

US EPA ARCHIVE DOCUMENT

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**DATA EVALUATION RECORD**

**STUDY TYPE:** Subchronic feeding - rodent; Guideline §82-1a

**EPA PESTICIDE CHEMICAL CODE:** 064104 (Na-OPP), 064103 (OPP)  
**TOXICOLOGY CHEMICAL NO:** 787 (Na-OPP), 623AA (OPP)  
**MRID NO.:** 921540-36 reformat of 407602-08

**TEST MATERIAL:** Sodium o-phenylphenate  
**SYNONYMS:** OPP-Na, Dowcide A, sodium 2-phenylphenate

**SPONSOR:** The Dow Chemical Company

**TITLE OF REPORT:** Phase 3 Reformat of MRID 407602-08: Subacute Toxicity of Sodium o-Phenylphenate by Food Administration to Rats

**TESTING FACILITY:** Tokyo Metropolitan Research Laboratory of Public Health, 3-24-1 Hyakunin-cho, Shinjuku-ku, Tokyo-to 160

**STUDY NUMBER:** Tokyo eiken Nenpo (Ann. Rep. Tokyo Metr. Res. Lab. P.H.), Vol. 30-2, pgs. 67-79, 1979

**AUTHOR(S):** S. Iguchi, K. Tayama, K. Hiraga

**REPORT ISSUED:** 1979, reformatted April 17, 1990

**CONCLUSIONS:** Dose levels of 0, 0.125, 0.250, 0.500, 1.000, 2.000, and 4.000% sodium orthophenylphenate in the diet were given to Kinko type Fischer (F344/DuCrj) albino rats from Nippon Charles River K. K. for a period of about 13 weeks. From the limited data provided, it was noted that Na-OPP at 0.5% and above in the diet produced reduced body weights with food consumption affected at the 4% dose level in males and females and also at the 2% dose level in females. The reduced food consumption was probably related to a palatability problem with the test compound mixed in with the feed (noted also in other studies). Other effects included an increase in absolute and relative liver and kidney weights. The effects on the liver also include decreases in enzyme activities (at 0.5% and above). No definitive conclusions can be drawn from these data; however, tentatively the NOEL for systemic toxicity is 0.5% Na-OPP with a LOEL of 1.0% Na-OPP. It must be noted that the percent active ingredient in the test compound was not provided.

**The study is classified as Core-Supplementary Data and does not satisfy the Guideline requirement (§82-1a) for a subchronic feeding study in rodents.**

**A. MATERIALS AND METHODS:** A copy of the materials and methods section from the investigators report is appended.

1. **Test compound:** Sodium o-phenylphenate  
Description - not provided  
Lot # - MM1044  
Purity - not provided
2. **Test animals:** Species: Albino rats  
Strain: "Kinko" type Fischer (F344/DuCrj)  
Age: 4 weeks at arrival  
Weight: 72.3 g (m), 68.5 g (f) at arrival  
Source: Nippon Charles River K. K.

### 3. Animal assignment

Animals were assigned to the following test groups:

Test Group	Dose in diet	# Animals/sex
1 Control	0%	10
2 Low (LDT)	0.125%	10
3 Low Mid (LMDT)	0.250%	10
4 Mid (MDT)	0.500%	10
5 High Mid (HMDT)	1.000%	10
6 Low High (LHDT)	2.000%	10
7 High (HDT)	4.000%	10

### 4. Diet Preparation

Test compound was added to Nippon Kurea's CE-2 solid diet. Diet preparation periods were not provided. No data were provided for analysis of diet mixtures in this document, a separate document entitled "Quantitative Analysis of Sodium o-Phenylphenol Added Into the Standard Animals Foods and Effect of Preservation" (MRID# 921540-34) was provided to support the subchronic study. No storage information was provided.

### 5. Animal Husbandry

Animals were kept under standard animal care conditions, acclimated for about 1 week and received food (CE-2 solid diet, Nippon Kurea, K.K.) and water *ad libitum*.

### 6. Clinical Observations:

Animals were inspected daily for "general condition".

### 7. Body Weight

Animals were weighed weekly for the experimental duration.

## 8. Food and Water Consumption and Compound Intake

Food and water consumption and food efficiency were determined every other week. Compound intake was calculated.

## 9. Ophthalmological Examinations

Ophthalmological examinations were not performed.

## 10. Hematology and Clinical Analysis

Blood was collected at the end of treatment (heparin treated). The following parameters (X) were examined.

### a. Hematology

X Hematocrit (HCT)*	Leukocyte differential count*
X Hemoglobin (HGB)*	X Mean corpuscular HGB (MCH)
X Leukocyte count (WBC)*	X Mean corpusc. HGB conc. (MCHC)
X Erythrocyte count (RBC)*	X Mean corpusc. volume (MCV)
Platelet count*	Reticulocyte count
Blood clotting measurements	
(Thromboplastin time)	
(Clotting time)	
(Prothrombin time)	

\* Required for subchronic and chronic studies

### b. Clinical Chemistry

#### Electrolytes:

Calcium\*  
Chloride\*  
Magnesium  
Phosphorous\*  
X Potassium\*  
X Sodium\*

#### Enzymes

X Alkaline phosphatase (ALK)  
Cholinesterase (ChE)#  
Creatinine phosphokinase\*^  
Lactic acid dehydrogenase (LAD)

X Serum alanine aminotransferase (also SGPT)\*  
X Serum aspartate aminotransferase (also SGOT)\*  
Gamma glutamyl transferase (GGT)  
Glutamate dehydrogenase

#### Other:

X Albumin\*  
Blood creatinine\*  
X Blood urea nitrogen\*  
X Cholesterol\*  
X Globulins  
X Glucose\*  
Total bilirubin  
X Total serum Protein (TP)\*  
Triglycerides  
Serum protein electrophoresis  
X Calculated Alb/Glob coeff.

\* Required for subchronic and chronic studies

^ Not required for subchronic studies

## 11. Urinalysis

Urine was collected 2 days before sacrifice. The following parameters (X) were examined.

Appearance*	X Glucose*
Volume*	X Ketones*
Specific gravity*	X Bilirubin*
X pH	X Blood*
Sediment (microscopic)*	Nitrate
X Protein*	X Urobilinogen

The above not required for subchronic studies

\* Required for chronic studies

## 12. Sacrifice and Pathology

All surviving animals were sacrificed at 13 weeks. The following organs were weighed. No gross pathological or histological examinations were conducted.

Digestive system	Cardiovas/Hemat.	Neurologic
Tongue	Aorta*	X Brain*+
Salivary glands*	X Heart*	Periph. nerve*#
Esophagus*	Bone marrow*	Spinal cord (3levels)*#
Stomach*	Lymph nodes*	X Pituitary*
Duodenum*	X Spleen	Eyes (optic n.)*#
Jejunum*	X Thymus*	<b>Glandular</b>
Ileum*	<b>Urogenital</b>	X Adrenal gland*
Cecum*	X Kidneys*+	Lacrimal gland#
Colon*	Urinary bladder*	Mammary gland*#
Rectum*	X Testes*+	Parathyroids*
X Liver *+	Epididymides	Thyroids*
<del>Gall bladder*</del>	X Prostate	<b>Other</b>
Pancreas*	Seminal vesicle≥	Bone*#
<b>Respiratory</b>	X Ovaries*+	Skeletal muscle*#
Trachea*	X Uterus*	Skin*#
X Lung*		All gross lesions
Nose		and masses*
Pharynx		
Larynx		

\* Required for subchronic and chronic studies.

# Subchronic studies, only if indicated by signs of toxicity or target organ involvement.

+ Organ weight required in subchronic and chronic studies.

## 13. Statistics

No procedures were mentioned; however, statistical methodology was utilized.

#### 14. Compliance

A signed "Statement of NO Data Confidentiality Claims" was provided.

A signed "Compliance with Good Laboratory Practice Standards" document was provided.

A signed "Flagging Statement Per 40 CFR 158.34" was provided, the study neither meets nor exceeds the criteria.

#### B. RESULTS:

##### 1. Clinical Observations:

According to the investigators: "There were no special appearance changes, but the spillage of the diet was great among 4% group male and female at the initial period, suggesting that there was abnormality in feeding activities during said period." No data were provided to support this statement.

##### 2. Body Weight

The following tables and figures (ratio of weight gain) present the body weight data. There were reduced body weights and body weight gains in the male 4% group and female 4%, 2% and 0.5% groups in comparison to control for the entire period. However, no individual animal data were provided.

		Body Weights [Body Weight Gains] (grams)					
		Males					
Week/Control	0.125%	0.250%	0.500%	1.000%	2.000%	4.000%	
0	86.3	87.7	85.3	85.8	86.1	86.4	86.2
1	112.9 [26.6]	112.5 [24.8]	109.8 [24.5]	109.8 [24.0]	109.3 [23.2]	108.2 [21.8]	88.3* [2.1]
7	199.5 [113.2]	212.8 [125.1]	205.0 [119.7]	190.2 [104.4]	199.2 [113.1]	203.8 [117.4]	163.1* [76.9]
13	261.7 [174.4]	271.2 [183.5]	264.3 [179.0]	249.8 [164.0]	259.7 [173.6]	261.0 [174.6]	217.7* [131.5]
% bw gains(13wks)	5.2	2.6	-6.0	-0.5	0	-24.6	
		Females					
0	78.9	79.4	77.7	78.3	79.2	77.5	79.6
1	98.7 [19.8]	98.0 [18.6]	95.7 [18.0]	94.4* [16.1]	97.8 [18.6]	91.3* [13.8]	81.9* [2.3]
7	143.4 [64.5]	149.2 [69.8]	137.6 [59.9]	130.7* [52.4]	142.3 [63.1]	123.7* [46.2]	118.1* [38.5]
13	166.5 [87.6]	168.6 [89.2]	156.6 [78.9]	147.2* [68.9]	161.2 [82.0]	138.6* [61.1]	136.2* [38.5]
% bw gains(13wks)	1.8	-10.0	-21.3	-6.4	-30.3	-56.1	

Data extracted from Tables 1 and 2 of the investigators report, body weight gains were calculated by the reviewer.

### 3. Food and Water Consumption and Compound Intake

The following tables provide food and water consumption, food efficiency and compound intake (no individual animal data were provided).

		Food Consumption (g/kg/day)					
		Males					
Week/Control	0.125%	0.250%	0.500%	1.000%	2.000%	4.000%	
0	101.5	94.4	101.0	103.1	99.3	86.6*	88.6*
1	90.7	92.6	95.0	93.6	92.2	91.8	95.1
7	53.2	53.3	53.1	53.1	53.9	56.7	53.9
11	50.5	48.4	49.3	51.4	49.7	50.1	53.9*
		Females					
0	101.5	89.5*	99.2	100.8	91.6*	73.4*	34.6*
1	98.1	94.7	95.0	93.5*	92.8*	98.2	95.4
7	53.5	57.1	53.9	51.3	54.9	51.1	51.2
11	55.8	55.4	53.6	54.4	54.4	54.9	55.2

Data extracted from Table 3 of the investigators report.

## Water Consumption (g/kg/day)

Week/Control	Males						
	0.125%	0.250%	0.500%	1.000%	2.000%	4.000%	
0	186.1	182.3	180.6	184.2	191.1	184.6	109.6*
1	128.1	127.2	125.7	129.3	135.9	148.0*	171.8*
7	69.0	76.9	71.3	71.6	80.7	86.7	95.4*
11	67.5	68.1	63.1	66.8	72.1	83.6*	101.3*
Week/Control	Females						
	0.125%	0.250%	0.500%	1.000%	2.000%	4.000%	
0	182.1	179.5	143.5	169.0	193.3	144.6	126.5*
1	142.2	138.4	138.8	143.2	148.3	159.4*	179.1*
7	78.1	84.2	77.7	76.3	95.4*	89.8	101.1*
11	83.5	83.6	84.8	86.0	96.9*	93.7*	106.9*

Data extracted from Table 7 of the investigators report.

## Food Efficiency (%)

Week/Control	Males						
	0.125%	0.250%	0.500%	1.000%	2.000%	4.000%	
0	42.1	43.3	39.9	36.9*	39.5	28.2*	-49.7*
1	27.0	28.5	27.9	24.5	22.7	22.0	25.8
7	25.7	19.6	18.1	16.4	22.0	17.5	16.8
11	12.0	10.5	13.3	13.0	11.1	15.3	16.2
Week/Control	Females						
	0.125%	0.250%	0.500%	1.000%	2.000%	4.000%	
0	35.5	36.8	36.8	34.7	39.6	30.8*	-66.0*
1	20.7	19.0	19.6	19.5	19.7	17.9	17.5
7	19.9	11.3	20.0	16.0	12.8	11.5	17.4
11	5.3	5.2	8.3	8.9	4.7	13.0	5.5

Data extracted from Table 5 of the investigators report.

The low high and high dose males and females consumed less food and food efficiency was lower. There was no apparent biologically relevant effect on water consumption. The compound intake was 85/87, 177/177, 353/352, 706/694, 1334/1388, and 2487/2431 mg/kg/day for the 0.125, 0.25, 0.5, 1.0, 2.0, and 4.0 % Na-OPP males/females, respectively.



#### 4. Hematology and Clinical Analysis

##### a. Hematology

The following table presents the results of the hematological tests (no individual animal data were provided):

Table 10 Hematological Tests

	0% (对照)(C)	4.0%	2.0%	1.0%	0.5%	0.25%	0.125%
WBC( $\times 10^3/\text{mm}^3$ )	7.06 $\pm$ 1.04	7.09 $\pm$ 0.85	7.29 $\pm$ 0.75	7.10 $\pm$ 0.96	6.56 $\pm$ 0.71	6.97 $\pm$ 0.57	6.46 $\pm$ 0.77
RBC( $\times 10^6/\text{mm}^3$ )	8.57 $\pm$ 0.25	8.14 $\pm$ 0.12*	8.46 $\pm$ 0.27	8.55 $\pm$ 0.34	8.66 $\pm$ 0.39	8.78 $\pm$ 0.26	8.64 $\pm$ 0.32
(a) Hgb(g/dl)	16.5 $\pm$ 0.35	15.5 $\pm$ 0.24*	16.1 $\pm$ 0.42	16.4 $\pm$ 0.41	16.4 $\pm$ 0.53	16.5 $\pm$ 0.41	16.3 $\pm$ 0.33
Hct(%)	44.3 $\pm$ 1.18	42.0 $\pm$ 0.65*	43.7 $\pm$ 1.24	44.5 $\pm$ 1.50	45.0 $\pm$ 1.94	44.8 $\pm$ 1.53	44.4 $\pm$ 1.28
MCV( $\mu^2$ )	52.7 $\pm$ 1.05	52.8 $\pm$ 1.27	52.6 $\pm$ 0.97	52.8 $\pm$ 0.79	52.8 $\pm$ 0.91	52.1 $\pm$ 1.10	52.1 $\pm$ 1.10
MCH( $\mu\text{g}$ )	19.5 $\pm$ 0.59	19.3 $\pm$ 0.44	19.3 $\pm$ 0.47	19.4 $\pm$ 0.54	19.3 $\pm$ 0.43	19.2 $\pm$ 0.47	19.2 $\pm$ 0.63
MCHC(%)	37.1 $\pm$ 0.74	36.8 $\pm$ 0.38	36.8 $\pm$ 0.50	36.7 $\pm$ 0.74	36.5 $\pm$ 0.70	36.8 $\pm$ 0.57	36.7 $\pm$ 0.80
WBC( $\times 10^3/\text{mm}^3$ )	7.36 $\pm$ 1.07	7.35 $\pm$ 0.86	6.37 $\pm$ 0.99*	6.48 $\pm$ 0.48*	7.05 $\pm$ 0.97	6.95 $\pm$ 0.96	8.11 $\pm$ 2.49
RBC( $\times 10^6/\text{mm}^3$ )	8.23 $\pm$ 0.18	8.15 $\pm$ 0.15	8.07 $\pm$ 0.16*	8.12 $\pm$ 0.21	8.12 $\pm$ 0.17	8.28 $\pm$ 0.30	8.23 $\pm$ 0.25
(b) Hgb(g/dl)	16.5 $\pm$ 0.28	15.8 $\pm$ 0.28*	15.7 $\pm$ 0.34*	16.1 $\pm$ 0.51*	16.1 $\pm$ 0.34*	16.4 $\pm$ 0.59	16.4 $\pm$ 0.28
Hct(%)	44.7 $\pm$ 1.14	43.2 $\pm$ 0.97*	42.5 $\pm$ 0.85*	43.4 $\pm$ 1.61*	43.4 $\pm$ 1.27*	44.1 $\pm$ 1.59	44.2 $\pm$ 1.35
MCV( $\mu^2$ )	55.2 $\pm$ 1.13	51.7 $\pm$ 0.67*	51.3 $\pm$ 0.67*	54.3 $\pm$ 0.67*	54.1 $\pm$ 0.73*	54.4 $\pm$ 1.57	54.4 $\pm$ 0.95
MCH( $\mu\text{g}$ )	20.4 $\pm$ 0.24	19.6 $\pm$ 0.40*	19.7 $\pm$ 0.28*	21.2 $\pm$ 0.19	20.1 $\pm$ 0.27*	21.1 $\pm$ 0.26	21.2 $\pm$ 0.25
MCHC(%)	36.9 $\pm$ 0.82	36.5 $\pm$ 0.70	36.9 $\pm$ 0.70	37.1 $\pm$ 0.48	37.0 $\pm$ 0.52	37.1 $\pm$ 0.25	37.1 $\pm$ 0.42

(d) 平均 $\pm$ SD \* 対照群と比較して $P < 0.05$

SE: (a) male; (b) female; (c) 0% (Reference);

(c) The values are the average of ten cases  $\pm$  SD. \*  $P < 0.05$  in comparison to Reference Group.

No biologically relevant differences were noted.

##### b. Clinical Chemistry

The following attached table presents the results of the clinical analysis of the blood. A dose related decrease in GOT levels (1.0% and above) in males and GPT levels (0.5% and above in males and 2.0% and above in females) were noted. The investigators noted increases in total amount of protein, albumin and cholesterol and decreases in amounts of glucose; however, the data do not show any consistent pattern and since no individual animal data were provided, it is difficult to determine if any of the effects are supportable.

Table 11. Serum Biochemical Tests

KEY: (a) male; (b) female; (c) 0% (Reference);  
 (d) The values are the average of ten cases  $\pm$  SD except special cases. ( ) number of cases \* P < 0.05 in comparison to Reference Group. a) measured according to the bromocresol green-method

	0% (21)(c)	4 0%	2 0%	1 0%	0 5%	0 25%	0 125%
COF(K U/ml)	126.3 $\pm$ 11.07	91.6 $\pm$ 15.38*(9)	100.0 $\pm$ 12.68*	102.6 $\pm$ 8.39*	115.2 $\pm$ 16.25	115.1 $\pm$ 23.34	121.7 $\pm$ 16.26
CPV(K U/ml)	65.5 $\pm$ 13.39	39.7 $\pm$ 6.07*(9)	45.4 $\pm$ 9.25*	47.9 $\pm$ 7.01*	51.1 $\pm$ 9.29*	64.8 $\pm$ 16.73	60.4 $\pm$ 12.15
ATP(KA U/h)	38.3 $\pm$ 4.05	36.0 $\pm$ 5.65(9)	37.5 $\pm$ 4.24	34.7 $\pm$ 3.02*	35.9 $\pm$ 2.33	36.2 $\pm$ 3.08	35.7 $\pm$ 3.62
TP(g/dl)	7.0 $\pm$ 0.17	7.4 $\pm$ 0.43*(9)	7.4 $\pm$ 0.34*	6.9 $\pm$ 0.28	6.9 $\pm$ 0.31	6.9 $\pm$ 0.28	7.0 $\pm$ 0.21
Alb(g/dl)*	5.2 $\pm$ 0.14	5.5 $\pm$ 0.36*(9)	5.5 $\pm$ 0.26*	5.2 $\pm$ 0.20	5.2 $\pm$ 0.23	5.1 $\pm$ 0.21	5.2 $\pm$ 0.17
HA/G	2.8 $\pm$ 0.16	2.8 $\pm$ 0.25(9)	2.9 $\pm$ 0.25	3.0 $\pm$ 0.13*	3.0 $\pm$ 0.13*	2.8 $\pm$ 0.21	2.8 $\pm$ 0.20
III(mg/dl)	20.1 $\pm$ 0.87	19.6 $\pm$ 1.32(9)	20.3 $\pm$ 1.70	19.3 $\pm$ 1.63	19.3 $\pm$ 0.91	19.9 $\pm$ 2.07	19.4 $\pm$ 1.11
GIU(mg/dl)	200.9 $\pm$ 18.22	174.8 $\pm$ 28.71*(9)	193.7 $\pm$ 22.03	196.6 $\pm$ 25.00	181.5 $\pm$ 11.41*	201.2 $\pm$ 36.41	181.2 $\pm$ 11.10*
CHO(mg/dl)	64.7 $\pm$ 6.97	80.4 $\pm$ 7.12*(9)	67.2 $\pm$ 4.73	55.8 $\pm$ 4.51*	61.0 $\pm$ 5.53	62.3 $\pm$ 5.85	61.0 $\pm$ 4.11
Ha(mEq/l)	136.0 $\pm$ 2.40	136.7 $\pm$ 3.59(9)	136.9 $\pm$ 2.02	137.9 $\pm$ 6.06	136.5 $\pm$ 3.10	136.1 $\pm$ 2.13	137.3 $\pm$ 1.88
K(mEq/l)	6.9 $\pm$ 0.53	6.8 $\pm$ 0.37(9)	6.9 $\pm$ 0.48	6.8 $\pm$ 0.49	6.7 $\pm$ 0.51	6.5 $\pm$ 0.58	6.9 $\pm$ 0.40
COF(K U/ml)	99.5 $\pm$ 17.72	100.0 $\pm$ 14.02	110.5 $\pm$ 19.91	108.2 $\pm$ 9.02	110.4 $\pm$ 20.67	108.1 $\pm$ 23.61	98.4 $\pm$ 15.91
CPV(K U/ml)	46.3 $\pm$ 6.25	36.2 $\pm$ 6.57*	40.2 $\pm$ 5.53*	44.0 $\pm$ 5.39	40.9 $\pm$ 9.91	47.7 $\pm$ 7.46	43.1 $\pm$ 7.08
ATP(KA U/h)	32.9 $\pm$ 4.93	32.6 $\pm$ 3.80	30.2 $\pm$ 5.77	31.0 $\pm$ 3.68	31.1 $\pm$ 7.01	32.3 $\pm$ 4.71	30.0 $\pm$ 1.39
TP(g/dl)	6.4 $\pm$ 0.17	6.9 $\pm$ 0.51*	6.4 $\pm$ 0.38	6.7 $\pm$ 0.33*	6.4 $\pm$ 0.31	6.4 $\pm$ 0.29	6.6 $\pm$ 0.28
Alb(g/dl)*	4.9 $\pm$ 0.11	5.2 $\pm$ 0.35*	4.9 $\pm$ 0.26	5.2 $\pm$ 0.23*	4.9 $\pm$ 0.26	4.9 $\pm$ 0.19	5.0 $\pm$ 0.20
HA/G	3.2 $\pm$ 0.21	3.1 $\pm$ 0.21	3.2 $\pm$ 0.22	3.3 $\pm$ 0.18	3.3 $\pm$ 0.15	3.2 $\pm$ 0.20	3.1 $\pm$ 0.16
III(mg/dl)	16.3 $\pm$ 1.63	18.2 $\pm$ 2.01*	17.7 $\pm$ 2.35	17.0 $\pm$ 1.49	16.2 $\pm$ 2.09	16.8 $\pm$ 1.81	16.4 $\pm$ 1.71
GIU(mg/dl)	178.1 $\pm$ 12.58	151.7 $\pm$ 10.76*	158.7 $\pm$ 13.15*	168.2 $\pm$ 8.90	169.6 $\pm$ 20.47	161.5 $\pm$ 10.58*	173.7 $\pm$ 15.80
CHO(mg/dl)	80.7 $\pm$ 6.12	90.0 $\pm$ 7.11*	82.0 $\pm$ 5.91	78.0 $\pm$ 8.43	75.5 $\pm$ 8.94	78.6 $\pm$ 4.67	80.8 $\pm$ 9.91
Ha(mEq/l)	133.3 $\pm$ 2.49	136.1 $\pm$ 1.79*	135.1 $\pm$ 2.58(8)	135.4 $\pm$ 1.35*	135.5 $\pm$ 2.95	135.9 $\pm$ 1.37*	135.2 $\pm$ 2.61
K(mEq/l)	6.3 $\pm$ 1.35	6.1 $\pm$ 0.44	6.2 $\pm$ 0.29(8)	6.1 $\pm$ 0.39	5.9 $\pm$ 0.44	6.1 $\pm$ 0.37	5.8 $\pm$ 0.29

(c) 6015504 12.5 10044\* ( ) 642 \* 210107 11.42 1.7 P < 0.05 a) ノマキロゾール法により測定

### 5. Urinalysis

The following table presents the results of the urinalysis (no individual animal data were provided):

TABLE II URINE TESTS

		0% (cont.)	4.0%	2.0%	1.0%	0.5%	0.25%	0.125%
Male	pH	5	3 <sup>1)</sup>	1	3	2	2	3
		6	7	5	4	5	5	6
		7		4	3	3	2	1
		8		2				
	Protein	-		1				
		30mg/dl >						
		30mg/dl	4	8	7	4	5	4
		100mg/dl	6	1	3	6	5	6
		300mg/dl						
	Glucose	-	10	10	10	10	10	10
	0.25g/dl							
Ketone Body	-	10	10	10	10	10	10	
	10mg/dl <							
Occult Blood	-	10	10	10	10	10	10	
	5+							
	10							
Bilirubin	0.2mg/dl >	10	10	10	10	10	10	
	0.2mg/dl <							
Urobilin	0.1-1E. U. <sup>2)</sup>	10	10	10	10	10	10	
	1E. U. <							
Female	pH	5						
		6	8	2	2	6	5	6
		7	2	3	3	3	2	3
		8		5	5	1	3	1
	Protein	-						
		30mg/dl >	1	5	1	3	2	1
		30mg/dl	3	5	9	7	7	7
		100mg/dl	1					1
		300mg/dl						
	Glucose	-	10	10	10	10	10	10
	0.25g/dl							
Ketone Body	-	10	10	10	10	10	10	
	10mg/dl <							
Occult Blood	-	10	10	10	10	10	10	
	5+							
	10							
Bilirubin	0.2mg/dl >	10	10	10	10	10	10	
	0.2mg/dl <							
Urobilin	0.1-1E. U. <sup>2)</sup>	10	10	10	10	10	10	
	1E. U. <							

1) No. of rats 2) No. of Red Blood Cells in the Range of View (x400) 3) E. U. = Ehrlich Units/dl

Although the investigators felt that there was an increase in pH and a decrease in protein, no consistent pattern was noted. A decrease in pH could be a physiological response to treatment with a chemical that is in an acid form such as is OPP and Na-OPP.

## 6. Organ Weights

The following table presents selected organ weight data, no individual animal data were provided. There appears to be an increase in absolute and relative liver weights at 2.0% and above in males and at 4.0% in females and absolute and relative kidney weights at 1.0% and above in males.

Organ Weights							
Males							
	Control	0.125%	0.250%	0.500%	1.000%	2.000%	4.000%
Liver (A = absolute g/rat, R = relative g/100 g b.w.)							
A	9.41	9.61	9.69	8.77	9.52	11.07*	10.22
R	3.59	3.52	3.63	3.48	3.65	4.22*	4.59*
Kidney - Left (A = mg/rat, R = mg/100 g b.w.)							
A	806.6	810.2	836.6	792.9	835.9	912.3*	874.3
R	308.1	310.7	319.1	318.3	321.9*	319.8*	405.2*
Kidney - Right							
A	793.6	831.1	824.4	791.8	837.4	893.2*	861.3
R	303.6	308.3	312.0	317.9*	323.0*	312.6*	400.5*
Females							
Liver							
A	5.08	5.31	4.90	4.69	5.20	4.71	5.57
R	3.05	3.15	3.11	3.17	3.21*	3.38	4.05*
Kidney - Left							
A	558.0	572.3	531.5	526.7	561.4	526.2	541.4
R	335.0	340.7	339.5	357.9*	349.6	381.3*	400.4*
Kidney - Right							
A	558.0	565.5	540.3	519.3*	562.0	521.4	538.2
R	334.8	335.8	315.4	353.4*	350.1	378.2*	397.3*

Data extracted from Tables 8 and 9 of the investigators report.

**C. DISCUSSION/CONCLUSIONS:**

Dose levels of 0, 0.125, 0.250, 0.500, 1.000, 2.000, and 4.000% sodium orthophenylphenate in the diet were given to Kinko type Fischer (F344/DuCrj) albino rats from Nippon Charles River K. K. for a period of about 13 weeks. Provided data were limited to body weights, food and water consumption, limited hematology, clinical chemistry and urinalysis parameters and organ weights. Tissues were not examined either grossly or histopathologically. No individual animal data were provided for any of the measured parameters. The provided data indicated that treatment with Na-OPP at 0.5% and above in the diet produced reduced body weights with food consumption affected at the 4% dose level in males and females and at the 2% dose level in females. The reduced food consumption may be related to a palatability problem with the test compound mixed in with the feed (also noted in other studies). Other effects included an increase in absolute and relative liver weights at 2.0% and above in males and at 4.0% in females and absolute and relative kidney weights at 1.0% and above in males. The effects on the liver also include decreases in enzyme activities (at 0.5% and above). No definitive conclusions can be drawn from these data; however, tentatively the **NOEL for systemic toxicity is 0.5% Na-OPP** with a **LOEL of 1.0% Na-OPP** based on the reduced body weights and food consumption, also the increase in absolute and relative liver weights and absolute and relative kidney weights along with the reduction in liver enzyme activities. It must be noted that the percent active ingredient in the test compound was not provided.

**Core Classification: Core-Supplementary Data, this study does not satisfy the Guideline requirement (§82-1a) for a subchronic feeding study in rodents.**

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ORTHOPHENYLPHENOL

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