High levels of dietary zinc under a cloud

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Key Points

- High level (2,500 – 3,000ppm) zing use (HZU) in feed for 1 to 2 weeks post weaning to counter enteric disease is perhaps the most widely adopted alternative to antibiotic use in pig production globally.
- The European Union just announced a ban on HZU in piglet feed, to be phased in over 5 years
- Banning of an effective and widely adopted alternative to antibiotics, at least in part due to perceived concerns about coselection of resistant bacteria, adds another layer of complexity to the development and validation of all interventions to replace antibiotics in food animal production.

In addition to being an essential nutrient that influences the function of over 300 enzymes in mammals, use of pharmacological levels of zinc (typically as zinc oxide) has had a central role in weaned pig management in the era of reduced antibiotic use. Phasing out antibiotics for growth promotion in Europe ushered in a period of increased problems of enteric disease in weaned pigs in many countries. Feeding high levels (2,500 – 3,000ppm) of zinc for 1 to 2 weeks post weaning to counter enteric disease is perhaps the most widely adopted alternative to antibiotic use in pig production globally. Within the EU, adoption of high zinc use (HZU) was variable due to bans in individual countries (e.g., Germany, Netherlands and France). However, the European Commission just announced an EU-wide ban on the HZU in piglet feed, to be phased in over 5 years. Concerns about HZU are twofold: 1) environmental contamination in pig dense regions, as most of the zinc is excreted in feces; and 2) potential co-selection of antibiotic resistant bacteria, specifically ST398 Methicillin-resistant Staphylococcus aureus (MRSA) which emerged in many EU swine industries after removal of growth promotant antibiotics.

The decision to phase out HZU was widely opposed by industry groups who fear it may have significant impact on pig health and welfare, as well as cost of production. The environmental risks are highly variable geographically and the banning of HZU, for the sake of regulatory uniformity, in regions known to have low levels of zinc in soil is clearly questionable. The ST398 MRSA issue remains highly politically charged, particularly in Denmark where invasive human infections have been documented in people without swine contact, albeit at very low incidence (Larsen et al., 2017). The relationship between HZU and ST398 MRSA raises questions about potential unintended consequences of regulatory changes, as a zinc resistance gene (*czr*) is carried on the same gene cassette as the *mecA* gene that encodes methicillin resistance in ST398 MRSA, providing a mechanism for co-selection by zinc. This relationship is also apparent in ST398 MRSA in pigs in North America, but not for the ST5 MRSA variants also found in US pigs.(Hau et al., 2017). The extent to which HZU actually influenced the emergence of ST398 is uncertain, as multiple factors are likely to be involved. However, the banning of an effective and widely adopted alternative to antibiotics, at least in part due to perceived concerns about coselection of resistant bacteria, adds another layer of complexity to the development and validation of all interventions to replace antibiotics in food animal production.

Larsen J, Petersen A, Larsen AR, Sieber RN, Stegger M, Koch A, Aarestrup FM, Price LB, Skov RL Emergence of livestock-associated methicillin-resistant *Staphylococcus aureus* bloodstream infections in Denmark. Clin Infect Dis. 2017 May 30. doi: 10.1093/cid/cix504.

Hau SJ, Frana T, Sun J, Davies PR, Nicholson TL. Zinc Resistance within Swine Associated Methicillin Resistant Staphylococcus aureus (MRSA) Isolates in the USA is Associated with MLST Lineage. Appl Environ Microbiol. 2017 May 19. pii: AEM.00756-17. doi: 10.1128/AEM.00756-17.