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

Risk Assessment Report

Ronidazole
(Veterinary Medicinal Products)

Food Safety Commission of Japan (FSCJ)
July 2014

ABSTRACT

FSCJ conducted a risk assessment of ronidazole（CAS No. 7681-76-7）, a parasiticide/antiprotozoan agent, based on documents such as assessment reports from the Joint FAO/WHO Expert Committee on Food Additives (JECFA) and the European Medicines Agency (EMEA).

Data used in the assessment include pharmacokinetics (rats, pigs and turkeys), residues (pigs and turkeys), genotoxicity, acute toxicity (mice, dogs and rabbits), subacute toxicity (rats and dogs), chronic toxicity and carcinogenicity (mice, rats and dogs), and reproductive and developmental toxicity (mice, rats and rabbits).

In vitro reverse mutation tests using bacteria and a fluctuation test were positive in genotoxicity studies of ronidazol. These results were likely due to nitroreductase activity of microorganisms per se used in the test, although as yet unproved. An *in vivo* dominant lethal test and a micronucleus test in mice were negative, while a sex-linked recessive lethal test in *Drosophila melanogaster* was positive. Induction of chromosome aberration has been reported, in contrast, by the mouse bone marrow chromosome aberration test. Because of the discrepancy between the data from the mouse micronucleus test and that from the chromosome aberration test, FSCJ can not judge the genotoxicity of ronidazole relevant to human health.

In addition, 3 carcinogenicity studies were conducted in mice and rats. In a carcinogenicity test in mice the incidences of benign and malignant lung tumors and of lung cancer significantly increased in mice given 10 mg/kg bw /day or more and 20 mg/kg bw/day or more, respectively. In 2 carcinogenicity studies in rats, mammary tumors significantly increased in females given 10 mg/kg bw/day or more. While these 3 studies thus suggested carcinogenicity of ronidazol, the mechanism is yet unknown and the relationship between the genotoxicity and carcinogenicity is also obscure. On the basis of the above findings, it was not possible to exclude the potential that the threshold in carcinogenicity of ronidazol exists.
Consequently, FSCJ concludes that the ADI of ronidazol should not be specified, since its genotoxicity could not be appropriately evaluated while its carcinogenicity was suggested.