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## Strategies for reduced antibiotic usage in dairy cattle farms

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#### ABSTRACT

The need for antibiotic treatments in dairy cattle farms can be reduced by a combined intervention scheme based on: (1) timely clinical inspections, (2) the assessment of animal-based welfare parameters, and (3) the use of predictive laboratory tests. These can provide greater insight into environmental adaptation of dairy cows and define animals at risk of contracting disease. In the long-term, an improved disease control justifies the adoption of such a combined strategy. Many antibiotic treatments for chronic disease cases are often not justified with a cost/benefit analysis, because the repeated drug administration does not give rise to the expected outcome in terms of animal health. In particular, compared with untreated cases, antibiotics may not lead to greater cure rates for some forms of mastitis. Lastly, a substantial reduction of antibiotic usage in dairy farms can be achieved through the proper use of immuno-modulators, aimed at increasing immunocompetence and disease resistance of cows.

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#### 1. Introduction

Production diseases of farm animals are complicated by the overuse of antibiotics, the generation of drug-resistant bacteria, and the transfer of the latter to the food chain. These issues were highlighted in a report issued in 2009 by the European Centre for Disease Prevention and Control and the European Medicines Agency (ECDC/EMEA, 2009), which stressed the discrepancy between the increasing occurrence of multidrug resistant bacteria in Europe and the poor development of antibiotic drugs to treat infections by such bacteria. The animal origin of some serious human infections caused by multidrug-resistant bacteria has also been highlighted by Fey et al. (2000).

The aforementioned risks can be traced to intensive animal production (Ingvartsen et al., 2003), compounded by mismanagement, especially in terms of nutrition, chemotherapy and housing conditions (Trevisi et al., 2006). Indeed, adequate animal welfare is not only achieved by eliminating pain, injury, disease, or distress, but also by proper management (Loor et al., 2013). High production levels and poor management often translate into increased replacement rates, reduction of life expectancy, more frequent occurrence of multifactorial diseases (Mulligan and Doherty, 2008), and increased use of veterinary drugs. The dairy farming

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sector is no exception to this general rule. A general improvement of milk quality has accompanied an impressive increase of milk yield in Friesian cows. According to the Italian Holstein Friesian Association (ANAFI), in 2011 the average milk yield of 1,128,626 Italian Holstein Friesian cows was 9190 kg with average contents of 3.67% and 3.35% for fat and protein, respectively. The impact of performances like these on animal welfare and health has been considerable. In this respect, as the genetic ability to produce milk increases, more cows are affected by production diseases. The associations between increased milk production and increased risk of production diseases, as well as reduced fertility, are well known, but less is known about the biological mechanisms behind these relationships (Ingvartsen et al., 2003; Oltenacu and Broom, 2010). Thus, the number of cows that reached 48 months of age in the North-Eastern USA decreased from 80% in 1957 to 13% in 2002, and the mean calving interval increased from 13 to 15.5 months (Oltenacu and Broom, 2010). In particular, as reviewed by Bertoni et al. (2009), the high yielding dairy cow (HYDC) is more susceptible to infectious diseases (namely mastitis) and metabolic stress, and this condition is exacerbated in times of reduced immunocompetence as it occurs during the transition from dry period to lactation (Lacetera et al., 2005; Sordillo et al., 2009a; Trevisi et al., 2011a).

In this framework, pending the enactment of a specific directive concerning welfare of dairy cows in Europe, dairy farms are still characterized by the presence of neglected sectors. In terms of housing, hygiene and feeding conditions, heifers and calves are

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often reared under substandard conditions as compared to lactating cows. This stance of farmers arises from lack of awareness of the crucial role of these animals for the maintenance of a good animal health status on farm, and of the repercussions of diseases early in life on the subsequent well-being and milk production levels (Bach, 2011). As a result, calves and heifers are often prone to suffer from opportunistic microbial infections which lead to a high infectious pressure in the herd. This may have a very negative impact on HYDC, that are not likely to mount an effective immune response because of the severe metabolic stress around calving and onset of lactation (Bertoni et al., 2008; Sordillo and Aitken, 2009b; Trevisi et al., 2012). Also, there is evidence of genome changes in HYDC. These may be associated with defective homeostatic control mechanisms, underlying more frequent occurrence of production diseases. Accordingly, some studies demonstrated unfavorable genetic correlations between milk vield and incidence of ketosis, ovarian cysts, mastitis and lameness in dairy cattle (Ingvartsen et al., 2003).

Owing to the above, the purpose of this manuscript is to define measures for a substantial reduction of drug usage in dairy cattle farms on the basis of published studies. The operational framework of these interventions also will be described against the background of the present needs and priorities of farming activities worldwide.

#### 2. Conceptual framework

The achievement of high production levels in animal husbandry translates into a greater difficulty of numerous animals to adapt to the environment. Dairy cows in the post-calving period represent a model of utmost importance and relevance for animal scientists. The current high-genetic merit cow phenotypes demand high technical and management skills, suitable logistical structures and intensive on farm controls. Therefore, an obvious gap may arise between the cow requirements and the actual environment in which they are reared. This fundamental risk condition may co-exist with the high level of performance for a period of time. However, performance will then decrease and eventually cease when clinical diseases and/or serious metabolic dysfunctions occur. Both conditions lead to the same result: early removal of the cows from the production enterprise and an overall increase of replacement rates in the farm. In this respect, the productive increase obtained through genetic selection is not in itself a cause of a reduction in animal welfare. It is a factor causing that a portion of the animal population is unable to respond with an adequate adaptation strategy to the environmental stressors associated with housing, feeding and farm management as a whole.

The disease control strategies in herds affected by production diseases and large antibiotic usage should be supported by adequate risk analysis and management. In this respect, a recent report (EFSA, 2012) provides a useful methodology for prioritization and management of risk factors underlying production diseases. In particular, production diseases are clearly indicated in the section "Consequence characterization flow chart of animal welfare", which outlines an interesting operational framework for intervention strategies. These can be conveniently supported by nation or region-wide information systems of food safety, as recently shown by the development of a risk prioritization model in the Veterinary Prevention Programme (VPP) adopted by the veterinary authorities in the Lombardy Region, Italy.

Secondly, the disease control measures should meet the consumers' expectations and ensure the quality of animal products along with animal health and welfare conditions. At the same time, the adopted measures should be conducive to optimal living conditions in rural areas for farmers and their families, as well as to reasonable prospects of economic sustainability and development of farms. Thus, the adopted measures should lead to lower rates of replacements on farm and improve animal-based welfare parameters. At the same time, livestock capital on farm must remain sufficiently profitable.

Thirdly, in terms of environmental sustainability, nitrogen, carbon dioxide and methane emissions from animal production account for a relevant percentage of the global warming effects (18% in developing Countries and 2–4% in industrialized Countries; Pulina et al., 2011). Moreover, world meat production should double by 2050 to keep up with consumption, thus creating a heavy impact on the biosphere (WWI, 2013). This means that intervention strategies for production diseases must be viewed in the perspective of new, environmentally-friendly husbandry activities.

#### 3. Alternatives to antibiotics

The recent OIE/IABS international conference on "Alternatives to antibiotics" (OIE/IABS, 2012) provided evidence that a reduction of antibiotic usage in farm animals can be achieved by a proper combination of natural antibacterial peptides, biological response modifiers (BRM), pre and probiotics, as well as by a correct development of the gut microbiome. Some of the above approaches have been successfully applied to disease models of cattle. In particular, there is evidence that probiotics can provide an important contribution to disease control in dairy cattle herds (Frola et al., 2012; Nader-Macías et al., 2008). Likewise, several BRM and non-antibiotic drugs proved effective in field trials in terms of disease resistance and thriftiness of treated cattle (Malinowski, 2002). The costs of such treatments are usually comparable to those of vaccines. However, their use implies a proper herd surveillance program, which must define the phases at risk for disease occurrence. In a global view, this means that a satisfactory level of veterinary control is highly-recommended before choosing the above intervention strategies.

On the whole, the authors agree with the conclusions of the OIE/IABS conference and believe that the possible interventions on farm can be widened to further areas of activity:

- The timely detection of disease signs, allowing for shorter and more effective drug treatments.
- A cost/benefit analysis of repeated antibiotic treatments in terms of animal health and farmer's convenience.
- A second generation diagnostic approach to production diseases. This should be based on clinical immunology and chemistry tests predictive of production diseases in dairy cattle, i.e. on robust, user-friendly parameters associated to poor environmental adaptation and relevant high risk of disease occurrence in cattle (Amadori et al., 1997; Trevisi et al., 2012; Loor et al., 2013).

Therefore, on the basis of their own experience and published results, the authors illustrate the possible contributions of the above approaches to an integrated strategy for reduction of antibiotic usage in dairy farms.

#### 4. Early diagnosis and predictive laboratory parameters

High disease rates are commonly reported among HYDC in the transition period, ranging from 3 weeks before to 3 weeks after calving. This period is characterized by the occurrence of an inflammatory response in terms of both positive and negative acute phase proteins (APP+ and APP-, respectively) (Bertoni et al., 2008; Trevisi et al., 2009). To measure the inflammatory response, we developed the Liver Functionality Index (LFI), which is based on some APP- responses (albumin, cholesterol *sensu stricto* + bilirubin) during the first month of lactation (Trevisi et al., 2011a). In this respect, low LFI values are associated with high inflammatory responses and disease occurrence (Trevisi

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