DEXAMETHASONE

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RESIDUE DEPLETION STUDY

Background

During the 42nd Meeting of JECFA in Rome, 7th February 1994, the sponsors submitted fresh data to facilitate the establishment of MRLs in horses (Bette, 1994). These results suggest that residue depletion of dexamethasone-21-isonicotinate in horses following a single intramuscular administration of VOREN^{R} suspension is in line with the findings previously presented for cattle and pigs.

Horses

Nine Welsh mountain ponies (1 control); age 14 years; ca. 300 kg, 1 male and 3 females per group were employed. VOREN^{R} suspension (1 mg dexamethasone-21-isonicotinate/mL in an injectable suspension containing microcrystalline particles, 20 μg/kg body weight) was administered as a single intramuscular injection into the neck.

Samples of blood were taken 3 hours post dose and muscle, liver, kidney, fat, and injecton site samples were acquired upon sacrifice. Dexamethasone in plasma and tissues were measured by HPLC/MS. Results are shown in Table 1.

Table 1 **Residue Depletion of Dexamethasone-21-isonicotinate in Horses Following a Single Intramuscular Administration of VOREN^{R} Suspension of 20 μg/kg BW**

Days post dosing	Mean Concentration (μg/kg)[a]				
	Muscle	Liver	Kidney	Fat	Injection Site
3	b	b	0.57	b	1698.2 (4)
21	b	b	b	b	11.68 (3)

a Geometric mean, values below the Limit of Quantification (LOQ) have been included in the calculation as the LOQ, the resulting average residue concentrations reported as "<values" (figures in brackets denote the numbers of samples above the LOQ).

b All values are below the LOQ of the assay (0.5 μg/kg for muscle, kidney, fat; 2.5 μg/kg for liver).

c μg dexamethasone found per injection site (ca. 300 g).

Nine cross bred ponies (1 control); age 12 years; ca. 300 kg, 2 males and 2 females per group were employed. VOREN^{R} depot (3 mg dexamethasone-21-isonicotinate/mL in an injectable suspension containing microcrystalline particles, 60 μg/kg body weight) was administered as a single intramuscular injection into the neck.

Samples of blood were taken 3 hours post dose and muscle, liver, kidney, fat, and injecton site samples were acquired upon sacrifice. Dexamethasone in plasma and tissues were measured by HPLC/MS. Results are shown in Table 2.

Table 2. Residue Depletion of Dexamethasone-21-isonicotinate in Horses Following a Single Intramuscular Administration of VOREN[R] depot of 20 μg/kg BW

Days post dosing	Mean Concentration (μg/kg)[a]				
	Muscle	Liver	Kidney	Fat	Injection Site
3	<0.70 (3)	b	1.34	b	6722.0 (4)
28	b	b	b	b	51.9 (4)

a Geometric mean, values below the Limit of Quantitation (LOQ) have been included in the calculation as the LOQ, the resulting average residue concentrations reported as "<values" (figures in brackets denote the numbers of samples above the LOQ).

b All values are below the LOQ of the assay (0.5 μg/kg for muscle, kidney, fat; 2.5 μg/kg for liver).

c μg dexamethasone found per injection site (ca. 300 g).

Residue studies in horses with Dexafort were expected in the summer of 1994 (Bette, 1994) but have not been made available for this evaluation.

APPRAISAL

Based on the limits of quantification of the HPLC/MS method and on the kinetics of depletion of the marker residue from the remaining food commodities the following MRLs common to cattle, and swine were proposed at the 42nd JECFA meeting:

Commodity	MRL [μg/kg]	Marker Residue
Muscle	0.5	dexamethasone
Liver	2.5	dexamethasone
Kidney	0.5	dexamethasone
Milk (cattle)	0.3 μg/l	dexamethasone

The data supplied for horses are in line with the data for other previously studied species. Therefore it is recommended that the temporary MRLs for residues in horses be the same as those proposed at the 42nd JECFA meeting for cattle, and swine.

REFERENCES

Bette, P. (1994). Submission to the 42nd JECFA Meeting, Rome, 7th February 1994 in answer to a question to the sponsors by the Expert Committee.

Quirke, J.F. and Höstermann, D. Corrigendum to the above submission, June 12, 1995.