

TDMS No. 20201 - 01
Test Type: 26-WEEK
Route: SKIN APPLICATION
Species/Strain: MICE/TG.AC HEMI

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS
TEF TRANSGENICS (TCDD)
CAS Number: 1746-01-6

Date Report Requested: 06/15/2006
Time Report Requested: 14:58:13
First Dose M/F: NA / 04/21/03
Lab: BAT

C Number: C20201A
Lock Date: 07/24/2004

Cage Range: ALL

Date Range: ALL

Reasons For Removal: ALL

Removal Date Range: ALL

Treatment Groups: Include 001 0 NG/KG

Include 002 121 NG/KG

Include 003 760 NG/KG

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**FOR ALL DOSES THE TUMOR RATES IN THE FOLLOWING TISSUES/ORGANS ARE BASED ON NUMBER OF TISSUES EXAMINED.
IN OTHER TISSUES/ORGANS RATES ARE BASED ON THE NUMBER OF ANIMALS NECROPSIED.**

Lung
Salivary Glands

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SUMMARY OF STATISTICALLY SIGNIFICANT ($P \leq .05$) RESULTS IN THE ANALYSIS OF TEF TRANSGENICS (TCDD)

FEMALE MICE

Organ

Skin

Skin, Site of Application

All Organs

Morphology

Basal or Sq. Cell Carcinoma, Carcinoma, Basosq. Tumor (M or B),
Basal Cell Adenoma, Adenoma, Papilloma, Sq Papilloma,
Keratoacanthoma, Trichoepithelioma
Squamous Cell Papilloma
Squamous Cell Papilloma, Papilloma, Squamous Cell Carcinoma or
Keratoacanthoma
Spindle Cell Carcinoma
Squamous Cell Carcinoma
Squamous Cell Papilloma
Benign Tumors
Malignant Tumors
Malignant and Benign Tumors

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**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN MICE(TG.AC HEMI)
 TERMINAL SACRIFICE AT 27 WEEKS**

DOSE	Females		
	0 NG/KG	121 NG/KG	760 NG/KG

Skin
 Basal or Sq. Cell Carcinoma, Carcinoma, Basosq. Tumor (M or B), Basal Cell Adenoma, Adenoma, Papilloma, Sq Papilloma, Keratoacanthoma, Trichoepithelioma

TUMOR RATES

	#	#	#
OVERALL (a)	0/20 (0%)	2/20 (10%)	6/20 (30%)
POLY-3 RATE (b)	0/17.89	2/15.4	6/16.07
POLY-3 PERCENT (g)	0%	13%	37.3%
TERMINAL (d)	0/17 (0%)	1/12 (8%)	3/11 (27%)
FIRST INCIDENCE	---	163	143

STATISTICAL TESTS

LIFE TABLE	P=0.003**	P=0.177	P=0.006**
POLY 3	P=0.003**	P=0.200	P=0.004**
POLY 1.5	P=0.004**	P=0.212	P=0.006**
POLY 6	P=0.002**	P=0.188	P=0.003**
LOGISTIC REGRESSION	P=0.006**	P=0.211	P=0.012*
COCH-ARM / FISHERS	P=0.008**	P=0.244	P=0.010**
ORDER RESTRICTED	P<0.001**	(e)	(e)
MAX-ISO-POLY-3	P=0.002**	(e)	(e)

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 TERMINAL SACRIFICE AT 27 WEEKS**

DOSE	Females		
	0 NG/KG	121 NG/KG	760 NG/KG

**Skin
 Squamous Cell Papilloma**

TUMOR RATES	#	#	#
OVERALL (a)	0/20 (0%)	2/20 (10%)	5/20 (25%)
POLY-3 RATE (b)	0/17.89	2/15.4	5/16.07
POLY-3 PERCENT (g)	0%	13%	31.1%
TERMINAL (d)	0/17 (0%)	1/12 (8%)	2/11 (18%)
FIRST INCIDENCE	---	163	143

STATISTICAL TESTS

LIFE TABLE	P=0.011*	P=0.177	P=0.015*
POLY 3	P=0.012*	P=0.200	P=0.014*
POLY 1.5	P=0.015*	P=0.212	P=0.017*
POLY 6	P=0.010**	P=0.188	P=0.011*
LOGISTIC REGRESSION	P=0.020*	P=0.211	P=0.028*
COCH-ARM / FISHERS	P=0.022*	P=0.244	P=0.024*
ORDER RESTRICTED	P=0.004**	(e)	(e)
MAX-ISO-POLY-3	P=0.007**	(e)	(e)

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 TERMINAL SACRIFICE AT 27 WEEKS**

	Females		
DOSE	0 NG/KG	121 NG/KG	760 NG/KG

**Skin
 Squamous Cell Papilloma, Papilloma, Squamous Cell Carcinoma or Keratoacanthoma**

TUMOR RATES	#	#	#
OVERALL (a)	0/20 (0%)	2/20 (10%)	6/20 (30%)
POLY-3 RATE (b)	0/17.89	2/15.4	6/16.07
POLY-3 PERCENT (g)	0%	13%	37.3%
TERMINAL (d)	0/17 (0%)	1/12 (8%)	3/11 (27%)
FIRST INCIDENCE	---	163	143

STATISTICAL TESTS

LIFE TABLE	P=0.003**	P=0.177	P=0.006**
POLY 3	P=0.003**	P=0.200	P=0.004**
POLY 1.5	P=0.004**	P=0.212	P=0.006**
POLY 6	P=0.002**	P=0.188	P=0.003**
LOGISTIC REGRESSION	P=0.006**	P=0.211	P=0.012*
COCH-ARM / FISHERS	P=0.008**	P=0.244	P=0.010**
ORDER RESTRICTED	P<0.001**	(e)	(e)
MAX-ISO-POLY-3	P=0.002**	(e)	(e)

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**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN MICE(TG.AC HEMI)
 TERMINAL SACRIFICE AT 27 WEEKS**

	Females		
DOSE	0 NG/KG	121 NG/KG	760 NG/KG

**Skin, Site of Application
 Spindle Cell Carcinoma**

TUMOR RATES

	#	#	#
OVERALL (a)	0/20 (0%)	0/20 (0%)	4/20 (20%)
POLY-3 RATE (b)	0/17.89	0/15.11	4/15.16
POLY-3 PERCENT (g)	0%	0%	26.4%
TERMINAL (d)	0/17 (0%)	0/12 (0%)	3/11 (27%)
FIRST INCIDENCE	---	---	155

STATISTICAL TESTS

LIFE TABLE	P=0.003**	(e)	P=0.024*
POLY 3	P=0.004**	(e)	P=0.031*
POLY 1.5	P=0.005**	(e)	P=0.039*
POLY 6	P=0.003**	(e)	P=0.024*
LOGISTIC REGRESSION	P=0.005**	(e)	P=0.034*
COCH-ARM / FISHERS	P=0.008**	(e)	P=0.053
ORDER RESTRICTED	P=0.002**	(e)	(e)
MAX-ISO-POLY-3	P=0.005**	(e)	(e)

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**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN MICE(TG.AC HEMI)
 TERMINAL SACRIFICE AT 27 WEEKS**

DOSE	Females		
	0 NG/KG	121 NG/KG	760 NG/KG

**Skin, Site of Application
 Squamous Cell Carcinoma**

TUMOR RATES

	#	#	#
OVERALL (a)	0/20 (0%)	0/20 (0%)	9/20 (45%)
POLY-3 RATE (b)	0/17.89	0/15.11	9/15.59
POLY-3 PERCENT (g)	0%	0%	57.8%
TERMINAL (d)	0/17 (0%)	0/12 (0%)	7/11 (64%)
FIRST INCIDENCE	---	---	151

STATISTICAL TESTS

LIFE TABLE	P<0.001**	(e)	P<0.001**
POLY 3	P<0.001**	(e)	P<0.001**
POLY 1.5	P<0.001**	(e)	P<0.001**
POLY 6	P<0.001**	(e)	P<0.001**
LOGISTIC REGRESSION	P<0.001**	(e)	P<0.001**
COCH-ARM / FISHERS	P<0.001**	(e)	P<0.001**
ORDER RESTRICTED	P<0.001**	(e)	(e)
MAX-ISO-POLY-3	P<0.001**	(e)	(e)

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**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN MICE(TG.AC HEMI)
 TERMINAL SACRIFICE AT 27 WEEKS**

DOSE	Females		
	0 NG/KG	121 NG/KG	760 NG/KG

**Skin, Site of Application
 Squamous Cell Papilloma**

TUMOR RATES	#	#	#
OVERALL (a)	1/20 (5%)	16/20 (80%)	19/20 (95%)
POLY-3 RATE (b)	1/17.89	16/17.25	19/20
POLY-3 PERCENT (g)	5.6%	92.8%	95%
TERMINAL (d)	1/17 (6%)	12/12 (100%)	10/11 (91%)
FIRST INCIDENCE	183 (T)	122	84

STATISTICAL TESTS

LIFE TABLE	P<0.001**	P<0.001**	P<0.001**
POLY 3	P<0.001**	P<0.001**	P<0.001**
POLY 1.5	P<0.001**	P<0.001**	P<0.001**
POLY 6	P<0.001**	P<0.001**	P<0.001**
LOGISTIC REGRESSION	P<0.001**	P<0.001**	P<0.001**
COCH-ARM / FISHERS	P<0.001**	P<0.001**	P<0.001**
ORDER RESTRICTED	P<0.001**	(e)	(e)
MAX-ISO-POLY-3	P<0.001**	(e)	(e)

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 TERMINAL SACRIFICE AT 27 WEEKS**

DOSE	Females		
	0 NG/KG	121 NG/KG	760 NG/KG

**Stomach, Forestomach
 Squamous Cell Papilloma**

TUMOR RATES	#	#	#
OVERALL (a)	5/20 (25%)	4/20 (20%)	4/20 (20%)
POLY-3 RATE (b)	5/17.89	4/15.11	4/16.2
POLY-3 PERCENT (g)	28%	26.5%	24.7%
TERMINAL (d)	5/17 (29%)	4/12 (33%)	1/11 (9%)
FIRST INCIDENCE	183 (T)	183 (T)	129

STATISTICAL TESTS

LIFE TABLE	P=0.530	P=0.571	P=0.563
POLY 3	P=0.535N	P=0.614N	P=0.567N
POLY 1.5	P=0.518N	P=0.568N	P=0.536N
POLY 6	P=0.560N	P=0.637	P=0.604N
LOGISTIC REGRESSION	P=0.588N	P=0.571	P=0.544N
COCH-ARM / FISHERS	P=0.510N	P=0.500N	P=0.500N
ORDER RESTRICTED	P=0.564N	(e)	(e)
MAX-ISO-POLY-3	P=0.568N	(e)	(e)

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 TERMINAL SACRIFICE AT 27 WEEKS**

DOSE	Females		
	0 NG/KG	121 NG/KG	760 NG/KG

Tooth
 Odontogenic Tumor

TUMOR RATES

	#	#	#
OVERALL (a)	6/20 (30%)	6/20 (30%)	2/20 (10%)
POLY-3 RATE (b)	6/18.15	6/16.02	2/15.29
POLY-3 PERCENT (g)	33.1%	37.5%	13.1%
TERMINAL (d)	5/17 (29%)	3/12 (25%)	1/11 (9%)
FIRST INCIDENCE	165	150	143

STATISTICAL TESTS

LIFE TABLE	P=0.207N	P=0.388	P=0.291N
POLY 3	P=0.115N	P=0.535	P=0.173N
POLY 1.5	P=0.092N	P=0.573	P=0.143N
POLY 6	P=0.156N	P=0.501	P=0.220N
LOGISTIC REGRESSION	P=0.103N	P=0.534	P=0.163N
COCH-ARM / FISHERS	P=0.079N	P=0.634N	P=0.118N
ORDER RESTRICTED	P=0.105N	(e)	(e)
MAX-ISO-POLY-3	P=0.139N	(e)	(e)

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 TERMINAL SACRIFICE AT 27 WEEKS**

DOSE	Females		
	0 NG/KG	121 NG/KG	760 NG/KG
All Organs			
Benign Tumors			
TUMOR RATES			
	#	#	#
OVERALL (a)	6/20 (30%)	16/20 (80%)	19/20 (95%)
POLY-3 RATE (b)	6/17.89	16/17.25	19/20
POLY-3 PERCENT (g)	33.6%	92.8%	95%
TERMINAL (d)	6/17 (35%)	12/12 (100%)	10/11 (91%)
FIRST INCIDENCE	183 (T)	122	84
STATISTICAL TESTS			
LIFE TABLE	P<0.001**	P<0.001**	P<0.001**
POLY 3	P<0.001**	P<0.001**	P<0.001**
POLY 1.5	P<0.001**	P<0.001**	P<0.001**
POLY 6	P<0.001**	P<0.001**	P<0.001**
LOGISTIC REGRESSION	P<0.001**	P<0.001**	P<0.001**
COCH-ARM / FISHERS	P<0.001**	P=0.002**	P<0.001**
ORDER RESTRICTED	P<0.001**	(e)	(e)
MAX-ISO-POLY-3	P<0.001**	(e)	(e)

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DOSE	Females		
	0 NG/KG	121 NG/KG	760 NG/KG

**All Organs
 Malignant Tumors**

TUMOR RATES

	#	#	#
OVERALL (a)	2/20 (10%)	1/20 (5%)	12/20 (60%)
POLY-3 RATE (b)	2/17.89	1/15.56	12/15.98
POLY-3 PERCENT (g)	11.2%	6.4%	75.1%
TERMINAL (d)	2/17 (12%)	0/12 (0%)	9/11 (82%)
FIRST INCIDENCE	183 (T)	150	151

STATISTICAL TESTS

LIFE TABLE	P<0.001**	P=0.602N	P<0.001**
POLY 3	P<0.001**	P=0.549N	P<0.001**
POLY 1.5	P<0.001**	P=0.530N	P<0.001**
POLY 6	P<0.001**	P=0.568N	P<0.001**
LOGISTIC REGRESSION	P<0.001**	P=0.526N	P<0.001**
COCH-ARM / FISHERS	P<0.001**	P=0.500N	P<0.001**
ORDER RESTRICTED	P<0.001**	(e)	(e)
MAX-ISO-POLY-3	P<0.001**	(e)	(e)

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 TERMINAL SACRIFICE AT 27 WEEKS**

DOSE	Females		
	0 NG/KG	121 NG/KG	760 NG/KG

**All Organs
 Malignant and Benign Tumors**

TUMOR RATES	#	#	#
OVERALL (a)	11/20 (55%)	17/20 (85%)	20/20 (100%)
POLY-3 RATE (b)	11/18.15	17/17.42	20/20
POLY-3 PERCENT (g)	60.6%	97.6%	100%
TERMINAL (d)	10/17 (59%)	12/12 (100%)	11/11 (100%)
FIRST INCIDENCE	165	122	84

STATISTICAL TESTS

LIFE TABLE	P<0.001**	P=0.003**	P<0.001**
POLY 3	P=0.003**	P=0.006**	P<0.001**
POLY 1.5	P=0.002**	P=0.009**	P<0.001**
POLY 6	P=0.004**	P=0.004**	P<0.001**
LOGISTIC REGRESSION	P<0.001**	P=0.005**	P<0.001**
COCH-ARM / FISHERS	P=0.003**	P=0.041*	P<0.001**
ORDER RESTRICTED	P<0.001**	(e)	(e)
MAX-ISO-POLY-3	P<0.001**	(e)	(e)

LEGEND

- (a) Number of tumor-bearing animals/number of animals examined at site.
 - (b) Number of tumor-bearing animals/Poly-3 number
 - (d) Observed incidence at terminal kill.
 - (f) Beneath the control incidence are the P-values associated with the trend test. Beneath the dosed group incidence are the P-values corresponding to pairwise comparisons between the controls and that dosed group. The life table analysis regards tumors in animals dying prior to terminal kill as being (directly or indirectly) the cause of death.
 - (e) Value of Statistic cannot be computed.
 - (g) Poly-3 adjusted lifetime tumor incidence.
 - (I) Interim sacrifice
 - (T) Terminal sacrifice
 - # Tumor rates based on numbers of animals necropsied.
 - * To the right of any statistical result, indicates significance at ($P \leq 0.05$).
 - ** To the right of any statistical result, indicates significance at ($P \leq 0.01$).
 - N Indicates a negative trend for all tests
- Logistic regression is an alternative method for analyzing the incidence of non-fatal tumors.
The Cochran-Armitage and Fishers exact tests compare directly the overall incidence rates.

*** END OF REPORT ***