Experiment Number: S0266
Route: IV, Gavage
Species/Strain: Mouse/B6C3F1

Toxicokinetics Data Summary
Compound: Oxymetholone/ **Analyte:** Oxymetholone
CAS Number: 434-07-1

Request Date: 7/11/2023
Request Time: 10:03:16
Lab: NIEHS CEDRA Corporation

Male

	Treatment Group (mg/kg)	
	20 IV Plasma[a,b]	**120 Gavage Plasma[a,c]**
Cmax (mg/L)		0.18
Tmax (hour)		1.0
Half-life (hour)	2.46	10.3
AUCinf_pred (mg*h/L)	3.62	2.53

LEGEND

MODELING SOFTWARE

Quattro Pro, Version 5.0 for Windows

MODELING METHOD & BEST FIT MODEL

[a]Quattro Pro (Version 5.0 for Windows, Borland International Inc ., Scotts Valley, CA) spreadsheet software. Non-compartmental analysis

EXCEPTIONS

[b]Plasma Concentration at 2 hours equals 0.510 mg/L. 7 timepoints with n of 3.
[c]Plasma Concentration at 2 hours equals 0.127 mg/L. 6 timepoints with n of 3.

ANALYTE

Oxymetholone

TK PARAMETERS

Cmax = Observed or Predicted Maximum plasma (or tissue) concentration
Tmax = Time at which Cmax predicted or observed occurs
Half-life = Lambda z Half life, t 1/2, the terminal elimination half-life based on non-compartmental analysis
AUCinf_pred = Area under the plasma concentration versus time curve, AUC, extrapolated to time equals infinity

TK PARAMETERS PROTOCOL

ANALYSIS METHOD

The animal experiments with blood collection were conducted at one laboratory. Plasma samples were frozen after collection, shipped overnight on dry ice to a second, different company laboratory, and analyzed within 24 hours of arrival to minimize effects of documented instability of oxymetholone in rat plasma even at -20 degree C. Plasma samples were analyzed by a validated method using reverse-phase high performance liquid chromatography (HPLC) with UV detection (285nm) using danazol as an internal standard. Calibration standards were prepared fresh each day of sample analysis. The validated concentration range was 0.1 to 10 ug/mL. Some samples had to be diluted. The limit of detection (LOD) was 0.005 ug/mL and the experimental limit of quantitation (ELOQ) was of 0.100 ug/mL. TK_INTRAVENOUS PLASMA

20 mg/kg, 120 mg/kg Male and Female

The number of animals per treatment-timepoint varied from 1-3 (See exception column). Experiments I and J were used to evaluate influence of gender in determining dose proportionality and the mice experiments L and M were used to evaluate species differences. The pharmacokinetic calculations were performed with noncompartmental methods using the Quattro Pro (Version 5.0 for Windows, Borland International Inc., Scotts Valley, CA) spreadsheet software. At each time point, the available concentrations were averaged. The elimination half-life (t1/2) was calculated as In(2) divided by the negative slope of the linear regression of the natural logarithm of the concentrations forming the terminal phase of the kinetic profiles. The area-under-the-curve (AUC) was calculated according to the linear trapezoidal rule, and extrapolated by dividing the last concentration by the elimination rate constant. The clearance was calculated as the dose divided by the AUC, and the volume of distribution (Vd) was obtained by dividing the clearance by the elimination rate constant The start date given here is the in-life start date. The average age of rats and mice at first dose for the related 2-year oxymetholone studies was 7 weeks.