52	16 470.6
	Range	4 578 – 10 011	12 735 – 19 867

*Data only available from three farms.
**In brackets this value is given as percentage of the average number of animals in the sample.

The calculations made encompass only the prices of the vaccines themselves. Labour costs for administering the vaccines were not included since this practice was assumed to be part of the regular tasks performed by farm personnel on their work schedule.

Despite recurrently resorting to vaccines, not all respondents were able to provide data on expenditures concerning this practice, as was seen in two meat farms, which may be due to the inexistence of vaccination records in those farms. Some reported values were also memory-based, which once again may lead to under or overestimations. It is worth mentioning that lack of information such as this makes it very difficult to assess the economic impact of BRD in terms of expenditures on medical prevention practices and benefits deriving from its use.

Given that, in 80% of farms, some vaccinated animals still developed disease, vaccine effectiveness was calculated recurring to the formula:

$$\text{Vaccine Effectiveness (\%)} = 100 - \left(\frac{\text{no. of sick animals previously vaccinated}}{\text{no. of vaccinated animals}} \times 100\right)$$

One dairy farm stood out as having a much lower vaccine effectiveness in comparison to the others (58.1%) (Table 9). This farm had the highest number of clinical cases within the group, with 310 affected animals, 200 of which were unweaned calves. Upon analyzing vaccination practices, it was seen that the vaccines Hiprabovis® Balance and Hiprabovis® Somni/Lkt were being used under the recommended age in unweaned calves, which might help explain the apparent vaccine failure. In addition, this farm also had management and biosecurity shortcomings, discussed further ahead, that might be contributing to this phenomenon. It is known that vaccines alone are not a miraculous solution in BRD risk minimization, with factors such as proper nutrition, calving conditions, calf housing and ventilation, hygiene and biosecurity acting as contributors to ensure that expected benefits derived from vaccination are experienced (Campbell, 2009).

Table 9: Vaccine effectiveness in dairy and meat farms

	Dairy Farms					Meat Farms*		
Vaccine Effectiveness	Farm A	Farm B	Farm C	Farm D	Farm E	Farm A	Farm B	Farm C
	93.7%	98.8%	58.1%	86.7%	100%	100%	95.3%	92.5%

*Two meat farms were unable to provide data on the number of vaccinated animals

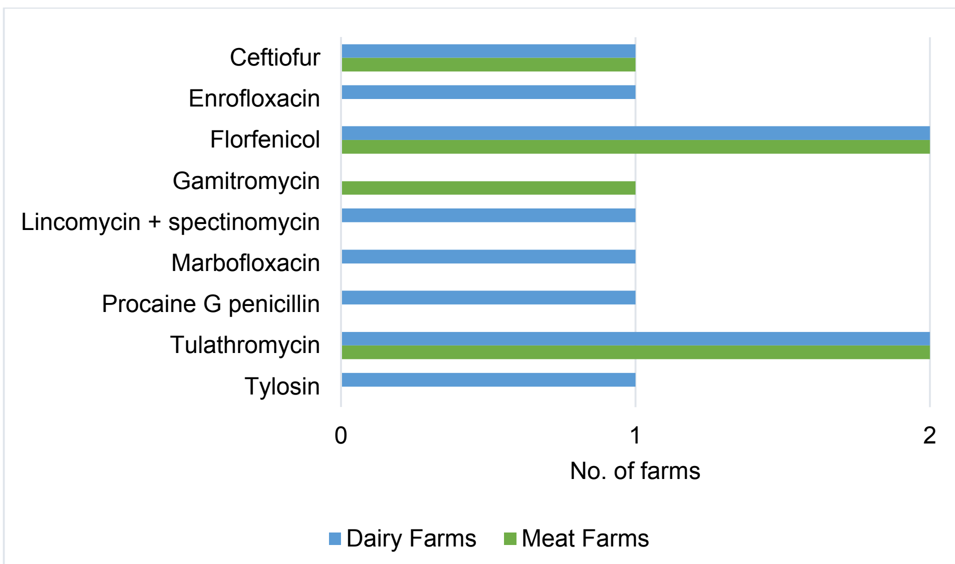
Considering the metaphylactic use of antimicrobials, only one meat farm had this practice instituted, recurring to tilmicosin, but no data was available on the cost of such practice.

All farms with BRD cases in the previous 12 months had instituted medical treatment of the disease. However, one meat farm was not able to provide information on products utilized.

Antimicrobials were always used on the remaining farms, with at least two molecules per farm. Given that only one dairy farm had performed antimicrobial susceptibility tests, the choice of antimicrobials used in the remaining farms is probably being done accordingly to previous cases and molecules successfully used, veterinary advice or on an empirical basis. All antimicrobials were approved for use against BRD, and many molecules were commonly used between dairy and meat farms, with florfenicol and tulathromycin being the most common (Graph 9).

Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) - namely carprofen and flunixin meglumine - were used in combination with antimicrobials in two dairy farms, one of which was the farm with the highest number of cases, and in the three meat farms with available information. NSAIDs are frequently used as ancillary drugs in BRD treatment despite the absence of sufficient data concerning the cost-benefits of their use in the long term (Potter, 2015). Also, their use must be a judicious one, since it has been shown that the inflammatory response does play a role in disease recovery.

Graph 9: Antimicrobials used in dairy and meat farms



It was seen that, in at least two dairy farms, sick animals sometimes had to receive more than one treatment, which might indicate therapeutic failure. This was particularly evident in the farm with the higher number of BRD cases (n=310), for which there were more than 400 treatment records. This farm did not routinely perform antimicrobial susceptibility tests, and therefore the molecules being used may not be the most adequate. Another interesting fact was these two dairy farms were the only ones that did not isolate sick animals, which might not only compromise their recovery but also facilitate disease spreading.

The diversity of antimicrobials used in our sample reflects the wide variety of molecules available in the market. There are currently more antimicrobials licensed for use against respiratory disease than any other cattle disease. However, antimicrobials are often prescribed in the absence of aetiological diagnosis and this, combined with the widespread use of these drugs, raises a red flag concerning the emergence of resistant pathogen strains, as well as possible human health risks (Potter, 2015).

Similarly to what was done with vaccination, farmer's expenditures on BRD treatment were also assessed and inserted into a spreadsheet. Given that more than one product was used per farm, and when data was available, the cost per treatment was multiplied by the number of animals treated with each product. The average values are presented on Table 10.

Table 10: Expenditures on treatment in dairy and meat farms

		Dairy Farms *	Meat Farms
Average no. of treated animals* **		149 (13%)	165 (7.4%) **
Treatment cost per animal (€)			
	Average	2.51	No data
	Range	1.88 – 3.03	No data
Total Expenditure on Treatment (€)			
	Average	373.99	No data
	Range	280.12 – 451.47	No data

* Data available only from three farms and, in two cases, partially incomplete;
** Data only available from two farms;
*** In brackets this value is given as percentage of the average number of animals in the sample.

The lack of data considering expenditures on BRD treatment in both groups of farms was notorious, particularly in meat farms, which might reflect the absence or poor organization of treatment records, once again rendering it very difficult to assess BRD's impact at farm level in terms of expenditures on treatment. The calculations made include only the prices of the medicines themselves. Labour costs for administering treatment were not included since this practice was assumed to be part of the regular tasks performed by farm personnel on their work schedule. Other costs not contemplated were veterinary fees, costs of materials used in product administration and the cost of isolating sick animals, when this practice was instituted at the farm.

When looking at treatment and vaccination costs, a preliminary conclusion might be that treating sick animals may be less demanding from a financial point of view. However, it is worth remembering that not all farms were able to provide data on treatment expenditures, so the values presented are underestimated. For example, the dairy farm with 3 affected cows, mostly likely to be suffering from Chronic Suppurative Pneumonia, was not able to provide data on their treatment, which is known to be quite long and have a low success rate, with animals frequently culled. Another thing to consider, especially in lactating cows, is the withdrawal period for the molecules used. Given that, unless this period is null, milk cannot be directed to human consumption, by multiplying the number of litres lost by the price per litre we obtain another parcel contributing to the total loss due to the presence of disease. The same can be seen in animals destined for meat production, which may need to be kept at the farm for an extended period accordingly to the molecules used. This will obviously come with increased costs in feed and housing, for instance. In addition to treatment costs, we must also consider production losses due to the presence of disease, some of which are known to affect animals not only in the short but also in the long term, compromising their productive life. A solid example of this would be what happens to sick heifers reared as dairy herd replacements, or what happens in meat cattle both in terms of carcase weight and quality.

As seen, and despite some lack of information, farmers seem to put much weight on vaccines and antimicrobials**.** Infectious agents are only one of several contributors to the development of BRD with other factors, like environmental ones, having to be as strongly targeted when aiming for an effective control of this disease at farm level. However, and despite the knowledge of the importance these factors have in the genesis of BRD, their management proves to be more difficult than the one related to infectious agents and, consequently, it does not seem strange that producers put so much weight on medical tools (Stilwell et al., 2008).

BRD seemed to be a strong negative input in both dairy and meat farms, impairing production through several ways (Table 11).

Table 11: BRD's production impacts in dairy and meat farms

BRD's Production Impacts	
Dairy Farms	**Meat Farms**
Liveweight reduction (*=4)	Stunted growth (*=5)
Stunted growth (*=4)	Mortality rate rise (*=5)
Milk production drop (*=4)	ADG decrease (*=4)
Mortality rate rise (*=4)	Liveweight reduction (*=3)
Culling rate rise (*=3)	Culling rate rise (*=1)
Increased age at 1st calving (*=3)	Bull fertility impairment (in the presence of IBR and/or BVD) (*=1)
SCC increase (*=3)	
Cow fertility impairment (*=1)	

* = number of times each impact was mentioned in surveyed farms

Despite the recognition of its economic importance, another hindering factor for assessing BRD's impact at farm level, transversal to the generality of our sample, was the lack of information concerning the magnitude of its negative impacts on production. This makes it impossible to calculate the exact impact of the disease in terms of losses, as well as the benefits that may derive from disease control in the form of avoided losses.

Two farms, however, were able to provide data on the quantification of two impacts verified: drops of milk yield of about 50% in affected cows in one dairy farm, and a total of seven dead unweaned calves in one meat farm. With the data collected, a spreadsheet was created recurring to the *Microsoft Office Excel 2013* program, and an estimation of those losses was made (Tables 12 and 13). In order to calculate the impact of each effect, the following formula was applied:

$$\text{Loss} = \text{no. of affected animals} \times \text{effect's magnitude} \times \text{effect's unitary value}$$

Table 12: Dairy farm production loss in milk yield

Data Required	Estimated Loss
• No. of affected cows = 3 • Milk loss magnitude = 50% of expected lactation yield • Expected lactation yield = 11 500 litres (early 2015 farm value) • Milk's price per litre = 0.294 (2015's average price for the mainland. Source: GPP, SIMA)	3 x (0.5 x 11 500) x 0.294 = **5 071.5 €**

By looking at the estimated loss in terms of milk yield of affected cows, which were assumed to be suffering from Chronic Suppurative Pneumonia due to farm history, the loss in terms of milk sale revenue corresponds to 0.7% of the yearly milk sale revenue (717 616€). Adding to this would be the cost per treatment of each cow (which the farm did not have available), milk excluded from human consumption in case of a not-null withdrawal period and the possibility of precocious culling. The observed milk loss magnitude is in accordance with previously reported values, in which milk production in cows suffering from Chronic Suppurative Pneumonia has been described to only reach 25% to 50% of expected yield (Scott, 2013).

Table 13: Meat farm production loss with dead unweaned calves

Data Required	Estimated Loss
• No. of affected calves = 7 • Effect magnitude = 100% (all affected calves died) • Unitary calf value = 662.5€ (Price per 6-8 months old and 250 Kg Charolais calf in November 2015. Source: GPP, SIMA)	7 x 1 x 662.5 = **4 637.5 €**

The loss due to calf mortality may be estimated by the lost revenue that would be obtained with animal sale. This farm sold Charolais calves after weaning, between six and seven months old. Taken this into account, the estimated mortality loss was of 4 637.5€, which corresponded to about 5.2% of the yearly calf sale revenue (90 000€). It should be noticed that the presented income derived from calf sale is overestimated, since we would need to take into account the costs of rearing the animals up to slaughter age. However, the farm had no available data on rearing costs. Mortality seems to be one of the major contributors to the total cost of suckler calf pneumonia, as reported by Andrews (2000), preceded only by weight loss and expenditures in medicines. In this case, we must also contemplate the fact that BRD treatment had been instituted in all seven animals before their deaths, which also carried a cost. However, there was no available data concerning treatment expenditures at the farm.

Respondents' level of knowledge concerning BRD was far from ideal, and appeared to be poorer amongst meat farm respondents when compared to their dairy peers, with all meat producers claiming not to be fully clarified concerning this disease and only one milk producer claiming to be fully clarified. Respondents from both groups viewed the Veterinary Practitioner as the main source of information concerning this disease, which may be an opportunity to strengthen the professional relationship between these two parts, with the Veterinarian playing not just a clinician role but the role of advisor as well. Other sources of information used by dairy farmers included pharmaceutical companies and publications, also used by meat producers along with farmer organizations, training actions and the internet.

Nearly 90% of respondents found it relevant to receive information and support concerning BRD from official entities, despite only one mentioning this source when actively searching for information about the disease. This apparent contradiction might mean that producers do not regard official entities as active partners in the first line of disease control, perhaps due to difficulties in communication, but will not decline their help if it is offered. This support was generally regarded as something that would aid producers in achieving a more efficient production but also a better understanding of BRD's geographical prevalence throughout the country.

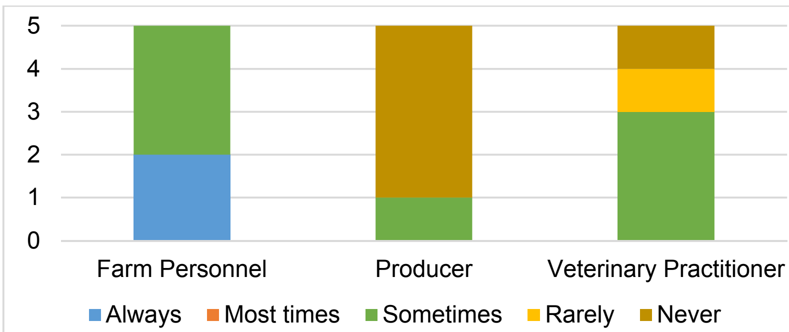
It is worth mentioning that the only respondent that did not find it relevant to receive support from official entities was the one from the dairy farm with the highest number of BRD cases, which might reveal some misinformation concerning the disease. The fact that this respondent names pharmaceutical companies as a common and valuable source of information might reflect the emphasis put on medical prophylaxis and treatment at this farm, overlooking management practices and biosecurity measures indispensable for an effective BRD control, which might help explain the high number of clinical cases in this farm.

6.4.3. Dairy Farm Management and Biosecurity Practices

All dairy farms had self-replacing herds, which decreases the risk of introducing infectious agents into the farm through the purchase of new animals.

Collective maternity areas were present in all farms, with calving supervision always done in one farm, performed most of the times in three farms and only sometimes on the remaining farm. Supervision was done by different intervenients (Graph 10). There was no apparent relationship between calving supervision frequency and intervenients and the occurrence of BRD on our sample.

Graph 10: Calving supervision on dairy farms



All farms performed the first colostrum feeding within six hours after birth and resorting to adequate methods (esophageal feeders and nursing bottles), therefore minimizing failure of passive transfer phenomena, but the amount of colostrum given was different amongst farms. It is known that providing calves with three to four litres of colostrum may diminish the prevalence of failure of passive transfer (Radostits, 2001). However, the farm that provided only 2.5 litres, a volume similar to the one obtained by naturally sucking calves (Radostits, 2001), was the only one that had not experienced any BRD cases, which might indicate that the volume was adequate for this farm. Colostrum evaluation was also performed in all farms, with four of them recurring to a colostrometer and the other performing only visual appraisal. This last farm was the one without any clinical cases.

Only two dairy farms privileged single housing in preweaned calves and, despite the absence of cases in one of these farms, the other had more clinical cases of BRD (n=30) when compared to a farm that kept preweaned calves exclusively in groups (n=3), which might indicate that an effective BRD control can be achieved even with grouped preweaned calves. An interesting fact about this last farm is that, despite keeping all calves grouped, it was the one with the smallest number of clinical cases in calves (three unweaned calves and one weaned calf), which probably indicates that other key management practices are being fulfilled, and are perhaps worthy of further investigation. For instance, this was the farm with the highest cleaning frequency, sanitizing the calves' barn more than once per week, and the only one performing calf navel tying in new born calves in addition to navel dipping, which was performed in all farms.

Calves' barns generally had natural ventilation systems, with one farm having artificial/mechanical ventilation. The farm which had had no cases of BRD had a mix of both methods, but no apparent relationship was found between the type of ventilation and the occurrence of BRD in other farms.

Weaned calves were usually kept in groups of more than ten animals, which has also been identified as a risk factor for BRD development. Three farms had experienced no cases of BRD on weaned calves and, despite one of them keeping groups between five to ten animals, with apparently less risk of BRD, the other two had larger groups, including the farm without any clinical cases, which makes it difficult to establish a correlation between the presence of BRD and this practice in our sample. Another fact worth mentioning is that the only farm that had an established all-in all-out system in the calves' facilities was the one without any clinical cases.

Considering preweaned calf feeding, all farms used whole discarded milk and/or colostrum and transition milk, despite only three of them possessing a pasteurizer. However, the farms that did not possess the device were the farms that had the smallest number of clinical BRD cases, and therefore not pasteurizing the milk did not appear to be an additional risk factor for the presence of disease. There was an apparent absence of relationship between milk feeding methods, with the majority of farms using automatic feeding systems, and BRD occurrence.

Calf weaning age differed amongst farms, ranging from two to four months of age. Calves from the farm with no clinical cases were the oldest weaned. Even though it makes sense that postponing stressful events like weaning may be beneficial, it is also true that performing this procedure at a younger age, if following good husbandry practices, may not come with an increased BRD risk. This seemed to be apparent in the dairy farm with the youngest weaning age, which had a much lower number of affected unweaned calves (n=3) when in comparison to other dairy farms.

With one exception, disbudding was performed at least a month prior to weaning, and it is known that distancing these two practices can be beneficial for BRD control. However, the farm that performed those practices at the same age (two months old), was the one with only four affected calves which, once again, demonstrates that other vital management practices are probably being followed. Considering pain control during disbudding, it was seen that the only farm that did not use local anesthesia - recurring only to flunixin meglumine - and that performed disbudding by application of caustic paste (the others performed cautery disbudding), had the highest number of calf pneumonia cases, with 200 unweaned sick calves and 40 weaned sick calves. Caustic paste is a widely used chemical dehorning method, known to induce significant pain and pain-related behavior – such as head shaking, lying and scratching – exacerbated when animals are exposed to direct sunlight (Stilwell, Lima & Broom, 2008). These authors, upon studying the effectiveness of flunixin meglumine upon caustic paste induced pain, concluded that this NSAID, when used alone, was not enough to control pain during disbudding. The distress experienced by these animals can render them more susceptible to BRD, which might help explain the numerous cases of enzootic calf pneumonia seen in this farm.

There seem to be some flaws considering biosecurity measures in dairy farms, with only three of them possessing physical barriers and providing protection equipment to external personnel, namely boots and overalls. Only two farms had foot baths, with another having both wheel baths and foot baths. Even though biosecurity may not be the main factor contributing to BRD prevention, by reducing pathogen exposure it can be a valuable contributor to an effective disease management programme (Callan & Garry, 2002). Considering BRSV, indirect transmission seems to play a major role in the virus's epidemiology (Ohlson et al. 2010) and therefore biosecurity measures should not be overlooked. In our sample, the dairy farm with the highest number of cases was the poorer one in terms of biosecurity, which might also act as a contributor to the heavy presence of BRD on this farm when in comparison to others.

6.4.4. Meat Farm Management and Biosecurity Practices

As consequence of the complexity of the meat cattle value chain, three farms purchased animals from different external sources, including high-risk locations like auction markets, and not all farms purchasing animals had established quarantine periods, another risk factor for the occurrence of BRD. The ones that did so had quarantine periods of one and two months, respectively. Animals purchased for fattening ranged between four and six months of age and arrived at a weekly basis in one farm, while the other had no data on the subject. Other farm bought breeding bulls every three years.

Vaccination of animals arriving at the farm (either from purchases or in the farm distributed between two locations) was not being done in the most adequate timing, being performed prior to transport on the day the animals were moved into fattening facilities, or in the first 24 to 48 hours after arrival at destination. Since, for an effective established active immunity, animals should be vaccinated two to three weeks prior to transport (Campbell, 2015), implemented vaccination practices may fail to reach expected positive results.

Fattening animals were always kept in groups, ranging from 12 to 100 heads per group, with animals sometimes from different locations and age/sizes being commingled, which may also act as a predisposing factor for BRD. However, the farm that registered the highest number of cases in fattening animals only grouped animals from the same sources and of similar ages/sizes, with many of them being kept outdoors, which might indicate that other factors were contributing to BRD occurrence. It should be noticed that this farm did not have an established quarantine period, despite frequently buying animals.

All farms kept animals outdoors, with three of them also keeping animals indoors, in sheds with natural ventilation. However, one of these farms was the one without any clinical case in the previous 12 months, even though the sheds were never cleaned and that the farm did not possess an established all-in all-out system. It is worth mentioning that this farm was the smallest in terms of animal density, with only 12 fattening animals, which may be decreasing the probability of BRD occurrence. On the contrary, the other two farms had had cases of BRD in these animals, of 40 and 150, respectively. These meat farms held the two largest herds, and therefore animal density in fattening facilities was substantially higher, which may be acting as a predisposing factor for BRD development, especially if factors like ventilation are not being optimized.

Two farms dehorned animals as a routinely practice, at 1.5 months and within 48 hours of birth. In the first case, the procedure was done by the Veterinarian Practitioner and under local anaesthesia, while on the second case it was performed by farm personnel and without any pain control. Interestingly, the farm in which dehorning was performed at a younger age and without pain control was the one with seven dead unweaned calves. The other farm was the one with the higher number of unweaned sick calves, which might indicate that dehorning is contributing to BRD occurrence in these farms, especially if in concomitance with other risk factors. None of the surveyed farms castrated animals.

Four farms had bulls and, of these, only three had established breeding seasons, namely: December to February and June to August; bulls kept separated from females during October and November, and between July and September. Only two farms performed andrological examinations (with an average cost of 78.5€ per bull), both with an adequate timing, that is, before the breeding season. One of these farms was the only one mentioning an impairment on bull fertility due to BRD, but did not have any data concerning the magnitude of such impact. The lack of information concerning bull fertility deriving from the absence of andrological examinations may stand as a challenge when analyzing the impact diseases such as BRD have on meat cattle enterprises.

There were some apparent biosecurity flaws in meat farms, with only three farms possessing physical barriers and only one providing protection equipment to external personnel - boots and overalls - and possessing foot baths and wheel baths. However, farms that did not possess physical barriers and that did not provide any protection equipment had lower cases when compared to the other farms. This may be because herds were kept in more extensive systems in these farms, where BRD pressure is lower. Another assumption is that these farms also received visits from external personnel less frequently. On the contrary, the farm with the highest number of cases was the one seemingly more complete in terms of biosecurity, which might suggest that BRD occurrence at this farm may be related to other risk factors like the lack of cow vaccination, dehorning or the purchase of animals and respective management practices.

Upon analysis of risk factors for BRD occurrence in both dairy and meat farms, we observed that not all previously reported risk factors need to be simultaneously present in order to generate disease. On the other hand, even though farms had indeed risk factors for the development of BRD, their presence was not always a synonym of bigger disease occurrence, which only reflects the multifactorial nature of this disease and that, when aiming for an effective disease control, dairy and meat farms must always be regarded in an individual basis.

Despite some interesting findings, it is worth mentioning again that the farms in which the questionnaires were implemented were chosen as a convenience sample, and therefore the reported results cannot be extrapolated to the general population. However, we believe this case study may act as a basis for a more detailed analysis in the future, considering that the importance of BRD as an economically important disease, both in dairy and meat farms, is globally recognized.

6.5. Preliminary Results in the UK Study

In order to investigate treatment and prevention costs, as well as animal management factors involved in the occurrence of BRD in unweaned calves, a questionnaire developed in the RVC under the European research project SAPHIR was implemented in 30 dairy farms in Wales, chosen as a convenience sample. Included in the questionnaire were questions related to farm characteristics, husbandry, management, treatment and vaccination practices, as well as the presence of respiratory disease at the farm in the previous 12 months.

After analyzing the data collected, the authors concluded that 87% of farms had experienced BRD cases in the previous 12 months, with unweaned calves being the main category of animals affected, similarly to our case study in Portugal, and treatment was administered in 83% of farms in response to the presence of clinical respiratory signs which, like in our study, reveals the importance of taking into account farm personnel's sensitivity in BRD diagnosis. Treatment and vaccination costs for both studies are presented in Table 14.

Table 14: Treatment and vaccination costs for the Portuguese and the Welsh case studies

		Portugal	UK (Wales)*
Treatment Cost Per Animal (€)**			
	Average	2.51	5.60 (per unweaned calf)
	Range	1.88 - 3.03	[a] – 65.11
Vaccination Cost Per Animal (€)**			
	Average	11.3	15.09 (per calf)
	Range	7.5 - 16.4	[a] – 115.34

*Estimated treatment costs did not include veterinary fees and labour. Vaccine costs included vaccine price and labour involved in administration.
**Exchange rate in 11th January 2017: £1 = 1.12183€. Source: *Conversor de Moeda do Banco de Portugal*, available at https://www.bportugal.pt/conversor-moeda?from=GBP&to=EUR&date=&value=1
[a]The minimum value was not included due to lack of clarification concerning its calculation.

An attempt was also made to investigate possible associations between the presence of BRD risk factors and disease incidence in unweaned calves. However, no significant correlation was found.

Another interesting finding, also similar to what we observed during our case study, was the heavy reliance of producers on memory-based data. In the Welsh study, it was concluded that this was the case in 97% of farms (n=29) which, as seen, may lead to under or overestimations of provided values.

CHAPTER VII: Conclusions and Future Work

Even though our analysis was based on a convenience sample, the presence of BRD in surveyed farms and the messages obtained from the study are quite relevant. As proposed, our case study identified future research ideas concerning BRD's control in both dairy and meat samples, namely: a need for a deeper knowledge of the meat cattle value chain, with a better understanding of purchase locations, history and husbandry practices in the farms of origin, as well as investigating the existence of detailed treatment and vaccination records at farm level. Knowledge of the real prevalences of BRD, as well as its incidence, is also desirable to ascertain the impact of this disease. Apart from epidemiological data, the much-needed information on the magnitude of negative impacts BRD has on production will allow for the estimation of losses due to the disease and, in parallel, of benefits that will arise from minimizing those losses, which might stand as a solid argument for future investments in disease control.
Given the lack of available data at farm level, the estimated losses in our case study represent only a modest parcel of the decrease in farm profitability attributed to BRD, with a yearly loss in milk sale revenue of about 0.7% in one dairy farm and a yearly loss of calf sale revenue of about 5% in a meat farm. However, these were not the only negative impacts observed in these farms, which means that BRD's true losses are being underestimated. Concerning expenditures on BRD treatment, our Portuguese study estimated an average cost per dairy animal of 2.51€, a value that reached 5.60€ in a similar study conducted in Wales. As for vaccination practices, the average cost per dairy animal was of 11.3€ in mainland Portugal and 15.09€ in Wales, with a vaccination cost per animal from meat farms of 9.7€ in Portuguese herds.

BRD has an endemic nature, being constantly present in most cattle populations, and is intimately connected to cattle's production systems. This, combined with the ubiquity of many of the infectious agents involved, may lead to the conclusion that eradication is perhaps not the most cost-effective goal when addressing the disease. Nonetheless, it is in farmers' best interest to minimize its impact on farm profitability, especially in the current conjuncture of tight profit margins. Endemic diseases generally attract less political intervention and surveillance when in comparison to epidemic diseases, being held as "a necessary evil" of modern animal production. It then falls on the private sector to control diseases such as BRD. That does not mean, however, that Governmental Entities do not have a role to play. An example of this role would be the Global Animal Health Plan in the Portuguese Azores region, which aims to eradicate, oversee and control certain cattle diseases (such as tuberculosis, bovine leucosis and bovine spongiform encephalopathy), as well as to minimize the occurrence and impact of the so called 'production diseases', such as IBR and BVD.

Official entities can and should take part in a transfer of knowledge to farmers, ensuring that they are properly clarified about BRD, its impacts and the control measures available, helping them make rational choices on the allocation of resources invested so as to optimize the relationship between verified losses and treatment and prevention expenditures. Veterinarian practitioners also stand as active intervenients in this, with their knowledge and expertise as clinicians enabling them to wear the shoes of advisors as well.

Taking into account the multifactoriality of BRD, with differences concerning the presence of risk factors and disease occurrence, each farm must be looked at on an individual basis when aiming for optimal disease control. In addition, our case study revealed that, in spite of substantial investments being made in medical prophylaxis and treatment of BRD, some farms still had considerable levels of disease, which may indicate the need for a more holistic disease approach, taking into account key management practices. Elucidating farmers on the importance of management practices when tackling BRD should also be a primary goal of this transfer of knowledge. If correctly addressed, these may reduce the need to resort to medical tools such as antimicrobials, an effort that, if generalized, can minimize the occurrence of antimicrobial resistance phenomena and therefore act as a positive externality.

Despite being a major contributor to the genesis of BRD, the current knowledge of BRSV is far from ideal, with identified gaps in knowledge that must be surpassed in order to fully clarify its epidemiology and optimize its control. This must start with a better understanding of the virus's transmission and persistence in cattle populations, with further investigation being needed in terms of carrier existence and occurrence of outbreaks of disease even in self-replacing herds, which will allow for the institution of more specific and effective preventive management and biosecurity practices. A deeper knowledge of viral pathogenesis, namely in terms of the observed host exacerbated response, is also desirable. In addition, there is a necessity for vaccines more effective at calf level, that are able to overcome the inhibitory effect of maternal antibodies as well as induce long-lasting immunity.

DIVA vaccines, and respective diagnostic tests, will be a vital tool for studying and controlling BRSV, and its development seems to be one of the priorities in the cattle production sector, as seen by its inclusion in the SAPHIR project.

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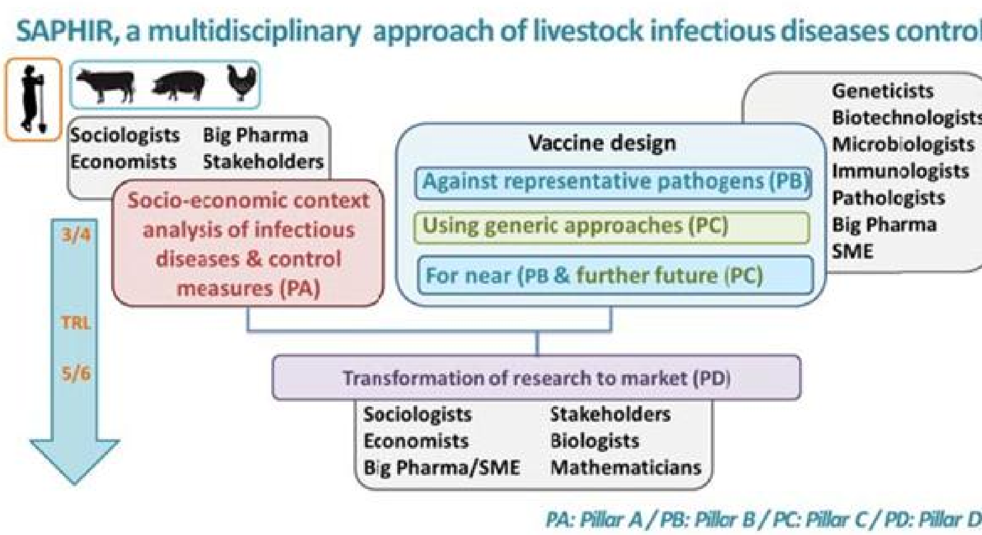
ANNEX I – The SAPHIR Project

SAPHIR, which stands for "Strengthening Animal Production and Health through the Immune Response", is a European research project whose objective is to develop innovative, effective and affordable vaccines against six pathogens that are responsible for highly costly endemic diseases of several livestock species. These vaccine strategies will allow for the combined results of maximizing profitability of food animal systems while at the same time ensuring animal welfare and promoting a reduction in the use of medicines such as antimicrobials, therefore also contributing to the safeguard of public health from a 'One Health' perspective. Apart from vaccine development, the project also aims to identify genetic markers that allow for future selection of animals with optimal vaccination response, therefore maximizing vaccination benefits. The targeted livestock species and pathogens are: cattle, with focus on BRSV and *M. bovis*; poultry, with the study of *Eimeria* spp. and *Clostridium perfringens*; and pigs, with focus on Porcine Reproductive and Respiratory Syndrome Virus (PRRSV) and *Mycoplasma hyopneumoniae*.
The objectives of this project are wide-ranging, comprising both technical and scientific goals such as the development, testing and implementation of effective vaccines as well as socio-economic goals, in which the impact of each pathogen-induced disease and the benefits that can arise from the prophylactic control through vaccination will be evaluated. In order to reach these objectives, a multidisciplinary approach is needed, considering different levels of intervention and contributors. This approach is illustrated in the figure bellow.

SAPHIR's Different Levels of Intervention and Pillars of Action



Source: http://www.h2020-saphir.eu/ambition.html

The project is structured over four different pillars of action, namely Pillars A to D. Pillar A, on which the RVC is an active participant, comprises the socio-economic analysis of SAPHIR-targeted pathogens, both in terms of economic impact due to the presence of disease and control measures already existent, including vaccination.

SAPHIR's Objective Concerning BRSV

The main objective of the programme in terms of BRSV control is the development of a DIVA vaccine, included in Pillar of action B. Even though there are already numerous vaccines against the virus throughout the European market, studies of their efficacy are far from consensual, with common reports of short-lasting immunity and even vaccine-induced disease shadowing their utilization. The development and implementation of a DIVA vaccine, by allowing the differentiation between infected and vaccinated animals, may allow for a more thorough evaluation of the virus concerning its actual prevalence and transmission patterns, as well as an easier monitoring of vaccine safety and efficacy and the possibility of undergoing eradication programmes against BRSV.

Preliminary Results Concerning Production Losses Caused by SAPHIR Pathogens and Induced Diseases

Evaluating productive losses due to a certain disease is the primordial step into determining the economic benefits that will arise from the introduction on the market of a new control measure, such as a vaccine. Therefore, the work being done at the RVC concerning Pillar A of the project comprised a literature review about quantitative estimated production losses concerning the pathogens targeted by the SAPHIR project. This literary review was performed through Google Scholar, with validation by a panel of scientific experts. Concerning the targeted cattle pathogens, and given their intrinsic relationship and contribution to BRD, studies that aimed to quantify the impact of undifferentiated BRD were also included. The main objective of this review was to evaluate the existent data on productive losses concerning the targeted pathogens, therefore identifying gaps in the current knowledge of these pathogens and their economic implications at farm level, also acting as a guide for future necessary research undertaken within the project.

Upon the conclusion of the literary review and compilation of an initial report, the main results concerning BRSV and BRD were as follows:

- There seems to be a significant lack of data concerning production losses due to specific pathogens, contrary to the more significant amount of published data concerning the productive impact of syndromic diseases. This can be seen by the general unavailability of data concerning productive losses especially attributed to BRSV in comparison to a vast number of studies focused on the impact of undifferentiated BRD.

- Despite the fact that BRSV mainly targets the respiratory tree, its negative impact is not restricted to that physiological system and its nefarious effects, especially in the long-term, are shown to affect cattle's productive performance in a variety of ways, both in the dairy and in the meat sectors. These wide-ranging, short and long term effects on production are also an obstacle when aiming for a broader, all-encompassing evaluation of the impact BRD has on the sector, especially considering the complexity of dairy and meat production chains.
- Another difficulty in evaluating the specific productive impacts of BRSV-induced disease is the fact that this virus commonly induces disease in synergy with other infectious agents, both viral and bacterial. The fact that BRD usually results from the action of several pathogens, whose combined effect manifests itself as clinical disease, makes it very difficult (if not nearly impossible), to attribute specific production losses to specific pathogens, which reversely also makes it more difficult to estimate the benefits that will arise from controlling that specific pathogens using a vaccine.
- The negative effect BRD has on cattle, especially beef cattle, transpires in many studies in the form of reduced ADG, translating the negative impact this syndrome has on meat production. On the contrary, not much has been published on the effect BRD has on another vital performance parameter, the FCR. This is due to the fact that this parameter is more difficult to estimate in cattle, especially considering that many herds may be loosely fed on pasture or forage.
- The vast majority of studies that aimed to evaluate the impact BRSV/BRD had on production were retrospective studies, centered on the availability of disease and production records from farms, slaughterhouses, official Veterinary services or national entities. There are several studies conducted at slaughterhouses whose approach is based on the evaluation of lung lesions at slaughter and their correlation with impaired performance or carcase quality. These have the advantage of being very informative concerning subclinical disease phenomena, of great importance when evaluating the economic impact BRD has on beef cattle, but the lack of a standardized scoring method makes it difficult to compare results from different studies.
- Most available studies were from either the United States or other non-European countries such as Canada. Concerning studies conducted in Europe, most of them were based in the UK, the Netherlands, Sweden and Norway. Scandinavian studies are mainly focused on the effect BRSV has on dairy herds, with well-documented effects on milk yield, SCC and age at first calving. American studies, on the other hand, are largely focused on the impact BRD has on feedlots, namely in terms of ADG and carcase quality impairment.

ANNEX II: Medicines Used in BRD Treatment in Portugal and in the UK

Antimicrobials used in BRD treatment in Portugal and the UK

Antimicrobial	Route of Administration	Labelled Dose	Duration of Treatment	Meat and Milk Withdrawal	Metaphylactic Use
Aminosidine	IM	10.5 mg/kg SID	3-5 days	Meat/offal: 24 days Milk: 4 days	No
Amoxicillin	IM	15 mg/kg (LA)	Single administration. If persistence of symptoms, repeat 48 hours later.	Meat/offal: 23 days; Milk: 3 days	No
		7 mg/kg SID	Up to 5 days	Meat/offal: 18 days Milk: 24 hours	
Amoxicillin/ Clavulanic Acid	IM, SC	8,75 mg/kg, SID	3-5 days	Meat/offal: 42 days Milk: 2 days	No
Ampicillin	IM	15 mg/kg	Single administration. If necessary repeat 48 hours later.	Meat/offal: 28 days Milk: 72 hours (Portugal); not approved (UK)	No
Ampicillin Trihydrate	IM	7.5 mg/kg SID	Up to 5 days	Meat/offal: 18 days Milk: 24 hours	
Cefquinome	SC	2.5 mg/kg (LA)	2 doses, 48 hours apart	Meat/offal: 13 days Milk: not approved	No
	IM	1 mg/kg SID	3-5 days	Meat/offal: 5 days Milk: 24 hours	
Ceftiofur	IM, SC	1 mg/kg, SID	3-5 days	Meat/offal: 2 days (IM); 8 days (SC) Milk: 0 hours	No
Danofloxacin	SC, IV	6 mg/kg	Single administration. If persistence of symptoms, repeat 48 hours later.	Meat/offal: 8 days Milk: 4 days	No
Doxycycline	PO	Calves: 10mg/kg SID	3-5 days	Meat/offal: 7 days Milk: not approved	Yes
Enrofloxacin	SC IV	5 mg/kg, SID 7.5 mg/kg (Single injection)	3-5 days	Meat/offal: 12 days (SC); 5 days (IV) Milk: 4 days (SC); 3 days (IV)	No
	PO	Calves: 2.5 mg/kg	3-5 days	Meat/offal: 7 days	
Erythromycin	IM	5 mg/kg SID	3-5 days	Meat/offal: 13 days Milk: 17 days	No
Florfenicol	IM, SC	IM: 20 mg/kg SC: 40 mg/kg	IM: 2 doses, 48 hours apart SC: Single injection	Meat/offal: 39 days (IM), 44 days (SC) Milk: not approved	Yes
Flumequine	PO	Calves: 10 mg/kg BID in drinking water/ milk	3-5 days	Meat/offal: 6 days Milk: not approved	Yes
Gamithromycin	SC	6 mg/kg	Single injection	Meat/offal: 64 days Milk: not approved	Yes
Lincomycin and Spectinomycin	IM	1 mL/5-10 kg, BID or SID	3-4 days	Meat/offal: 14 days Milk: 72 hours	No

Marbofloxacin	IM	8 mg/kg	Single injection	Meat/offal: 3 days Milk: 72 hours	No
	IM, SC, IV	2 mg/kg SID	3-5 days	Meat/offal: 6 days Milk: 36 hours	
Oxytetracycline	PO	Calves: 9-18 mg/kg/day Adults: 2-4 mg/kg/day	3-5 days	Meat: 10 days Milk: 0 days	Yes
	IM, SC, IV, IP	5-10 mg/kg	Single injection Repeat up to 5 days in severe cases.	Meat/offal: 10 days (IM, SC, IP); 5 days (IV) Milk: 3-12 days	Yes
Procaine Penicillin	IM	10 mg/kg SID	3-5 days	Meat/offal: 7 days Milk: 84 hours	No
Procaine Penicillin + Streptomycin	IM	8 mg/kg of procaine-penicillin and 10 mg/kg of Streptomycin, SID	3-5 days Until 1-2 days after symptoms disappear.	Meat/offal: 23 days Milk: 5 days	No
Spectinomycin	IM	5-10 mg/kg, SID Calves: 20-39 mg/kg SID	5 days maximum	Meat/offal: 5 days; 32 days (calves) Milk: 12 hours	No
Spiramycin	IM	100.000 UI/kg	Treatment: 2 doses, with 48 hours apart Metaphylaxis: Single injection	Meat/offal: 28 days (Portugal); 75 days (UK) Milk: not approved	Yes
Sulfadoxine-Trimethoprim	IM, SC, IV	15 mg/kg	3-5 days	Meat/offal: 10 days Milk: 2 days	No
Tildipirosin	SC	4 mg/kg	Single injection	Meat/offal: 47 days Milk: not approved	Yes
Tilmicosin	PO	Calves: 12.5 mg/kg, BID	3-5 days	Meat/offal: 42 days	Yes
	SC	10 mg/kg	Single injection	Meat/offal: 77 days Milk: 36 days (UK); not approved (Portugal)	
Tulathromycin	SC	2,5 mg/kg	Single injection	Meat/offal: 22 days Milk: not approved	Yes
Tylosin	PO	Calves: 10-20 mg/kg, BID in drinking water/milk	7-14 days	Meat/offal: 12 days	Yes
	IM	5-10 mg/kg SID	2-5 days	Meat/offal: 28 days Milk: 5 days	

Sources: Simposium Veterinário Apifarma, available at http://www.apifarma.pt/simposiumvet/Paginas/default.aspx
Veterinary Medicines Directorate, available at www.vmd.defra.gov.uk

Anti-Inflammatory drugs used in BRD treatment in Portugal and in the UK

Anti-Inflammatory Drug	Route of Administration	Labelled Dose	Duration of Treatment	Milk/Meat Withdrawal
Acetylsalicylic acid	PO	50-100 mg/kg SID	3-5 days	Meat/offal: 1 day Milk: not approved
Carprofen	SC, IV	1.4 mg/kg	Single injection	Meat/offal: 21 days Milk: 0 days
Dexamethasone	IM, SC, IV	0.06 mg/kg	Single injection. Can be repeated after 24-48 hours	Meat/offal: 7 days Milk: 3 days
Flunixin Meglumine	IV	2.2 mg/kg, SID	3 days maximum	Meat/offal: 4 days Milk: 1 day
Ketoprofen	IV, IM	3 mg/kg SID	1-3 days	Meat/offal: 4 days Milk: 12 hours
Meloxicam	SC, IV	0.5 mg/kg	Single injection	Meat/offal: 15 days Milk: 5 days
Sodium Salicylate	PO	40 mg/kg SID	1-3 days	Meat/offal: 0 days Milk: not approved
Tolfenamic acid	IM	2 mg/kg	Single injection. If necessary, repeat after 48 hours	Meat/offal: 10 days Milk: 0 days

Sources: Simposium Veterinário Apifarma, available at http://www.apifarma.pt/simposiumvet/Paginas/default.aspx
Veterinary Medicines Directorate, available at www.vmd.defra.gov.uk

Other auxiliary drugs used in BRD treatment in Portugal and the UK

Name and Class	Route of Administration	Labelled Dose	Duration of Treatment	Milk/Meat Withdrawal
Adrenaline (sympathomimetic agent)	SC, IM	0.004-0.018 mg/kg	Single injection	Meat/offal: 0 days Milk: 0 days
Bromhexine (mucolytic agent)	IM PO	0.2-0.5 mg/kg SID	5 days	Meat/offal: 0 days Milk: not approved
Dihydrochlorothiazide (diuretic agent)	IV, IM, SC	10-20 mL/day (adults) 2 ml/40 kg SID (calves)	2-3 days	Meat/offal: 72 hours Milk: 48 hours

Sources: Simposium Veterinário Apifarma, available at http://www.apifarma.pt/simposiumvet/Paginas/default.aspx
Veterinary Medicines Directorate, available at www.vmd.defra.gov.uk

ANNEX III: BRSV vaccines currently available in Portugal and in the UK

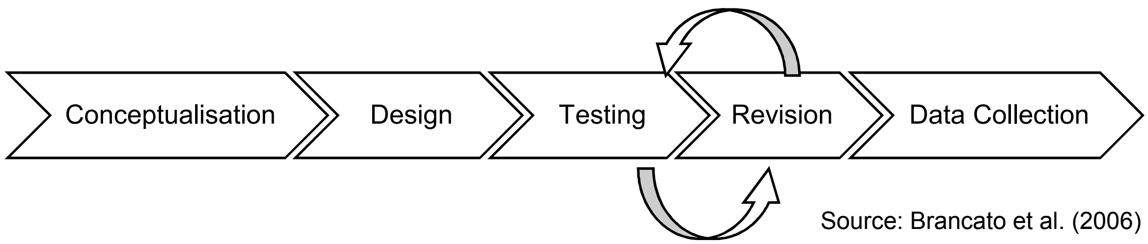
Name	Induces Protection Against	Dose and Route	Basic Immunization	Booster dose	Use during pregnancy / lactation	Duration of Immunity
Bovilis Bovipast® RSP	▪ BRSV (inactivated) ▪ PI_3V (inactivated) ▪ *Mannheimia haemolytica* (inactivated)	5 mL SC	Calves with approximately 2 weeks of age: 2 doses, 4 weeks apart	If required, vaccinate with a Single injection approximately 2 weeks before a risk period	Safe	Not established Peak of antibody immunity 2 weeks after basic immunization
Hiprabovis® 4	▪ IBR (inactivated) ▪ PI_3V (inactivated) ▪ BVDV (inactivated) ▪ BRSV (live)	3mL IM SC	2 doses, 3 weeks apart Calves Dams Heifers(1 month before 1st service)	1 vaccination annually	Safe	32 weeks (at least) Effective immunity 3 weeks after vaccination
Hiprabovis® Balance	▪ PI_3V (inactivated) ▪ BVDV (inactivated) ▪ BRSV (inactivated)	3 mL IM SC	2 doses, 21-30 days apart Calves (>4 weeks) Dams Heifers(1 month before 1st service)	1 vaccination annually	Safe	12 months Effective immunity 3 weeks after vaccination
Rispoval®3	▪ PI_3V (modified live) ▪ BRSV (modified live) ▪ BVDV (inactivated)	4 mL IM	2 doses, 3 or 4 weeks apart Calves >12 weeks Calves should be vaccinated at least 3 weeks before a risk period, or in early Autumn	Re-vaccinate after 6 months if protection against BRSV and/or BVDV is required	Not safe	6 months for BRSV and BVDV No info on PI_3 Onset of immunity 3 weeks after vaccination
Rispoval®4	▪ IBR (inactivated) ▪ BVDV (inactivated) ▪ PI_3V (modified live) ▪ BRSV (modified live)	5 mL IM	Calves >3 months ▪ 2 doses, 3/4 weeks apart Calves <3 months ▪ Repeat vaccination scheme (probable interference with maternal antibodies)	If animals are at risk after a period of 6 months since 1st vaccination	Not safe (lack of info)	6 months (at least)
Rispoval® IntraNasal RS + PI_3	▪ BRSV (modified live) ▪ PI_3V (modified live)	2 mL IN	Calves > 3 weeks ▪ Single injection Calves should be vaccinated at least 10 days before risk period, or in early Autumn. Vaccinating all the calves in the farm is advised.	Not appliable	Not safe	9 weeks (at least)
Rispoval® RS	▪ BRSV (live, attenuated)	2 mL IM	Calves ≥ 4 months:		Safe	4 months (at least)

	▪ 2 doses, 3 or 4 weeks apart Calves <4 months: ▪ 2 doses, 3 or 4 weeks apart + 3rd dose at 4 months (an interval of at least 14 days must be observed between the 2nd and 3rd injection)		Onset of immunity occurs up to 7 days after vaccination.

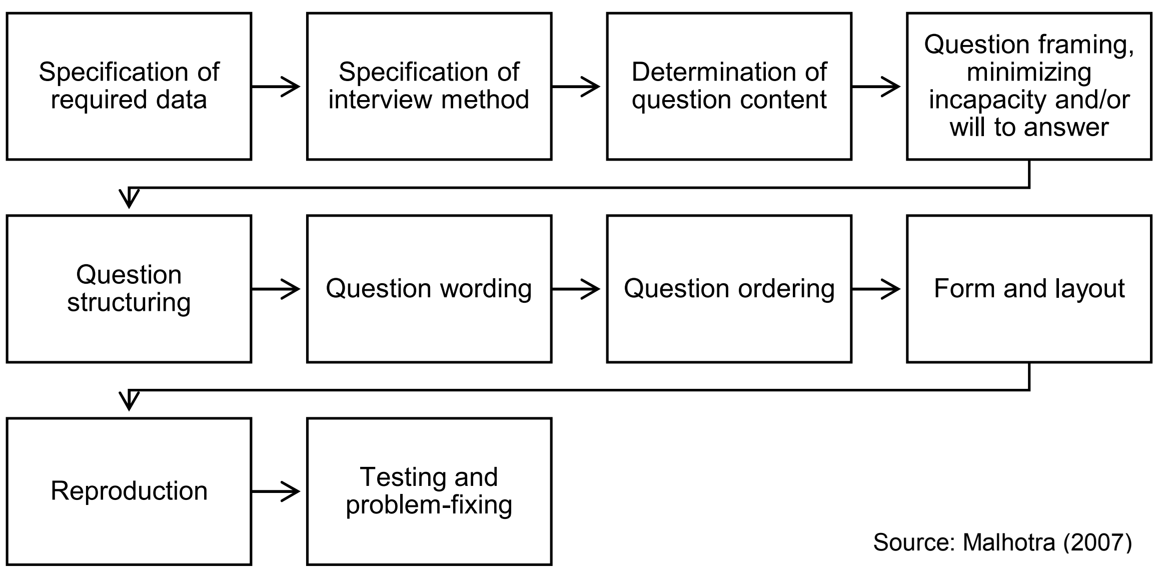
BRSV Vaccines Currently Available in Portugal and in the UK (continuation)

<u>Sources</u>*:* Simposium Veterinário Apifarma, available at http://www.apifarma.pt/simposiumvet/Paginas/default.aspx
Veterinary Medicines Directorate, available at www.vmd.defra.gov.uk

ANNEX IV – Steps of constructing and implementing a questionnaire, adapted from Brancato et al. (2006) and Malhotra (2007)



Source: Brancato et al. (2006)



Source: Malhotra (2007)

ANNEX V – Bovine Respiratory Disease in Dairy Farms: a Questionnaire

Doença Respiratória Bovina em Explorações Leiteiras

O presente questionário, realizado no âmbito do Mestrado Integrado em Medicina Veterinária da Universidade de Lisboa, destina-se a reunir informação acerca da presença de Doença Respiratória Bovina (DRB) em explorações leiteiras nacionais, como base para a análise do impacto económico desta doença no sector da produção bovina. Um melhor conhecimento acerca dos efeitos da DRB no sector pode contribuir para, e sustentar, uma melhor atuação no seu maneio e prevenção.
Todos os dados recolhidos são de carácter anónimo, e não há respostas certas e erradas, pelo que se pede que as respostas sejam o mais sinceras possível.

Muito obrigada pela sua colaboração! Data: / /

Grupo I: Caracterização da Exploração

1. **Localização geográfica da exploração (concelho)**

   ____

2. **Indique os tipos de produção praticados na sua exploração (pode assinalar mais do que uma opção).**

   ☐ Produção leiteira

   ☐ Recria de vitelas e novilhas para reposição do efetivo

   ☐ Recria de vitelos para produção de carne

   ☐ Outras (especifique): ______________________________

   ____

   ____

3. **Indique as raças utilizadas na exploração.**

   ☐ Puras. Quais? ______________________________

   ____

   ____

   ☐ Cruzadas. Quais? ______________________________

   ____

   ____

4. **Indique o número aproximado de animais de cada categoria presentes na exploração.**

☐ Vacas em lactação: __________

☐ Vacas secas: __________

☐ Novilhas gestantes: __________

☐ Novilhas não-gestantes (> 6 meses): __________

☐ Vitelas não-desmamadas: __________

☐ Vitelas desmamadas (2 a 6 meses): __________

☐ Touros: __________

5. **Indique a procedência dos animais na exploração (pode assinalar mais do que uma opção).**

☐ Exploração fechada (não compra animais de fora)

☐ Compra de animais de outras explorações. Se sim, por favor indique:

Que animais: ____

Com que frequência: ____

☐ Compra de animais em leilão. Se sim, por favor indique:

Que animais: ____

Com que frequência: ____

☐ Outros (especifique): ______________________________

____

____

6. **No caso de comprar animais, estes provêm sempre das mesmas fontes?**

☐ Sim

☐ Não

7. **No caso de comprar animais, estes são mantidos isolados antes de os introduzir no resto do efetivo?**

☐ Sim. Durante quanto tempo? ______________________________

☐ Não

8. **Indique o tipo de mão-de-obra na exploração (pode assinalar mais do que uma opção)**

☐ Mão-de-obra permanente. Número de trabalhadores: _______ Salário mensal bruto / trabalhador (encargo para o empregador):______________

☐ Mão-de-obra familiar / não-assalariada. Número de trabalhadores: _______

☐ Mão-de-obra temporária. Número de horas:________________ € / hora:__________________

Em que situações recorre a mão-de-obra temporária?

____

____

Grupo II: Práticas de Maneio

Maternidade e Cuidados com Vitelos Recém-Nascidos

1. Existe maternidade na exploração?

☐ Sim. De que tipo? ☐ Individual ☐ Coletiva

☐ Não

2. Os partos são supervisionados?

☐ Sempre

☐ A maioria das vezes

☐ Algumas vezes

☐ Raramente

☐ Nunca

Caso haja alguma supervisão, quem a executa? E com que frequência?

	Sempre	Algumas vezes	Raramente	Nunca
Trabalhadores da exploração				
Produtor				
Médico-Veterinário				

3. A primeira administração de colostro é efetuada quanto tempo após o nascimento?

☐ Menos de 4 horas

☐ Entre 4 a 6 horas

☐ Mais de 6 horas

4. Como é administrado o colostro?

☐ Balde

☐ Tetina

☐ Entubação

☐ Outro (especifique): ____________________

5. **Qual a quantidade média de colostro dada a cada vitelo na primeira refeição?** _________ litros

6. **Procede à avaliação da qualidade do colostro?**

☐ Sim. Por que método? ☐ Apreciação visual

☐ Colostrómetro

☐ Outro (especifique):____________

☐ Não

7. **Após o parto, os umbigos dos vitelos são sujeitos a desinfeção ou atadura?**

☐ Desinfeção

☐ Atadura

☐ Não

Alojamento de Vitelos

8. **Qual, ou quais, os modos de alojamento dos vitelos até ao desmame? Pode assinalar mais do que uma opção.**

☐ Individual. Que tipo de alojamento? ☐ Iglô ☐ Cubículo ☐ Outro (especifique): ________________________

☐ Coletivo. Indique o número médio de animais por grupo: ☐ até 5 animais ☐ 5-10 animais ☐ mais de 10 animais

9. **No agrupamento de vitelos desmamados, indique o número médio de animais por grupo:**

☐ Até 5 animais

☐ 5-10 animais

☐ Mais de 10 animais

10. **Indique o tipo de ventilação nos pavilhões**

☐ Natural

☐ Artificial / Mecânica

11. **Qual a frequência de limpeza das instalações dos vitelos?**

☐ Mais do que uma vez por semana

☐ Semanal

☐ A cada duas semanas

☐ Mensal

☐ Outra: Especifique: ____

12. **É utilizado um sistema de *all-in all-out (*limpeza e vazio sanitário depois da saída da totalidade de animais do grupo) no viteleiro?**

☐ Sim

☐ Não

Alimentação Pré-Desmame

---

13. **Que tipo de leite é dado aos vitelos após encolostramento? Pode assinalar mais do que uma opção.**

☐ Leite inteiro descartado

☐ Colostros e leite de transição

☐ Leite de substituição

☐ Outro. Especifique: ____________________________

O leite usado é previamente pasteurizado? ☐ Sim ☐ Não

14. **Qual, ou quais, os métodos usados na exploração para a alimentação dos vitelos pré-desmame?**

☐ Balde sem tetina

☐ Balde com tetina

☐ Alimentadores automáticos

☐ Outro. Especifique: ________________________

____

Desmame

---

15. **Com que idade são desmamados os vitelos na exploração?** __________________

Descorna

---

16. **Com que idade se procede à descorna dos vitelos na exploração?** _____________

17. **Que método é utilizado na descorna?**

☐ Termocautério

☐ Descorna Química (produtos cáusticos)

☐ Outro (especifique): _____________

18. É efetuado controlo da dor na descorna?

☐ Sim, anestesia

☐ Sim, anestesia + analgesia

☐ Não

Biossegurança

---

19. Possui barreiras físicas com o objetivo de limitar o acesso de pessoas e/ou veículos à sua exploração?

☐ Sim

☐ Não

20. Aquando da entrada de pessoal externo (visitantes, veterinário, inseminador, etc) na exploração, é-lhes providenciado algum tipo de equipamento de proteção?

☐ Sim. Que material? ☐ Botas ☐ Macacão ☐ Outros: ______________________________________

☐ Não

21. Possui rodilúvios e/ou pedilúvios na exploração?

☐ Sim, rodilúvios.

☐ Sim, pedilúvios.

☐ Sim, ambos.

☐ Não.

Grupo III: Doença Respiratória Bovina na Exploração

1. Nos últimos 12 meses, ocorreram casos de doença respiratória na exploração?

☐ Sim

☐ Não

2. No caso de ter respondido 'Sim' à questão anterior, que animais foram afetados? E em que número?

☐ Vitelos não-desmamados. Quantos? __________

☐ Vitelos desmamados. Quantos? __________

☐ Novilhas. Quantas? __________

☐ Vacas em lactação. Quantas? __________

☐ Touros. Quantos? __________

3. **Tem alguma estimativa da prevalência de doença respiratória na sua exploração?**

☐ Sim. Quanto? _________%

☐ Não

4. **Quem procede ao diagnóstico dos casos clínicos de doença respiratória na exploração? E com que frequência?**

	Sempre	Algumas vezes	Raramente	Nunca
Trabalhadores da exploração				
Produtor				
Médico-Veterinário				

5. **Nos últimos 12 meses, contactou um Médico Veterinário devido à ocorrência de doença respiratória na sua exploração?**

☐ Sim. Quantas vezes? __________ Qual foi o custo total das visitas? ________________

☐ Não

6. **Que sinais clínicos são usados na exploração para o diagnóstico de doença respiratória? Pode assinalar mais do que uma opção.**

☐ Redução de apetite

☐ Febre

☐ Depressão

☐ Tosse

☐ Corrimento nasal e/ou ocular

☐ Respiração anormal

☐ Outros (especifique): _____________________________________

____

____

7. **Para além dos sinais clínicos, faz uso de algum outro método para diagnosticar casos de doença respiratória na exploração?**

☐ Sim. Especifique: ____

☐ Não

8. **Após o diagnóstico, procede ao isolamento dos animais doentes?**

☐ Sim

☐ Não

9. **Já foram identificados na exploração agentes infeciosos de doença respiratória?**

☐ Sim. Quais (pode assinalar várias opções):

  ☐ Vírus Respiratório Sincicial Bovino

  ☐ Vírus Parainfluenza 3

  ☐ Herpesvirus Bovino 1

  ☐ Vírus da Diarreia Viral Bovina

  ☐ Coronavírus Bovino

  ☐ *Pasteurella multocida*

  ☐ *Mannheimia haemolytica*

  ☐ *Histophilus somni*

  ☐ *Mycoplasma bovis*

☐ Não

10. **No caso de já terem sido identificados agentes bacterianos de DRB na exploração, foram feitos testes de sensibilidade aos antibióticos?**

☐ Sim

☐ Não

11. **Já foram identificados casos de resistência a antimicrobianos na exploração?**

☐ Sim. A que substâncias? ____

☐ Não

12. **Vacinou animais contra agentes infeciosos de doença respiratória nos últimos 12 meses?**

☐ Sim

☐ Não

No caso de ter respondido 'Sim' à questão 12, por favor indique:

Nome da Vacina	*Idade dos animais vacinados*	*Número de animais vacinados*	*Preço por dose de vacina*

13. Nos últimos 12 meses, foram efetuados tratamentos de casos clínicos de doença respiratória na exploração?

☐ Sim

☐ Não

No caso de ter respondido 'Sim' à questão 13, por favor indique:

Nome do Produto	*Dose Usada*	*Nº de dias de Tratamento*	*Nº de animais tratados*	*Custo por Tratamento*

14. Que efeitos negativos observa nos seus animais que sofrem de doença respiratória? Pode assinalar mais do que uma opção.

☐ Perda de peso. Quanto? _____________ Kg ☐ Sem dados

☐ Atrasos de crescimento. Número de dias de crescimento compensatório: _____________ ☐ Sem dados

☐ Aumento da taxa de mortalidade. Em quanto? _________ % ☐ Sem dados

☐ Aumento da taxa de refugo. Em quanto? _________ % ☐ Sem dados

☐ Aumento da idade ao 1º parto. Em quantos dias? ___________ ☐ Sem dados

☐ Redução da produção leiteira.

Quantos litros? _____________ Durante quanto tempo? ___________________________ ☐ Sem dados

☐ Aumento da Contagem de Células Somáticas no leite.

Que valores registou? ___________________ cél./mL ☐ Sem dados

☐ Outros (especifique):

____

____

____

15. Sente-se esclarecido no que toca ao conhecimento da Doença Respiratória Bovina, nomeadamente acerca dos agentes da doença, sinais clínicos, diagnóstico, tratamento, prevenção, bem como impactos económicos dela recorrentes?

☐ Sim

☐ Não

16. De onde obteve, ou de onde acha que deve obter, informação acerca desta doença?

☐ Médico Veterinário

☐ Organizações de Produtores Pecuários (OPPs)

☐ Entidades oficiais (ex: DGAV)

☐ Outros produtores

☐ Internet

☐ Outros (especifique): ____

17. Acharia relevante receber informação e acompanhamento acerca desta doença por parte de entidades oficiais?

☐ Sim.

Porquê?

____

☐ Não.

Porquê?

____

ANNEX VI – Bovine Respiratory Disease in Meat Cattle: a Questionnaire

Doença Respiratória Bovina em Explorações de Bovinos de Carne

O presente questionário, realizado no âmbito do Mestrado Integrado em Medicina Veterinária da Universidade de Lisboa, destina-se a reunir informação acerca da presença de Doença Respiratória Bovina (DRB) em explorações nacionais de bovinos de carne, como base para a análise do impacto económico desta doença no sector da produção bovina. Um melhor conhecimento acerca dos efeitos da DRB no sector pode contribuir para, e sustentar, uma melhor atuação no seu maneio e prevenção.
Todos os dados recolhidos são de carácter anónimo, e não há respostas certas e erradas, pelo que se pede que as respostas sejam o mais sinceras possível.

Muito obrigada pela sua colaboração! Data: / /

Grupo I: Caracterização da Exploração

1. Localização geográfica da exploração (concelho)

____

2. Indique os tipos de produção praticados na sua exploração (pode assinalar mais do que uma opção).

- ☐ Cria
- ☐ Recria
- ☐ Engorda de novilhos de tipo intensivo (abate dos 12 aos 18 meses)
- ☐ Engorda de novilhos de tipo semi-intensivo (abate dos 18 aos 30 meses)
- ☐ Engorda de novilhos do tipo extensivo (abate acima dos 30 meses)
- ☐ Outras (especifique): ______________________________

____

____

3. Indique o regime de produção adotado na exploração.

- ☐ Intensivo
- ☐ Semi-intensivo
- ☐ Extensivo

4. Indique as raças utilizadas na exploração.

☐ Puras. Quais? ______________________________________

____

☐ Cruzadas. Quais? ______________________________________

____

5. Indique o número de animais de cada categoria presentes na exploração.

☐ Vitelos não-desmamados: __________

☐ Vitelos desmamados: __________

☐ Novilhos(as) destinados a abate para produção de carne: __________

☐ Novilhas de substituição: __________

☐ Vacas: __________

☐ Touros reprodutores: __________

6. Indique a procedência dos animais na exploração (pode assinalar mais do que uma opção).

☐ Exploração fechada (não compra animais de fora)

☐ Compra de animais de outras explorações. Se sim, por favor indique que tipo de animais:

☐ Reposição Idade:________

☐ Engorda Idade:_________

Com que frequência: ____

☐ Compra de animais em leilão. Se sim, por favor indique que tipo de animais:

☐ Reposição Idade:________

☐ Engorda Idade:________

Com que frequência: ____

☐ Outros (especifique): __________________________________

____

____

7. No caso de comprar animais, estes provêm sempre das mesmas fontes?

☐ Sim

☐ Não

8. **No caso de comprar animais, estes são mantidos isolados (quarentena) antes de os introduzir no efetivo?**

☐ Sim. Durante quanto tempo? ______________________________

☐ Não

9. **Os animais que chegam à exploração são sujeitos a (pode assinalar mais do que uma opção):**

☐ Vacinações

☐ Desparasitações

☐ Descorna

☐ Castração

☐ Desmame

Este(s) procedimento(s) são realizados:

☐ Antes do transporte, no local de origem. Quanto tempo antes?

____

☐ Após o transporte e chegada à exploração. Quanto tempo depois?

____

10. **Indique o tipo de mão-de-obra na exploração (pode assinalar mais do que uma opção).**

☐ Mão-de-obra permanente. Número de trabalhadores: _______ Salário mensal bruto / trabalhador (encargo para o empregador):______________

☐ Mão-de-obra familiar / não-assalariada. Número de trabalhadores: _______

☐ Mão-de-obra temporária. Número de horas:_________________ € / hora:___________________

Em que situações recorre a mão-de-obra temporária?

____

____

Grupo II: Práticas de Maneio

*Responda apenas às questões que se enquadram no(s) tipo(s) de produção praticados na sua exploração***.**

Alojamento

1. **Possui animais alojados em grupo?**

☐ Sim. Que animais? ___________________________________

Quantos animais por grupo? ___________________________

Os animais do grupo: ☐ Provêm da(s) mesma(s) fonte ☐ Provêm de diferentes fontes

Os animais do grupo: ☐ Têm idades e/ou tamanhos semelhantes ☐ Têm idades e/ou tamanhos diferentes

☐ Não

2. **Indique o tipo de instalação ocupada pelos animais. Pode assinalar mais do que uma opção.**

☐ Exterior (ao ar livre)

☐ Interior (em pavilhões)

☐ Outras. Especifique:

____

3. **No caso de possuir pavilhões de alojamento de animais, indique o tipo de ventilação.**

☐ Natural

☐ Artificial / Mecânica, permanente

☐ Artificial / Mecânica, em dias quentes

4. **Qual a frequência de limpeza das instalações de alojamento de animais?**

☐ Mais do que uma vez por semana

☐ Semanal

☐ A cada duas semanas

☐ Mensal

☐ Outra: Especifique: ____________________________________

5. **É utilizado um sistema de *all-in all-out* (limpeza e vazio sanitário depois da saída da totalidade de animais das instalações)?**

☐ Sim

☐ Não

Desmame

6. **Com que idade são desmamados os vitelos na exploração?**

☐ Antes dos 6 meses

☐ Entre os 6-7 meses

☐ Depois dos 7 meses

Descorna e Castração

7. **Procede à descorna dos animais da sua exploração?**
   - ☐ Sim. Com que idade? ____________________________
   - ☐ Não

No caso de ter respondido 'Sim' à questão 7, indique quem normalmente executa a descorna.

- ☐ Médico-Veterinário
- ☐ Pessoal da exploração
- ☐ Pessoal externo à exploração (contratos)

8. **Procede à castração dos animais da sua exploração?**
   - ☐ Sim. Quando? ____
   - ☐ Não

No caso de ter respondido 'Sim' à questão 8, indique quem normalmente executa a castração.

- ☐ Médico-Veterinário
- ☐ Pessoal da exploração
- ☐ Pessoal externo à exploração (contratos)

9. **É efetuado controlo da dor na descorna e/ou castração?**
   - ☐ Sim, anestesia
   - ☐ Sim, anestesia + analgesia
   - ☐ Não

Maneio Reprodutivo dos Touros

10. **Possui época de reprodução definida na exploração?**
    - ☐ Sim. Especifique:

      ____
    - ☐ Não, o touro está com as vacas todo o ano.

11. **Os touros são sujeitos a exame andrológico?**
    - ☐ Sim. Quando? ____
    - ☐ Não

No caso de ter respondido 'Sim' à questão 11, indique qual o custo anual dos exames andrológicos.

____

Biossegurança

12. Possui barreiras físicas com o objetivo de limitar o acesso de pessoas e/ou veículos à sua exploração?

☐ Sim

☐ Não

13. Aquando da entrada de pessoal externo (visitantes, veterinário, inseminador) na exploração, é-lhes providenciado algum tipo de equipamento de proteção?

☐ Sim. Que material? ☐ Botas ☐ Macacão ☐ Outros: ________________________________

☐ Não

14. Possui rodilúvios e/ou pedilúvios na exploração?

☐ Sim, rodilúvios.

☐ Sim, pedilúvios.

☐ Sim, ambos.

☐ Não.

Grupo III: Doença Respiratória Bovina na Exploração

1. Nos últimos 12 meses, ocorreram casos de doença respiratória na exploração?

☐ Sim

☐ Não

2. No caso de ter respondido 'Sim' à questão anterior, que animais foram afetados? E em que número?

☐ Vitelos não-desmamados. Quantos? __________

☐ Vitelos desmamados. Quantos? __________

☐ Novilhos(as). Quantos? __________

☐ Vacas. Quantas? __________

☐ Touros. Quantos? __________

3. **Tem alguma estimativa da prevalência de doença respiratória na sua exploração?**

☐ Sim. Quanto? _________%

☐ Não

4. **Quem procede ao diagnóstico dos casos clínicos de doença respiratória na exploração? E com que frequência?**

	Sempre	Algumas vezes	Raramente	Nunca
Trabalhadores da exploração				
Produtor				
Médico-Veterinário				

5. **Nos últimos 12 meses, contactou um Médico Veterinário devido à ocorrência de doença respiratória na sua exploração?**

☐ Sim. Quantas vezes? __________ Qual foi o custo total das visitas? ________________

☐ Não

6. **Que sinais clínicos são usados na exploração para o diagnóstico de doença respiratória? Pode assinalar mais do que uma opção.**

☐ Redução de apetite

☐ Febre. Qual o valor indicativo? _________ºC

☐ Depressão

☐ Tosse

☐ Corrimento nasal e/ou ocular

☐ Respiração anormal

☐ Outros (especifique): ______________________________________

____

____

7. **Para além dos sinais clínicos, faz uso de algum outro método para diagnosticar casos de doença respiratória na exploração?**

☐ Sim. Especifique:

____

☐ Não

8. **Após o diagnóstico, procede ao isolamento dos animais doentes?**

☐ Sim

☐ Não

9. **Já foram identificados na exploração agentes infeciosos de doença respiratória?**

☐ Sim. Quais (pode assinalar várias opções):

  ☐ Vírus Respiratório Sincicial Bovino

  ☐ Vírus Parainfluenza 3

  ☐ Herpesvirus Bovino 1

  ☐ Vírus da Diarreia Viral Bovina

  ☐ Coronavírus Bovino

  ☐ *Pasteurella multocida*

  ☐ *Mannheimia haemolytica*

  ☐ *Histophilus somni*

  ☐ *Mycoplasma bovis*

☐ Não

10. **No caso de já terem sido identificados agentes bacterianos de DRB na exploração, foram feitos testes de sensibilidade aos antibióticos?**

☐ Sim

☐ Não

11. **Já foram identificados casos de resistência a antimicrobianos na exploração?**

☐ Sim. A que substâncias? ____

☐ Não

12. **Vacinou animais contra agentes infeciosos de doença respiratória nos últimos 12 meses?**

☐ Sim

☐ Não

No caso de ter respondido 'Sim' à questão 12, indique:

Nome da Vacina	***Idade dos animais vacinados***	***Número de animais vacinados***	***Preço por dose de vacina***

13. **Nos últimos 12 meses, foram efetuados tratamentos de casos clínicos de doença respiratória na exploração?**

☐ Sim

☐ Não

No caso de ter respondido 'Sim' à questão 13, indique:

Nome do Produto	***Dose Usada***	***Nº de dias de Tratamento***	***Nº de animais tratados***	***Custo por Tratamento***

14. **Possui algum plano metafilático para Doença Respiratória Bovina na exploração?**

Por plano metafilático entende-se a administração de agentes antimicrobianos à totalidade de animais de um grupo no qual existem em simultâneo animais com sinais clínicos de doença e animais aparentemente sãos.

☐ Sim. Neste caso, indique:

Antibiótico Usado	***Em que situações***	***Animais tratados***	***Custo por animal***

☐ Não

15. Que efeitos negativos observa nos seus animais que sofrem de doença respiratória? Pode assinalar mais do que uma opção.

☐ Diminuição do Ganho Médio Diário. Em quanto? _____________ Kg/dia ☐ Sem dados

☐ Diminuição do peso ao abate. Quanto? _____________ Kg ☐ Sem dados

☐ Atrasos de crescimento. Número de dias de crescimento compensatório: _____________ ☐ Sem dados

☐ Aumento da taxa de mortalidade. Em quanto? _________ % ☐ Sem dados

☐ Aumento da taxa de refugo. Em quanto? _________ % ☐ Sem dados

☐ Diminuição da fertilidade dos touros.

De que forma? ____ ☐ Sem dados

☐ Outros (especifique):

____

____

16. Sente-se esclarecido no que toca ao conhecimento da Doença Respiratória Bovina, nomeadamente acerca dos agentes da doença, sinais clínicos, diagnóstico, tratamento, prevenção, bem como impactos económicos dela recorrentes?

☐ Sim

☐ Não

17. De onde obteve, ou de onde acha que deve obter, informação acerca desta doença?

☐ Médico Veterinário

☐ Organizações de Produtores Pecuários (OPPs)

☐ Entidades oficiais (ex: DGAV)

☐ Ações de formação ou publicações

☐ Internet

☐ Outros (especifique): ____

18. Acharia relevante receber informação e acompanhamento acerca desta doença por parte de entidades oficiais?

☐ Sim.

Porquê?

____

☐ Não.

Porquê?

____