Packet 2

DEPARTMENT OF HEALTH & HUMAN SERVICES — Public Health Service

Memorandum

Date December 14, 1988

From Group Leader, IIMS Group
Standards and Monitoring Branch (HFF-156)

Subject FAP 7M-3971; Safety of irradiating poultry products at levels of 1.5-3 kGy (150-300 kRad). Related Petition: 8M-3422.

To George Pauli, Ph.D.
Food Additive Policy Staff (HFF-330)

FOOD ADDITIVE PETITION No.7M-3971 — Food Safety and Inspection Service, USDA
Washington, D.C. 20250

At your request, I have collected all information present in our files pertaining to the safety of irradiated chicken in order to re-evaluate the safety of irradiating poultry products at levels up to 3 kGy (300 kRad) as petitioned in FAP 7M-3971. (See also my memo of February 11, 1986.)

The following studies were used for this evaluation (numbers at the beginning of the title refer to the reference number in the review of FDA's Irradiated Foods Task Force):

A. Subchronic and chronic feeding studies in rats, mice and dogs:

= 97: Multi-generation study in rats with radiation-pasteurized chicken; De Knecht-van Eekelen, A.; Van der Meulen, H.C.;Til, H.P.& de Groot, A.P.; 1971; CIVO Tech.Report R3622.

This multigeneration reproduction study in rats fed diets with 35% chicken irradiated up to 6 kGy (600 kRad) was well conducted and did not show any adverse effects of feeding irradiated chicken on reproduction parameters. A 90-day subchronic study performed with third generation offspring reported slight changes in heart, liver and kidney weights and a decrease of serum glutamic-pyruvic acid transferase (SGPT) and alkaline phosphatase (AP). These observations were not considered to be of toxicological significance.
The Agency requested, received and reviewed the working sheets of individual animal observations (including histopathology). These records were not useful for verification of the reported results. However, in view of the excellent reputation of the performing laboratory, and the excellent design of the study DTRE considers this study acceptable as part of the safety evaluation.

this study was resolved by the Director of the Canadian General Food Directorate in a letter to Dr. Sanford Miller (Jan. 9, 1987) as being based on a typographical error. The incidence of liver pathology in the final report was not related to the ingestion of irradiated chicken. In the final analysis the study was considered to be adequate to support the safety of irradiated chicken.

= 16 Irradiated sterilized chicken meat: A chronic toxicity and reproductive performance study in Beagle dogs; Ralston Purina; 1982; FMF00239,V.30,p.26609.

I have not been able to locate a review memo on this 999 day dog study with diets containing 35% chicken irradiated up to 59 kGy (5900 kRad). However, on the "longform" of the Irradiated Foods Review Task Force, the restriction of the feeding for preventing obesity was considered by the reviewer to be a compromising factor. Dogs consuming irradiated chicken developed increased levels of serum globulin and some had ocular abnormalities. The toxicological significance of these findings has not been established. The high protein content of the diet may be related to the changes in globulin levels. No effects were noted on reproductive performance of the dogs.

= 231 One-year feeding study with low-dose irradiated chicken in Beagle dogs; Til, H.P.;Willems, M.I.;Huismans, J.W. & de Groot, A.P.; 1971; Tech.Rep.CIVO R3443.

Dogs were fed a diet with 35% chicken irradiated up to 6 kGY (600 kRad) for 1 year and were found to be free of adverse findings due to feeding of irradiated chicken. The individual data sheets of this study were reviewed and found to support the absence of adverse effects.

Special Study on potential Thiamine deficiency:

= 218 Investigation of possible antithiamin properties in irradiation sterilized chicken; McGown, E.L.; Lewis, C.M. & Waring, P.P.; 1979; Contract DL-47.

This special study was designed to evaluate whether rats fed a diet with 35% chicken irradiated at 47 kGy (4700 kRad) would develop signs of thiamine deficiency. The activity of the thiamine dependent enzyme transketolase in erythrocytes was not significantly altered by feeding rats diets with irradiated chicken indicating that the rats' thiamine status was sufficient. However, since the duration of this study was not reported this finding is of limited value for our safety evaluation.

B. Teratological Studies:

= 90 Animal feeding study for irradiated sterilized test foods: hamster teratology study: Dahlgren, R.R. et al.; 1980; Contract DAMD17-76-C-6047.

Feeding diets with 35% chicken irradiated up to 45 kGy (4500 kRad) to hamsters during organogenesis did not result in developmental abnormalities in the offspring. This study was reviewed in-depth and was found to be of good quality.

= 90 Irradiated Chicken rabbit teratology study; Dahlgren, R.R.; 1978; Contract.

This negative teratology study in rabbits fed chicken irradiated up to 45 kGy (4500 kRad) was reviewed in-depth and was found to be of good quality.

= 353 Mouse teratology study; Thomson, G.M.; Dahlgren, R.R. et al.; 1977; Contract DAMD-76-C-6047.

This negative teratology study in mice fed 35% of their diet with chicken irradiated up to 45 kGy (4500 kRad) was of limited value due to procedural flaws (see memo Tom Collins, March 9, 1988)

= 79 Teratology study with gamma or electron irradiated chicken meat in rats: Christopher, J.P.; 1983; Contract Report.

This teratolgy study was reviewed in-depth and, although sacrifice was performed 1 day early (day 20 of gestation), no evidence of teratogenicitywas found. The study therefore supports the absence of teratogenicity.

C. Potential for Genetic Toxicity:

= 45 Dominant lethal study; Black, C.M. et al.; no date reported; Contract.

This dominant lethal study in mice fed 35% of their diet as irradiated chicken was rejected, because no irradiation dose was reported and because the positive control (triethylenemelamine) was found to be negative.

= 199 Evaluation of the mutagenicity of irradiated sterilized chicken by the sex-linked recessive lethal test in Drosophila melanogaster; Lusskin, R.M.; 1979; Contract Rep.

Raising Drosophila on a medium containing extracts of chicken irradiated at doses up to 55.8 kGy (5580 kRad) resulted in a decrease in the number of offspring. However, the control with extracts of unirradiated chicken was also toxic to Drosophila (see memo Benz, November 8, 1988). The

implications of these observations for mutagenic potential of irradiated chicken is unclear. The test is considered to be negative for sex-linked recessive lethal mutations.

= 15 Application of the Ames Mutagenicity test for the assessment of mutagenic activity of thermally processed, frozen, electron irradiated, and gamma irradiated chicken; Anon; 1980; Contract PAMD17-76-C-6017.

A well conducted Ames test with extracts from chicken irradiated at levels up to 59 kGy (5900 kRad) with negative results.

= 265 An investigation of genetic toxicology of irradiated foodstuffs using short-term test systems. I. Digestion in vitro & testing of digests in the S.Thyphymurium mutation test; Phillips, B.J.; Kranz, E. & Elias, P.S.; 1980; Fd Cosm.Tox. 18:371-375.

Water extracts of irradiated chicken (dose 7 kGy, equivalent to 700 kRad) did not have mutagenic acitivity. The in-depth review of this study raised questions about the procedures used in this study; e.g., not all test strains were subjected to adequate positive controls, and the high protein content of the extracts may be a compromising factor for this test. (see memo M.J.Prival, May 9, 1986).

= 266 An investigation of genetic toxicology of irradiated foodstuffs using short-term test systems. II. Sister chromatid exchanges and mutation assays in cultures CHO cells; Phillips, B.J.; Kranz, E. & Elias, P.S.; 1980; Fd Cosm. Tox.18:471-475.

Although negative, this study was considered to be flawed by experimental design and cannot be used for support of non-mutagenicity (see Memo ofMoreland to Dunkel, March 28, 1986).

= 305 In vivo mutagenicity testing of irradiated chicken, fish and dates; Renner, H.W.; 1980; Contract Rep.#78/1

Chicken irradiated at 7 kGy (700 kRad) and fed to rats, mice or hamsters for 3 days (100% of diet) did not cause increases in micronucleated bone marrow cells. Sister Chromatid exchanges (SCE) in bone marrow cells of mice and hamsters as well as SCE in spermatogonia of mice were studied and were shown not to be affected by the irradiated chicken diet (see Memo of May 19,1986).

Summary

In summary, 15 different types of studies with diets containing irradiated chicken at different radiation dose levels, ranging from 6 to 59 kGy (600 to 5900 kRad) are available to support the safety of irradiated chicken.
The following table summarizes the studies that are available in our files for support of the safety of irradiated chicken:

no	study	species	duration	radiation dose kRad	effects
97	subchronic/repro	rat	90	600	none
98	chronic	rat	730	600	none
79	chronic/repro	mouse	730	5900	kidney Ca
277	chronic	mouse	580	700	none
16	chronic/repro	dog	999	5900	serum glob.
354	chronic	dog	365	600	none
218	subchr./special	rat		4700	none
90	teratology	hamster	5	4500	none
90	teratology	rabbit	14	4500	none
353	teratology	mouse	18	4500	none
79	teratology	rat	20	5900	none
199	mutation	Drosophila	5	5580	extract toxic
15	Ames	S.thyphim	0	5900	none
265	Ames	S.typhim	2	700	none
305	SCE/micronuc/spe	rat,mouse	4	700	none

The above studies were thoroughly reviewed and when necessary individual animal data or microscopic slides were reviewed by FDA scientists. We have not identified any studies that indicate adverse reactions to the consumption of irradiated chicken up to a radiation dose of 59 kGy (5900 kRad). It has been established that the formation of radiation products has a linear relationship to the radiation dose (Bureau of Foods Irradiation Committee Report, 1981). The innocuousness in animal studies of chicken irradiated at doses up to 59 kGy (5900 kRad) Provides sufficient evidence for the safety of irradiating poultry at the petitioned level up to 3 kGy (300 kRad).

Therefore, DFFE believes that the use of ionizing radiation of chicken at levels not to exceed 3 kGy (300 kRad) does not raise toxicological concerns.

Pertinent memoranda mentioned in this review, and not present in your file, are attached.

12/14/88

Hiltje Irausquin, Ph.D.

INIT:CJKokoski 12/14/88

cc:
HFF-100
HFF-152
HFF-156
HFF-158
HFF-415

HFF-156:HIrausquin:472-5767:hir:FW-ii:MemoV:Chicken:12/9/88:
final:12/14/88

DEPARTMENT OF HEALTH & HUMAN SERVICES — Public Health Service

Memorandum

Date December 11, 1998

From SCIENTIFIC SUPPORT BRANCH (HFS-207)

Subject Evaluation of the Use of Approved Sources of Ionizing Radiation as a Physical Process for the Pasteurization of Fresh Shell Eggs to Kill Salmonella

To REGULATORY POLICY BRANCH (HFS-206)

ATTENTION: WILLIAM J. TROTTER

FAP 8M4584
Vol 1-4

Food Science and Nutrition Research Center
University of Rhode Island, West Kingston
Rhode Island 02892-1802

Edward S. Josephson, Ph.D. (Professor, Food Science and Nutrition Research Center, University of Rhode Island) has submitted a petition requesting that 21 CFR part 179 of the food additive regulations be amended to allow the use of approved sources including ^{60}Co, ^{137}Cs and X-rays up to 5MeV of ionizing radiation as a physical process for the pasteurization of fresh shell eggs to kill Salmonella enteritides. Eating of raw or undercooked eggs has been cited as the primary cause of human infection with this pathogen. The stated purpose of irradiating fresh shell eggs is to reduce the incidence of foodborne illness and to prevent loss of human life due to Salmonella food poisoning. The radiation dose range given in the petition is from 0.7 to 1.7 kGy.

Toxicological Safety Information of Irradiated Eggs Submitted by the Petitioner

The petitioner submitted a large number of published articles and study reports containing data and information related to eggs and other kinds of food in the areas of radiation chemistry, toxicology, nutrition, microbiology and economics (see attachment Table 1). The petitioner submitted several of these articles/information to establish that many of the outbreaks of illness caused by Salmonella enteritidis in the United Kingdom and in the United States (especially in northeast and mid-Atlantic areas of US) were due to the consumption of raw or undercooked eggs. Some of these eggs were even uncracked and sanitized Grade A eggs. To control or reduce the number of Salmonella organisms in eggs is one of the methods to reduce food poisoning in both healthy and immune-compromised individuals.

No conventional animal toxicity feeding studies on irradiated eggs were submitted in the petition. The petitioner's argument for the toxicological safety evaluation of irradiated eggs is based on international reports and reviewed articles. We have reviewed the

when performed in accordance with good manufacturing practice... " (see Irausquin memo of 4/20/95). FAP 4M4428 was approved and the final rule was published in the Federal Register (12/3/97).

Additional Toxicological Safety Information

We further checked the Agency's file and the WHO Report entitled "Safety and Nutritional Adequacy of Irradiated Food" (1994). A variety of irradiated foods including red meat, chicken, fish, eggs, etc. had been tested in the earlier animal feeding toxicity studies, in nutritional studies, as well as in genotoxicity studies. The study designs and parameters measured varied in these studies; in some cases, the research was designed to test several different irradiated foods simultaneously. In the evaluation of individual studies by different FDA reviewers, some of the earlier individual study reports can not stand alone to provide definitive answers, however, taken together as whole, these studies present a consist finding of no harm when irradiated foods were tested in animal feeding studies and genetic toxicity studies (see OPA, Hattan memo of 11/20/97).

Among these studies, three studies/reports, directly relevant to this petition for irradiated eggs, were identified and further evaluated (see FDA's file "Data Summary Form for Irradiated Foods # 175, 238 and 239). In these studies, irradiated eggs were fed the testing animals in the diet, they are:

1. An article entitled "Establish the Toxicological Safety of Feeding Whole (Irradiated) Eggs to Rats throughout their Life-span" by Morre (1974).

This study was conducted in Laboratoire Central de Recherches Veterinaries, Paris, France. In this study 10 to 30 rats/sex/group were fed to a diet containing irradiated whole eggs (0.5 Mrad) at 25% dry weight base as biscuits for two generations (1080 days). The author concluded that no significant findings in the test animals and irradiated whole eggs in diet did not affect their health as compared to animals fed with non-irradiated eggs. This study was reviewed by FDA previously and the study was accepted, although "with reservation" because it was only a summary report (Khalsa of 1/7/82). Nevertheless, the reviewer found no basis for disagreement with the author's conclusions, indicating that "no adverse effects in any generation" were found in this study.

2. A report entitled "The Possible Carcinogenicity of Irradiated Foods" by Kline and Teply (Final Report-Dept. of Army, Office of the Surgeon General, Contract No. DA-49-007-MD-583, 1959) was conducted in Laboratories of the Wisconsin Alumni Research Foundation.

In this study 48 mice/group (sex not specified) and 20 Sprague Dawley rats/sex/group

were fed a diet containing irradiated pork brain and dried eggs (at 9.3 Mrad) for a period of 15 months. The investigator concluded that no carcinogenic effect could be attributed to the irradiated food preparations (including irradiated eggs). This study was reviewed previously by FDA and "rejected" (Van Gemert of 1/6/82). The reason for "rejection" was that there were many studies in the report and each study was not clearly stated and, thus, hard to follow. However, as we have indicated, in some of the earlier toxicity studies, the research was designed to test several different irradiated foods simultaneously. Even though some of these earlier individual study reports can not stand alone to provide definitive answers, taken together as a whole, these studies present a consist finding of no harm when irradiated foods were tested in animal feeding studies and genetic toxicity studies (see OPA, Hattan memo of 11/20/97). Nevertheless, the reviewer indicated that "no effects" attributable to irradiation were found in these particular studies of irradiated pork brain and eggs.

3. A study entitled "Acute and Chronic Toxicity Study of Frozen Canned Eggs Irradiated at 0.5 Mrad" by Morre (1972) was conducted in Laboratoic de Radiobiologic Paris, France.

Thirty rats/sex/group were fed canned irradiated eggs in the diet for two generations (in lifespan). This study was reviewed previously and accepted (Irausquin of 2/12/82). However, this study was identified as a weak study because only a few toxicological parameters were measured and reported, and no histopathology data available. Thus, the data were not suitable for evaluation on carcinogenicity of irradiated eggs. Nevertheless, the reviewer indicated that "no effects" attributable to irradiation were found in these studies.

In summary, all of the submitted review articles regarding toxicity studies were based on more or less the same data base, in which most of the toxicity feeding studies were conducted on a variety of irradiated foods. Only a few reports describe studies conducted specifically on irradiated eggs. In review some of these individual study reports considered in isolation, may not be able to stand alone to provide definitive answers. However, taken together, the totality of evidence from these data/studies indicates that irradiated foods present no harm when tested in animal feeding studies (see OPA, Hattan memo of 11/20/97) and supports a conclusion that the petitioned use of irradiation on fresh shell eggs is safe.

In addition, irradiated whole and powder eggs or egg products at dose range from 3 to 10 kGy were approved in Croatia (from 1994), France (from 1990), Mexico (from 1995), South Africa (from 1989) and Yugoslavia (from 1984). This information was based on Food Irradiation Newsletter (Joint FAO/IAEA Division of Nuclear Techniques in Food

DATA SUMMARY FORM FOR IRRADIATED FOODS Ref # 238

I. Study Identification

a. Study Title Establish The toxicological safety of feeding (irradiated) whole eggs to rats throughout their life-spa

b. Author's name/ Date Morre J., 1974

c. Type of Report Published. Fd. Irrad. Inf. (3) IAEA, Suppl. p. 4

d. Reviewer/ Date of Review L. H. Khalsa, 1/7/82. MVB 1-28-82

e. FAIS Document Type & Number loose file (# 201)

f. Testing Facility/ FAIS # DIRECTION DES SERVICES VETERINAIRES, LABORATOIRE CENTRAL DE RECHERCHES VETERINAIRES, PARIS

g. Preliminary Evaluation Accept, with reservation although it is a summary.

h. Reason for Rejection Abstract only

i. Summary of Effects/ Irradiation Dose No adverse effects in any generation.

Comments

II. Experimental Design Life time Study.

a. Test Type/ Date/ FAIS Test Name Code

b. Test Subject Species/ FAIS Test Subject Code Rats.

c. Test Subject Strain Wistar Rats.

d. Test Duration, Specified in Days 1080

e. Group Size/ Sex 10-30/sex/gr. Groups (i) 10/sex – Normal diet rat
(ii) 30/sex – Non-irrad. diet – Eggs
(iii) 30/sex – irrad. eggs at 2.5% etc
(iv) 20/sex (F_1) .. .. ..
(v) 30/sex (F_2) .. .. ..
(vi) 16/sex (F_1 + ve control) | Non-ir
(vii) 30/sex (F_2 + ve control)

f. Irradiation Conditions:

- Type of Food Irradiated Eggs
- Dose and Source 0.5 ~~krad~~ Mrad Cs^{137} – (γ-irradiation)
- Time after Irradiation
- Atmosphere Nitrogen atmosphere at ambient temp.
- Temperature Stored as frozen, subsequently as biscuits packed in polyethylene bags and stored in a Nitrogen atmosphere at ambient temp.

Ref # 175

DATA SUMMARY FORM FOR IRRADIATED FOODS

I. Study Identification

a. Study Title THE POSSIBLE CARCINOGENICITY OF IRRADIATED FOODS

b. Author's name/ Date KLINE, B.E. TEPLY, L.J. DEC. 1959

c. Type of Report FINAL REPORT - DEPT OF ARMY, OFFICE OF THE SURGEON GENERAL - CONTRACT NO. DA-49-007-MD-583

d. Reviewer/ Date of Review M. VAN GEMERT 1-6-82

e. FAIS Document Type & Number FAP3M0890 Vol. 3 pg 925

f. Testing Facility/ FAIS # WISCONSIN ALUMNI RESEARCH FOUNDATION U. OF WISCONSIN

g. Preliminary Evaluation Reject

h. Reason for Rejection Summary of many studies

i. Summary of Effects/ Irradiation Dose NO effects

Comments

II. Experimental Design

a. Test Type/ Date/ FAIS Test Name Code Chronic

b. Test Subject Species/ FAIS Test Subject Code Mice, Rats

c. Test Subject Strain Sutter Swiss, C_3H JAY, SPRAGUE DAWLEY

d. Test Duration, Specified in Days NR

e. Group Size/ Sex 48-60/group, Sex not specified

f. Irradiation Conditions:

- Type of Food Irradiated PORK BRAIN, EGGS, fish, cheese, milk, Veg. oil, Sterol conc.
- Dose and Source krad/ Mrad
- Time after Irradiation NR
- Atmosphere NR
- Temperature NR

2 French

DATA SUMMARY FORM FOR IRRADIATED FOODS

Ref # 239A

I. Study Identification

a. Study Title: Acute and chronic toxicity of frozen, canned eggs irradiated at 0.5 Mrad

b. Author's name/ Date: J. Moore et al (1972)

c. Type of Report: Published literature: Revue gén. Froid 63: 805-13

d. Reviewer/ Date of Review: Dr. Hiltje Irausquin 2/12/82 Hi. 3/22/82

e. FAIS Document Type & Number: Loose File # 258

f. Testing Facility/ FAIS #: Laboratoire de Radiobiologie à Paris XVème

g. Preliminary Evaluation: accept / ~~reject~~ weak study

h. Reason for Rejection: only a few parameters studied; data presentation not suitable for evaluation

i. Summary of Effects/ Irradiation Dose: none | For carcinogenicity or histopathology no data available

Comments

II. Experimental Design

a. Test Type/ Date/ FAIS Test Name Code: Chronic / 03 (reproduction/14 oncogenicity/12)

b. Test Subject Species/ FAIS Test Subject Code: rat /110

c. Test Subject Strain: Windsbar

d. Test Duration, Specified in Days: 2-gen. - lifespan

e. Group Size/ Sex: 30 M, 30 F

f. Irradiation Conditions:

- Type of Food Irradiated: egg
- Dose and Source: 0.5 ~~krad~~/ Mrad ^{137}Cs
- Time after Irradiation: NR
- Atmosphere: NR
- Temperature: NR

NAME OF PETITIONER: *Food Irradiation Coalition*

ADDRESS: National Food Processors Association
1350 I Street, NW Suite 300
Washington, DC 20005

DATE: August 23, 1999

NAME OF FOOD ADDITIVE: Approved Sources of Ionizing Radiation

PROPOSED USE: Treatment of certain refrigerated, frozen or dried human food products derived from meat, poultry, fruits or vegetables to help control microbial pathogens and infectious protozoa, with a concomitant reduction in numbers of common spoilage microorganisms, thereby inactivating harmful microorganisms and extending shelf-life of subject products.

EXPEDITED REVIEW: Petitioner believes its petition meets the criteria for expedited review delineated in the agency's guidance document entitled "Food Additive Petition Expedited Review -- Guidance for Industry and Center for Food Safety and Applied Nutrition Staff" (Jan. 4, 1999).

Petitions Control Branch
Food and Drug Administration
Dept. of Health and Human Services
Washington, D.C. 20204

Dear Sir or Madam:

The undersigned, ***Food Irradiation Coalition*** submits this petition pursuant to section 409(b)(1) of the Federal Food, Drug, and Cosmetic Act with respect to the approved sources of ionizing radiation for the treatment of human foods consisting of (a) edible tissue of animal food sources, or (b) plant material (including seeds, sprouts, and the expressed or extracted juices of fruit or vegetables used as a beverage), with or without other approved food additives and ingredients to help control illness-causing microbial pathogens (e.g., *Bacillus cereus, Clostridium perfringens, Campylobacter jejuni, Escherichia coli* O157:H7, *Listeria monocytogenes, Salmonella spp.* and *Shigella spp., Staphylococcus aureus* and *Yersinia* spp.) and infectious protozoa (e.g., *Cyclospora cayetanensis* and *Cryptosporidium parvum),* thereby reducing related incidents of foodborne illnesses and loss of life. Further, achieving this primary objective of pathogen control can also be expected to result in the concomitant extension of nonfrozen (i.e., refrigerated) edible-marketable life. The shelf-life extension results from the simultaneous reduction in numbers of the non-pathogenic spoilage microflora that are common to such food materials, thus delaying the onset of typical, recognizable spoilage patterns by a matter of days to a week or more in the dose ranges of interest and under existing and anticipated packaging, handling, marketing and distribution/display systems.

b.) Toxicological Significance

i.) Processed Meat and Poultry

Toxicologically, chemical compounds formed during food irradiation at doses up to 10 kGy are insignificant and are the same as those already found in small quantities in foods or as formed during traditional processes like heating and drying. (WHO, 1994). As with heating and drying, radiolytic products formed increase with dosage. Thus, frozen foods have fewer radiolytic products than those irradiated at room temperature. This accounts for the often preferred utility of irradiation under low temperature conditions, reduced oxygen, or in the presence of antioxidants (WHO, 1994).

Radiolytic products of any food product irradiated up to 10 kGy have been determined by the Joint Food and Agriculture Organization of the United Nations/International Atomic Energy Agency/WHO Expert Committee on the Wholesomeness of Irradiated Food (WHO, 1980) to be toxicologically insignificant. The Committee's opinion was based on a multitude of animal feeding studies carried out on different classes of food and on the evaluation of the chemical compounds formed by the irradiation of the principal components of food. The Committee also reviewed the results of studies of multi-generational animal colonies reared on irradiated diets either sterilized at 25-44 kGy or treated to destroy pathogens at 15 kGy. (WHO, 1994).

The WHO Report of 1994 concludes that radiolytic products of foods have been well-investigated toxicologically, and the database indicates no adverse effects in the radiation doses tested. The Joint Committee has reiterated its position (WHO, 1997) that food irradiation will not lead to toxicological changes adverse to human health and will not lead to nutrient losses that have adverse health effects. The WHO position on lack of unique, adverse radiolytic products in irradiated food has also been expressed in the review of Crawford and Ruff (1996). They note that low to medium doses of irradiation have little negative effect on vitamins and other nutrients. Further, they cite that world-renowned scientists, health organizations, and agencies agree that radiolytic products formed during the irradiation process pose no danger to human health. Crawford and Ruff conclude that at doses up to 10 kGy, irradiation of food is safe and effective.

A positive effect of irradiating bacon at 3 Mrad (30 kGy) was noted by Fiddler, Gates, Pensabene, and Wierbicki (1980): the reduction of residual nitrite prior to frying so that less nitrosation of residual amine occurred. Dixon (1961) tested for formation of toxic or carcinogenic compounds in fat of irradiated bacon. Mice were fed the lipids of irradiated (56 kGy) and fried bacon fat such that this constituted 20% of their diet. There was no significant difference between mice eating lipids of unirradiated bacon or irradiated bacon. Kraybill et al, (1956) reported investigating irradiated foods (at commercial processing dosage and twice that level) that included ground beef, fresh ham, sliced bacon, green beans, sliced beets, frozen strawberries, and sliced peaches as dry solids fed to rats. The diets were satisfactory as far as growth and feed efficiency and were non-toxic based on the 8 week trial and diet continuation through two successive generations. A feeding study by Blood et al (1966) showed that rats could be fed up to two years on irradiated beef as dry solids with no adverse effects as evidenced

by growth, hematologic change, food efficiency, reproduction, mortality, and pathology. Genetic toxicology on irradiated, cooked chicken (7 kGy) and dried dates (1 kGy) has been studied in small rodents and *Drosophila melanogaster* by Renner et al (1982). None of the tests provided any evidence of toxicity induced by irradiation. Elias (1989) has written a good review of animal feeding studies and mutagenicity testing.

ii.) Fruits and Vegetables

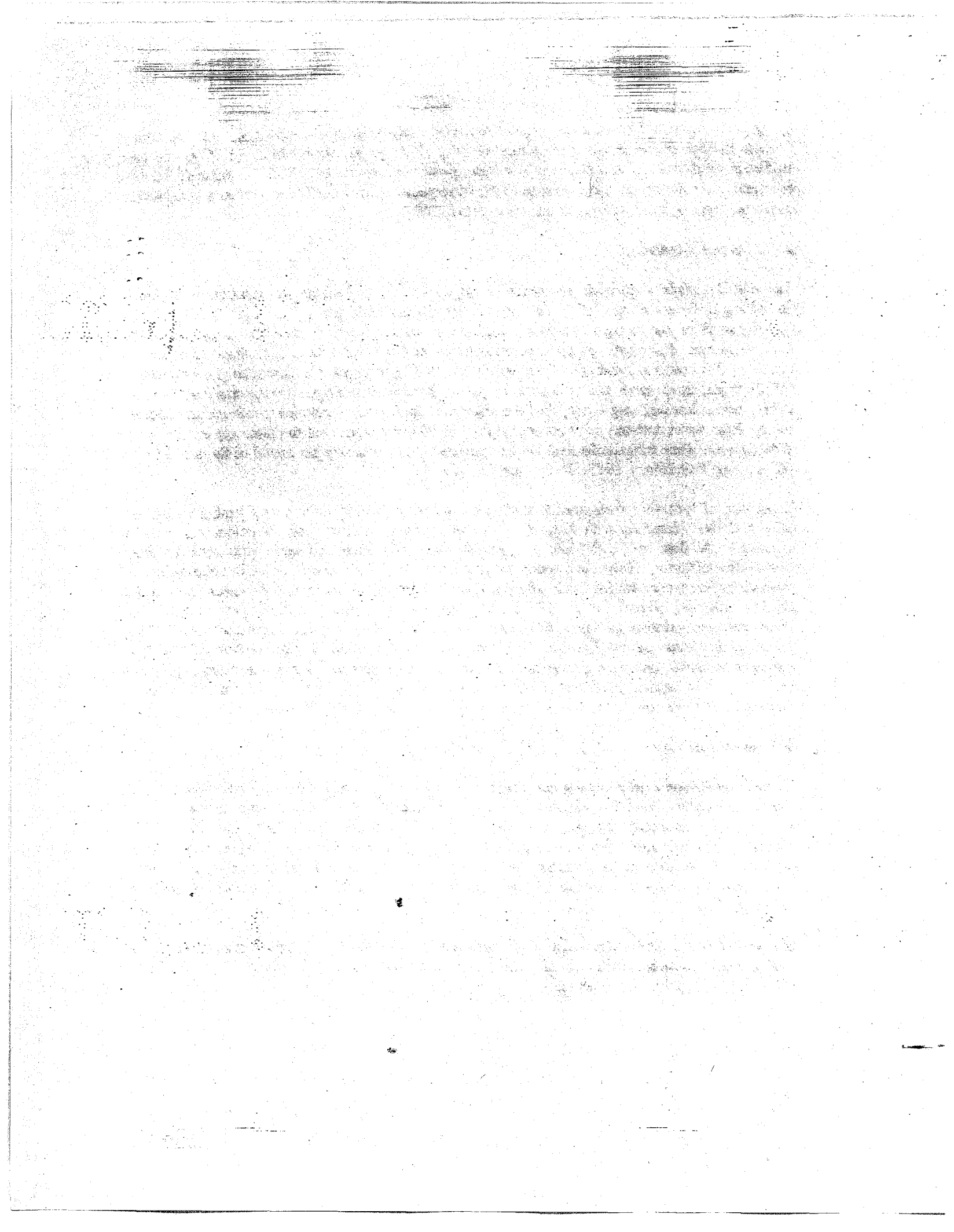
The chemi-generic clearance approach is applicable to the safety of irradiation of fruits. According to Basson et al, (1983), data from fruits is applicable among all fruits. This was based on their work on the mango, strawberry, and lemon, the radiolytic products of which were very close in spectra. Radiolytic products in fruits originate from the carbohydrate fraction (Basson et al 1983). The result is carbonylic compounds and hydrogen peroxide. Interestingly, Beyers et al (1983) found three times the carbonyls in thermally treated mangoes versus irradiated. Kader (1986) noted that ionizing energy in the presence of fruits and vegetables produces free radicals mostly from water and oxygen because produce is 80-95% water and the intercellular spaces are 20% oxygen. Free radicals formed are the same as those naturally produced in the human body (Hassan and Schellborn, 1988; Wefers and Sies, 1988).

Irradiation of fruits is a well-studied subject because of the FDA approval of irradiation up to 1 kGy in 1986. Irradiation is helpful in sprout inhibition, insect disinfestation, and delayed ripening. A dose of 2.25 kGy is generally the maximum exposure tolerated by fresh commodities (Kader, 1986). Mutagenic effects noted for carbohydrates alone in solution are not observed when the actual food is irradiated, even at higher doses, as noted for dates (and cooked chicken and fish) (Renner et al., 1982) and fruits and their juices (Den Drijver et al., 1986). Dilute sucrose solution (a mimic for whole grapes and strawberries) irradiated with 20 kGy produced the toxic agents hydroxyalkyl peroxides derived from the interaction of radiolytic hydrogen peroxide and α, β-unsaturated carbonyls from radiolysis of sucrose (Schubert, 1969). However, strawberries irradiated at 2 kGy do not show any amounts of the peroxides or carbonyls. Similar results have been noted by Basson et al, (1979) with mangoes.

iii.) Formulated Foods

To date, most food irradiation applications have been based on irradiating the food either in a whole form or the whole food divided into discrete pieces. Studies and literature reviews addressing the toxicological safety of irradiated foods have consequently focused on the properties of whole foods. Petitions granted by the FDA, for the most part, involve irradiating a whole food. This petition is requesting approval for ready-to-eat whole foods and ready-to-eat formulated foods as well. Formulated foods would be mixtures of food components with added food ingredients.

In considering the toxicological safety of irradiated formulated foods, we must rely on any available information and also consider the further application of any principles of irradiation chemistry to help us judge the safety of irradiated formulated foods.



DATA SUMMARY FORM FOR IRRADIATED FOODS Ref # 177

I. Study Identification

a. Study Title Wholesomeness of gamma-irradiated foods fed to rats

b. Author's name/ Date HF Kraybill et al / 1956

c. Type of Report Published literature: Fed Proc. 15: 933-7 (1956)

d. Reviewer/ Date of Review Dr. Hiltje Irausquin 1/18/82 MVG 2-1-82

e. FAIS Document Type & Number FAP 7F1 2056, v. 3, p. 683 petitions ref # 17

f. Testing Facility/ FAIS # US Army Medical Nutrition Lab

g. Preliminary Evaluation Reject

h. Reason for Rejection Group size not given.

i. Summary of Effects/ Irradiation Dose increased liver cytochrome oxidase.

Comments Reproduction study still in progress

II. Experimental Design

a. Test Type/ Date/ FAIS Test Name Code reproduction / 14
short-term / 02

b. Test Subject Species/ FAIS Test Subject Code rat / 110

c. Test Subject Strain NR

d. Test Duration, Specified in Days 56 ; reproduction 4 generation

e. Group Size/ Sex NR / male

f. Irradiation Conditions:

- Type of Food Irradiated ground beef, bacon, haddock fillet, strawberry peach, cereal, ham, milk powder

- Dose and Source 3; 6 ~~krad~~/ Mrad γ-rays

- Time after Irradiation NR

- Atmosphere NR

- Temperature NR

g. Controls:

- Basic Diet ☐
- Non-irradiated Food ☐
- Cooked Food(incl.microwave) ☐
- Other(specify) ☐

h. Diet: Ref #177 P82

- Composition
- Antioxidants
- Palatability
- Processing & Storage
- Dose of Irradiated Food 35

Comments: diet supplemented with vitamins

III. Results:

Parameters Studied:		Effects Due to Irradiated Food
1. Appearance, Behavior	☐	
2. Body Weight	☑	none
3. Food Consumption	☑	none
4. Hematology	☐	
5. Blood Chemistry	☐	
6. Urinalysis	☐	
7. Mortality	☐	
8. Gross Pathology	☐	
9. Organ Weights	☐	
10. Histopathology	☑	none
11. Tumor Incidence	☐	
12. Reproduction	☑	Suggestion of higher incidence of sterility in males
13. Teratology	☐	
14. Other(specify) liver cytochrome oxidase	☑	increased

Comments:

* no data given → evaluation not possible.

Ref #48

DATA SUMMARY FORM FOR IRRADIATED FOODS

I. Study Identification

a. Study Title Feeding of irradiated beef to Rats

b. Author's name/ Date Blood, F.R., Darby, W.J., Elliott G.A. and Wright, M.S. 1966

c. Type of Report Published Paper., Tox. appl. Pharmacol. 8: 235-240, 1

d. Reviewer/ Date of Review J.H. Khalsa, 12/22/81 MNG 1-29-82

e. FAIS Document Type & Number Published lit. # 74

f. Testing Facility/ FAIS # Vanderbilt University, TN.

g. Preliminary Evaluation Accept. (AR) *Too small/group

h. Reason for Rejection

i. Summary of Effects/ Irradiation Dose

No adverse effects were found.

Comments

II. Experimental Design

a. Test Type/ Date/ FAIS Test Name Code Multigeneration (4 generation) / 24 months

b. Test Subject Species/ FAIS Test Subject Code Rats,

c. Test Subject Strain Rats, Sprague-Dawley

d. Test Duration, Specified in Days 24 months / Multigen. study

e. Group Size/ Sex 9/Sex/group. ① Control - ② 1X - irradiat 2-79 ③ 2X irrad. 5-58 in Rats

f. Irradiation Conditions:

- Type of Food Irradiated Beef
- Dose and Source 2.79-5.58 ~~krad~~ Mrad, (35% in diet)
- Time after Irradiation 4 months - 1 year
- Atmosphere
- Temperature 5°C

g. Controls:

- Basic Diet ☐
- ✓ Non-irradiated Food ☒
- ✓ Cooked Food(incl.microwave) ☒
- Other(specify) ☐

h. Diet: CF TO PG 2

- Composition ✓
- Antioxidants
- Palatability
- Processing & Storage see below
- Dose of Irradiated Food 35 % solids

Comments: non-irradiated control beef was stored in the frozen state until used. Beef cooked in pressure cooker at 15 psi for 20 min before incorporation into diet

III. Results:

Parameters Studied:		Effects Due to Irradiated Food
1. Appearance, Behavior	☒	none
2. Body Weight	☒	none
3. Food Consumption	✓	
4. Hematology	☐	
5. Blood Chemistry	☒	at 12 wk. intervals.
6. Urinalysis	☐	
7. Mortality	☒	none
8. Gross Pathology	☐	
9. Organ Weights	☒	none
10. Histopathology	☒	Bone renal ~~damage~~ damage in 67% of all rats.
11. Tumor Incidence	☐	
12. Reproduction	☒	none
13. Teratology	☐	
14. Other(specify)	☐	

Comments:

Ref # 109

DATA SUMMARY FORM FOR IRRADIATED FOODS

I. Study Identification

a. Study Title Incidence of irradiated bacon lipids on body growth, incidence of cancer, & other pathological chg in

b. Author's name/ Date Dixon, M.A., Mayer, D.L., Zeldis, L.J. & McKee, R.W. 196

c. Type of Report Published literature, J. Food Sci. 26: 611-61 196

d. Reviewer/ Date of Review J. H. Khalsa, 12/21/81 MVG1-29-82

e. FAIS Document Type & Number # 70

f. Testing Facility/ FAIS # Univ. UCLA,

g. Preliminary Evaluation good, accept. (AR) ~~Group size not~~ reported

h. Reason for Rejection —

i. Summary of Effects/ Irradiation Dose no effects as a result of feeding irradiated bacon for 2 yrs. in mice

Comments

II. Experimental Design

a. Test Type/ Date/ FAIS Test Name Code Life-time / 2 yrs.

b. Test Subject Species/ FAIS Test Subject Code

c. Test Subject Strain Mice, C3H/He Crgl. and A/crgl.

d. Test Duration, Specified in Days c.a. 750 days.

e. Group Size/ Sex Gr. size/sex not reported, but 98 C3H controls, 149 irrad. gr. ~~149~~ unirr. mice. A mice = 91, 136, & 136 in 3 grps.

f. Irradiation Conditions:

- Type of Food Irradiated Bacon
- Dose and Source 5.58 ~~krad~~/ Mrad
- Time after Irradiation 5 months
- Atmosphere ~~air~~ packed in vac. cans
- Temperature Stored at 5° until used.

g. Controls:

- ✓ Basic Diet ☒
- ✓ Non-irradiated Food ☒
- ✓ - Cooked Food(incl.microwave) ☒
- Other(specify) ☐

h. Diet:

- ✓ Composition 23% Crude protein, 4.5% Crude fat, 44% N-free extr. + 6% crude fiber, 9% ash.
- Antioxidants
- Palatability
- Processing & Storage
- Dose of Irradiated Food NR %

Comments: uncured bacon was packed in #10 cans - unirradiated bacon was shipped frozen + held at -20° until use

III. Results:

Parameters Studied:		Effects Due to Irradiated Food
1. Appearance, Behavior	☒	normal.
2. Body Weight	☒	No effects, although mice on non-irr. & irradiated bacon gained more bwt. as a result of 10-25% more lipids in di
3. Food Consumption	☐	
4. Hematology	☐	
5. Blood Chemistry	☐	
6. Urinalysis	☐	
7. Mortality	☐	
8. Gross Pathology	☒	
9. Organ Weights	☐	
10. Histopathology	☒	No significant effects observed in ba
11. Tumor Incidence	☒	Not significantly different from controls.
12. Reproduction	☐	
13. Teratology	☐	
14. Other(specify)	☐	

Comments:

hem. Toxic. Vol. 20, pp. 867 to 878, 1982
ed in Great Britain.

0278-6915/82/060867-12$03.00/0

AN INVESTIGATION OF THE GENETIC TOXICOLOGY OF IRRADIATED FOODSTUFFS USING SHORT-TERM TEST SYSTEMS. III—*IN VIVO* TESTS IN SMALL RODENTS AND IN *DROSOPHILA MELANOGASTER*

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(*Received 20 November 1981; revision received 29 January 1982*)

Abstract—Six *in vivo* genetic toxicity tests were carried out on irradiated or unirradiated cooked chicken, dried dates and cooked fish. The tests were as follows: sex-linked recessive lethal mutations in *Drosophila melanogaster* (dried dates only), chromosome aberrations in bone marrow of Chinese hamsters, micronucleus test in rats, mice and Chinese hamsters, sister-chromatid exchange in bone marrow of mice and Chinese hamsters and in spermatogonia of mice, and DNA metabolism in spleen cells of Chinese hamsters. None of the tests provided any evidence of genetic toxicity induced by irradiation. However, dried dates, whether irradiated or not, showed evidence of some genetic toxicity in their effect on DNA metabolism in spleen cells and SCE induction in bone marrow. Feeding irradiated fish affected DNA metabolism in the spleen cells of Chinese hamsters. This effect could be interpreted as an induction of an immunoactive compound, although it could also be explained by the persistence of an immunoactive compound due to the removal by irradiation of spoilage organisms that would normally degrade it.

INTRODUCTION

The treatment of food with ionizing radiation for reservation purposes can give rise to complex chemi- changes which are dependent on food composition d irradiation conditions (for a review see Elias & ohen, 1977). The production of mutagenic and/or rcinogenic compounds cannot be excluded. There- re genetic toxicity screening using a variety of short- rm test systems has to be included in a thorough xicological evaluation of irradiated food. The pre- ous papers in this series (Phillips, Kranz & Elias, 80a; Phillips, Kranz, Elias & Münzer, 1980b) have described the *in vitro* short-term tests applied to irradiated foodstuffs including an *in vitro* digestion procedure (Phillips & Elias, 1978) designed to overcome the special problems presented by using food, composed as it is of complex macromolecules and other smaller chemical moieties, as a test substrate. Since *in vitro* tests alone cannot form a total genetic toxicity screen, especially for a material such as food, *in vivo* investigations were also carried out at three European laboratories, in collaboration with the International Food Irradiation Project's own laboratory at Karlsruhe. These studies, which cover six short-term tests in four different species, complete the genetic toxicity screening of irradiated chicken, dates and fish as representatives of three different classes of food, and the results are presented in this paper.

EXPERIMENTAL

Because the investigations were carried out in three different Institutes† on several animal species, some

breviations: BudR = Bromodeoxyuridine; CPA = cyclo- phosphamide; IFIP = International Food Irradiation Project; MMS = methyl methanesulphonate; SCE = ister-chromatid exchange.

*To whom requests for reprints should be addressed.

†The names of the individual research workers involved re given in Table 1.

Table 7. *Mean number of micronuclei-containing immature (polychromatic) and mature (normochromatic) erythrocytes per thousand cells examined in rats, mice and hamsters given diets of unirradiated or irradiated chicken, dates or fish for 4 days (Test 3)*

Diet or treatment		Mean* no. of micronuclei-containing cells/1000 cells among					
		Rat erythrocytes		Mouse erythrocytes		Hamster erythrocytes	
		Normochromatic	Polychromatic	Normochromatic	Polychromatic	Normochromatic	Polychromatic
Control		3·3(1–6)	3·5(0–6)	2·9(1–5)	3·3(0–6)	2·9(1–6)	3·1(1–6)
Chicken:	unirradiated	2·8(0–4)	2·8(0–5)	2·4(1–4)	2·8(1–5)	2·7(1–4)	3·0(1–5)
	irradiated	2·7(0–5)	2·5(0–5)	2·5(1–4)	2·9(1–7)	2·8(0–4)	3·1(2–5)
Dates:	unirradiated	3·0(1–6)	2·7(1–4)	2·5(1–4)	2·7(1–7)	3·0(1–6)	2·9(1–5)
	irradiated	2·7(1–5)	2·7(0–6)	2·5(1–4)	2·7(1–5)	2·9(2–5)	2·6(0–6)
Fish:	unirradiated	3·1(2–4)	3·1(0–5)	2·5(1–5)	3·0(1–6)	3·2(1–4)	3·9(2–7)
	irradiated	3·1(1–5)	2·9(0–6)	2·4(1–5)	3·0(1–6)	2·4(0–4)	3·3(1–7)
CPA (positive control)		ND	ND	2·5(1–5)	12·1(7–17)	2·0(0–4)	11·0(7–15)

CPA = Cyclophosphamide ND = Not done

*Values are means (range in brackets) for groups of 15 animals given the chicken, dates or fish diets, groups of 11 rats, ten mice and ten hamsters given the control diet and groups of eight mice and four hamsters (positive controls) injected ip with 20 mg CPA/kg body weight 30 and 6 hr before they were killed.

chicken than in either the negative control group or the group given unirradiated chicken.

Test 3. Micronucleus test

The results of the micronucleus test are summarized in Table 7. The counts of micronucleated erythrocytes per thousand were similar in the control and experimental groups and the means fell in the range 2·4 to 3·9. Thus the level of micronucleus formation was independent of animal species, sex, test diet and irradiation status of the test diet. As expected the positive control groups of mice and hamsters treated with CPA both showed an increased incidence of micronuclei in polychromatic erythrocytes, but not in normal mature erythrocytes.

Tests 4 and 5. SCE in bone marrow and spermatogonia

The results of the SCE test in the bone marrow of mice and Chinese hamsters, summarized in Table 8, show that the numbers of SCEs per cell were the same for the control groups and those fed unirradiated or irradiated chicken and fish, irrespective of species or sex. The groups of animals fed on dates, both irradiated and unirradiated, all showed an increase in the number of SCEs per cell compared to the other experimental and control groups. The investigations with dates were therefore repeated using a new batch of unsulphurized dates and sulphurized dates. The results (not presented here) confirmed that raised SCE levels also occurred with those two new batches of dates.

In the spermatogonial SCE test in mice (Table 9) there was no increase in the number of the SCEs per cell when any of the test diets were fed to these animals, the numbers of SCEs in all of the test groups being very similar to that in the control group. The number of SCEs per cell increased with increasing CPA concentration in the positive control groups, thus confirming that for a pure chemical this method can be used for the measurement of SCEs *in vivo*.

Test 6. DNA metabolism in spleen cells

The results of the measurement of semiconservative DNA replication are summarized in Table 10. Only in date-fed animals was there a significant loss in body weight compared to controls during the 2-day treatment period. Food consumption was also considerably lower in date-fed animals but significantly higher in chicken- and fish-fed groups when compared with controls. DNA synthesis was markedly inhibited in the date-fed test groups independently of irradiation. The degree of suppression was similar to that caused by CPA at 100 mg/kg body weight. With both chicken and fish (irradiated and unirradiated), the rate of DNA synthesis was markedly increased compared to control values. With chicken-fed animals and the individual spleens of fish-fed animals, no difference between irradiated and unirradiated diets was seen. Only with the pooled spleens from fish-fed animals was the rate of DNA synthesis significantly greater in the groups given the irradiated diet than in the group given unirradiated fish.

Autoradiographs exposed for 14 days showed no evidence of unscheduled DNA synthesis, even in the positive control (CPA-treated animals), although evidence of incisions in DNA had been seen in sedimen-

National Fisheries Institute

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June 25, 1999

Name of Petitioner:
National Fisheries Institute

Address:
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703-524-8883
Attn: Robert Collette

Co-Petitioner:
State of Louisiana

Address:
Department of Agriculture and Forestry
P.O. Box 3334
Baton Rouge, LA 70821-3334
225-922-1280
Attn: Roy Johnson

Name of food Additive: Approved Sources of Ionizing Radiation

Proposed Use: Inactivation in shellfish of all Vibrio present and a reduction in levels of coexisting *Salmonella* and *Listeria* species, thereby reducing the potential for outbreaks of food poisoning from this food source.

Petitions Control Branch
Food and Drug Administration
Department of Health and Human Services
200 C St., S.W., HFS 200
Washington, DC 20204
Attention: Hansen/Trotter

1999 JUN 29 A 7:50

Dear Sir or Madam:

The undersigned, Mr. Robert Collette, submits this petition, pursuant to section 409(b)(1) of the Federal Food, Drug and Cosmetic Act, with respect to the use of approved sources of ionizing radiation as a physical process for the pasteurization of fresh or frozen shellfish to kill all *Vibrio* species and to reduce coexisting *Salmonella* and *Listeria* species, thereby reducing related incidences of foodborne illness. The minimum radiation dose range we are petitioning approval for is 0.5 kGy and a maximum not to exceed 7.5 kGy.

Vibrio bacteria are naturally occurring marine microorganisms that are sometimes found in seafood. When present in sufficient numbers some strains of these bacteria can cause human illness. *Vibrios* represent a particular concern to high-risk groups, such as those with underlying chronic diseases and/or immune deficiencies, and can inflict serious illness in these individuals. The use of this process, in conjunction with HACCP and current regulatory requirements for the

individuals cannot be ignored, but in terms of the general population this statement is true. Thus concerns about nutritional value are presently unwarranted.

Nevertheless, a few general comments are included below. The effects on other vitamins, proteins, fats, and carbohydrates are as submitted in Section E of the Egg Petition (Josephson 1997) and demonstrate that ionizing radiation, in the dose range requested has no significant impact on macro or micro nutrient levels. Josephson has also provided an overview of this aspect (Josephson; Thomas, and Calhoun 1978).

Vitamins

Brook et al. (Brooke; Ravesi; Gadbois, and Steinberg 1964) found no significant changes in any of the B vitamins or free amino acid content or irradiated clams. This would suggest that the overall affect on the B vitamins is minimal but any such effect is likely to be species specific. Liuzzo (Liuzzo; Lagarde, and Novak 1969) studied irradiated gulf oysters and found no effects on any of the macro nutrients, namely, crude protein, sugars, ash, glycogen and non-protein nitrogen. While Liuzzo claimed that ash content decreased with storage time, this is not readily apparent from the data presented, other than an initial drop at the first time point, namely day 5.

Organoleptic Properties

Organoleptic assessments that have been made would suggest that an irradiation dose up to 7.5 kGy can reasonably be tolerated for most unshucked shellfish, before organoleptic properties begin to significantly diminish. Organoleptic concerns will not be a problem for shucked product because lower doses will be required. It is certain that not all product will withstand 7.5 kGy, but this will permit maximum flexibility to maximize the inactivation of other pathogens while retaining good organoleptic properties. Evidence of the variable response of different species of shellfish is provided by Rodrick and Dixon (1994) for two species of oysters.

Other sensory characteristics that have been evaluated were taste, texture, odor and appearance. Adverse effects on these parameters were species specific and depended upon whether the meat had been shucked or was still in the shell (ICGFI 1998). When compared with unirradiated shellfish, no statistically significant differences were obtained for irradiated product (ICGFI 1998) at radiation doses sufficient to provide for complete inactivation of *Vibrio*.

Toxicological Safety

The fundamental question to be addressed in this section can be expressed as follows: Does the radiation pasteurization of molluscan shellfish generate stable radiolysis products that, by virtue of their structure, reactivity and concentration pose significant toxicological risk?

This question has been rather exhaustively, but indirectly addressed in recent decades by animal (including short-term human) feeding studies and in *vitro* tests. Direct analytical chemical analysis has also been used. There are a large number of books, monographs and review articles that are in-part or entirely devoted to the toxicological safety of irradiated food. Several of the more authoritative and detailed of these are cited and listed in recent overviews, (Thayer 1994), (Crawford and Ruff 1996) (Kaferstein and Moy 1993). The remaining arguments are as submitted in the Egg Petition (Josephson 1997).

In addition, the WHO has recently stated that a review of the literature indicates that there is no toxicological problem with food irradiated to 70 kGy (WHO 1997). As this is an order of magnitude greater than the level we are requesting, there should be no toxicological consequence to the irradiation of fresh raw shellfish.

Performance Characteristics

We refer here to the draft guidelines published by the International Consultative Group on Food Irradiation (ICGFI 1998), for approximate dose ranges to obtain the greatest bacterial reduction with the least disturbance to desired organoleptic properties. It will be noted that these fall within the requested radiation doses of 0.5 to 7.5 kGy.

Summary

Considering the above comments, we believe that there is not need to conduct toxicological studies of irradiated shellfish, especially in view of the low dose requested for this application.

The joint FAO/WHO Food Standard Program was instituted for foods in international trade. The Codex Alimentarius Commission developed two standards for irradiated foods:

1. International General Standard for Irradiated Foods and
2. International Code of Practice for the Operation of Radiation Facilities used for the Treatment of Foods.

These are accepted by GATT countries.

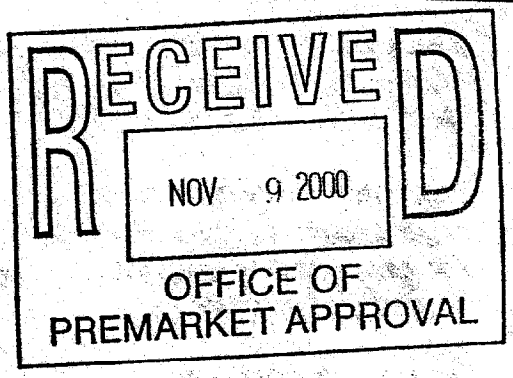
We submit that on all the foregoing counts there are no significant toxicological safety implications in connection with the irradiation of shellfish to eliminate *Vibrio*.

Reference List

Basak, J. Characterization of the Adaptive Response of Ionizing Radiation Induced by Low Doses of X-rays to Vibrio cholerae Cells. Mutat Res. 1996; 372(1): 115-118.

FISHERIES INSTITUTE
Arlington, VA 22209

CFS 75250 FAP 1M4827



Date: November 7, 2000

Name of Petitioner:

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Attn: Robert Collette

Supporting Organizations:

Mr. Peter Kunstadt
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Baton Rouge, LA 70821

Mr. Pat Adams
IBA Food Safety Division
1661 International Dr. Suite 350
Memphis Tenn. 38120

Name of food additive: Approved sources of ionizing radiation

Proposed Use: The inactivation, in crustaceans, of *Vibrio, Salmonella, and Listeria spp. and other pathogens* to a level which is not likely to cause food borne illness or to sufficiently low numbers to inhibit their recovery and regrowth. The use of ionizing radiation is intended to significantly reduce the potential for outbreaks of food borne illness from this food source, and may also result in a concomitant reduction in numbers of common food spoilage microorganisms. Regardless of the reason for treatment, irradiated crustaceans must be held under proper storage conditions during the refrigerator or freezer shelf life of the product.

2 kGy but then was scored lower with higher doses due to the perceptibility of browning from possible Maillard Reactions in the chemical matrix of the crawfish tail meat (Andrews and Grodner 1991).

From the above discussion, it is easy to see that the D_{max} will be well controlled by the organoleptic effects of radiation and this varies by species and sub-species. It will up to the processor to determine the optimum dose and storage time for the particular product to be irradiated.

Toxicological Safety

The fundamental question to be addressed in this section can be expressed as follows: Does the radiation pasteurization of crustaceans generate stable radiolysis products that, by virtue of their structure, reactivity and concentration pose significant toxicological risk?

This question has been rather exhaustively, but indirectly, addressed in recent decades by animal (including short - term human) feeding studies and *in vitro* tests. Direct analytical chemical analysis has also been used. There are a large number of books, monographs and review articles that are in - part or entirely devoted to the toxicological safety of irradiated food. Several of the more authoritative and detailed of these include Thayer, 1994; Crawford and Ruff, 1996; Kaferstein and Moy, 1993; WHO, 1999. The remaining arguments are as submitted in the Egg Petition (Josephson,1997).

In addition, the WHO has recently stated that a review of the literature indicates that there is no toxicological problem with food irradiated to 70 kGy (WHO 19997, 1999). As this is an order of magnitude far greater than the level we are requesting, there would appear to be no toxicological consequence to the irradiation of crustaceans.

Performance Characteristics

We refer here to the draft guidelines published by the International Consultative Group on Food Irradiation (ICGFI 1998), for approximate dose ranges to obtain the greatest bacterial reduction with the least disturbance to desired organoleptic properties. It will be noted that these fall within the requested radiation doses.

Summary

Considering the above comments, we feel that there is no need to conduct toxicological studies of irradiated crustaceans, especially in view of the low dose requested for this application.

The Joint FAO/WHO Food Standard Program was instituted for foods in international trade. The Codex Alimentarius Commission developed two standards for irradiated foods: