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

Risk Assessment Report

N^{pro} and *E*^{rns} gene defect bovine viral diarrhea viruses (type 1 and type 2) live vaccine (Bovela)

(Veterinary Medicinal Product)

Food Safety Commission of Japan (FSCJ)
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ABSTRACT

The FSCJ conducted a risk assessment of a live vaccine (Bovela) for *N*^{pro} and *E*^{rns} gene defect bovine viral diarrhea viruses (BVDV: type 1 and type 2), based on application documents for approval of manufacturing and marketing this veterinary medicinal product.

The production strains of this formulation's main ingredient are ddBVD Tub 1 and ddBVD Tub 2 strains. They are genetically modified viruses created by deleting all bases except the first sequence of four amino acids (methionine, glutamic acid, leucine and phenylalanine) of *N*^{pro} gene, and three bases (CAT) of the 394th codon (Histidine) of *E*^{rns} gene from BVDV-1 KE-9 and BVDV-2NY-93 strains as parental strains, which are pathogenic.

It is viewed that these production strains do not contain any exogenous gene and seem to inherit the characteristics of BVDV except the effects of defects of the target gene region (attenuated and not showing pathogenicity). BVDV's host range is restricted to Cloven-hoofed animals, and BVDV is not pathogenic to humans. Consequently, bovine viral diarrhea (BVD) is not regarded as a zoonotic disease.

In addition, there are no reports on the productivity of harmful physiologically active substances in BVDV. Therefore, it is thought that no harmful substance would be generated in the production strains as well, which inherit the characteristics of BVDV. Furthermore, it was demonstrated that even gene sequence database search did not identify sequences having high homology with allergic substances.

Based on the above, the production strains of the main agent of this formulation were considered to have no pathogenicity to humans.

The FSCJ presumed that the additives included in this formulation would have negligible effects on health in the case of consuming this substance, considering its usage, existing toxicity assessments, directions, and dosage.

In safety studies in bovines, no particular concern for the effects on bovines was found due to the intake of this formulation.

Given the above, the FSCJ concluded that the probability of causing adverse effects on human health through food would be negligible as long as this formulation is appropriately applied.