ゾコーバ錠 125mg，同錠 25mg

第 2 部 (モジュール 2) : CTD の概要 (サマリー)

2.6 非臨床試験の概要文及び概要表

2.6.7 毒性試験概要表

塩野義製薬株式会社

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略号及び用語定義一覧表

略号	英語
AUC	area under the plasma concentration-time curve
$AUC_{0\text{-}24h}$	area under the plasma concentration-time curve from time 0 to 24 hours post-dose
C_{max}	maximum plasma concentration
DRF	dose range-finding
F	female
GLP	Good Laboratory Practice
M	male
MC	methylcellulose aqueous solution
N/A	not applicable
NOAEL	no observed adverse effect level
PND	postnatal day
T_{max}	time to maximum plasma concentration

2.6.7 毒性試験概要表

2.6.7.1 毒性試験： 一覧表

Test Article: Ensitrelvir fumaric acid

Type of Study	Species/Strain	Method of Administration	Duration of Dosing	Doses [a] (mg/kg/day)	GLP Compliance	Testing Facility	Study Number	Location in CTD
DRF Juvenile Animal Toxicity	Rat/Sprague Dawley	Oral gavage	PND 21 to 28	0, 30, 120, 1000	No	[redacted]	S-217622-TF-102-R	4.2.3.5.4-01
Juvenile Animal Toxicity	Rat/Sprague Dawley	Oral gavage	PND 21 to 28	0, 30, 90, 1000	Yes	[redacted]	S-217622-TF-111-L	4.2.3.5.4-02
	Rat/Sprague Dawley	Oral gavage	PND 29 to 36	0, 30, 90, 1000	Yes	[redacted]	S-217622-TF-111-L	4.2.3.5.4-02
	Rat/Sprague Dawley	Oral gavage	PND 37 to 45	0, 30, 90, 1000	Yes	[redacted]	S-217622-TF-111-L	4.2.3.5.4-02

DRF = dose range-finding; GLP = Good Laboratory Practice; PND = postnatal day

a As free form. Unless otherwise specified, for DRF Juvenile Animal Toxicity and Juvenile Animal Toxicity, the NOAEL (No Observed Adverse Effect Level) is underlined.

2.6.7.2 トキシコキネティクス： トキシコキネティクス試験の一覧表

Test Article: Ensitrelvir fumaric acid

Type of Study	Test System	Method of Administration	Doses [a] (mg/kg/day)	GLP Compliance	Study Number	Location in CTD
Juvenile repeat-dose toxicity study	Rat	Oral gavage	0, 30, 90, 1000	Yes	S-217622-TF-111-L	4.2.3.5.4-02

a As free form.

2.6.7.3 トキシコキネティクス： トキシコキネティクス試験成績の一覧

Test Article: Ensitrelvir fumaric acid

Daily Dose [a] (mg/kg)	Steady State C_{max} (µg/mL)			Steady State AUC_{0-24hr} (µg·hr/mL)		
	Rats		Humans	Rats		Humans
	M	F	M & F	M	F	M & F
30	53.2 [b], 38.5 [c], 41.0 [d]	63.9 [b], 54.1 [c], 64.4 [d]	N/A	734 [e], 446 [f], 562 [g]	715 [e], 571 [f], 809 [g]	N/A
90	127 [b], 113 [c], 142 [d]	145 [b], 120 [c], 168 [d]	N/A	1870 [e], 1770 [f], 1890 [g]	2340 [e], 1660 [f], 2530 [g]	N/A
1000	266 [b], 193 [c], 185 [d]	248 [b], 221 [c], 305 [d]	N/A	4030 [e], 3000 [f], 2360 [g]	4440 [e], 3740 [f], 3530 [g]	N/A
375/125 mg (>=40 kg)	N/A	N/A	32.1 [h]	N/A	N/A	754.6 [i]
250/125 mg (30 to 40 kg))	N/A	N/A	37.2 [j]	N/A	N/A	853.5 [k]
150/75 mg (20 to <30 kg)	N/A	N/A	29.9 [l]	N/A	N/A	666.0 [m]

AUC_{0-24hr} = area under the plasma concentration-time curve from time 0 to 24 hours post-dose; C_{max} = maximum plasma concentration; F = female; M = male; N/A = not applicable

a. As free form
b. The C_{max} on Day 8 of a repeat-dose toxicity study in juvenile rats in Cohort-1 (Study No.: S-217622-TF-111-L)
c. The C_{max} on Day 8 of a repeat-dose toxicity study in juvenile rats in Cohort-2 (Study No.: S-217622-TF-111-L)
d. The C_{max} on Day 9 of a repeat-dose toxicity study in juvenile rats in Cohort-3 (Study No.: S-217622-TF-111-L)
e. The AUC_{0-24hr} on Day 8 of a repeat-dose toxicity study in juvenile rats in Cohort-1 (Study No.: S-217622-TF-111-L)
f. The AUC_{0-24hr} on Day 8 of a repeat-dose toxicity study in juvenile rats in Cohort-2 (Study No.: S-217622-TF-111-L)
g. The AUC_{0-24hr} on Day 9 of a repeat-dose toxicity study in juvenile rats in Cohort-3 (Study No.: S-217622-TF-111-L)
h. The estimated C_{max} on Day 5 in clinical dosing regimen of 375/125 mg (375 mg on day 1 of dosing, 125 mg once daily on days 2 to 5 of dosing) for pediatric population from 6 to < 12 years old with body weight of >=40 kg by a population PK analysis (Study No.: S-217622-CPK-025-B [Location in CTD 5.3.3.5-01])
i. The estimated AUC_{0-24hr} on Day 5 in clinical dosing regimen of 375/125 mg (375 mg on day 1 of dosing, 125 mg once daily on days 2 to 5 of dosing) for pediatric population from 6 to < 12 years old with body weight of >=40 kg by a population PK analysis (Study No.: S-217622-CPK-025-B [Location in CTD 5.3.3.5-01])
j. The estimated C_{max} on Day 5 in clinical dosing regimen of 250/125 mg (250 mg on day 1 of dosing, 125 mg once daily on days 2 to 5 of dosing) for pediatric population from 6 to < 12 years old with body weight of 30 to 40 kg by a population PK analysis (Study No.: S-217622-CPK-025-B [Location in CTD 5.3.3.5-01])
k. The estimated AUC_{0-24hr} on Day 5 in clinical dosing regimen of 250/125 mg (250 mg on day 1 of dosing, 125 mg once daily on days 2 to 5 of dosing) for pediatric population from 6 to < 12 years old with body weight of 30 to 40 kg by a population PK analysis (Study No.: S-217622-CPK-025-B [Location in CTD 5.3.3.5-01])
l. The estimated C_{max} on Day 5 in clinical dosing regimen of 150/75 mg (150 mg on day 1 of dosing, 75 mg once daily on days 2 to 5 of dosing) for pediatric population from 6 to < 12 years old with body weight of 20 to <30 kg by a population PK analysis (Study No.: S-217622-CPK-025-B [Location in CTD 5.3.3.5-01])
m. The estimated AUC_{0-24hr} on Day 5 in clinical dosing regimen of 150/75 mg (150 mg on day 1 of dosing, 75 mg once daily on days 2 to 5 of dosing) for pediatric population from 6 to < 12 years old with body weight of 20 to <30 kg by a population PK analysis (Study No.: S-217622-CPK-025-B [Location in CTD 5.3.3.5-01])

2.6.7.4 毒性試験： 被験物質 (ロット毎) 一覧

Test Article: Ensitrelvir fumaric acid

Batch No.	Content (on the anhydrous basis) (%)	Specified Impurities (%)	Study Number	Type of Study
		Related substance		
B170021	81.0 [a]	0.11	S-217622-TF-111-L	Juvenile toxicity in rats

a as ensitrelvir free basis

2.6.7.5 単回投与毒性試験

該当する試験なし.

2.6.7.6 反復投与毒性試験： 重要な試験以外の試験

該当する試験なし.

2.6.7.7 反復投与毒性試験： 重要な試験

該当する試験なし.

2.6.7.8 In Vitro 遺伝毒性試験

該当する試験なし.

2.6.7.9 In Vivo 遺伝毒性試験

該当する試験なし.

2.6.7.10 がん原性試験

該当する試験なし.

2.6.7.11 生殖発生毒性試験： 重要な試験以外の試験

該当する試験なし.

2.6.7.12 生殖発生毒性試験： 受胎能及び着床までの初期胚発生に関する試験

該当する試験なし.

2.6.7.13 生殖発生毒性試験： 胚・胎児発生に関する試験

該当する試験なし.

2.6.7.14 生殖発生毒性試験： 出生前及び出生後の発生並びに母体の機能に関する試験

該当する試験なし.

2.6.7.15 新生児を用いた試験

2.6.7.15.1 幼若ラットにおける反復経口投与毒性試験： 重要な試験以外の試験

Test Article: Ensitrelvir fumaric acid

<table>
<tr><th>Species/Strain</th><th>Method of Administration (Vehicle/ Formulation)</th><th>Duration of Dosing</th><th>Doses a (mg/kg/day)</th><th>Gender and No. per Group</th><th>Noteworthy Findings</th><th>Study Number [Location in CTD]</th></tr>
<tr><td>Rat/ Crl:CD (Sprague Dawley)</td><td>Oral gavage (0.5% methylcellulose aqueous solution (MC) /Suspension)</td><td>8 days (Age at start of dosing: PND 21)</td><td>0, 30, 120, 1000</td><td>5M and 5F</td><td>1000:
Decreased corpuscular hemoglobin concentration (M only)
Increased ratio of reticulocyte (F only)
Increased Gamma- glutamyltransferase
≥ 120:
Decreased direct bilirubin (F only)
Decreased total cholesterol
Decreased calcium (M only)

Toxicokinetics (n = 4, mean value)
<table>
<tr><th rowspan="2">Dose (mg/kg/day)</th><th rowspan="2">Day</th><th colspan="2">C_{max} (μg/mL)</th><th colspan="2">$AUC_{0\text{-}24hr}$ (μg·hr/mL)</th></tr>
<tr><th>M</th><th>F</th><th>M</th><th>F</th></tr>
<tr><td rowspan="2">0</td><td>1</td><td>N/A</td><td>N/A</td><td>N/A</td><td>N/A</td></tr>
<tr><td>8</td><td>N/A</td><td>N/A</td><td>N/A</td><td>N/A</td></tr>
<tr><td rowspan="2">30</td><td>1</td><td>56.3</td><td>59.6</td><td>669</td><td>747</td></tr>
<tr><td>8</td><td>61.5</td><td>63.7</td><td>796</td><td>763</td></tr>
<tr><td rowspan="2">120</td><td>1</td><td>173</td><td>163</td><td>2740</td><td>2720</td></tr>
<tr><td>8</td><td>216</td><td>215</td><td>3380</td><td>3570</td></tr>
<tr><td rowspan="2">1000</td><td>1</td><td>341</td><td>378</td><td>6140</td><td>5960</td></tr>
<tr><td>8</td><td>378</td><td>346</td><td>5500</td><td>5430</td></tr>
</table></td><td>S-217622-TF-102-R [4.2.3.5.4-01]</td></tr>
</table>

N/A = not applicable; PND = postnatal day

2.6.7.15.2 幼若ラットにおける反復経口投与毒性試験

Test Article: Ensitrelvir fumaric acid

Report Title: Repeated Oral Toxicity Study of S-217622 fumaric acid in Juvenile Rats		
Species/Strain: Rat/Crl:CD(Sprague Dawley)	**Duration of Dosing:** Cohort-1 and -2: 8 days, Cohort-3: 9 days	**Study No. [Location in CTD]** S-217622-TF-111-L [4.2.3.5.4-02]
Age at Start of Dosing: Cohort-1: PND 21 Cohort-2: PND 29 Cohort-3: PND 37	**Duration of Postdose (Age at Necropsy of Postdose):** Cohort-1: 22 days (PND 51) Cohort-2: 14 days (PND 51) Cohort-3: 13 days (PND 59)	**Date of First Dose:** Cohort-1: [redacted] Cohort-2: [redacted] Cohort-3: [redacted]
Method of Administration: Oral gavage	**Vehicle/Formulation:** 0.5 w/v% methylcellulose aqueous solution (MC) /Suspension	**GLP Compliance:** Yes
Special Features: None		
NOAEL: 90 mg/kg/day (animals that dose from PND 21) 1000 mg/kg/day (animals that dose from PND 29 and 37)		

Dose (mg/kg/day, as free form)	0 (control)[a]		30		90		1000	
Number of Animals	M: 4	F: 4	M: 4	F: 4	M: 4	F: 4	M: 4	F: 4
Toxicokinetics								
Cohort-1								
C_{max} (µg/mL)								
Day 1	N/A	N/A	41.7	46.1	123	144	333	310
Day 8	N/A	N/A	53.2	63.9	127	145	266	248
T_{max} (hr)								
Day 1	N/A	N/A	8.0	3.0	3.0	8.0	8.0	8.0
Day 8	N/A	N/A	3.0	1.0	3.0	8.0	1.0	3.0
$AUC_{0\text{-}24hr}$ (µg·hr/mL)								
Day 1	N/A	N/A	687	722	1950	2270	6310	5750
Day 8	N/A	N/A	734	715	1870	2340	4030	4440

All individual values in the control group were below the lower limit of quantification (< 0.100 µg/mL).
The first day of dosing was designated as Day 1.
N/A = not applicable; PND = postnatal day
a 0.5% MC

Dose (mg/kg/day, as free form)	0 (control)[a]		30		90		1000	
Number of Animals	M: 4	F: 4	M: 4	F: 4	M: 4	F: 4	M: 4	F: 4
Toxicokinetics								
Cohort-2								
C_{max} (µg/mL)								
Day 1	N/A	N/A	45.7	44.5	119	108	268	256
Day 8	N/A	N/A	38.5	54.1	113	120	193	221
T_{max} (hr)								
Day 1	N/A	N/A	3.0	3.0	3.0	3.0	8.0	3.0
Day 8	N/A	N/A	3.0	1.0	3.0	1.0	3.0	1.0
$AUC_{0\text{-}24hr}$ (µg·hr/mL)								
Day 1	N/A	N/A	400	503	1730	1630	4590	4850
Day 8	N/A	N/A	446	571	1770	1660	3000	3740
Cohort-3								
C_{max} (µg/mL)								
Day 1	N/A	N/A	33.7	49.1	125	146	265	293
Day 9	N/A	N/A	41.0	64.4	142	168	185	305
T_{max} (hr)								
Day 1	N/A	N/A	3.0	3.0	3.0	8.0	8.0	8.0
Day 9	N/A	N/A	3.0	1.0	3.0	1.0	1.0	1.0
$AUC_{0\text{-}24hr}$ (µg·hr/mL)								
Day 1	N/A	N/A	403	683	1580	2360	4720	5070
Day 9	N/A	N/A	562	809	1890	2530	2360	3530

All individual values in the control group were below the lower limit of quantification (< 0.100 µg/mL).
The first day of dosing was designated as Day 1.
N/A = not applicable
a 0.5% MC

Cohort-1								
Dose (mg/kg/day, as free form)	0 (control)[a]		30		90		1000	
Number of Animals	M: 20	F: 20	M: 20	F: 20	M: 20	F: 20	M: 20	F: 20
Noteworthy Findings								
Found Dead or Sacrificed Moribund[b]	0	0	0	0	0	0	0	0
Clinical Signs	–	–	–	–	–	–	–	–
Body Weight (g)[c]								
Day 1	60.9	56.7	59.0	55.9	59.2	57.4	58.7	54.7
Day 3	72.8	67.3	69.6	66.6	70.8	67.9	65.9*	61.7*
Day 5	85.0	78.0	81.6	76.8	82.7	78.2	76.8**	71.6*
Day 8	105.6	95.3	100.8	93.2	102.3	95.2	95.4**	87.3*
Body Weight Gain (g)[c]								
Days 1 to 3	11.9	10.7	10.7	10.7	11.7	10.6	7.3**	7.1**
Days 3 to 5	12.3	–	12.0	–	11.9	–	10.9*	–
Food Consumption (g/animal/day)[d]								
Days 1 to 3	9.0	8.5	8.3	8.3	8.4	8.3	6.0**	5.9**
Days 3 to 5	11.3	10.1	10.6	10.0	10.4	10.1	9.4**	8.6**
Days 5 to 8	12.8	11.8	12.3	11.1	12.1	11.4	11.0**	10.5**
Evaluation of Genital Development	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

– = No noteworthy findings; N/A = not applicable

a 0.5% MC

b Numerals represent the number of animals.

c Mean values of all animals are shown.

d Mean values of 8 cages

* $p < 0.05$, ** $p < 0.01$: Significantly different from control.

Cohort-1								
Dose (mg/kg/day, as free form)	0 (control)[a]		30		90		1000	
Number of Animals	M: 10	F: 10	M: 10	F: 10	M: 10	F: 10	M: 10	F: 10
Noteworthy Findings								
Hematology	–	–	–	–	–	–	–	–
Blood Chemistry[b]								
Total bilirubin (mg/dL)	0.044	–	0.041	–	0.041	–	0.026*	–
Total cholesterol (mg/dL)	75.0	82.1	70.7	70.0	46.5**	46.2**	41.8**	48.2**
Triglyceride (mg/dL)	61.1	36.4	50.4	33.6	33.7*	27.0	29.3**	27.1
Urea nitrogen (mg/dL)	12.66	13.83	12.48	12.36	14.05	14.43	15.85*	17.59**
Calcium (mg/dL)	9.04	–	8.98	–	8.89	–	8.62*	–
Necropsy	–	–	–	–	–	–	–	–
Bone Length Measurement (mm)	–	22.1	–	22.1	–	21.5*	–	21.3**
Organ Weight[b]	–	–	–	–	–	–	–	–
Liver (absolute, g)	3.440	3.095	3.418	3.118	3.561	3.304	4.046**	3.678**
Liver (relative, g/100gBW)	3.500	3.463	3.530	3.575	3.689	3.739*	4.476**	4.550**
Histopathology[c]								
Liver								
Hypertrophy, hepatocyte, centrilobular								
Very slight	0	0	0	0	0	0	6 (#66 to 68, 70, 146, 147)	4 (#79, 80, 156, 160)

( ) Animal number, − = No noteworthy findings

a 0.5% MC

b Mean values of all animals are shown.

c Numerals represent the number of animals.

* $p < 0.05$, ** $p < 0.01$: Significantly different from control.

Cohort-2								
Dose (mg/kg/day, as free form)	0 (control)[a]		30		90		1000	
Number of Animals	M: 20	F: 20	M: 20	F: 20	M: 20	F: 20	M: 20	F: 20
Noteworthy Findings								
Found Dead or Sacrificed Moribund[b]	0	0	0	0	0	0	0	0
Clinical Signs	–	–	–	–	–	–	–	–
Body Weight	–	–	–	–	–	–	–	–
Food Consumption (g/animal/day)[c]		–		–		–		–
Days 1 to 3	15.5		15.4		15.3		14.1**	
Evaluation of Genital Development	N/A	–	N/A	–	N/A	–	N/A	–
Number of Animals	M: 10	F: 10	M: 10	F: 10	M: 10	F: 10	M: 10	F: 10
Hematology	–	–	–	–	–	–	–	–
Blood Chemistry[d]								
Total bilirubin (mg/dL)	0.051	–	0.043	–	0.043	–	0.029**	–
Direct bilirubin (mg/dL)	0.043	0.027	0.038	0.030	0.037	0.024	0.028**	0.018**
Total cholesterol (mg/dL)	80.3	76.8	75.8	66.2	50.0**	46.0**	62.0**	69.7
Triglyceride (mg/dL)	72.0	50.2	67.9	42.0	33.1**	33.0	35.0**	30.0*

– = No noteworthy findings; N/A = not applicable

a 0.5% MC

b Numerals represent the number of animals.

c Mean values of 8 cages

d Mean values of all animals are shown.

* $p < 0.05$, ** $p < 0.01$: Significantly different from control.

Cohort-2								
Dose (mg/kg/day, as free form)	0 (control)[a]		30		90		1000	
Number of Animals	M: 10	F: 10	M: 10	F: 10	M: 10	F: 10	M: 10	F: 10
Noteworthy Findings								
Necropsy	–	–	–	–	–	–	–	–
Bone Length Measurement	–	–	–	–	–	–	–	–
Organ Weight[b]								
Liver (absolute, g)	5.302	4.292	5.351	4.219	5.763	4.447	6.216**	4.952**
Liver (relative, g/100gBW)	3.348	3.474	3.354	3.502	3.621**	3.618	3.803**	4.077**
Histopathology[c]								
Liver								
Hypertrophy, hepatocyte, centrilobular								
Very slight	0	0	0	0	0	0	5 (#366, 446, 447, 449, 450)	4 (#378, 456, 459, 460)

– = No noteworthy findings, ( ) Animal number

a 0.5% MC

b Mean values of all animals are shown.

c Numerals represent the number of animals.

* $p < 0.05$, ** $p < 0.01$: Significantly different from control.

Cohort-3								
Dose (mg/kg/day, as free form)	0 (control)[a]		30		90		1000	
Number of Animals	M: 20	F: 20	M: 20	F: 20	M: 20	F: 20	M: 20	F: 20
Noteworthy Findings								
Found Dead or Sacrificed Moribund[b]	0	0	0	0	0	0	1	0
Clinical Signs	–	–	–	–	–	–	–	–
Body Weight	–	–	–	–	–	–	–	–
Food Consumption (g/animal/day)[c]		–		–		–		–
Days 1 to 3	19.6		19.3		19.4		18.3**	
Evaluation of Genital Development	–	N/A	–	N/A	–	N/A	–	N/A
Number of Animals	M: 10	F: 10	M: 10	F: 10	M: 10	F: 10	M: 9	F: 10
Hematology	–	–	–	–	–	–	–	–
Blood Chemistry[d]								
Total bilirubin (mg/dL)	–	0.016	–	0.016	–	0.012	–	0.004*
Total cholesterol (mg/dL)	73.8	–	72.9	–	62.6	–	64.6	–
Triglyceride (mg/dL)	54.0	–	40.9	–	32.8**	–	28.1**	–
Necropsy	–	–	–	–	–	–	–	–
Bone Length Measurement	–	–	–	–	–	–	–	–
Organ Weight	–	–	–	–	–	–	–	–
Histopathology	–	–	–	–	–	–	–	–

– = No noteworthy findings
a 0.5% MC
b Numerals represent the number of animals.
c Mean values of 8 cages
d Mean values of all animals are shown.
* $p < 0.05$, ** $p < 0.01$: Significantly different from control.

Cohort-1								
Dose (mg/kg/day, as free form)	0 (control)[a]		30		90		1000	
Postdose Evaluation								
Number of Animals	M: 10	F: 10	M: 10	F: 10	M: 10	F: 10	M: 10	F: 10
Noteworthy Findings								
Found Dead or Sacrificed Moribund[b]	0	0	0	0	0	0	0	0
Clinical Signs	–	–	–	–	–	–	–	–
Body Weight (g)[c]		–		–		–		–
Day R1	112.8		105.6		109.3		99.6*	
Food Consumption	–	–	–	–	–	–	–	–
Hematology	–	–	–	–	–	–	–	–
Blood Chemistry	–	–	–	–	–	–	–	–
Evaluation of Genital Development	–	–	–	–	–	–	–	–
Necropsy	–	–	–	–	–	–	–	–
Bone Length Measurement	–	–	–	–	–	–	–	–
Organ Weight	–	–	–	–	–	–	–	–
Histopathology	–	–	–	–	–	–	–	–

– = No noteworthy findings: R = recovery

a 0.5% MC

b Numerals represent the number of animals.

c Mean values of all animals are shown.

* $p < 0.05$: Significantly different from control.

Cohort-2								
Dose (mg/kg/day, as free form)	0 (control)[a]		30		90		1000	
Postdose Evaluation								
Number of Animals	M: 10	F: 10	M: 10	F: 10	M: 10	F: 10	M: 10	F: 10
Noteworthy Findings								
Found Dead or Sacrificed Moribund[b]	0	0	0	0	0	0	0	0
Clinical Signs	–	–	–	–	–	–	–	–
Body Weight	–	–	–	–	–	–	–	–
Food Consumption	–	–	–	–	–	–	–	–
Hematology	–	–	–	–	–	–	–	–
Blood Chemistry	–	–	–	–	–	–	–	–
Evaluation of Genital Development	–	–	–	–	–	–	–	–
Necropsy	–	–	–	–	–	–	–	–
Bone Length Measurement	–	–	–	–	–	–	–	–
Organ Weight	–	–	–	–	–	–	–	–
Histopathology	–	–	–	–	–	–	–	–

– = No noteworthy findings

a 0.5% MC

b Numerals represent the number of animals.

Cohort-3								
Dose (mg/kg/day, as free form)	0 (control)[a]		30		90		1000	
Postdose Evaluation								
Number of Animals	M: 10	F: 10	M: 10	F: 10	M: 10	F: 10	M: 10	F: 10
Noteworthy Findings								
Found Dead or Sacrificed Moribund[b]	0	0	0	0	0	0	0	0
Clinical Signs	−	−	−	−	−	−	−	−
Body Weight	−	−	−	−	−	−	−	−
Food Consumption	−	−	−	−	−	−	−	−
Hematology	−	−	−	−	−	−	−	−
Blood Chemistry	−	−	−	−	−	−	−	−
Evaluation of Genital Development	−	N/A	−	N/A	−	N/A	−	N/A
Necropsy	−	−	−	−	−	−	−	−
Bone Length Measurement	−	−	−	−	−	−	−	−
Organ Weight	−	−	−	−	−	−	−	−
Histopathology	−	−	−	−	−	−	−	−

− = No noteworthy findings; N/A = not applicable

a 0.5% MC

b Numerals represent the number of animals.

2.6.7.16 局所刺激性試験

該当する試験なし.

2.6.7.17 その他の毒性試験

該当する試験なし.