アクリル酸=2 - ヒドロキシエチルのマウスを用いた 経口投与による 13 週間毒性試験(混水試験)報告書

試験番号:0324

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TABLE 1 SURVIVAL ANIMAL NUMBERS AND BODY WEIGHT CHANGES OF MALE MICE IN THE 13-WEEK DRINKING WATER STUDY OF 2-HYDROXYETHYL ACRYLATE

Group	C	Control		$375~\mathrm{ppm}$			$750~\mathrm{ppm}$			$1500\;\mathrm{ppm}$			3000 ppm			$6000~\mathrm{ppm}$	
		<10>		<10>		<10>		<10>		<10>			<10>				
Week	Survival	BW	Survival	l BW	7	Surviva	l BW	r	Survival	I BV	V	Survival	BW	Ţ	Surviva	ıl BW	T
on Study	No.	g	No.	g	%	No.	g	%	No.	g	%	No.	g	%	No.	g	%
0	10	23.1 (10)	10	23.1 (10)	100	10	23.0 (10)	100	10	23.1 (10)	100	10	23.1 (10)	100	10	23.1 (10)	100
1	10	24.0 (10)	10	23.8 (10)	99	10	23.8 (10)	99	10	23.9 (10)	100	10	23.1 (10)	96	10	21.4 (10)	89 **
2	10	24.3 (10)	10	24.9 (10)	102	10	24.5 (10)	101	10	25.0 (10)	103	10	24.0 (10)	99	10	22.5 (10)	93 **
3	10	25.5 (10)	10	25.6 (10)	100	10	25.6 (10)	100	10	26.0 (10)	102	10	24.5 (10)	96 *	10	23.5 (10)	92 **
4	10	26.8 (10)	10	26.7 (10)	100	10	26.2 (10)	98	10	26.9 (10)	100	10	24.7 (10)	92 **	10	24.3 (10)	91 **
5	10	27.6 (10)	10	27.8 (10)	101	10	27.2 (10)	99	10	27.6 (10)	100	10	25.6 (10)	93 **	10	24.8 (10)	90 **
6	10	28.5 (10)	10	28.8 (10)	101	10	27.6 (10)	97	10	28.2 (10)	99	10	25.9 (10)	91 **	10	25.0 (10)	88 **
7	10	29.1 (10)	10	29.5 (10)	101	10	28.6 (10)	98	10	29.3 (10)	101	10	26.3 (10)	90 **	10	25.5 (10)	88 **
8	10	29.8 (10)	10	30.4 (10)	102	10	29.1 (10)	98	10	29.5 (10)	99	10	26.7 (10)	90 **	10	25.9 (10)	87 **
9	10	30.9 (10)	10	31.4 (10)	102	10	29.8 (10)	96	10	30.7 (10)	99	10	27.9 (10)	90 **	10	26.2 (10)	85 **
10	10	31.7 (10)	10	32.8 (10)	103	10	31.0 (10)	98	10	31.4 (10)	99	10	28.4 (10)	90 **	10	26.6 (10)	84 **
11	10	32.4 (10)	10	33.4 (10)	103	10	31.7 (10)	98	10	31.9 (10)	98	10	28.7 (10)	89 **	10	26.6 (10)	82 **
12	10	33.3 (10)	10	33.9 (10)	102	10	32.0 (10)	96	10	32.4 (10)	97	10	29.9 (10)	90 **	10	26.9 (10)	81 **
13	10	34.3 (10)	10	35.5 (10)	103	10	33.1 (10)	97	10	33.3 (10)	97	10	29.5 (10)	86 **	10	27.4 (10)	80 **

< > : No.of effective animals, (): No.of measured animals, % : Percent of control group Significant difference, *: $p \le 0.05$, ** : $p \le 0.01$, Test of Dunnett

TABLE 2 SURVIVAL ANIMAL NUMBERS AND BODY WEIGHT CHANGES OF FEMALE MICE IN THE 13-WEEK DRINKING WATER STUDY OF 2-HYDROXYETHYL ACRYLATE

Group	C	Control		$375~\mathrm{ppm}$			$750~\mathrm{ppm}$			$1500~\mathrm{ppm}$		3000 ppm				6000 ppm	
		<10>		<10>		<10>		<10>		<10>		<10>					
Week	Survival	BW	Survival	BW	7	Survival	l BW	I	Survival	BV	V	Survival	BW	<i>T</i>	Surviva	l BW	I
on Study	No.	g	No.	g	%	No.	g	%	No.	g	%	No.	g	%	No.	g	%
0	10	19.2 (10)	10	19.2 (10)	100	10	19.2 (10)	100	10	19.2 (10)	100	10	19.2 (10)	100	10	19.2 (10)	100
1	10	19.2 (10)	10	19.3 (10)	101	10	19.1 (10)	99	10	19.7 (10)	103	10	19.0 (10)	99	10	17.9 (10)	93 **
2	10	19.7 (10)	10	19.8 (10)	101	10	20.1 (10)	102	10	19.9 (10)	101	10	19.8 (10)	101	10	18.7 (10)	95 *
3	10	20.4 (10)	10	20.1 (10)	99	10	20.4 (10)	100	10	20.4 (10)	100	10	19.8 (10)	97	10	19.0 (10)	93 **
4	10	21.3 (10)	10	20.8 (10)	98	10	21.0 (10)	99	10	21.0 (10)	99	10	20.4 (10)	96	10	19.8 (10)	93 **
5	10	21.9 (10)	10	21.7 (10)	99	10	22.2 (10)	101	10	22.2 (10)	101	10	21.3 (10)	97	10	20.8 (10)	95 *
6	10	21.6 (10)	10	21.5 (10)	100	10	21.6 (10)	100	10	21.7 (10)	100	10	21.5 (10)	100	10	20.9 (10)	97
7	10	22.4 (10)	10	22.4 (10)	100	10	22.2 (10)	99	10	22.6 (10)	101	10	21.8 (10)	97	10	21.3 (10)	95 *
8	10	22.6 (10)	10	22.7 (10)	100	10	22.6 (10)	100	10	22.8 (10)	101	10	22.3 (10)	99	10	21.7 (10)	96
9	10	23.1 (10)	10	23.1 (10)	100	10	23.2 (10)	100	10	22.9 (10)	99	10	22.1 (10)	96	10	22.3 (10)	97
10	10	23.2 (10)	10	23.3 (10)	100	10	23.5 (10)	101	10	23.8 (10)	103	10	22.7 (10)	98	10	22.8 (10)	98
11	10	23.8 (10)	10	23.7 (10)	100	10	23.5 (10)	99	10	24.0 (10)	101	10	23.4 (10)	98	10	22.9 (10)	96
12	10	23.3 (10)	10	23.0 (10)	99	10	23.3 (10)	100	10	23.7 (10)	102	10	24.0 (10)	103	10	23.6 (10)	101
13	10	24.8 (10)	10	24.5 (10)	99	10	25.1 (10)	101	10	25.1 (10)	101	10	23.5 (10)	95	10	22.8 (10)	92 **

< >: No.of effective animals, (): No.of measured animals, %: Percent of control group
Significant difference, *: $p \le 0.05$, **: $p \le 0.01$, Test of Dunnett

TABLE 3 WATER CONSUMPTION CHANGES OF MALE MICE IN THE 13-WEEK DRINKING WATER STUDY OF 2-HYDROXYETHYL ACRYLATE

Group	Control	375 ppm	750 ppm	1500 ppm	3000 ppm	6000 ppm
Week	<10> WC	<10> WC	<10> WC	<10> WC	<10> WC	<10> WC
n Study	g	g %	g %	g %	g %	g %
1	4.4 (10)	3.9 (10) 89	3.2 (10) 73 *	3.3 (10) 75	2.4 (10) 55 **	1.8 (10) 41 **
2	4.1 (10)	4.1 (10) 100	3.3 (10) 80	3.3 (10) 80	2.3 (10) 56 **	1.8 (10) 44 **
3	4.2 (10)	3.8 (10) 90	3.2 (10) 76	3.1 (10) 74 *	2.1 (10) 50 **	1.8 (10) 43 **
4	4.2 (10)	3.7 (10) 88	3.0 (10) 71 **	2.8 (10) 67 **	2.0 (10) 48 **	1.8 (10) 43 **
5	4.1 (10)	3.9 (10) 95	3.1 (10) 76	2.7 (10) 66 **	2.1 (10) 51 **	1.8 (10) 44 **
6	4.0 (10)	3.7 (10) 92	3.2 (10) 80 *	2.9 (10) 72 **	2.2 (10) 55 **	2.0 (10) 50 **
7	4.1 (10)	4.2 (10) 102	3.4 (10) 83	2.8 (10) 68 **	2.2 (10) 54 **	2.0 (10) 49 **
8	4.0 (10)	4.0 (10) 100	3.2 (10) 80	2.6 (10) 65 **	2.0 (10) 50 **	1.9 (10) 47 **
9	3.9 (10)	4.0 (10) 103	3.3 (10) 85	2.7 (10) 69 **	2.1 (10) 54 **	1.9 (10) 49 **
10	3.8 (10)	4.1 (10) 108	3.1 (10) 82	2.6 (10) 68 *	2.0 (10) 53 **	1.8 (10) 47 **
11	3.7 (10)	3.5 (10) 95	3.0 (10) 81	2.5 (10) 68 **	2.0 (10) 54 **	2.0 (10) 54 **
12	3.7 (10)	3.3 (10) 89	2.8 (10) 76 *	2.5 (10) 68 **	2.4 (10) 65 **	1.7 (10) 46 **
13	3.7 (10)	3.5 (10) 95	3.0 (10) 81 **	2.5 (10) 68 **	2.1 (10) 57 **	1.9 (10) 51 **

< >: No.of effective animals, (): No.of measured animals, %: Percent of control group
Significant difference, *: $p \le 0.05$, **: $p \le 0.01$, Test of Dunnett

TABLE 4 WATER CONSUMPTION CHANGES OF FEMALE MICE IN THE 13-WEEK DRINKING WATER STUDY OF 2-HYDROXYETHYL ACRYLATE

Group	Control	375 ppn	n	750 pp	m	1500 p	pm	3000 p	pm	6000 g	pm
_	<10>	<10>		<10>		<10>		<10>		<10>	
Week	WC	WC		WC		WC		WC		WC	
on Study	g	g	%	g	%	g	%	g	%	g	%
1	4.0 (10)	3.3 (10)	83 **	3.1 (10)	78 **	2.9 (10)	72 **	2.4 (10)	60 **	1.6 (10)	40 **
2	4.2 (10)	3.6 (10)	86	3.1 (10)	74	2.7 (10)	64 **	2.3 (10)	55 **	1.7 (10)	40 **
3	4.1 (10)	3.3 (10)	80	3.4 (10)	83	2.8 (10)	68 *	2.2 (10)	54 **	1.4 (10)	34 **
4	4.4 (10)	3.4 (10)	77	3.4 (10)	77	2.7 (10)	61 **	2.3 (10)	52 **	1.6 (10)	36 **
5	4.5 (10)	3.8 (10)	84	3.3 (10)	73	2.7 (10)	60 **	2.3 (10)	51 **	1.7 (10)	38 **
6	4.8 (10)	3.9 (10)	81	3.3 (10)	69	2.8 (10)	58 **	2.4 (10)	50 **	1.8 (10)	38 **
7	4.3 (10)	3.7 (10)	86 **	3.3 (10)	77 **	2.8 (10)	65 **	2.3 (10)	53 **	1.8 (10)	42 **
8	4.4 (10)	3.6 (10)	82 **	3.3 (10)	75 **	2.8 (10)	64 **	2.4 (10)	55 **	1.9 (10)	43 **
9	4.8 (10)	3.8 (10)	79	3.3 (10)	69	3.0 (10)	62 **	2.4 (10)	50 **	2.0 (10)	42 **
10	4.8 (10)	4.1 (10)	85	3.4 (10)	71 *	3.1 (10)	65 **	2.6 (10)	54 **	2.1 (10)	44 **
11	4.2 (10)	4.2 (10) 1	100	3.3 (10)	79	2.7 (10)	64 **	2.4 (10)	57 **	2.1 (10)	50 **
12	4.3 (10)	4.0 (10)	93	3.1 (10)	72	2.7 (10)	63 **	2.8 (10)	65 **	2.0 (10)	47 **
13	4.4 (10)	3.9 (10)	89	3.2 (10)	73	2.7 (10)	61 **	2.4 (10)	55 **	2.0 (10)	45 **

< >: No.of effective animals, (): No.of measured animals, %: Percent of control group
Significant difference, *: $p \le 0.05$, **: $p \le 0.01$, Test of Dunnett

TABLE 5 FOOD CONSUMPTION CHANGES OF MALE MICE IN THE 13-WEEK DRINKING WATER STUDY OF 2-HYDROXYETHYL ACRYLATE

Group	Control	375 ppm	750 ppm	1500 ppm	3000 ppm	6000 ppm
•	<10>	<10>	<10>	<10>	<10>	<10>
Week	FC	FC	FC	FC	FC	FC
on Study	g	g %	g %	. g %	g %	g %
1	3.9 (10)	3.7 (10) 95	3.7 (10) 95	3.7 (10) 95	3.5 (10) 90 *	3.2 (10) 82 **
2	3.7 (10)	3.7 (10) 100	3.5 (10) 95	3.7 (10) 100	3.4 (10) 92	3.4 (10) 92
3	3.8 (10)	3.6 (10) 95	3.7 (10) 97	3.8 (10) 100	3.4 (10) 89 *	3.5 (10) 92
4	3.8 (10)	3.7 (10) 97	3.6 (10) 95	3.8 (10) 100	3.3 (10) 87 **	3.5 (10) 92
5	3.8 (10)	3.9 (10) 103	3.7 (10) 97	3.8 (10) 100	3.4 (10) 89 *	3.5 (10) 92
6	3.8 (10)	3.8 (10) 100	3.6 (10) 95	3.7 (10) 97	3.4 (10) 89	3.5 (10) 92
7	3.9 (10)	4.0 (10) 103	3.8 (10) 97	3.9 (10) 100	3.4 (10) 87 **	3.5 (10) 90 **
8	3.9 (10)	4.0 (10) 103	3.8 (10) 97	3.8 (10) 97	3.5 (10) 90 **	3.6 (10) 92 *
9	4.0 (10)	4.0 (10) 100	3.8 (10) 95	3.9 (10) 97	3.6 (10) 90 *	3.5 (10) 88 **
10	4.0 (10)	4.1 (10) 103	3.9 (10) 97	3.9 (10) 97	3.6 (10) 90 **	3.5 (10) 88 **
11	4.2 (10)	4.0 (10) 95	4.0 (10) 95	3.8 (10) 90	3.5 (10) 83 **	3.4 (10) 81 **
12	4.1 (10)	4.1 (10) 100	3.9 (10) 95	3.9 (10) 95	3.8 (10) 93	3.5 (10) 85 **
13	3.9 (10)	4.1 (10) 105	3.9 (10) 100	3.9 (10) 100	3.4 (10) 87 **	3.5 (10) 90 **

< > : No.of effective animals, (): No.of measured animals, %: Percent of control group
Significant difference, *: $p \le 0.05$, **: $p \le 0.01$, Test of Dunnett

TABLE 6 FOOD CONSUMPTION CHANGES OF FEMALE MICE IN THE 13-WEEK DRINKING WATER STUDY OF 2-HYDROXYETHYL ACRYLATE

Group	Control	375 ppm	750 ppm	1500 ppm	3000 ppm	6000 ppm	
-	<10>	<10>	<10>	<10>	<10>	<10>	
Week	FC	FC	FC	FC	FC	FC	
on Study	g	g %	g %	g %	g %	g %	
1	3.3 (10)	3.2 (10) 97	3.2 (10) 97	3.3 (10) 100	3.0 (10) 91 *	2.7 (10) 82 **	
2	3.1 (10)	3.0 (10) 97	3.2 (10) 103	3.0 (10) 97	3.1 (10) 100	3.0 (10) 97	
3	3.3 (10)	3.2 (10) 97	3.3 (10) 100	3.3 (10) 100	3.1 (10) 94 **	3.0 (10) 91 **	
4	3.6 (10)	3.4 (10) 94	3.4 (10) 94	3.3 (10) 92 *	3.2 (10) 89 **	3.2 (10) 89 **	
5	3.6 (10)	3.5 (10) 97	3.7 (10) 103	3.5 (10) 97	3.4 (10) 94	3.4 (10) 94	
6	3.6 (10)	3.4 (10) 94	3.5 (10) 97	3.4 (10) 94	3.4 (10) 94	3.3 (10) 92	
7	3.7 (10)	3.7 (10) 100	3.7 (10) 100	3.6 (10) 97	3.4 (10) 92 **	3.6 (10) 97	
8	3.7 (10)	3.7 (10) 100	3.7 (10) 100	3.5 (10) 95	3.5 (10) 95	3.4 (10) 92	
9	3.7 (10)	3.7 (10) 100	3.8 (10) 103	3.6 (10) 97	3.5 (10) 95 **	3.6 (10) 97	
10	3.8 (10)	3.7 (10) 97	3.7 (10) 97	3.7 (10) 97	3.5 (10) 92	3.7 (10) 97	
11	3.6 (10)	3.7 (10) 103	3.7 (10) 103	3.5 (10) 97	3.5 (10) 97	3.5 (10) 97	
12	3.8 (10)	3.7 (10) 97	3.8 (10) 100	3.7 (10) 97	3.7 (10) 97	3.8 (10) 100	
13	3.7 (10)	3.7 (10) 100	3.7 (10) 100	3.6 (10) 97	3.3 (10) 89 **	3.5 (10) 95	

< > : No.of effective animals, () : No.of measured animals, % : Percent of control group
Significant Difference, * : $p \le 0.05$, ** : $p \le 0.01$, Test of Dunnett

TABLE 7 HEMATOLOGY OF MALE MICE IN THE 13-WEEK DRINKING WATER STUDY OF 2-HYDROXYETHYL ACRYLATE (SELECTED)

Group	Control	$375~\mathrm{ppm}$	750 ppm	1500 ppm	$3000~\mathrm{ppm}$	$6000~\mathrm{ppm}$
No. of examined animals	<8>	<9>	<9>	<9>	<10>	<9>
Red blood cell ($10^6/\mu\mathrm{L}$)	10.40 ± 0.71	10.36 ± 0.38	$10.48~\pm~0.45$	$10.57~\pm~0.34$	10.62 ± 0.43	10.46 ± 0.24
Hemoglobin (g/dL)	$15.9~\pm~0.5$	$15.4~\pm~0.4$	$15.6~\pm~0.5$	$15.8~\pm~0.2$	$15.8~\pm~0.5$	$15.6~\pm~0.5$
Hematocrit (%)	$47.4 ~\pm~ 3.3$	$47.0~\pm~1.7$	48.0 ± 1.9	48.4 ± 1.3	$48.3~\pm~1.9$	$48.0~\pm~1.1$
MCV (fL)	$45.6~\pm~0.3$	$45.4~\pm~0.7$	45.8 ± 0.8	$45.8~\pm~0.5$	$45.5~\pm~0.5$	$45.9~\pm~0.5$
MCH (pg)	$15.3~\pm~0.7$	$14.9~\pm~0.3$	$14.9~\pm~0.3$	$15.0~\pm~0.4$	$14.8~\pm~0.2$	$14.9~\pm~0.3$
MCHC (g/dL)	33.7 ± 1.6	32.8 ± 0.8	$32.5~\pm~0.5$	$32.8~\pm~0.7$	$32.6~\pm~0.5$	$32.5~\pm~0.7$
Platelet $(10^3/\mu L)$	$1447 ~\pm~ 140$	$1450~\pm~71$	$1463~\pm~109$	$1412~\pm~97$	$1456~\pm~113$	$1462~\pm~126$
WBC $(10^3/\mu\mathrm{L})$	1.80 ± 0.58	$1.40~\pm~0.69$	1.51 ± 0.84	$1.51~\pm~0.81$	1.31 ± 0.30	$1.08~\pm~0.71$
Differential WBC (%)						
N-SEG	14 ± 3	18 ± 6	16 ± 4	15 ± 3	14 ± 4	21 ± 6 **
LYMPHO	82 ± 4	78 ± 6	79 ± 4	81 ± 3	83 ± 4	76 ± 7

Significant difference, **: $p \le 0.01$, Test of Dunnett

TABLE 8 HEMATOLOGY OF FEMALE MICE IN THE 13-WEEK DRINKING WATER STUDY OF 2-HYDROXYETHYL ACRYLATE (SELECTED)

Group	Control	375 ppm	750 ppm	1500 ppm	$3000~\mathrm{ppm}$	$6000~\mathrm{ppm}$
No. of examined animals	<10>	<10>	<8>	<9>	<10>	<8>
Red blood cell ($10^6/\mu$ L)	$10.46~\pm~0.30$	$10.44~\pm~0.53$	10.38 ± 0.27	$10.45~\pm~0.41$	$10.08~\pm~0.45$	$10.37~\pm~0.38$
Hemoglobin (g/dL)	$15.8~\pm~0.4$	$15.7~\pm~0.7$	$15.5~\pm~0.4$	$15.7~\pm~0.7$	$15.3~\pm~0.4$	$15.5~\pm~0.5$
Hematocrit (%)	$47.6~\pm~1.3$	$47.4~\pm~2.5$	$47.0~\pm~1.3$	$47.2~\pm~2.0$	$45.5~\pm~2.1$	$47.0~\pm~1.9$
MCV (fL)	$45.5~\pm~0.3$	$45.4~\pm~0.5$	$45.3~\pm~0.4$	$45.1~\pm~0.3$	$45.1~\pm~0.5$	$45.3~\pm~0.7$
MCH (pg)	$15.1~\pm~0.2$	$15.1~\pm~0.5$	$15.0~\pm~0.2$	$15.0~\pm~0.1$	$15.2~\pm~0.4$	$15.0~\pm~0.4$
MCHC (g/dL)	$33.3~\pm~0.4$	33.3 ± 1.2	$33.1~\pm~0.2$	$33.2~\pm~0.2$	33.7 ± 1.0	$33.0~\pm~1.1$
Platelet $(10^3/\mu L)$	$1338~\pm~67$	$1335~\pm~82$	$1331~\pm~91$	$1242~\pm~101$	$1314~\pm~110$	$1311~\pm~58$
WBC $(10^3/\mu L)$	$1.28~\pm~0.58$	$1.22~\pm~0.87$	$0.80~\pm~0.51$	$0.92~\pm~0.49$	$0.79~\pm~0.71$	0.79 ± 0.71
Differential WBC (%)						
N-SEG	16 ± 4	16 ± 4	16 ± 4	17 ± 5	16 ± 4	22 ± 8
LYMPHO	81 ± 4	80 ± 3	81 ± 5	79 ± 4	80 ± 3	74 ± 8

TABLE 9 BIOCHEMISTRY OF MALE MICE IN THE 13-WEEK DRINKING WATER STUDY OF 2-HYDROXYETHYL ACRYLATE

Group	Control	375 ppm	750 ppm	1500 ppm	3000 ppm	6000 ppm
No. of animals examined	<9>	<10>	<9>	<9>	<10>	<9>
Total protein (g/dL)	$5.1~\pm~0.2$	$5.0~\pm~0.2$	$5.0~\pm~0.2$	$4.9~\pm~0.1$	$4.8~\pm~0.2~^{**}$	4.6 ± 0.2 **
Albumin (g/dL)	$3.0~\pm~0.1$	$2.9~\pm~0.1$	$2.8~\pm~0.1$	$2.9~\pm~0.1$	2.8 ± 0.1 *	$2.7~\pm~0.1~$
A/G ratio	$1.4~\pm~0.1$	$1.4~\pm~0.1$	$1.3~\pm~0.2$	$1.4~\pm~0.1$	$1.5~\pm~0.1$	$1.4~\pm~0.1$
T-Bilirubin (mg/dL)	$0.17~\pm~0.01$	$0.21~\pm~0.14$	$0.20~\pm~0.05$	$0.17~\pm~0.01$	0.16 ± 0.01	0.17 ± 0.02
Glucose (mg/dL)	$235~\pm~67$	207 ± 35	208 ± 35	$209~\pm~29$	188 ± 38	$179~\pm~25$
T-Cholesterol (mg/dL)	87 ± 7	83 ± 6	82 ± 11	78 ± 4 *	76 ± 4 **	77 ± 6 **
Triglyceride (mg/dL)	$34~\pm~16$	34 ± 13	33 ± 19	$34~\pm~15$	$27~\pm~9$	22 ± 9
Phospholipid (mg/dL)	$175~\pm~17$	167 ± 14	$165~\pm~20$	$160~\pm~12$	$158~\pm~10$	$158~\pm~17$
GOT (IU/L)	53 ± 12	49 ± 7	55 ± 21	44 ± 6	47 ± 6	50 ± 15
GPT (IU/L)	20 ± 8	18 ± 3	$23~\pm~12$	16 ± 2	17 ± 3	$20~\pm~7$
LDH (IU/L)	$236~\pm~47$	$233~\pm~92$	$294~\pm~157$	$186~\pm~41$	$202~\pm~29$	$238~\pm~101$
ALP (IU/L)	$155~\pm~14$	$156~\pm~21$	$151~\pm~14$	$153~\pm~11$	$150~\pm~13$	$148~\pm~9$
γ -GTP (IU/L)	2 ± 1	1 ± 1	1 ± 1	2 ± 1	1 ± 1	1 ± 1
CPK (IU/L)	91 ± 66	63 ± 21	108 ± 101	$59~\pm~30$	$70~\pm~24$	86 ± 59
Urea nitrogen (mg/L)	$26.6~\pm~4.7$	$25.2~\pm~5.3$	24.6 ± 3.9	$23.9~\pm~2.5$	$24.9~\pm~4.2$	$25.2~\pm~3.6$
Sodium (mEq/L)	$150~\pm~2$	152 ± 2	151 ± 1	151 ± 1	151 ± 1	151 ± 2
Potassium (mEq/L)	4.6 ± 0.3	4.9 ± 0.6	$4.8~\pm~0.5$	$4.4~\pm~0.3$	$4.5~\pm~0.3$	$4.6~\pm~0.3$
Chloride (mEq/L)	$122~\pm~3$	123 ± 3	121 ± 3	$122~\pm~1$	$122~\pm~3$	$122~\pm~3$
Calcium (mg/dL)	8.8 ± 0.2	8.8 ± 0.3	$8.7~\pm~0.4$	$8.8~\pm~0.2$	8.8 ± 0.2	8.6 ± 0.3
Inorganic phosphorus (mg/dL)	$7.7~\pm~1.3$	7.3 ± 0.9	7.6 ± 1.6	$7.0~\pm~1.2$	6.8 ± 1.2	6.4 ± 1.2

Significant difference, *: $p \le 0.05$, **: $p \le 0.01$, Test of Dunnett

TABLE 10 BIOCHEMISTRY OF FEMALE MICE IN THE 13-WEEK DRINKING WATER STUDY OF 2-HYDROXYETHYL ACRYLATE

Group	Control	375 ppm	750 ppm	1500 ppm	3000 ppm	6000 ppm
No. of examined animals	<10>	<10>	<9>	<10>	<10>	<8>
Total protein (g/dL)	$5.0~\pm~0.1$	$5.1~\pm~0.2$	$5.0~\pm~0.2$	$5.0~\pm~0.2$	4.8 ± 0.3 *	4.7 ± 0.2 **
Albumin (g/dL)	$3.1~\pm~0.1$	$3.1~\pm~0.2$	$3.1~\pm~0.1$	$3.1~\pm~0.2$	$3.0~\pm~0.1$	$3.0~\pm~0.1$
A/G ratio	$1.7~\pm~0.1$	$1.6~\pm~0.2$	$1.6~\pm~0.2$	$1.6~\pm~0.1$	$1.7~\pm~0.1$	$1.7~\pm~0.1$
T-Bilirubin (mg/dL)	$0.16~\pm~0.01$	$0.19~\pm~0.05$	$0.17~\pm~0.02$	$0.17~\pm~0.02$	$0.17~\pm~0.02$	$0.16~\pm~0.01$
Glucose (mg/dL)	$167~\pm~19$	$156~\pm~18$	$156~\pm~28$	$156~\pm~16$	$174~\pm~13$	$170~\pm~11$
T-Cholesterol (mg/dL)	78 ± 6	71 ± 8	77 ± 8	72 ± 7	66 ± 7 **	77 ± 11
Triglyceride (mg/dL)	$22~\pm~55$	19 ± 5	$23~\pm~7$	$21~\pm~6$	$19~\pm~4$	15 ± 3
Phospholipid (mg/dL)	$153~\pm~17$	$135~\pm~17$	$151~\pm~18$	$144~\pm~15$	130 ± 18 *	$147~\pm~19$
GOT (IU/L)	51 ± 7	61 ± 11	64 ± 11	60 ± 12	59 ± 13	61 ± 14
GPT (IU/L)	19 ± 4	21 ± 4	$22~\pm~5$	22 ± 5	19 ± 3	21 ± 3
LDH (IU/L)	$225~\pm~32$	$273~\pm~85$	$251~\pm~71$	$250~\pm~55$	$253~\pm~52$	$252~\pm~56$
ALP (IU/L)	$245~\pm~24$	$253~\pm~28$	$247~\pm~29$	$239~\pm~35$	$248~\pm~38$	$250~\pm~34$
γ -GTP (IU/L)	2 ± 1	2 ± 2	2 ± 1	1 ± 1	2 ± 1	1 ± 1
CPK (IU/L)	$106~\pm~55$	$101~\pm~33$	$82~\pm~40$	101 ± 34	$124~\pm~73$	$98~\pm~42$
Urea nitrogen (mg/L)	$20.4~\pm~3.5$	$22.0~\pm~3.4$	$20.6~\pm~2.9$	$20.4~\pm~2.7$	$21.6~\pm~2.7$	25.2 ± 2.6 **
Sodium (mEq/L)	$151~\pm~2$	$152~\pm~2$	151 ± 3	$152~\pm~2$	$151~\pm~2$	151 ± 1
Potassium (mEq/L)	$4.5~\pm~0.2$	$4.8~\pm~0.6$	4.8 ± 0.4	$4.6~\pm~0.4$	$4.6~\pm~0.4$	$4.5~\pm~0.3$
Chloride (mEq/L)	$122~\pm~2$	$122~\pm~5$	$122~\pm~3$	$123~\pm~3$	$122~\pm~2$	$122~\pm~2$
Calcium (mg/dL)	8.8 ± 0.3	8.6 ± 0.2	8.6 ± 0.3	$8.9~\pm~0.2$	$8.7~\pm~0.3$	$8.7~\pm~0.2$
Inorganic phosphorus (mg/dL)	$6.3~\pm~0.7$	$6.4~\pm~1.0$	$6.2~\pm~0.7$	$6.3~\pm~0.4$	$5.9~\pm~0.4$	$6.1~\pm~0.7$

Significant difference, *: $p \le 0.05$, **: $p \le 0.01$, Test of Dunnett

TABLE 11 URINALYSIS OF MALE MICE IN THE 13-WEEK DRINKING WATER STUDY OF 2-HYDROXYETHYL ACRYLATE (SELECTED)

Group		Control	375 ppm	750 ppm	1500 ppm	3000 ppm	6000 ppm
Number of anima	ls examined	<10>	<10>	<9>	<10>	<10>	<10>
pН	6.0	0	0	0	0	0	1 *
•	6.5	0	0	0	1	0	4
	7.0	1	0	2	3	2	4
	7.5	2	2	2	4	6	1
	8.0	5	6	4	2	2	0
	8.5	2	2	1	0	0	0
	(Grade)						
Protein	_	0	0	0	0 *	0 **	0 **
	土	1	1	1	0	0	0
	+	9	9	4	4	2	1
	2+	0	0	4	4	8	9
	3+	0	0	0	2	0	0
Ketone body	_	4	4	0	0 *	0 **	0 *
	±	5	6	6	4	2	3
	+	1	0	3	6	8	7
	2+	0	0	0	0	0	0

Significant difference, *: $p \le 0.05$, **: $p \le 0.01$ Chi square test

TABLE 12 URINALYSIS OF FEMALE MICE IN THE 13-WEEK DRINKING WATER STUDY OF 2-HYDROXYETHYL ACRYLATE (SELECTED)

Group		Control	375 ppm	750 ppm	1500 ppm	3000 ppm	6000 ppm
Number of animal	s examined	<10>	<10>	<10>	<10>	<10>	<10>
pН	6.0	0	2	1	2	3 *	5 **
P	6.5	0	3	2	3	4	4
	7.0	3	2	4	3	2	0
	7.5	4	0	2	1	1	1
	8.0	3	3	1	1	0	0
	8.5	0	0	0	0	0	0
	(Grade)						
Protein	-	0	0	0	0	0 *	0
11000111	±	1	0	0	0	0	0
	+	7	8	6	4	2	3
	2+	2	2	4	6	8	7
	3+	0	0	0	0	0	0
Ketone body		6	1	0 *	0 **	0 **	0 **
	<u>.</u>	4	8	9	4	1	3
	+	Ô	1	1	6	8	6
	2+	ŏ	$\tilde{0}$	0	0	1	1

Significant difference, *: $p \le 0.05$, **: $p \le 0.01$ Chi square test

TABLE 13 ORGAN WEIGHTS OF MALE MICE IN THE 13-WEEK DRINKING WATER STUDY OF 2-HYDROXYETHYL ACRYLATE

Group		$\operatorname{Control}$	350 ppm	750 ppm	1500 ppm	3000 ppm	6000 ppm
No. of anim		<10>	<10>	<10>	<10>	<10>	<10>
Liver	(g)	1.115 ± 0.069	1.143 ± 0.055	1.116 ± 0.063	1.130 ± 0.083	1.052 ± 0.056	1.037 ± 0.060 *
	(%)	3.688 ± 0.127	3.662 ± 0.206	3.812 ± 0.130	3.803 ± 0.220	$3.972 \pm 0.163 **$	4.148 ± 0.156 **
Kidney	(g)	0.417 ± 0.019	0.439 ± 0.035	0.439 ± 0.019	$0.457~\pm~0.028~^{**}$	0.443 ± 0.030	0.433 ± 0.023
	(%)	1.383 ± 0.089	1.406 ± 0.114	1.500 ± 0.063	$1.542 \pm 0.123 **$	$1.674 \pm 0.160 **$	$1.733 \pm 0.080 **$
Thymus	(g)	0.033 ± 0.007	0.033 ± 0.006	0.030 ± 0.007	0.029 ± 0.006	0.027 ± 0.004	0.029 ± 0.003
	(%)	0.108 ± 0.020	0.105 ± 0.020	0.102 ± 0.025	0.098 ± 0.018	0.103 ± 0.014	0.115 ± 0.012
Adrenal	(g)	0.011 ± 0.004	0.012 ± 0.002	0.010 ± 0.001	0.011 ± 0.003	0.011 ± 0.003	0.010 ± 0.001
	(%)	0.038 ± 0.013	0.039 ± 0.005	0.034 ± 0.004	0.037 ± 0.008	0.040 ± 0.010	0.038 ± 0.005
Testis	(g)	0.229 ± 0.032	0.232 ± 0.018	0.240 ± 0.024	0.230 ± 0.017	0.222 ± 0.027	0.219 ± 0.029
	(%)	0.758 ± 0.115	0.744 ± 0.066	0.823 ± 0.101	0.774 ± 0.059	0.842 ± 0.137	0.876 ± 0.116
Heart	(g)	0.146 ± 0.009	0.158 ± 0.016	0.149 ± 0.014	0.154 ± 0.011	0.141 ± 0.009	0.136 ± 0.009
	(%)	0.485 ± 0.028	0.506 ± 0.054	0.509 ± 0.035	0.520 ± 0.032	$0.532 \pm 0.023 *$	0.543 ± 0.032 **
Lung	(g)	0.163 ± 0.013	0.158 ± 0.007	0.158 ± 0.007	0.156 ± 0.012	0.152 ± 0.006 *	0.148 ± 0.007 **
	(%)	0.540 ± 0.044	0.505 ± 0.029	0.541 ± 0.027	0.526 ± 0.056	0.576 ± 0.048	0.594 ± 0.032 *
Spleen	(g)	0.051 ± 0.007	0.052 ± 0.005	0.050 ± 0.005	0.046 ± 0.004	0.045 ± 0.004 *	0.048 ± 0.004
•	(%)	0.169 ± 0.019	0.166 ± 0.015	0.170 ± 0.013	0.155 ± 0.013	0.171 ± 0.017	0.193 ± 0.015 *
Brain	(g)	0.440 ± 0.011	0.442 ± 0.011	0.440 ± 0.013	0.441 ± 0.011	0.444 ± 0.008	0.437 ± 0.009
	(%)	1.462 ± 0.135	1.416 ± 0.071	1.505 ± 0.085	1.489 ± 0.090	$1.680 \pm 0.103 **$	$1.750 \pm 0.079 *$

Significant difference, *: $p \le 0.05$, **: $p \le 0.01$, Test of Dunnett

TABLE 14 ORGAN WEIGHTS OF FEMALE MICE IN THE 13-WEEK DRINKING WATER STUDY OF 2-HYDROXYETHYL ACRYLATE

Group		Control 375 ppm 750 ppm		1500 ppm	3000 ppm	6000 ppm	
No. of anim		<10>	<10>	<10>	<10>	<10>	<10>
Liver	(g) (%)	0.869 ± 0.029 4.118 ± 0.117	0.854 ± 0.038 4.141 ± 0.166	0.910 ± 0.054 4.302 ± 0.250	0.921 ± 0.049 4.299 ± 0.251	0.909 ± 0.051 4.326 ± 0.164	0.941 ± 0.061 ** 4.491 ± 0.193 **
Kidney	(g) (%)	0.284 ± 0.012 1.346 ± 0.062	0.298 ± 0.014 1.444 ± 0.081 *	0.359 ± 0.144 * 1.705 ± 0.712 **	0.327 ± 0.017 ** 1.529 ± 0.090 **	0.340 ± 0.014 ** 1.618 ± 0.055 **	0.357 ± 0.017 ** 1.704 ± 0.055 **
Thymus	(g) (%)	$\begin{array}{c} 0.040 \pm 0.005 \\ 0.187 \pm 0.024 \end{array}$	0.037 ± 0.005 0.180 ± 0.023	0.037 ± 0.006 0.175 ± 0.029	0.042 ± 0.004 0.194 ± 0.016	0.036 ± 0.004 0.169 ± 0.017	0.036 ± 0.005 0.174 ± 0.027
Adrenal	(g) (%)	0.013 ± 0.002 0.060 ± 0.011	0.012 ± 0.002 0.056 ± 0.011	0.012 ± 0.002 0.056 ± 0.006	0.012 ± 0.002 0.057 ± 0.006	0.011 ± 0.001 0.054 ± 0.005	$0.011 \pm 0.001 \\ 0.051 \pm 0.005$
Ovaries	(g) (%)	0.040 ± 0.004 0.191 ± 0.019	0.033 ± 0.002 ** 0.158 ± 0.012 **	0.032 ± 0.004 ** 0.152 ± 0.014 **	0.033 ± 0.005 ** 0.153 ± 0.025 **	$0.031 \pm 0.006 ** $ $0.148 \pm 0.027 **$	0.031 ± 0.005 ** 0.150 ± 0.022 **
Heart	(g) (%)	0.119 ± 0.004 0.565 ± 0.013	0.121 ± 0.008 0.588 ± 0.036	0.120 ± 0.004 0.569 ± 0.030	0.125 ± 0.008 0.585 ± 0.039	0.123 ± 0.005 0.585 ± 0.029	0.118 ± 0.005 0.562 ± 0.027
Lung	(g) (%)	0.153 ± 0.009 0.727 ± 0.050	0.148 ± 0.008 0.718 ± 0.047	0.144 ± 0.012 0.678 ± 0.041	0.149 ± 0.009 0.696 ± 0.035	0.148 ± 0.013 0.706 ± 0.054	0.142 ± 0.009 0.677 ± 0.037
Spleen	(g) (%)	0.057 ± 0.005 0.269 ± 0.021	0.051 ± 0.003 0.247 ± 0.015	0.057 ± 0.010 0.269 ± 0.034	0.054 ± 0.005 0.254 ± 0.018	0.052 ± 0.006 0.246 ± 0.024	0.052 ± 0.005 0.249 ± 0.020
Brain	(g) (%)	0.454 ± 0.016 2.153 ± 0.082	0.458 ± 0.016 2.222 ± 0.074	0.458 ± 0.018 2.166 ± 0.083	0.457 ± 0.016 2.135 ± 0.125	0.455 ± 0.010 2.169 ± 0.113	0.443 ± 0.009 2.118 ± 0.071

Significant difference, *: $p \le 0.05$, **: $p \le 0.01$, Test of Dunnett

TABLE 15 HISTOLOGICAL LESIONS OF MALE MICE IN THE 13-WEEK DRINKING WATER STUDY OF 2-HYDROXYETHYL ACRYLATE (SELECTED)

Group		Control	375 ppm	750 ppm	1500 ppm	3000 ppm	6000 ppm
No. of animals examined		<10>	<10>	<10>	<10>	<10>	<10>
	Grade						
Stomach							
Ulcer : forestomach	+	0	0	0	0	0	3
	2+	0	0	0	0	1	2
Hyperplasia : forestomach	+	0	0	0	0	2	0
	2+	0	0	0	0	1	5
	3+	0	0	0	0	0	2
Kidney							
Vacuolization of proximal tuble	+	4	6	8	9	5	2
	2+	6	4	1	0	0	0

Grade +: Slight 2+: moderate 3+: Marked

TABLE 16 HISTOLOGICAL LESIONS OF FEMALE MICE IN THE 13-WEEK DRINKING WATER STUDY OF 2-HYDROXYETHYL ACRYLATE (SELECTED)

Group		Control	375 ppm	750 ppm	1500 ppm	3000 ppm	6000 ppm
No. of animals examined	Grade	<10>	<10>	<10>	<10>	<10>	<10>
Stomach							
Ulcer: forestomach	+	0	0	0	0	0	6
	2+	0	0	0	0	0	1
Hyperplasia : forestomach	+	0	0	0	0	1	1
VI 1	2+	0	0	0	0	0	8
	3+	0	0	0	0	0	1

Grade +: Slight 2+: moderate 3+: Marked