This is provisional English translation of an excerpt from the original full report.

Risk Assessment Report

Virginiamycin

(Veterinary Medicinal Products)

Food Safety Commission of Japan (FSCJ)
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ABSTRACT

FSCJ conducted the hazard identification on antimicrobial-resistant bacteria selected by using virginiamycin, a streptogramin antibiotic designated as a feed additive for food animals, in accordance with the Assessment Guideline for the Effect of Food on Human Health Regarding Antimicrobial-Resistant Bacteria Selected by Antimicrobial Use in Food Animals [1].

Vancomycin-resistant *Enterococcus* (VRE) infection in human is treated with streptogramin antibiotics, and possibly arising from consumption of foods of pig and poultry origins. Streptogramin antibiotics used in human medicine confer a cross-resistance to virginiamycin. VRE, which possibly affects human health, is occasionally harbored in intestines of chickens and pigs, although the bacterium is not the main pathogen in these animals. The use of virginiamycin in chickens and pigs has the potential to cause resistance to virginiamycin. Virginiamycin resistant enterococci possibly causes infectious diseases in human via foods, or via hospital environments which may be contaminated via some pathways. Vancomycin-resistant *Enterococcus faecium* is susceptible to quinupristin and dalfopristin, which belong to the streptogramin class of antibiotics as one of the primary antibiotics for treatment of VRE infections in humans. Streptogramin antibiotics are not primary antibiotics for non-VRE enterococci, but some strains of them harbor resistance factors against streptogramin antibiotics, and possibly transfer the resistance gene to VRE. Therefore, the hazard to be assessed were identified as *Enterococci* that acquired antibiotic resistance attributing to the use of virginiamycin in chickens and pigs. Based on the results of the release assessment, exposure assessment and consequence assessment, FSCJ estimated the risk arising from the use of virginiamycin.

The release assessment suggested possible selection of the hazard after the use of virginiamycin in chickens and pigs. The monitoring conducted under the Japanese Veterinary Antimicrobial Resistance Monitoring System suggested a trend of the decrease in the rate of resistance in *Enterococcus faecium* isolates from chickens and pigs. However, this may be due to the recent trend of the decrease in the amount of virginiamycin approved for use. The risk level of *Enterococcus* hazard was thus estimated to be “Medium”[2], because the usage of virginiamycin as a feed additive and future occurrence of resistance

[1] Food Safety Commission of Japan, September 30, 2004

needs to be carefully monitored.

The exposure assessment suggested that consumption of chickens and pigs is unlikely to cause directly infectious diseases in humans. *E. faecium* isolates from food animals, healthy population, hospitalized patients and nosocomial infections are not genetically identical. Therefore, livestock-derived *E. faecium* is unlikely to colonize in human intestinal tract for long and to cause infectious diseases in humans. However, livestock-derived *E. faecium* isolates carrying antimicrobial resistant gene have been found to colonize transiently in human intestinal tract, and to transfer resistance genes to *E. faecium* from humans. Furthermore, the prevalence of *Enterococci* is high in retail chicken products. Thus, the exposure assessment suggested the risk level to be "Moderate"[2].

In the consequence assessment, the risk level was judged as "Medium"[2], because the therapeutic efficacy of streptogramin antibiotics for human infectious diseases will be possibly reduced or lost based on the comprehensive consideration of the current status of medical treatments.

The feed additive use of virginiamycin in chickens and pigs may possibly select the hazard to which humans may be exposed through foods of chicken and pig origin, resulting in decreased and/or abolished therapeutic efficacy of antibiotics for humans. The risk for hazard was judged to be "Medium" as a result of the estimation of the risk based on scientific findings and information obtained.

Regarding antimicrobial-resistant bacteria, detailed scientific findings and information are not sufficiently available at this point, and an internationally accepted methodology for the risk assessment has not yet been established. Therefore, it is necessary to keep up with the latest scientific findings and information including the development of discussion in international organizations.

Currently in Japan, virginiamycin is not used in chickens and pigs, however, future use possibly increases the rate of the resistance. Quinupristin and dalfopristin are the primary antibiotics for treatment of VRE infection in humans, and have the cross-resistance with virginiamycin. Therefore, risk management measures need to be strengthened to ensure the prudent use of virginiamycin.

The effective monitoring of resistant bacteria is achieved by monitoring the dynamics of resistant bacteria in the process from food animals via food commodities to humans. Detailed information through genetic analysis on the status of the presence of resistance factors in isolated resistant bacteria is beneficial for understanding of a causal-result relationship. Prevalence of antimicrobial resistance needs to be surveyed and monitored through continued collaboration among risk management agencies in construction of a comprehensive monitoring system which can withstand epidemiological evaluation and verification.

[2] Food Safety Commission of Japan. Fluoroquinolone Antimicrobials for Chickens. Summary. Food Safety. 2014, 2, 171-5.

Detailed data are not available at this point on bacteria resistant to virginiamycin assessed here as a feed additive, and therefore new scientific findings and information need to be continuously collected. Furthermore, risk assessment of this feed additive should be conducted again, if necessary, based on the status of the use of the feed additive, results of monitoring of resistant bacteria in food animals, and the status of investigation and discussion in international organizations.