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Industrial **BIO-TEST Laboratories, Inc.**
1810 FRONTAGE ROAD
NORTHBROOK, ILLINOIS 60062

REPORT TO
ATOMIC ENERGY COMMISSION
THREE-GENERATION REPRODUCTION STUDY WITH
LOW DOSE IRRADIATED PAPAYAS
IN ALBINO RATS
RESULTS OF ALL THREE GENERATIONS

CONTRACT NO. AT (11-1)-2014
REPORT NO. COO-2014-16

OCTOBER 25, 1971

IBT NO. B7041

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Industrial **BIO-TEST** *Laboratories, Inc.*

1810 FRONTAGE ROAD
NORTHBROOK, ILLINOIS 60062

October 25, 1971

Mr. Harold N. Miller, Director
Contracts Division
U. S. Atomic Energy Commission
Chicago Operations Office
9800 South Cass Avenue
Argonne, Illinois 60439

Dear Mr. Miller:

Re: IBT No. B7041 - Three-Generation Reproduction
Study with Low Dose Irradiated Papayas in Albino
Rats - Contract No. AT (11-1)-2014

We are submitting herewith our laboratory report dated
October 25, 1971, prepared in connection with the above study.

Very truly yours,

J. C. Calandra
President

JCC/kjl

cc: Dr. Murray Schulman
Radiation Biologist, Biology Branch
Division of Biology and Medicine
U. S. Atomic Energy Commission
Washington, D. C. 20545

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I. Introduction

A two-year chronic and three-generation reproduction study employing albino rats subjected to oral administration of low dose irradiated papayas was conducted. This report summarizes the results of all three generations of the reproduction portion of the investigation.

II. Summary

A two-year chronic and three-generation reproduction study employing albino rats fed low dose irradiated papayas was conducted. The following results were obtained during the reproduction portion of the experiment.

Investigation of the following parameters revealed no differences between test and control animals which could be attributed to the ingestion of low dose irradiated papayas.

A. Parental Animals

1. Body weight gain.
2. Mortality and reactions.
3. Hematologic and clinical blood chemistry.
4. Pathologic studies.
5. Reproductive performance.

B. Progeny

1. Numbers delivered and viable.
2. Survival.
3. Body weight at weaning.
4. Hematologic and clinical blood chemistry.
5. Pathologic studies.
6. Reactions.

Respectfully submitted,

INDUSTRIAL BIO-TEST LABORATORIES, INC.

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October 25, 1971

trm:lam;bb:psh

III. Procedure

A. Experimental Animals

The animals employed in the study were Charles River strain* albino rats. A total of 400 rats (200 males and 200 females) was selected to form two test groups, a papaya control and negative control group for the two-year longevity portion of the investigation. Following ten weeks of feeding, 30 males and 30 females were selected from each group to serve as the first generation parental animals. Following breeding, these animals were returned to the longevity portion of the study. Parental animals of each generation, after having reached maturity, were bred and produced two litters. At the time of weaning the second litters (F1b and F2b), weanlings were isolated and maintained on the prescribed diet for one week. Parental animals were then chosen for each succeeding generation (F1 and F2). The reproduction study terminated following the weaning of the F3b weanlings. The design for the production of the three generations is presented in Figure 1.

B. Organization of Groups

A structural outline of the experiment is presented in Table I.

* Charles River Breeding Laboratories, Inc., North Wilmington, Mass.

FIGURE 1

TEST MATERIAL: Irradiated Papayas

Design of Experiment

TABLE I

TEST MATERIAL: Irradiated Papayas

Three-Generation Reproduction Study - Albino Rats

Outline of Experiment

Group	Treatment	Number of Parental Animals per Generation					
		Fo		F1		F2	
		Male	Female	Male	Female	Male	Female
C	None	30	30	50	50	35	35
PC	Non-irradiated papayas	30	30	50	50	35	35
T-I	Irradiated papayas (75 krads)	30	30	50	50	35	35
T-II	Irradiated papayas (200 krads)	30	30	50	50	35	35

C. Diets and Feeding

Diets were prepared in the central diet room of this laboratory. The diet for any given group was prepared by blending the calculated weight of papaya (15 percent wet weight of the total diet) with a pre-weighed portion of the stock ration* in a high speed mixer.

The amount of food allotted per day to each rat was sufficient for ad libitum feeding.

D. Body Weight

Parental animals were weighed weekly until mating trials commenced. Females were also weighed one and 21 days post-partum.

E. Mortality, Reactions and General Observations

Animals in each generation were observed daily for mortality and abnormal behavioral reactions. In addition, these animals were observed for fertility, length of gestation and lactation performance.

All pups were examined for physical anomalies at birth and the number of viable and stillborn members of each litter was recorded. Survival indices were calculated at various points during the gestation period. Litters of more than eight pups were reduced to that number (four males and four females when possible) on the fourth day of lactation.

F. Mating Procedure

Mating trials were initiated when the parental animals were 100 days old. Each of the females was mated with a male from within the same dietary level. Daily vaginal examinations were conducted to

* Purina Laboratory Chow, Ralston Purina Company, St. Louis, Mo.

determine if copulation had occurred. Each male was given a one-week mating trial before being replaced by another male from the same group. Males were rotated at weekly intervals until conception was confirmed or until a female was considered sterile.

The first litters (F1a, F2a, F3a) obtained were weaned 21 days post-partum. The females were given a 7-day rest period and rebred, the above procedure being repeated to obtain the second (F1b, F2b, F3b) litters. Females that did not become pregnant during the first mating trials were not rebred.

G. Pathologic Examinations

A complete gross necropsy and histopathological examination were conducted on any animals that were obviously ill or that developed tumors to ascertain the cause of the condition. The second and third generation parental animals were sacrificed following the weaning of the second litters and gross necropsies were conducted. Grossly abnormal tissues were examined histologically.

Gross pathologic examination was performed on all progeny appearing abnormal; no such examination was performed on pups which appeared outwardly normal until the weaning of the final litters (F3b), at which time ten male and ten female weanlings were chosen from each dietary group for pathologic examination. Five male and five female weanlings from each group were examined histologically.

H. Hematologic Studies

Hematological examinations were conducted on the peripheral blood of four male and four female parental animals from each dietary group. These examinations were conducted during each generation after one, three, and six months of testing.

Erythrocyte count, hemoglobin concentration, hematocrit and both total and differential leukocyte counts were determined. Serum glutamic-oxalacetic transaminase (SGOT) activity was also measured at the same intervals.

Investigation of the same parameters was also conducted upon one male and one female weanling from each of the F3b litters obtained.

I. Statistical Analysis

Statistical analyses (analysis of variance followed by multi-treatment comparisons) were conducted upon data in which quantitative differences were measured. Comparisons were made between the control group and the groups receiving irradiated or non-irradiated papayas. Further comparisons were made between the group receiving non-irradiated papayas and the groups receiving irradiated papayas. Statistically significant differences are noted in the tables discussed in the text.

IV. Results

A. Parental Animals

1. Body Weights

Body weight data are presented in Tables II and III. Included in the tables are the total weight gains for the first 70 days of the feeding period.

Table IV represents the mean weights of females on lactation days one and 21.

TABLE II

TEST MATERIAL: Irradiated Papayas
 Three-Generation Reproduction Study - Albino Rats
 Mean Body Weight and Weight Gain Data

Parental Male Rats

Group	Generation	Mean Body Weight (grams)											Total Weight Gain (grams)
		0	7	14	21	28	35	42	49	56	63	70	
C	F ₀	137	188	240	298	337	360	390	418	440	455	447	340
	F ₁	114	161	214	264	302	327	356	386	412	430	449	335
	F ₂	90	133	189	229	266	294	323	355	384	404	421	331
PC	F ₀	137	229	228	286	319	356	388	410	430	447	463	326
	F ₁	109	153	200	249	284	318	347	347	398	418	435	326
	F ₂	81	127	172	212	250	279	306	338	367	388	407	326
T-I	F ₀	137	186	237	298	333	355	382	396	419	438	447	310
	F ₁	116	160	207	255	295	312	345	371	402	417	436	320
	F ₂	96	133	117	212	257	270	308	346	384	397	424	328
T-II	F ₀	137	188	240	304	341	365	388	406	432	447	458	321
	F ₁	110	159	206	254	296	315	344	372	402	416	432	322
	F ₂	83	130	172	203	250	265	301	339	372	385	407	324

TABLE III

TEST MATERIAL: Irradiated Papayas

Three-Generation Reproduction Study - Albino Rats

Mean Body Weight and Weight Gain Data

Parental Female Rats

Group	Generation	Mean Body Weight (grams)											Total Weight Gain (grams)
		0	7	14	21	28	35	42	49	56	63	70	
C	Fo	123	157	174	198	211	221	237	246	253	264	273	150
	F1	102	134	160	182	196	208	226	236	244	252	258	156
	F2	80	111	147	165	182	196	215	227	236	240	242	162
PC	Fo	123	158	178	203	213	227	235	240	255	263	266	143
	F1	100	134	160	184	198	211	222	231	245	254	262	162
	F2	77	109	141	165	182	194	209	221	234	246	257	180
T-I	Fo	123	159	179	204	213	232	239	249	267	270	272	149
	F1	108	134	160	182	196	216	224	234	248	253	261	153
	F2	78	111	141	160	179	199	210	219	228	237	249	171
T-II	Fo	123	158	181	211	220	234	242	251	260	267	273	150
	F1	101	134	166	188	204	221	228	236	244	253	248	147
	F2	79	110	152	166	188	208	213	221	229	239	224	145

TABLE IV

TEST MATERIAL: Irradiated Papayas

Three-Generation-Reproduction Study - Albino Rats

Lactating Female Body Weights

Group	Litter	Body Weight (grams) Lactation Day:	
		1	21
C	F1a	322	315
	F1b	366	340
	F2a	303	310
	F2b	355	333
	F3a	296	304
	F3b	352	331
PC	F1a	321	306
	F1b	359	323
	F2a	301	305
	F2b	353	317
	F3a	324	302
	F3b	367	341
T-I	F1a	316	315
	F1b	340	319
	F2a	301	300
	F2b	350	316
	F3a	311	286
	F3b	361	344
T-II	F1a	324	296
	F1b	360	343
	F2a	304	314
	F2b	352	329
	F3a	306	291
	F3b	362	329

2. Mortality

Mortality data are presented in Tables V and VI.

3. Reactions

No untoward reactions were noted among the parental animals during the investigation.

TABLE V

TEST MATERIAL: Irradiated Papayas

Three-Generation Reproduction Study - Albino Rats

Mortality Data

Parental Generation Males

Group	Generation	Mortality Data					Total
		Pre-M	First Mating M	Post-M	Second Mating M	Post-M	
C	F ₀	0	0	0	0	0	0
	F ₁	0	0	0	0	0	0
	F ₂	0	0	2	0	1	3
PC	F ₀	0	0	0	0	0	0
	F ₁	0	0	0	0	0	0
	F ₂	0	0	1	0	0	1
T-I	F ₀	0	0	0	0	0	0
	F ₁	0	0	0	0	0	0
	F ₂	0	2	0	2	0	4
T-II	F ₀	0	0	0	0	0	0
	F ₁	0	0	0	0	0	0
	F ₂	0	0	0	0	1	1

Pre-M = Pre-Mating Period

M = Mating Period

Post-M = Post-Mating Period

TABLE VI

TEST MATERIAL: Irradiated Papayas

Three-Generation Reproduction Study - Albino Rats

Mortality Data

Parental Generation Females

Group	Generation	Pre-M	First Mating					Second Mating					Total
			M	G	P	L	R	M	G	P	L	Post-W	
C	Fo	0	0	0	0	1	0	0	0	0	0	0	1
	F1	0	1	0	0	0	0	1	0	1	1	1	5
	F2	0	0	0	0	0	0	0	0	0	0	0	0
PC	Fo	0	0	0	0	0	0	0	0	0	0	0	0
	F1	0	0	0	0	0	0	1	0	0	1	1	3
	F2	0	0	0	0	1	0	0	0	0	0	0	1
T-I	Fo	0	0	0	0	0	0	0	0	0	0	0	0
	F1	0	0	0	0	0	0	0	0	2	0	1	3
	F2	0	0	0	0	0	1	0	0	1	0	0	2
T-II	Fo	0	0	0	0	0	0	0	0	0	0	0	0
	F1	0	0	0	0	0	0	0	0	0	0	0	0
	F2	0	0	0	0	1	0	0	0	2	3	0	6

Pre-M = Pre-Mating Period

M = Mating Period

G = Gestation Period

P = Parturition

L = Lactation

R = Rest Period

Post-W = Post-Weaning

4. Hematologic Studies

Results of the parental blood studies are summarized in Tables VII and VIII. Included in Table VII are the results obtained from the determinations of serum glutamic-oxalacetic transaminase (SGOT) activity.

5. Pathologic Studies

Gross pathologic examinations performed on the second and third generation animals revealed no differences between test and control animals which could be attributed to the ingestion of irradiated papayas.

Pathologic examinations of the first generation parental animals were performed only during the longevity portion of the study.

TABLE VII

TEST MATERIAL: Irradiated Papayas

Three-Generation Reproduction Study - Albino Rats

Hematologic and Clinical Blood Chemistry Data

Summary of Mean Values

Group	Sex	Generation	Total Leukocyte Count (thousands/mm ²)			Erythrocyte Count (millions/mm ²)			Hemoglobin Concentration (g/100 ml)			Hematocrit (%)			SGOT (Dade Units)		
			Month:			Month:			Month:			Month:			Month:		
			1	3	6	1	3	6	1	3	6	1	3	6	1	3	6
C	M	Fo	-	-	9.7	-	-	8.37	-	-	15.7	-	-	47.4	-	-	94
		F1	14.0	15.4	10.1	8.16	8.25	8.71	17.1	17.7	15.7	51.3	49.7	41.2	127	87	109
		F2	9.4	14.9	10.4	6.95	8.10	8.27	16.1	15.6	15.3	42.1	43.8	43.3	100	92	92
	F	Fo	-	-	6.0	-	-	7.50	-	-	15.0	-	-	44.9	-	-	70
		F1	9.1	9.4	6.7	7.50	7.72	7.38	16.9	17.4	14.1	50.2	47.6	42.5	133	93	88
		F2	10.2	9.3	9.9	7.10	7.20	7.43	16.3	14.7	14.9	44.0	39.3	39.4	109	77	81
	M	Fo	-	-	12.2	-	-	8.68	-	-	15.4	-	-	46.6	-	-	97
		F1	15.6	10.4	9.7	7.79	8.04	8.00	16.8	16.9	14.2	50.5	48.0	41.4	142	76	92
		F2	4.3	14.0	13.2	6.90	7.30	8.23	15.0	14.5	15.3	41.7	39.9	42.6	161	92	95
PC	F	Fo	-	-	5.8	-	-	7.44	-	-	14.3	-	-	43.0	-	-	86
		F1	15.6	9.0	7.7	7.42	7.68	7.55	15.8	16.1	13.6	46.8	48.4	40.5	129	90	89
		F2	21.7	12.4	9.8	7.70	7.03	7.71	16.3	13.6	15.0	46.0	36.5	40.2	163	75	82

TABLE VII continued

TEST MATERIAL: Irradiated Papayas

Three-Generation Reproduction Study - Albino Rats

Hematologic and Clinical Blood Chemistry Data

Summary of Mean Values

Group	Sex	Generation	Total Leukocyte Count (thousands/mm ²)			Erythrocyte Count (millions/mm ²)			Hemoglobin Concentration (g/100 ml)			Hematocrit (%)			SGOT (Dade Units)		
			Month:			Month:			Month:			Month:			Month:		
			1	3	6	1	3	6	1	3	6	1	3	6	1	3	6
T-I	M	Fo	-	-	9.6	-	-	7.85	-	-	15.3	-	-	46.1	-	-	91
		F1	13.8	12.7	11.2	8.34	7.63	8.20	16.8	17.2	14.0	51.9	47.3	43.3	156	94	79
		F2	6.8	18.9	15.4	6.57	7.87	8.33	14.8	15.2	15.2	40.0	41.5	42.1	133	75	99
	F	Fo	-	-	6.2	-	-	7.37	-	-	14.3	-	-	43.0	-	-	85
		F1	10.4	9.9	7.3	6.94	7.90	7.85	16.2	17.0	13.7	50.7	47.1	41.3	145	75	101
		F2	8.6	13.5	15.6	7.05	7.52	7.32	16.1	15.4	14.7	43.8	41.1	39.6	121	89	89
T-II	M	Fo	-	-	11.7	-	-	8.27	-	-	14.8	-	-	44.4	-	-	104
		F1	12.5	13.0	9.8	8.52	8.15	6.76	15.6	17.6	13.8	48.7	47.2	42.4	110	83	94
		F2	5.9	19.7	14.6	7.76	7.50	7.86	16.0	15.2	15.0	46.3	41.4	40.8	127	80	93
	F	Fo	-	-	7.9	-	-	7.50	-	-	14.5	-	-	43.1	-	-	99
		F1	11.8	10.3	6.1	6.81	7.47	7.06	16.6	17.8	13.9	49.7	47.5	40.7	117	90	83
		F2	4.8	12.7	8.4	7.39	7.23	7.51	15.4	15.0	15.5	44.7	39.2	40.1	229	82	109

- = Analyses not conducted.

TABLE VIII

TEST MATERIAL: Irradiated Papayas

Three-Generation Reproduction Study - Albino Rats

Hematologic Data

Summary of Mean Values

Group	Sex	Generation	Differential Leukocyte Count (number of cells/hundred)														
			Lymphocytes			Neutrophils			Monocytes			Eosinophils			Basophils		
			Month:			Month:			Month:			Month:			Month:		
			1	3	6	1	3	6	1	3	6	1	3	6	1	3	6
C	M	Fo	-	-	79.5	-	-	19.0	-	-	0.0	-	-	1.5	-	-	0.0
		F1	82.0	86.6	80.4	16.0	11.4	18.6	0.8	0.0	0.0	1.4	2.0	1.0	0.0	0.0	0.0
		F2	89.8	90.3	82.0	10.2	9.5	16.5	0.0	0.0	0.3	0.0	0.2	1.2	0.0	0.0	0.0
	F	Fo	-	-	85.2	-	-	14.0	-	-	0.0	-	-	0.8	-	-	0.0
		F1	83.0	86.6	86.8	15.4	11.6	11.8	0.0	0.0	0.0	1.0	1.8	1.4	0.0	0.0	0.0
		F2	90.8	90.5	85.6	8.8	8.5	13.0	0.0	0.5	0.2	0.4	0.5	1.0	0.0	0.0	0.2
PC	M	Fo	-	-	77.5	-	-	21.0	-	-	0.0	-	-	1.5	-	-	0.0
		F1	89.0	84.4	79.8	9.6	15.2	18.8	0.2	0.0	0.0	0.6	0.4	1.4	0.0	0.0	0.0
		F2	91.0	89.5	81.0	8.5	10.0	16.8	0.0	0.0	0.2	0.5	0.5	2.0	0.0	0.0	0.0
	F	Fo	-	-	78.2	-	-	20.3	-	-	0.0	-	-	1.5	-	-	0.0
		F1	91.4	86.0	82.8	8.4	13.6	17.2	0.0	0.0	0.0	0.2	0.4	0.0	0.0	0.0	0.0
		F2	75.0	91.5	76.4	24.5	8.2	22.8	0.0	0.0	0.0	0.5	0.5	0.8	0.0	0.0	0.0

TABLE VIII continued

TEST MATERIAL: Irradiated Papayas

Three-Generation Reproduction Study - Albino Rats

Hematologic Data

Summary of Mean Values

Group	Sex	Generation	Differential Leukocyte Count (number of cells/hundred)														
			Lymphocytes			Neutrophils			Monocytes			Eosinophils			Basophils		
			Month:			Month:			Month:			Month:			Month:		
			1	3	6	1	3	6	1	3	6	1	3	6	1	3	6
T-I	M	Fo	-	-	80.3	-	-	18.2	-	-	0.0	-	-	1.5	-	-	0.0
		F1	85.8	85.4	83.4	12.6	13.8	15.8	0.6	0.0	0.0	1.4	2.0	1.0	0.0	0.0	0.0
		F2	79.0	88.8	84.0	21.0	10.7	15.2	0.0	0.0	0.0	0.0	0.5	0.8	0.0	0.0	0.0
	F	Fo	-	-	79.3	-	-	18.5	-	-	0.0	-	-	1.7	-	-	0.0
		F1	92.0	89.6	78.8	7.6	10.0	19.4	0.6	0.0	0.0	1.0	1.8	1.4	0.0	0.0	0.0
		F2	89.5	93.0	77.7	10.5	6.0	21.8	0.0	0.0	0.0	0.0	1.0	0.5	0.0	0.0	0.0
T-II	M	Fo	-	-	84.0	-	-	14.5	-	-	0.0	-	-	1.5	-	-	0.0
		F1	88.2	79.6	85.8	10.8	12.2	13.8	0.0	0.0	0.0	1.0	0.2	0.4	0.0	0.0	0.0
		F2	84.5	81.8	84.0	15.5	18.0	15.2	0.0	0.0	0.0	0.0	0.2	0.8	0.0	0.0	0.0
	F	Fo	-	-	85.8	-	-	14.0	-	-	0.0	-	-	0.2	-	-	0.0
		F1	92.2	92.2	79.6	7.4	7.8	20.2	0.0	0.0	0.0	0.4	0.2	0.2	0.0	0.0	0.0
		F2	86.0	74.5	77.7	12.0	25.3	21.8	0.3	0.2	0.0	1.7	0.0	0.5	0.0	0.0	0.0

- = Analyses not conducted.

6. General Data

General data for parental animals are presented in Table IX.

The indices employed are defined below:

$$\text{Mating Index} = \frac{\text{Number of Copulations*}}{\text{Number of Estrus Cycles Required}} \times 100$$

$$\text{Fertility Index} = \frac{\text{Number of Pregnancies}}{\text{Number of Copulations}} \times 100$$

$$\text{Incidence of Pregnancy} = \frac{\text{Number of Pregnancies}}{\text{Number of Females Mated}} \times 100$$

$$\text{Incidence of Parturition} = \frac{\text{Number of Parturitions}}{\text{Number of Pregnancies}} \times 100$$

* Only one copulation counted per estrus cycle.

TABLE IX

TEST MATERIAL: Irradiated Papayas

Three-Generation Reproduction Study - Albino Rats

General Data

Parental Animals

Reproductive Performance

Group	Litter	Mating Index		Incidence of Pregnancy		Fertility Index		Incidence of Parturition		Gestation Time (Days)	
		Fraction	%	Fraction	%	Fraction	%	Fraction	%	Mean	Range
C	F1a	32/52	61.5	30/30	100.0	30/32	93.8	30/30	100.0	22	20-23
	F1b	28/50	56.0	26/28	92.9	26/29	89.7	26/26	100.0	21	20-23
	F2a	54/72	75.0	49/50	98.0	49/54	90.7	48/49	97.9	21	19-23
	F2b	50/68	73.5	47/50	94.0	47/50	94.0	46/47	97.9	22	20-23
	F3a	37/45	77.8	35/35	100.0	35/35	100.0	35/43	97.1	22	19-23
	F3b	37/44	84.1	32/35	91.4	32/37	86.5	30/32	93.8	21	19-23
PC	F1a	31/58	53.4	30/30	100.0	30/31	96.8	29/30	96.7	22	20-23
	F1b	28/40	70.0	27/28	96.4	27/28	96.4	27/27	100.0	22	20-23
	F2a	61/66	92.4	49/50	98.0	49/61	80.3	48/49	97.9	22	19-23
	F2b	53/62	85.5	46/49	93.9	46/53	86.8	46/46	100.0	22	19-23
	F3a	37/44	89.1	35/35	100.0	35/37	94.6	34/35	97.4	21	20-23
	F3b	36/50	72.0	33/35	94.3	33/36	91.7	30/33	90.9	22	21-22

TABLE IX continued

TEST MATERIAL: Irradiated Papayas

Three-Generation Reproduction Study - Albino Rats

General Data

Parental Animals

Reproductive Performance

Group	Litter	Mating Index		Incidence of Pregnancy		Fertility Index		Incidence of Parturition		Gestation Time (Days)	
		Fraction	%	Fraction	%	Fraction	%	Fraction	%	Mean	Range
T-I	F1a	35/46	76.1	30/30	100.0	30/35	87.5	29/30	96.7	22	20-23
	F1b	35/37	61.4	25/30	88.3	25/30	71.4	24/25	96.0	22	20-23
	F2a	50/55	90.9	49/49	100.0	49/50	98.0	49/49	100.0	21	19-23
	F2b	52/62	83.9	49/50	98.0	49/52	94.2	49/49	100.0	22	20-23
	F3a	35/41	85.4	34/34	100.0	34/36	94.4	33/34	97.1	22	19-23
	F3b	34/37	91.9	33/33	100.0	33/33	100.0	31/33	93.9	21	18-22
T-II	F1a	32/54	59.3	30/30	100.0	30/32	93.8	30/30	100.0	22	20-23
	F1b	33/52	63.5	24/29	82.8	24/33	72.7	24/24	100.0	22	20-23
	F2a	58/85	68.2	48/50	96.0	48/58	82.8	48/48	100.0	22	19-23
	F2b	53/64	82.8	49/50	98.0	49/53	92.4	49/49	100.0	21	19-23
	F3a	35/45	77.8	34/34	100.0	34/35	97.1	34/34	100.0	21	19-23
	F3b	29/40	72.5	28/28	100.0	28/29	96.6	28/28	100.0	22	21-23

B. Progeny

1. Population Data

Population data for all litters are presented in Table X.

All pups appeared outwardly normal and displayed normal growth through their lactation period. At weaning, an examination of each pup for external abnormalities was conducted and all pups were judged to be free of gross external abnormalities.

TABLE X

TEST MATERIAL: Irradiated Papayas

Three-Generation Reproduction Study - Albino Rats

Population Data

Progeny

Group	Litter	Number of Pups Delivered		Number of Pups Stillborn		Number of Viable Pups Born		Number of Pups at Lactation Day 1	
		Total	Mean/Litter	Total	Mean/Litter	Total	Mean/Litter	Total	Mean/Litter
C	F1a	367	12.2	4	0.1	363	12.1	334	11.1
	F1b	337	13.0	1	0.1	336	12.9	330	12.2
	F2a	536	11.2	15	0.3	521	10.9	500	10.4
	F2b	504	10.7	7	0.2	496	10.6	488	10.4
	F3a	408	12.0	11	0.3	397	11.7	385	11.3
	F3b	396	13.2	16	0.4	380	12.8	371	12.4
PC	F1a	337	11.6	10	0.3	327	11.2	310	10.7
	F1b	338	12.5	7	0.3	331	12.3	325	12.0
	F2a	549	11.4	26	0.5	525	10.9	481	11.6
	F2b	554	12.3	11	0.2	520	11.6	496	10.1
	F3a	375	11.0	9	0.3	366	10.7	358	10.5
	F3b	366	12.6	10	0.3	356	12.3	338	11.7

TABLE X continued

TEST MATERIAL: Irradiated Papayas

Three-Generation Reproduction Study - Albino Rats

Population Data

Progeny

Group	Litter	Number of Pups Delivered		Number of Pups Stillborn		Number of Viable Pups Born		Number of Pups at Lactation Day 1	
		Total	Mean/Litter	Total	Mean/Litter	Total	Mean/Litter	Total	Mean/Litter
T-I	F1a	320	11.0	4	0.1	361	10.9	314	10.8
	F1b	253	10.5	10	0.4	242	10.1	230	9.6
	F2a	550	11.2	20	0.4	530	10.8	496	10.1
	F2b	575	11.7	22	0.5	553	11.3	542	11.1
	F3a	358	10.8	5	0.2	353	10.6	335	10.2
	F3b	354	11.8	4	0.1	350	11.7	345	11.3
T-II	F1a	362	12.1	9	0.3	353	11.8	339	11.3
	F1b	300	12.5	3	0.1	297	12.2	291	12.1
	F2a	573	11.9	14	0.3	559	11.7	535	11.2
	F2b	557	11.6	17	0.4	540	11.3	515	10.7
	F3a	348	10.2	10	0.3	338	9.9	328	9.7
	F3b	285	11.9	9	0.4	276	11.5	242	10.0

TABLE X continued

TEST MATERIAL: Irradiated Papayas

Three-Generation Reproduction Study - Albino Rats

Population Data

Progeny

Group	Litter	Number of Pups at Lactation Day 4		Number of Pups Retained at Lactation Day 4				Number of Pups Weaned at Lactation Day 21			
		Total	Mean/Litter	Males	Females	Total	Mean/Litter	Males	Females	Total	Mean/Litter
C	F1a	279	9.3	103	102	205	6.8	66	64	310	4.3
	F1b	311	11.5	106	103	209	7.7	100	97	197	7.3
	F2a	473	9.9	170	171	341	7.1	153	153	306	6.4
	F2b	469	9.9	173	172	345	7.3	170	142	312	6.6
	F3a	361	10.6	129	125	254	7.5	119	107	226	6.7
	F3b	348	11.6	112	112	224	7.5	86	80	175	5.8
PC	F1a	294	10.1	115	107	222	7.6	107	94	201	6.9
	F1b	299	11.1	99	99	198	7.3	93	91	184	6.8
	F2a	467	9.7	114	112	326	6.8	146	144	290	6.0
	F2b	493	11.0	121	122	343	7.6	145	135	280	6.2
	F3a	348	10.2	126	125	251	7.4	98	84	182	5.4
	F3b	330	11.4	110	110	220	7.6	86	78	165	5.7

TABLE X continued

TEST MATERIAL: Irradiated Papayas

Three-Generation Reproduction Study - Albino Rats

Population Data

Progeny

Group	Litter	Number of Pups at Lactation Day 4		Number of Pups Retained at Lactation Day 4				Number of Pups Weaned at Lactation Day 21			
		Total	Mean/Litter	Males	Females	Total	Mean/Litter	Males	Females	Total	Mean/Litter
T-I	F1a	264	9.1	96	101	197	6.8	75	79	154	5.3
	F1b	220	9.2	92	80	172	7.2	87	75	162	6.8
	F2a	462	9.4	119	120	339	6.9	154	163	317	6.5
	F2b	533	10.9	130	134	364	7.4	141	126	267	5.5
	F3a	329	10.0	123	123	246	7.5	113	112	225	6.8
	F3b	339	11.3	115	116	231	7.7	106	84	190	6.3
T-II	F1a	261	8.7	99	93	192	6.4	68	59	127	4.2
	F1b	285	11.9	97	93	190	7.9	97	92	189	7.9
	F2a	492	10.3	122	124	346	7.2	146	171	317	6.6
	F2b	497	10.4	175	176	351	7.3	134	145	279	5.8
	F3a	304	8.9	119	121	240	7.1	89	88	177	5.2
	F3b	250	10.4	132	128	160	6.7	63	61	124	5.2

2. Survival Data

Survival data for progeny are presented in Table XI. The number of pups per female was reduced to eight, four males and four females whenever possible, on the fourth day of the lactation period.

Indices employed are defined below.

$$\text{Live Birth Index} = \frac{\text{Number of Viable Pups Born}}{\text{Total Number of Pups Born}} \times 100$$

$$\text{24-Hour Survival Index} = \frac{\text{Number of Pups Viable at Lactation Day 1}}{\text{Number of Viable Pups Born}} \times 100$$

$$\text{5-Day Survival Index} = \frac{\text{Number of Pups Viable at Lactation Day 4}}{\text{Number of Viable Pups Born}} \times 100$$

$$\text{Lactation Index} = \frac{\text{Number of Pups Viable at Weaning (Day 21)}}{\text{Number of Pups Retained at Lactation Day 4}} \times 100$$

TABLE XI

TEST MATERIAL: Irradiated Papayas

Three-Generation Reproduction Study - Albino Rats

Survival Indices

Progeny

Group	Litter	Live Birth Index	24-Hour Survival Index	4-Day Survival Index	Lactation Index
C	F1a	98.9	92.0	76.9	63.4
	F1b	99.7	94.6	92.3	94.0
	F2a	97.2	96.0	90.8	89.7
	F2b	98.4	98.4	94.6	90.4
	F3a	97.3	94.4	88.5	89.8
	F3b	96.0	97.6	91.5	78.1
PC	F1a	97.0	94.8	89.9	90.5
	F1b	97.9	98.2	90.3	92.9
	F2a	95.6	91.6	89.0	91.4
	F2b	98.0	95.8	90.8	81.6
	F3a	97.6	97.8	97.2	72.5
	F3b	98.3	93.9	97.6	75.0
T-I	F1a	98.9	99.4	83.5	78.2
	F1b	95.7	95.0	90.9	92.4
	F2a	96.4	93.6	87.2	93.5
	F2b	96.2	98.0	96.4	73.4
	F3a	98.6	94.9	93.2	91.5
	F3b	98.9	98.6	96.9	81.4
T-II	F1a	97.5	96.0	73.9	66.1
	F1b	99.0	98.0	96.0	99.5
	F2a	97.6	95.7	88.0	91.6
	F2b	97.0	95.4	92.0	79.5
	F3a	97.1	97.0	89.9	73.8
	F3b	96.8	87.7	85.9	78.1

3. Body Weight Data

Body weight data for weanlings are presented in Table XII.

TABLE XII

TEST MATERIAL: Irradiated Papayas
Three-Generation Reproduction Study - Albino Rats

Progeny

Weanling Body Weight Data

Group	Litter	Mean Body Weight (grams)	
		Males	Females
C	F1a	43.4	38.3
	F1b	54.6	40.0
	F2a	44.2	41.3
	F2b	61.7	59.8
	F3a	41.1	40.1
	F3b	51.3	45.1
PC	F1a	47.5	43.9
	F1b	44.9	43.6
	F2a	42.4	38.9
	F2b	57.2	54.3
	F3a	41.1	39.8
	F3b	43.2	42.3
T-I	F1a	45.4	44.5
	F1b	45.3	42.5
	F2a	40.8	38.9
	F2b	58.2	53.6
	F3a	41.5	39.2
	F3b	47.8	47.2
T-II	F1a	36.2	34.7
	F1b	44.3	41.4
	F2a	42.3	39.2
	F2b	55.0	51.9
	F3a	42.7	40.7
	F3b	46.8	44.0

4. Hematological Studies

Results of the F3b weanling blood studies are summarized in Tables XIII and XIV. Included in Table XIII are the results obtained from the determinations of serum glutamic-oxalacetic transaminase (SGOT) activity.

TABLE XIII

TEST MATERIAL: Irradiated Papayas

Three-Generation Reproduction Study - Albino Rats

Hematologic and Clinical Blood Chemistry Data - F3b Weanlings

Summary of Mean Values

Group	Sex	Total Leukocyte Count (thousands/mm ²)	Erythrocyte Count (millions/mm ²)	Hemoglobin Concentration (g/100 ml)	Hematocrit (%)	SGOT (Dade Units)
C	M	8.0	6.31	14.1	39.3	160
	F	8.2	6.62	14.6	40.2	157
PC	M	6.4	6.55	14.0	39.5	161
	F	7.2	6.62	14.2	39.9	176
T-I	M	8.2	6.32	13.7	38.2	154
	F	9.6	5.97	14.0	38.5	150
T-II	M	7.0	6.27	13.7	38.0	152
	F	8.3	6.30	13.8	38.1	155

TABLE XIV

TEST MATERIAL: Irradiated Papayas

Three-Generation Reproduction Study - Albino Rats

Hematologic Data - F3b Weanlings

Summary of Mean Values

Group	Sex	Differential Leukocyte Count (number of cells/hundred)				
		Lymphocytes	Neutrophils	Monocytes	Eosinophils	Basophils
C	M	80.9	18.9	0.1	0.1	0.0
	F	85.5	14.2	0.1	0.2	0.0
PC	M	83.4	16.6	0.0	0.0	0.0
	F	84.6	14.9	0.0	0.5	0.0
T-I	M	82.0	17.8	0.1	0.1	0.0
	F	82.6	17.0	0.1	0.3	0.0
T-II	M	83.7	15.7	0.1	0.5	0.0
	F	86.7	12.8	0.2	0.3	0.0

5. Pathologic Studies

Gross pathologic examinations were conducted upon ten male and ten female F3b weanlings from each dietary group. Tissues from one-half (five male and five female) of these animals were examined microscopically.

These examinations failed to reveal any differences between the test and control groups which could be attributed to the ingestion of irradiated papayas. The data are presented in Table XV.

6. Reactions

No untoward reactions were noted among test or control progeny.

TABLE XV

TEST MATERIAL: Irradiated Papayas

Three-Generation Reproduction Study - Albino Rats

Histopathologic Findings

F3b Weanling Sacrifice

Group	Sex	Tissue	Finding	Incidence	Grade
Control	M	Trachea	Focal inflammation	1	0.5
		Lung	Hyperemia	1	0.5
	F		Focal inflammation	1	0.5
		Trachea	Focal inflammation	2	0.5
		Lung	Hyperemia	2	0.5
Positive Control	M	Trachea	Focal inflammation	1	2.0
		Liver	Focal lymphoid infiltration	1	0.5
		Kidney	Focal inflammation	1	0.5
	F	Trachea	Focal inflammation	1	0.5
		Lung	Focal inflammation	1	0.5
T-I	M	Trachea	Focal inflammation	1	0.5
		Lung	Focal inflammation	1	0.5
	F	Trachea	Focal inflammation	1	0.5
		Lung	Inflammation	1	5.0
			Focal inflammation	1	0.5
T-II	M	Trachea	Focal inflammation	1	0.5
		Lung	Hyperemia	1	0.5
			Focal inflammation	1	1.0
		Liver	Focal lymphoid infiltration	1	0.5
	F	Trachea	Inflammation	1	3.0
		Lung	Hyperemia	2	0.5
		Liver	Hyperemia	2	0.5
			Focal lymphoid infiltration	1	0.5

All other tissues and organs examined histologically were normal.

Grading System

0.5 = minimal

2.0 = mild

4.0 = severe

1.0 = slight

3.0 = moderate

5.0 = extreme