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Memorandum

Date December 28, 1982

From Food Additives Evaluation Branch, HFF-156

Subject Administrative File from the Toxicology Data on Irradiated Foods

To Clyde Takegucni, Ph.D.
Petitions Control Branch, (HFF-334)
Through: Chief:
Food Additives Evaluation Branch (HFF-156) *[Signature]* 1/3/83

The data review process on the irradiated foods toxicology data was completed by March 25, 1982, with a final report issued to Dr. Flamm dated April 9, 1982. You had requested a compilation of the administrative file for these toxicology studies and it is now complete. All the study reports and most of the miscellaneous documents have been delivered to you, and the remaining material is being transmitted with this memo. These remaining materials include:

1. A summary of the study reports that claimed to show adverse effects from irradiated foods. (tab A)
2. A bibliography of all the study reports that were evaluated. (tab B)
3. All the "short" and "long" form evaluations of the study reports in alphabetical order. (tab C)
- ④ 4. A copy of the final report of the Task Group for the Review of Toxicology Data on irradiated Foods dated April 9, 1982. (tab D)

The data review proceeded in three phases. In the initial phase, all relevant toxicology studies were identified from computer printouts, SIREN searches of our files, and review papers. In the second phase, the obtainable toxicology studies were summarized on "short" summary forms. Four-hundred-forty-one short forms were completed. This number is somewhat lower than the original estimate of 800 studies because of the many duplications in the papers, reports and documents available. Many reports were also unavailable from the open literature and some were unsuitable for review. Of the 441 summarized studies, 266 were "accepted" or "accepted with reservation," 147 were "rejected" and 28 were not categorized because they were general reviews. Only 409 studies appear in the bibliography because some studies were reviewed twice. Studies were considered in the "rejected" category if any of the following conditions were met:

1. Irradiation dose not reported,
2. Irradiation dose less than 10 krad or more than 10 Mrad,
3. Group size not reported,
4. Group size for rodents less than 5, for days less than 4,
5. Inadequate diet,
6. No non-irradiated diet controls,
7. Administration other than oral,
8. Type of food not reported, and
9. Studies done by IBT.

Studies were "accepted with reservation" (AR) or called questionable if the study report, on initial summary review, appeared acceptable but had some serious deficiencies interfering with interpretation of the data other than the "reject" criteria mentioned above. These deficiencies were detailed on the summary forms if the need arose. Study reports were categorized as "accepted" if on initial examination they appeared to be reasonably complete.

In the third phase, all studies that either appeared to show adverse effects or to support safety were then examined in detail on the "long" summary forms. Thirty-two studies indicating adverse results and 37 studies that appeared to support safety were examined in this phase. On detailed examination of these 69 studies, only 5 studies were judged to support safety, and all the remaining 64 were determined to be deficient. The deficiencies in these studies fell into two general categories, 1) problems associated with diet, and 2) inadequate experimental design. Some examples of these categories are presented below:

1. DIETARY PROBLEMS

- a. General dietary, vitamin, mineral and/or protein deficiency,
- b. Restricted food intake,
- c. Unpalatable diet, e.g., increased peroxidation of oils,

2. INADEQUATE EXPERIMENTAL DESIGN

- a. Inadequate control diet,
- b. "Replicate" experiments,
- c. Too few animals/sex/group, use of one sex, or numbers of animals were not reported,
- d. Combining data such as "total tumors," which is currently considered inappropriate,
- e. Inadequate presentation of the final report, or insufficient data for evaluation, e.g., only a summary was presented,
- f. Addition of antioxidants such as BHT or ethoxyquin to diet either before or after irradiation,
- g. Insufficient recovery time for female animals between breedings in a reproduction study,
- h. Lack of random selection of animals for groups,
- i. Questionable culling practices, and/or sibling matings, in reproduction studies,
- j. Inadequate histopathology,
- k. Use of animals too old for breeding purposes.
- l. Addition of extra animals in the middle of experiments, and,
- m. Inadequate length of time for a study. e.g., carcinogenicity.

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Our conclusions concerning these studies have been detailed in the short and long forms (tab C), the summary of study reports (tab A) and in the final report sent to Dr. Flamm dated April 9, 1982. All documents and written evaluations on the toxicological aspects of irradiated foods are now in your possession.

M. van Gemert 12 28 82

M. van Gemert, Ph.D.
Chairman, Task Group for the
Review of Toxicology Data on
Irradiated Foods

cc: HFF-156 (Kokoski, Bleiberg, Hattan, Misra, Khalsa, Irausquin,
F. Lin)
HFF-102 (Dunkel, Sheu)
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HFF-100

September 15, 1982

STUDY REPORTS INDICATING ADVERSE EFFECTS FROM IRRADIATED FOODS

The studies which indicated adverse effects from irradiated foods are listed below, with a summary of the adverse effects seen in these studies, and a short evaluation of the data. For a more detailed review of these reports, refer to the long summary forms located in the administrative record located under their appropriate reference numbers.

1. The Growth, Reproduction, Longevity and Histopathology of Rats fed Gamma Irradiated Pork, Jam, Carrots, Peaches and Flour. I.J. Tinsley, I.F. Bone, E.C. Bubl. Contract DA-49-007-MD-580, 1960. Ref. # 358, 360. Located in FAP 7M 2056, Vol. 7, pg. 1697.

EFFECTS:

2nd and 3rd generation animals showed higher growth rates but inferior breeding performance.

EVALUATION:

The data were rejected for the following reasons. For a more detailed review, please refer to the long summary forms.

- A. Culling procedures of final report and published paper don't coincide.
 - B. Results of weight gains and decreases in pregnant females were not significant, no decrease in litter size was apparent.
 - C. Extremely poor animal husbandry was practiced.
 - D. Very questionable histopathology practices were used.
 - E. Data from published paper and final report didn't coincide. eg. published paper claimed an increased weight gain and feed efficiency, however, review of the final report revealed only modest (10%) weight gain for all groups including controls.
2. Series of studies showing vitamin K, E, and methionine deficiency in irradiated diets.

- A. Feeding of Irradiated Beef to Rats. F. Blood et al. Tox and Appl. Pharmacol. 8, 235-240, 1966. Ref. # 48.
- B. Influence of Age, Sex, Strain of Rat and Fat-soluble Vitamins on Hemorrhagic Syndromes in Rats fed Irradiated Beef. Melette, S.J., Leone, L.A., Fed. Proc. 19, 1045-9, 1960. Ref. #223
- C. Effect of Methionine and Age of Rat on the Occurrence of Hemorrhagic Diathesis in Rats fed a Ration containing Irradiated Beef. J. Nutr. 80, 85-90, 1963. Malhotra, O.P., Reber, E.F., Ref.# 205
- D. On the Cause of Vitamin K Deficiency in Male Rats fed Irradiated Beef and the Production of Vitamin K Deficiency using an Amino Acid Synthetic Diet. M.S. Mameesh, et.al. J. Nutr. 77, 165-170, 1962. Ref. #212
- E. Vitamin K Deficiency in Rats induced by the Feeding of Irradiated Beef. Metta, V.C., et al. J. Nutr. 69, 18-21, 1959. Ref. #227

- F. Effect of Methionine and Vitamin K3 on Hemorrhages induced by Feeding a Ration Containing Irradiated Beef. Malhotra, O.P., Reber, E.F., Norton, H.W., *Tox. Appl. Pharm.* 7: 402-8, 1965. Ref. #208
- G. Methionine and Testosterone Effect on Occurrence of Hemorrhagic Diathesis in Rats. Malhotra, O.P., Reber, E.F., *Am. J. Physiol.* 205: 1089-92, 1963. Ref. # 204
- H. The Effects of Methionine on Blood Coagulation in Rats Fed a Vitamin K Deficient Ration. O.P. Malhotra, E.F. Reber, Abstract only. Ref. # 202
- I. Mechanism of the Hemorrhagic Phenomen produced in Male Rats by Feeding Irradiated Beef. Mellette, S.J., Leone, L.A., Report from the Office of the Surgeon General. U.S.D.A.-49-007-MD-951. 1959. Ref. # 222

COMMENTS ON THE ABOVE 9 STUDIES:

1. It appears that during gamma irradiation of beef at a dose of 2.79 or 5.58 Mrad, vitamin K is destroyed. This is of little consequence for the human diet, because beef is a poor source of vitamin K. Richer sources are foods like the leafy vegetables, cauliflower, bran and liver. In addition, the major part of the vitamin K supply is synthesized by the intestinal flora.
2. The diet in the studies under consideration was clearly inadequate in vitamin K. One study, by another investigator using the same concentration of irradiated beef in another basic diet, had no hemorrhagic deaths for over 9 months.
3. The effect was sex-dependent. Only males were affected. In castrated males, the effect was much less apparent. Testosterone did aggravate the effect, and estrogens protected. In females, no hemorrhagic deaths were reported, but after castration females became susceptible to the vitamin K deficiency symptoms. Apparently Sprague-Dawley is an unusually susceptible strain for this effect.
4. Most of the studies were of nutritional quality, studying the interactions of vitamin K, methionine, vitamin E in the diet. The development of hemorrhagic diathesis is clearly of nutritional origin and has not been caused by toxic substances in the irradiated beef.

3. Studies on the Effect of Food Irradiation on some Blood Serum Enzymes in Rats. O.M. Metwalli, *Z. Ernährungswiss* 16: 18, 1977 Ref. # 228

EFFECT:

Significant decrease of SGOT activity in only female rats of both 2.5 and 4.5 Mrad dose

EVALUATION:

No dose-response relationship was found. Effects were only found in one sex, and were only marginally significant statistically. Effects therefore are questionable.

4. Long-term Feeding Studies; Irradiated Oranges. Phillips, A.W., Newcomb, H.R., Shanklin, D., Dept. of Army Contract # DA-49-007-MD-791, 1961. Ref. #268

EFFECT:

3rd generation showed decreased weight gain, significantly lower weaning weights for 2nd breeding of parent, 2nd and 3rd generations.

EVALUATION:

Observed effect was small. It is not possible to evaluate if weight reduction occurred during lactation or in utero, because birth weights were not given, neither are maternal weights. Rats make up for the weight depression after weaning. This is another indication that the observed effect was lactational. The decreased reproductive performance in controls and experimental groups in the second breedings raises the suspicion that females were not given enough recovery time between breedings. This would augment a nutritional effect on lactation.

5. Growth, Food Consumption, and Feed Efficiency of Rats fed a Diet containing either Irradiated or Non-irradiated Mushrooms. L. Vlieland, C. Chappel, AEC Contract Report # 149, 1969. Ref. #382

EFFECT:

Feed efficiency slightly decreased and food intake and weight gain were decreased in the 500 krad group.

EVALUATION:

The data in this study were rejected. This study was started to confirm data found in an earlier study Ref# 381, where the decrease in food efficiency was very questionable. It may have been caused by large fluctuations in the weekly weight gains, and food intakes. There is a possibility of palatability problems with the 500 krad mushrooms which was never explored. The possibility of nutritional deficiencies cannot be explored because no data are available concerning the composition of the diet. (these data are not given in the original report either.) The lack of individual data further complicates the evaluation of this study (e.g. no standard deviations on body weights are given).

6. The Effects of Feeding Irradiated Beef to Dogs. I. Growth. E.F. Reber et al. Am. J. Vet. Res. 21, 267-270, 1960. Ref. # 295.

EFFECTS:

Decrease in feed efficiency proportional to the increase in radiation dose was seen. Dogs fed 5.58 Mrad irradiated beef required more feed than those fed 2.79 Mrad irradiated or non-irradiated beef.

EVALUATION:

This was an extremely poor study. The groups were too small (2/sex/group) and there was no random selection of animals. Apparently there was a large variation in initial weights. This together with the small experimental groups makes the data uninterpretable.

7. Vitamin A and E Levels in the Liver and Serum of Rats kept on Irradiated Food. J. Barna, M. Kramer, Acta Physiol. Acad. Sci. Hung. 41: 383, 1972. Ref. # 30.

EFFECT:

A decrease in liver vitamin A depot was seen in both the parents and weanling rats.

EVALUATION:

This study cannot be further evaluated. It is an abstract only. Dose dependent decreases in Vitamin E and vitamin A in the food due to irradiation are reflected by decreases in liver vitamin A. No changes in serum vitamin A or in serum or liver vitamin E could be seen. The study did not detect any toxicity.

8. Effects of Feeding X-irradiated Pork to Rats on their Thiamine Nutrition as reflected in the Activity of Erythrocyte Transketolase. M. Brin, A.S. Ostashever, M. Tai, H. Kalinsky. J. Nutr. 75: 29-34, 1961, Ref. # 53

EFFECTS:

92-98% thiamine was destroyed at 2.79 and 5.58 Mrad and there was decreased weight gain and erythrocyte transketolase.

EVALUATION:

This is not a toxicology study, but is rather a nutritional study. The authors showed destruction of thiamine in irradiated pork, with consequences of decreased thiamine and decreased thiamine-dependent enzymes.

9. Effects of Feeding X-irradiated Pork to Rats on their Pyridoxine Nutrition as reflected in the Activity of Plasma Transaminases. M. Brin, A.S. Ostashever, M. Tai, H. Kalinsky. J. Nutr. 75: 35, 1961. Ref. # 54.

EFFECTS:

Depression of alanine transaminase activity was seen in plasma, possibly due to its effect on pyridoxine content in pork.

EVALUATION:

This is not a toxicology study, but is a nutrition study. Effects are probably due to a pyridoxine deficiency in the diet and not considered a toxic effect.

10. Long-term Rat Feeding Studies: Irradiated Chicken Stew and Cabbage. A.W. Phillips, H.R. Newcomb, D. Shanklin, Army Contract # DA-49-007-MD-783. 1961. Ref. # 268A

EFFECTS:

Weanling rats have reduced alkaline phosphatase in duodenal tissue.

EVALUATION:

These were replicate experiments and the group size of 5/sex/dose was too small to adequately evaluate the data. There were no significant toxicological effects observed in rats fed irradiated chicken stew and cabbage for their lifetime carried over two additional generations.

11. Study the Effects of Radurized Onions when fed to Beagle Dogs. K.L. Gabriel, R.S. Edmonds, 1976. Food Irrad. Inf. (6) 1976. Ref. # 128.

EFFECTS:

Increased spleen weights were seen, and were said to be due to congestion, pigmentation, myeloid metaplasia, and reticuloendothelial hyperplasia; pigmentation of liver and kidneys was also seen, along with mild leucocytosis.

EVALUATION:

There were too few animals /sex/group for an adequate evaluation. They were summary data only. (2 page summary) The effects seen were in both control and experimental animals.

12. Pathomorphology of the Kidneys in Rats after Prolonged Ingestion of Irradiated Foods. A.E. Levina, A.E. Ivanov. Bull. Exp. Biol. Med. 85(2) 236-238, 1978, Ref. # 187

EFFECTS:

At the 0.25-5.6 Mrad dose, they claimed to have seen necrobiotic changes in the kidneys, increased cells in glomeruli over controls, marked stromal sclerosis, periarteritis nodosa type changes in juxtamedullary zone vessels. At the 2.5-560 Krad dose, sclerotic

changes developed slowly, the response was mainly cellular, with (in particular) infiltration by eosinophils, small intestinal hemorrhages were observed, the number of glomeruli per field of vision in these rats was increased.

EVALUATION:

The spread of irradiation dose was extremely wide. Data were only in a short summary form, with no supporting data. It is impossible to verify their data, they not having even a table of numbers to evaluate.

13. Long-term Feeding Study for Testing the Wholesomeness of an Irradiated Diet with a High Content of Free Radicals. D. Reichelt. H.W. Renner, Diehl, Zbl. Vet. Med. B. 20: 648-660, 1973. Ref. # 307

EFFECTS:

Decreased body weights were seen in the first year but disappeared in the later generation.

EVALUATION:

After the animals received vitamin supplements no growth changes were seen. Vitamin A, E, and B levels were decreased in the milk powder. Decreased body weights appear to be a nutritional effect.

14. The Effect of Fresh Fish, Exposed to Gamma Irradiation on the Organism of Albino Rats. I Shillinger, I.N. Osipova, Voprosy Pitaniya 29: 45, 1970. Ref. # 330.

same study but published elsewhere

To Ascertain the Possibility of Toxic Properties in Irradiated Cod-fish and their Effects on Reproduction and Progeny when the Product is fed to Albino Rats. Fd. Irrad. Inf. (7) IAEA Suppl. pg. 151, 1977 (summary only;) #328

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EFFECTS:

Albumin/globulin ratio in blood was said to be decreased because of increased globulin fraction; changes in serum enzyme levels were seen, testicular atrophy, prolonged estrus cycles were seen.

EVALUATION:

Authors indicate that there was a 42% reduction in blood BCE activity in rats indicating protein deficiency. Protein deficiency may be due to reduced intake or decreased wholesomeness of fish, or perhaps to a change in the nutritional value of irradiated fish protein. The diet appeared very inadequate and no supplemental vitamins or minerals were given. Reproductive function indices were rather questionable. (a) frequency of activity of spermatozoa (measured in "arbitrary units",

(b) sperm resistance to a 1% solution of "cooking" salt, (c) testicular weight. No data were presented on their "offspring", or "births", or number of stillborn or survival rates or organ weights, etc., all of which were referred to in the text. Data from this study are of very questionable value.

15. Apollo Diet Evaluation: a Comparison of Biological and Analytical Methods including Bioisolation of Mice and Gamma Radiation of Diet.
Aerospace Med. 44: 888-901, 1973. T.D. Luckey, M.H. Bengson, M.C. Smith. Ref. # 198.

EFFECTS:

Anemia was seen in the irradiated diet-fed mice. Mice in bioisolation on irradiated diet appeared to grow slower.

EVALUATION:

The data were rejected for the following reasons.

A. The unirradiated Apollo diet (control diet) is deficient for mice in: phosphorous, calcium, iron, copper, cobalt, manganese, according to the authors. Vitamin deficiencies for mice in this diet also included riboflavin, thiamin, vitamin B₆, pantothenate, folate.

Since irradiation results in a loss of 11.2% of the riboflavin, 1.8% of vitamin B₆, 2.2% of the pantothenate. These deficiencies will be exacerbated in the irradiated diet. The diet is also marginal in some of the amino acids.

B. The inadequacies in the diet are reflected in the growth curves. At 42 days of age the average weight of mice on the Apollo diet was 22g. for males and females. Mice on control lab chow weighed 30g for males and 26g for females at that age.

C. Although the mice on irradiated diet, reared in bioisolation seemed to grow slower than non-irradiated controls (and irradiated Apollo diet, but reared in the open laboratory) in the first generation, this disadvantage was reversed in the second and third generation, where the irradiated diet-bioisolation reared mice were heavier than controls. (and irradiated diet, open laboratory reared)

D. This laboratory appears to have serious problems with fertility. Mice reared on untreated lab chow produced 7 litters (out of 12 females in study) with 34 mice weaned. Mice on autoclaved chow: pregnancy rate 5/12 with 14 mice weaned. The mice on Apollo diet (non-irradiated) produced 2 litters (out of 12 females) and 11 mice were weaned (One of these two litters died before weaning.) For the second generation 11 animals of the irradiated Apollo diet group were added to the remaining 11 weaned mice to form the non-irradiated diet control. Thus these animals were exposed to irradiated food in utero and during lactation.

E. The food efficiency data presented are invalid, because the animals on lab chow were already past their growth spurt, while

the animals on Apollo diet had an unusually large weight difference during the 4 days food intake was measured.
F. Hematology (Hgb and WBC) reflects an inadequate diet: low Hgb in all Apollo-diet groups, along with low WBC.
G. The inadequacy of the Apollo diet for mice and other irregularities in the protocol of this study, as pointed out, render the results of this study uninterpretable. The findings can be explained by the deficiencies of the diet.

16. Studies on the Wholesomeness of Irradiated Fish. J.R. Hickman, A.W. Law. F.J Ley. 1969, UK Atomic Energy Authority Technical Report AERE R-6015, 1969. Ref. # 138.

EFFECTS:

Reproductive organ atrophy was reported.

EVALUATION:

Tissues of the reproductive organs were not examined histopathologically in all animals. All animals were not run concurrently. Due to the limited availability of this substrain, it was not possible to obtain sufficient numbers at any one time, so mice were entered into the test as they became available. Considerable variation in weight was also noted upon arrival. Age at start of experiment was not accurately known. Female mice on irradiated diet may have been younger, since their initial weights were lower. Background testicular atrophy is unusually high, only the severity appears to be moderately increased in the irradiated foods group. Since no uteri were examined histopathologically, the so-called "increase" in uterine atrophy is not real. The evidence for reproductive organ atrophy is extremely weak.

17. A Comparison between Irradiated and Autoclaved Diets for Breeding Mice with Observations on Palatability. G. Porter, M. Festing, Lab. Animals 4: 203-213, 1970. Ref. # 274.

EFFECTS:

Fewer litters were produced with irradiated diet but the total number of animals weaned was about the same.

EVALUATION:

The difference was not significant statistically.

18. Ninety Day Rat Feeding Study on Irradiated Strawberries. H.G. Vekschuuren, G.J.. van Esch, J.G. van Kooy. Food Irradiation 7(1-2) A17-A21, 1966. Ref. # 274.

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EFFECTS:

Male rats that received 500 krad strawberry powder showed a statistically significant growth retardation.

EVALUATION:

The Data were rejected for the following reasons:

1. The groups which had basic diet mixed with 5% strawberry powder were on a restricted diet, resulting in a slower growth than the groups on gavage strawberry juice and ad lib basic diet. Growth (in groups 4,5 and 6) virtually stopped after 6 weeks on the diet (10 weeks of age) and the body weight of males (only) on a diet with 5000 krad irradiated strawberries actually dropped.
2. The investigators didn't insure adequacy of the diet. No vitamin or mineral mixtures were added to the basic diet. The growth retardation in males consuming 5000 krad strawberry powder (group 6) is therefore possibly due to destruction of a nutrient in an already marginal diet. It is not clear, however, why only males would be affected by this possible deficiency unless the males were challenged more than the females by the restricted intake. Hematology data are not supportive of an overall general deficiency.

19. Growth, Reproduction, Survival and Histopathology of Rats fed Beef Irradiated with Electrons. C.E. Poling et al. Fd. Res. 20: 193-214, 1955. Ref. # 272.

EFFECTS:

There were some effects on growth, feed efficiency, reproduction, adult body size and survival.

EVALUATION:

The data were rejected because of clinically evident vitamin E deficiency. Flb had high mortality shortly after weaning, but this condition may have been caused by Vitamin E deficiency. In the presence of no change in weight gain and zero weaning mortality, the decreased survival day 0-9 occurs for F2A experimental animals of 28%. It occurs but is not reproduced in any other litter or generation other than non-vitamin E supplemented flb and the effect is not reproducible.

20. Short-term Rat Feeding Studies with Gamma Irradiated Food Products. II. Beef and Pork Stored at Elevated Temperatures. M.S. Read, H.M. Trabosh, W.S. Worth, H.F. Kraybill, N.F. Witt. Tox. Appl. Pharm. 1, 417-425, 1959. Ref. #286.

EFFECTS:

Increased liver cytochrome oxidase was noted. This effect increases if the 2.79 Mrad irradiated beef is cooked before feeding.

EVALUATION:

The biological significance of this phenomenon is not clear. It may be associated with essential fatty acid deficiency, but this is probably not the cause in this experiment, since there are ample supplies of corn oil in the basic diet, and another symptom of EFA was not demonstrated (decrease in hypotonic endogenous respiration). In other studies, E.D. Wills (1978, Ref. # 390) reports a depression in drug metabolism and oxidase activities contrary to this effect.

21. Studies of Irradiated Food with Special Reference to its Lipid Peroxidase Content and Carcinogenic Potential. E.D. Wills. Technical Report to IFIP- R48, 1978. Ref. # 390.

EFFECTS:

Reduced growth rate at 400 krad dose was seen.

EVALUATION;

Reduced growth as well as reduced food intake was seen. Addition of BHT to oils before irradiation will restore normal growth. Study measured the increase in the oil's peroxide content from irradiation. The reduced growth and food intake probably correlated with increased oxidation and rancidity of the oil, making it less palatable. The results of reduced growth rate are very questionable.

22. To Investigate the Wholesomeness of Low-dose Irradiated Strawberries in Poultry. P.O. Nees, Fd. Irrad. Ins. (6) IAEA Suppl. pg. 131-2, 1976. Ref. # 252.

EFFECT:

At 300 krad there was poor performance by the first hatch chicks. (performance meant egg reproduction, fertility of eggs, embryo survival and hatchability.)

EVALUATION:

The authors claimed that protein deficiency involving methionine inadequacy in the strawberry-supplemented starter rations was the factor behind the poor performance in the first hatch chicks of the parent generation. The report was a two page summary, and evaluation of the data is impossible. Reproduction in two mammalian species (rat and dog) was not affected in studies done by the same laboratory Refs #149 and 151)

23. Gamma Ray Irradiation to Semi-purified Diet, Peroxide Formation and Its Effects on Chicks. A. Takigawa, H. Danbara, J. Ohyama, Jap. J. Zotech. Sci. 47: 292-302, 1976. Ref. # 344.

EFFECTS:

1. Decreases in feed consumption and feed efficiency were seen in the 3 and 6 Mrad groups.
2. Increases of % organ wt/body wt in liver, pancreas, intestines and gizzard were seen, but decreases of the ratio in spleen in the 3 and 6 Mrad groups were also seen.
3. Increases of hemolysis and fragile erythrocytes in 0.6 and 3 Mrad groups were seen, but not in the 6 Mrad group.
4. Encephalomalacia was found in 2 chicks of the 3 Mrad group.

EVALUATION:

1. The increase in organ wt/body wt ratios may be due to decreased body weights. There was no difference in absolute organ weights.
2. Encephalomalacia occurred in 1 control chick, 2 chicks in the 3 Mrad group and 0 chicks in the 6 Mrad group. This problem does not appear to be irradiated-food related.
3. Increases in hemolysis and fragile erythrocytes is not irradiation-dose related and also occurs after high-oxidized oil ingestion.
4. Symptoms are probably due to peroxidation of soybean oil in the diet. Whole diet + soybean oil, when irradiated together, was shown to have greater peroxide formation, probably due to the increased surface area and oxygen availability. Decreased body weights and food consumption are most likely associated with a palatability problem due to peroxide formation.

24. Nutritional and Biochemical Effects of Irradiation. R.R. Becker, H.C. Kung, N.F. Barr, C.G. King, 1956. Food Technol. 10, 61, 1956. Ref. #33.

EFFECTS:

The reproductive performance of experimental animals was below that of the control group. The difference for the first generation was higher than that for the second or third generation.

EVALUATION:

There was no non-irradiated food control (butterfat + skim milk) to compare the irradiated food group with. It also appears that littermates were mated. Female animals were mated almost continuously, allowing very little time for rest between litters. If there was a nutrition or oil peroxidation and palatability problem with the diet, this would be exacerbated by the continuous breeding of the females. There were fewer litters in the irradiated foods group, however the number of pups born was approximately the same. There were slightly more pups/litter in the irradiated foods group. It is impossible to say if the second generation was from the first litter or from subsequent litters.

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25. Safety of Irradiated Fats, K. Lang. Zernahrungswiss 2: 141-6, 1962. Ref. #182.

and:

26. Toxicity of Irradiated Fat, K. Lang. Food Cosmet. Toxicol. 1: 125, 1963. Ref. # 183.

EFFECTS:

Increased mortality was seen that was claimed to be dose-dependent in rats starting at ten Mrad. Doses were 2.5, 10, 50, 100 Mrep of beta rays. There was decreased growth at 50 Mrep and higher, with liver, thyroid, and heart function affected.

EVALUATION:

It is impossible to evaluate this study because effects are mentioned in the text but not substantiated with data. These effects were seen at the higher doses (10 Mrep or higher). No-effect dose was 2.5 Mrad. The radiation doses except for 2.5 Mrad were higher than we considered suitable for evaluation.

27. The Long-term Effects of Irradiated Foods upon Rats with Special Reference to Tissue Enzyme Systems. N.F. Witt, et al. 1955-1961 Contract Report DA 49-007-MD-549. Ref. # 393.

and:

Successive Generation Rat Feeding Studies with a Composite Diet of Gamma -irradiated Foods. M.S. Read, H.F. Kraybill. et al. Tox. and Appl. Pharm. 3: 153-173, 1961. Ref. # 291A.

EFFECTS:

Increased liver cytochrome oxidase was seen in all generations except for the 4th.

EVALUATION:

Unexplained breeding problems in the control animals may point to a dietary origin. Litter data of the first and second (and third in some cases) was lumped together. It was not possible to make a distinction between the first and second litters of each generation. There was a high incidence of stillborn litters in the F1 controls: (12/43). There was a high incidence of litters dying during lactation in controls and experimentals. These problems point to dietary problems. Final report and published paper based on data from the final report (ref # 291A) do not have data that agree. Methodology described in interim reports is contradicted by the final report. Data are too haphazardly reported to be adequately evaluated.

28. The Effect of Feeding Irradiated Flour to Dogs: II. Reproduction and Pathology. E.F. Reber, O.P. Maihotra, J. Simon, J.P. Krier, et al. Tox. Appl. Pharm. 3, 568-573, 1961. Ref. # 297.

EFFECTS:

Subacute to chronic thyroiditis was seen with atrophic acini. This effect appeared to increase with increasing radiation dose.

EVALUATION:

The groups were too small (2/sex/dose) to give statistical significance. There were difficulties in whelping. Apparently one litter in the control group and one litter in the low dose group got lost. There also appears to be a problem with lactation, because a high number of pups died before weaning. This effect was not related to irradiation. Chronic thyroiditis is not unusual in Beagles, and is therefore impossible to classify as a toxic response.

29. Growth and Fertility of Mice fed an Irradiated Diet for Two years. C. Biagini, et al. G. Med. Milit. 117, 347-368, 1967. Ref. # 42.

EFFECTS:

Decreased growth and fertility were seen.

EVALUATION:

The reduction in growth difference is less than 10%. Fertility problems appear to be nutritional and the investigators didn't rotate the males to non-pregnant females. It also looks like there was a palatability problem with the diet.

30. Long-term Dog Feeding Tests on Irradiated Green Beans and Fruit Compote: Final Report. P.S. Larson and H.B. Haag. FAP 6M 1833, vol. 2 pg. 256-296. Ref. # 184.

EFFECTS:

Irradiated fruit compote caused increased spleen weights in the two doses tested.

EVALUATION:

The study was rejected because there were too few animals (2/sex/group) to have any meaningful evaluation of the data. Statistics could not be done on such small group sizes, and spleen weights varied within each group. Authors claimed that spleens varied widely in weight and this at time of autopsy was interpreted as related to the amount of blood which bled out at the time of sacrifice. Histologically the only consistent difference noted between the heavier and lighter spleens was the degree of congestion of the pulp and did not appear to be the result of intrinsic changes.

31. Growth, Reproduction, Mortality and Pathologic Changes in Rats Fed Gamma-irradiated Potatoes. Brownell, L.E., Burns, C.H., Abrams, G.O., Army Contract Report No. DA-49-007-MD-581, 1959. Ref. # 56.

and

Necrotizing Arteritis in Rats used in a Toxicity Study of Irradiated Potatoes. Burns, G.H., Abrams, G.D., Army Contract Report # DA-49-007-Md-581, 1961. Ref. # 65.

EFFECTS:

Increased mortality was seen with irradiated potatoes among the males of the first generation and among both sexes of the second generation. There was claimed to be a decreased pregnancy rate and low birth rate for females on the IX diet. Pathologic changes were seen in the vasculature with increased pneumonia, with major lesions in the colon. Other digestive lesions such as intestinal nephritis were seen, along with prostatic changes, skin and muscle changes in the irradiated potato group.

EVALUATION:

The study has a number of deficiencies that make the results less than acceptable.

1. The level of decay of the potatoes fed was directly associated with the dose level of irradiation, and the potatoes were considered to be in poor condition.
2. There appeared to be a rather high level of vitamins and minerals fed, and the diet was changed during the experiment. After one year thiamine and biotin levels were increased.
3. There was a very serious lack of agreement between the pathology reports of the U. of Michigan and the Armed Forces Institute of Pathology on the same slides and animals on test.
4. The pathologic changes and the increased mortality were said to be attributed to necrotizing arteritis. The increased mortality in the 1st generation males was said not to be significant as measured by the Student Fisher T test and the 2nd generation females who showed increased mortality were by that time already off irradiated diet.
5. The second study (ref # 56), which examined necrotizing arteritis, showed about a 50% incidence, and the animals in the initial study showed a similar incidence, suggesting the possibility of some genetic influence.

32. Studies done at the National Institute of Nutrition, in Hyderabad India claimed to have found polyploidy in animals and children who were fed freshly irradiated wheat. These reports along with the slides and raw data were examined by a special commission of the WHO. Their final report is attached refuting the finding of increased polyploidy.