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Public consultation on potential candidates for substitution

Substance name: **Cyanamide**

Third party submission of information on potential candidates for substitution

NON-CONFIDENTIAL

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Since my experimental thesis on „Investigations on dysentery treatment of pigs: combination of vaccination and chemotherapy“ at the University of Veterinary Medicine Hannover in 1993 I have been frequently involved in studies on the various treatment options for the control and eradication of *Brachyspira hyodysenteriae*.

Swine dysentery has long been recognized as a major cause of loss to pig industry throughout the world. The causative bacterium was identified back in the 1960s and is now referred to as *Brachyspira hyodysenteriae*.

B. hyodysenteriae live in the large intestine and are passed out with the faeces. This is why it is so easily

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spread on claws, boots, vehicles, equipment as well as by vectors like rodents and flies (Harlizius 2004, 2014).

Treatment of infected herds by reliance solely on antimicrobial medication is not sufficient (Heinritzi 2002). This may at least partly be due to the fact that a decrease of antimicrobial susceptibility to the main drugs used against *B. hyodysenteriae* has been observed worldwide. Resistance to antimicrobials can develop if not all pathogens are killed, especially if the treatment duration is not long enough and/or if the concentration given is too low. The latter problem often occurs in acutely infected animals when antibiotics are supplied in feed because those animals do not eat or drink enough. Consequently, they need to get correct antimicrobial dose by injection.

As animals discharge in their faeces and urine between 10%-90% of the administered antibiotic unchanged or in active metabolites resistance can potentially also develop in the manure and after the manure is spread onto the field (Massé et al. 2014).

Due to the increasing threat of drug-resistant infections in animals as well as humans the European Commission considers antimicrobial resistance (AMR) a priority problem and has recently published "Guidelines for the prudent use of antimicrobials in veterinary medicine" (Anonymus 2015).

One of the key elements for reducing the need to use antimicrobials is the disease prevention by implementing hygiene and biosecurity measures (Commission Notice, chapter 6).

This is especially important for the prevention of *B. hyodysenteriae* caused dysentery as today only a few antimicrobials are effective against these bacteria (Figi et al. 2014).

In case of *B. hyodysenteriae* the most important disease prevention methods are the eradication of vectors like flies and rodents (Harlizius and Hennig Pauka 2014, Harlizius 2004) and the disinfection of the highly contagious liquid manure of which in most cases residuals remain in the slurry pit after the end of a fattening cycle and the pumping out of the slurry. The elimination of the *B. hyodysenteriae* bacteria in the liquid pig manure is also important in order to avoid the manure becoming a possible source of antibiotic resistant bacteria as high rates of (multi-) resistant bacteria have already been found in pig manure (Hölzel et al. 2010). Resistance genes can even be enriched in manure from antibiotic-exposed farm animals, and thus have the potential to survive in soil through horizontal gene transfer events, and to be transported to other environmental compartments (Heuer et al. 2011).

The main advantages of using the biocidal product ALZOGUR® for the treatment of the residual liquid pig manure are as follows:

- Cyanamide, the active substance of ALZOGUR, controls *Brachyspira hyodysenteriae* as well as the fly larvae and therefore effectively interrupts the reinfection-cycles in the affected pig houses otherwise the healthy new piglets would be infected via flies and other vectors.
- In contrary to many other disinfectants cyanamide is known to be effective also at lower temperatures. This is particularly important during the winter months when *B. hyodysenteriae* can longer survive in the liquid pig manure.
- Although cyanamide has been used in pig-farming for decades, resistance of Brachyspires or flies has never been reported. This can be explained due to the mode of action as a multi-site inhibitor. Therefore, it is not expected that resistance to cyanamide will develop in future from its use in pig stables.
- The action of cyanamide is not interfered even by high organic load, as is present in liquid manure.
- The efficacy of using cyanamide for treatment of residual slurry as an essential element of a swine dysentery eradication program has recently been demonstrated on a Swiss sow breeding farm with 170 sows and 600 gilts/fatteners (Figi et al. 2014). The eradication program not only eliminated *B. hyodysenteriae* from the entire farm but also resulted in significantly higher daily weight gain.
- A retrospective study from 2019 showed that Cyanamid is the only possibility for treatment of slurry (Cadetg et al. 2019).

Conclusion on suitability and availability of an alternative

In consideration of the worldwide crucial situation with the fight against pig dysentery and the above described characteristics of Alzogur there is currently no alternative biocide or any other method available for the disinfection of liquid manure in pig houses against *Brachyspira hyodysenteriae*.

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