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

Risk Assessment Report

Diethylstilboestrol

(Veterinary Medicinal Products)

Food Safety Commission of Japan (FSCJ)

July 2019

ABSTRACT

FSCJ conducted a risk assessment of diethylstilboestrol (DES) (CAS No. 56-53-1), a non-steroidal synthetic hormone with estrogenic activity, based on reports from the International Agency for Research on Cancer (IARC) and other documents.

Data used in the assessment include ADME data (mice, rats, guinea pigs, cattle and sheep), residue data of livestock, chronic toxicity/carcinogenicity (mice, rats, hamster, squirrel monkey and frogs), reproductive and developmental toxicity (mice and rats), genotoxicity and other information on toxicity.

In genotoxicity studies, DES induced aneuploidy characterized by an abnormal number of chromosomes, but DES did not induce mutagenicity. The mechanism of aneuploidy was presumed to be inhibition of tubulin polymerization to microtubules.

DES showed carcinogenicity in F_1 generations of mice, rats and hamsters when the animals were perinatally exposed. FSCJ attributed mechanisms of these carcinogenicities to combinations of multiple factors. The major factors involved were activation of estrogen receptor alpha (ERα) resulting in stimulation of estrogen dependent cell proliferation and invation. Inhibition of tubulin polymerization to microtubules resulting aneuploidy was also considered as a factor.

In reproductive developmental toxicity studies, inciedences of tumors in reproductive tracts increased through multiple generations.

On the basis of human cases, a relationship between exposure to DES during pregnancy and increased incidence of breast cancer was reported. Increased cancers in female reproductive system were also reported in females exposed to DES at fetuses.

Possible mechanisms for the DES-induced carcinogenesis have been proposed as mentioned above. However, FSCJ recognized information to consider mechanisms for carcinogenesis observed through multiple generations or to specify the NOAEL is limited.
Consequently, FSCJ concluded it inappropriate to specify an ADI of DES.