# Wholesomeness of irradiated food

---

Report of a Joint FAO/IAEA/WHO
Expert Committee

Published by FAO and WHO

World Health Organization
Technical Report Series
604

FAO Food and Nutrition
Series
6

---

World Health Organization Geneva 1977

ISBN 92 4 120604 7

PRINTED IN SWITZERLAND

# CONTENTS

# JOINT FAO/IAEA/WHO EXPERT COMMITTEE ON THE WHOLESOMENESS OF IRRADIATED FOOD

*Geneva, 31 August – 7 September 1976*

*Members :*

Dr H. Blumenthal, Acting Director, Division of Toxicology, Bureau of Foods, Food and Drug Administration, Washington, DC, USA (*Chairman*)

Professor D. O. Cliver, Food Research Institute and Department of Bacteriology, University of Wisconsin, Madison, WI, USA

Professor J. F. Diehl, Director, Federal Research Centre for Nutrition, Karlsruhe, Federal Republic of Germany

Professor L. Ehrenberg, Department of Radiobiology, Wallenberg Laboratory, University of Stockholm, Sweden

Dr J. Farkas, Deputy Director, Central Food Research Institute, Budapest, Hungary

Dr Akira Matsuyama, Head, Radiobiology Laboratory, Institute of Physical and Chemical Research, Wako-shi, Saitama-ken, Japan

Professor M. J. Rand, Department of Pharmacology, University of Melbourne, Victoria, Australia (*Rapporteur*)

Mr L. Saint-Lebe, Chief, Radiation Conservation of Foodstuffs Group, Radiation Agronomy Service, Cadarache Centre for Nuclear Studies, St Paul-lès-Durance, France

Dr S. G. Srikantia, Director, National Institute of Nutrition, Indian Council of Medical Research, Hyderabad, Andhra Pradesh, India

Dr K. Sundaram, Director, Biomedical Group, Bhabha Atomic Research Centre, Bombay, India

Professor T. Tashev, Director, Centre of Hygiene, Medical Academy, Sofia, Bulgaria (*Vice-Chairman*)

Professor B. Underdal, Head, Department of Food Hygiene, Veterinary College of Norway, Oslo, Norway

Dr A. N. Zajcev, Head, Laboratory for Hygienic Examination of Food Additives, Institute of Nutrition of the Academy of Medical Sciences of the USSR, Moscow, USSR

*Observers (invited by FAO/IAEA) :*

Mr W. T. Potter, Project Secretary, International Food Irradiation Project, Nuclear Energy Agency, Organization for Economic Cooperation and Development, Paris, France

Dr G. F. Wilmink, Chairman of the Codex Committee on Food Additives, Ministry of Agriculture and Fisheries, The Hague, Netherlands

*Secretariat* :

Dr C. Agthe, Chief, Food Additives Unit, Division of Environmental Health, WHO, Geneva (*WHO Joint Secretary*)

Dr R. Angelotti, Associate Bureau Director, Office of Food Compliance, Bureau of Foods, Food and Drug Administration, Washington, DC, USA (*WHO Temporary Adviser*)

Mr D. Clegg, Head, Pesticide Section, Toxicological Evaluation Division, Bureau of Chemical Safety, Department of National Health and Welfare, Ottawa, Ontario, Canada (*WHO Temporary Adviser*)

Dr P. S. Elias, Project Director, International Project in the Field of Food Irradiation, Institute of Radiation Technology, Karlsruhe, Federal Republic of Germany (*FAO/IAEA Temporary Adviser*)

Professor H. Glubrecht, Deputy Director-General for Research and Isotopes, International Atomic Energy Agency, Vienna, Austria

Professor M. Ingram, formerly Director, Meat Research Institute, Langford, Bristol, England (*FAO/IAEA Temporary Adviser*)

Dr G. Kapsiotis, Senior Officer (Technology), Food Policy and Nutrition Division, FAO, Rome, Italy (*FAO Joint Secretary*)

Dr W. Keller, Nutrition Unit, Division of Family Health, WHO, Geneva

Dr L. Ladomery, Food Standards Officer, Food Standards Branch, Food Policy and Nutrition Division, FAO, Rome, Italy

Professor C. G. Lamm, Deputy Director, Joint FAO/IAEA Division of Atomic Energy in Food and Agriculture, IAEA, Vienna, Austria

Dr F. C. Lu, Formerly Chief, Food Additives Unit, Division of Environmental Health, WHO, Geneva (*WHO Consultant*)

Dr L. Reinius, Veterinary Public Health Unit, Division of Communicable Diseases, WHO, Geneva

Dr K. Vas, Head, Food Preservation Section, Joint FAO/IAEA Division of Atomic Energy in Food and Agriculture, IAEA, Vienna, Austria (*IAEA Joint Secretary*)

# WHOLESOMENESS OF IRRADIATED FOOD

## Report of a Joint FAO/IAEA/WHO Expert Committee

A Joint FAO/IAEA/WHO Expert Committee on the Wholesomeness of Irradiated Food met in Geneva from 31 August to 7 September 1976. The meeting was opened by Dr A. S. Pavlov, Assistant Director-General of WHO, and by Dr H. Glubrecht, Deputy Director-General of IAEA, on behalf of the Directors-General of the Food and Agriculture Organization of the United Nations, the International Atomic Energy Agency and the World Health Organization.

## 1. INTRODUCTION

To meet the increasing need for food throughout the world, many approaches are utilized. One of the most important is the reduction of food loss. This may be achieved by the use of chemicals (e.g., antimicrobials, insecticides, and sprout inhibitors), but such use involves potential health hazards not only of the chemicals themselves but of their metabolic products and interaction products (such as nitrosamines). For this reason, much work has been done on the use of irradiation in the conservation of food and on determining the wholesomeness of the food that has been irradiated.

At the international level, the need to consider the wholesomeness of irradiated food was emphasized at a meeting sponsored by FAO, IAEA and WHO in Brussels in 1961. The appropriate studies required to ascertain the wholesomeness of irradiated food were discussed by an expert committee sponsored by the three organizations in Rome in 1964 (*7*, *28*). A further joint expert committee was convened in Geneva in April 1969 (*30*). Its main task was to assess the wholesomeness of irradiated wheat, potatoes, and onions. In the light of the available data, the Committee recommended temporary acceptance of wheat and wheat products irradiated with doses of up to 0.75 kGy (75 krad) and of white potatoes irradiated with doses not exceeding 0.15 kGy (15 krad).[1] It further specified certain studies to be carried out on

---

[1] In this report absorbed dose is expressed in terms of the gray (Gy), as recommended by the International Organization for Standardization. Values expressed in terms of the rad are given in parenthesis. Conversion factor : 1 rad = $10^{-2}$ Gy.

these irradiated foods. The data were considered inadequate to assess the wholesomeness of irradiated onions.

Much additional information has since been provided, notably from studies sponsored by the International Project in the Field of Food Irradiation (IFIP). The studies cover not only the foods specified by the 1969 meeting but also other irradiated foods. In addition, data have been provided in response to a circular letter from WHO to its Member States, which supplement those resulting from a WHO consultation group that met in 1974 to review data on irradiated food and an FAO/IAEA consultants' meeting on microbiological aspects of food irradiation (*34*). The present Expert Committee was convened to review and assess these data.[1]

## 2. GENERAL CONSIDERATIONS

### 2.1 Principles

The Committee reviewed the principles and guidelines described in the reports of the 1964 and the 1969 Joint FAO/IAEA/WHO Expert Committees referred to in the previous section and concluded that, for the most part, these were sound and should be followed. The present Committee re-emphasized, however, that the safety for human consumption of irradiated food must be based on the following considerations: (1) the absence of microorganisms and microbial toxins harmful to man, (2) the nutritional contribution to the total diet of the irradiated food, and (3) the absence of any significant amounts of toxic products formed in the food as a result of the irradiation process.

### 2.2 Irradiation as a food-treatment process

Irradiation is a physical process for treating foods and as such it is comparable to the heating or freezing of foods for preservation. The only unique feature of irradiation is the particular type of energy employed, and it is this feature that has aroused special attention.

The question of wholesomeness has been raised in relation to the irradiation of foods with gamma-rays, yet the wholesomeness of foods treated with radiation of longer wavelengths (heat or microwaves) has not been questioned to the same extent. The Committee stressed that

---

[1] A summary of the data considered by the Joint Expert Committee (document WHO/Food Add/77.45) is available from Food Additives, World Health Organization, 1211 Geneva 27, Switzerland.

the microbiological, nutritional and toxicological approaches to the assessment of the wholesomeness of irradiated food must be based on the concept of food irradiation as a process.

In the past the approach has been taken that irradiation " adds " something to the treated food and that it should therefore be considered as a food additive and not as a process. This view was adopted by some national authorities, whereas others regulated food irradiation by controlling it as a process. The " food additive " approach to food irradiation meant that evaluation of the toxicological aspects of wholesomeness had to be based on the concepts of an acceptable daily intake and safety factors, as is the case with food additives or pesticide residues in food. However, the Committee considered that the approach needed in the toxicological evaluation of the wholesomeness of irradiated food differs from that used in the safety evaluation of chemicals. It is impracticable to exaggerate the feeding levels of irradiated foods in animal studies beyond a modest degree, nor is it appropriate to exaggerate the radiation dosage much beyond that to be used in practice. Either of these practices gives rise to effects which are not relevant to the toxicological potential of the irradiated food. The evaluation of the wholesomeness of irradiated foods therefore poses problems of a different kind from those encountered with food additives or contaminants and it consequently requires a different approach.

It is recognized that public concern about the hazards of radiation generally may be reflected in a distrust of irradiated foods. It will be necessary to educate and reassure the public as to the safety of irradiation as a food process, because in many parts of the world and for many commodities there are good reasons to use this process.

## 2.3 Extrapolation of data from one food to another

The Joint FAO/IAEA/WHO Expert Committee that met in 1964 (*28*) considered that too little information was available at that time to establish general principles for extrapolation of data on the wholesomeness of some irradiated foods. It was expected that this would become possible in time.

The Joint FAO/IAEA/WHO Expert Committee that met in 1969 (*30*) concluded that data on the wholesomeness of one irradiated food had relevance to other irradiated foods. Any generally applicable data that could be identified would add reliability to the evaluation of specific foods treated by irradiation. This approach represented progress compared to the earlier views.

A WHO Consultation held in 1974 considered that data on a specific variety of a food crop were applicable to all varieties of that food crop. For groups of foods exhibiting differences extending beyond intraspecies variety (e.g., the applicability of data collected on wheat to maize, barley or oats) it might be possible to use simpler wholesomeness testing procedures when the radiation dose is below 10 kGy (1 Mrad). Thus studies on a single representative variety of irradiated food could cover other varieties of the same food. Similarly, toxicological and chemical data could be used across a class of related irradiated foods with minimal toxicological testing requirements for new foods in that class.

The Committee was presented with evidence on the great similarity in radiolytic products in related foods treated with radiation doses of the order of 10 kGy and on the uniformity of reaction of the protein, lipid and carbohydrate constituents of foods to radiation (see section 4). It is considered, therefore, that it is possible to generalize to a considerable extent about the radiation chemistry of foods. Most of the radiolytic products identified in irradiated foods can also be found in non-irradiated foods, and many of them are generated in foods by other processing procedures. For those radiolytic products that have been identified, the concentrations of the most abundant, even with radiation doses of up to 60 kGy (6 Mrad), are only in the mg/kg range. With dose ranges below 10 kGy (1 Mrad)—i.e., in the range that achieves the technical requirement for foods considered by the present Committee—the concentrations of radiolytic products are much lower. The available data on the chemical structures of radiolytic products in food and the very low concentrations at which they occur (see section 4) suggest the general conclusion that the health hazard they might represent is negligible.

The Committee agreed with the view that evidence of safety of one form of irradiated food could be applied to other forms of the same food. To the extent that foodstuffs can be placed in a relatively small number of major categories and for doses below 10 kGy (1 Mrad), the Committee accepted that data may be extrapolated from one member of a class to related members. It employed these principles when evaluating the wholesomeness of the starch-containing foods potato, wheat and rice by including in its evaluation information on maize starch. In the case of the wholesomeness evaluation of certain irradiated fresh fish, the evaluation was facilitated by information on a large variety of other irradiated fish and fish products; in future the totality of the data on irradiated fish may allow the acceptance of irradiation for all fish.

From such considerations the Committee envisaged that for doses of up to 5 kGy (500 krad) radiation chemical data (along with negative evidence from animal feeding studies) may eventually indicate that food items in general are safe for consumption by man. If certain radiation chemical and toxicological studies are continued it may even prove possible to use a purely chemical approach to the wholesomeness evaluation of irradiated food. These conclusions regarding the safety of the radiation process may even be extended to dose levels higher than 5 kGy.

However, the acceptance of these principles does not militate against the questions that might be asked about any new process. Thus irradiation must be proved to be an acceptable means of processing food and one that does not impair its wholesomeness, and it may be premature to base an evaluation of a new irradiated food solely on data obtained with other foods, even though they may be of closely related types.

## 3. TECHNICAL ASPECTS

### 3.1 Dosimetry

Careful dosimetry is required in the irradiation of test foods to be used in animal feeding studies as well as in the irradiation of foods for human consumption. Satisfactory methods of dosimetry exist and have been used for years in the commercial radiation-sterilization of medical products, laboratory animal diets, and some other items. Suitable procedures are described in detail in a handbook entitled *Dosimetry manual for industrial irradiators*, which is being prepared by IAEA.

In the technical specifications for the irradiation of various foods described in this report, a dose range is given for each food. This indicates that no part of the foods to be irradiated shall receive less than the minimum dose or more than the maximum dose indicated.

Dosage has to be expressed in terms of a range not only because it is impracticable to have a completely uniform dose distribution in an irradiator but also because an optimum average radiation dose cannot be fixed. For instance, different potato varieties require somewhat different doses for optimum sprout inhibition and storage life ; thus one variety may require an average dose of 0.07 kGy (range 0.05–0.09 kGy) and another may require an average dose of 0.12 kGy (range 0.09–0.15 kGy). Similarly, climatic conditions and insect populations prevailing in one country may require wheat to be irradiated with about 0.5 kGy (range 0.4–0.6 kGy) whereas in another country half that dose may suffice. In order to encompass all such variations it is necessary to specify a range of dosage.

As a matter of principle, the applied dose should not be higher than is needed to achieve the desired effect. It is therefore necessary to set maximum dose values. The setting of minimum dose values is critical in those cases where the desired effect is the elimination of pathogenic organisms or of plant pests for which quarantine regulations exist. In other instances adherence to the prescribed minimum dose is necessary to achieve the technological purpose.

### 3.2 Processing conditions for irradiation

Beyond indicating a dose range and the type of radiation to be used, it is beyond the scope of this report to prescribe all the technologically important details of various radiation processes. To take potato irradiation as an example, some of the factors to be considered are : whether the potatoes are irradiated immediately after harvest or after several weeks of storage ; whether they are irradiated loose or packaged, and if packaged, what sort of packaging material or container should be used ; and whether storage after irradiation is at ambient temperature or at 10°C. The answers to these questions may depend on local needs and conditions. Potatoes to be stored for eight months and to be used for industrial processing into chips will require conditions different from those needed for potatoes to be stored for four months and to be sold for household use.

With regard to the irradiation of a food used in experiments for testing wholesomeness, the irradiation conditions specified should be as close as possible to those to be used when the food is irradiated for human consumption.

On the other hand, radiation chemical data show that extrapolation within a wide range of irradiation conditions (with regard, for example, to water content and dose rate) is permissible ; therefore an evaluation of wholesomeness that is arrived at under one set of conditions will often be valid for practical application under a different set of conditions.

### 3.3 Methods of identifying irradiated foods

The search for methods that permit the identification of irradiated foods is not without scientific interest, but the availability of such methods should not be made a condition for permitting food irradiation or trade with irradiated foods. Food irradiation cannot be done in a clandestine fashion ; indeed it will be carried out in government-licensed installations. To ascertain the dose, existing methods of dosimetry are more reliable than any analysis of the food. In only a few cases can irradiation of foods be reliably detected by chemical methods.[1]

### 3.4 Packaging of irradiated food

Irradiation should not adversely affect the functional properties of packaging materials and should not cause the release of deleterious substances that may migrate into the food.

Methods of testing the functional properties of packaging materials and detecting migrating compounds are well established and must be applied to non-irradiated as well as irradiated packaging materials.

### 3.5 Repeated irradiation

The Committee considers that repeated irradiation of food is to be avoided, for a number of reasons. For example, the evaluations of toxicological and microbiological safety and nutritional quality are in respect of foods treated within specific ranges of radiation ; furthermore, the product should be correctly identified to the consumer in terms of the processing to which it has been subjected.

Even though radiolytic products accumulate with repeated irradiation, the concentrations are so low that the toxicological hazard likely to arise from repeated irradiation is minimal. However, the food is likely to be degraded in terms of organoleptic acceptability and nutritional quality.

Because there are no readily available tests for detecting repeated irradiation of a product, the main procedures for preventing this practice are proper labelling, record-keeping, and surveillance. The records should be sufficiently comprehensive to avoid irradiation of secondary products of previously irradiated foods—for example, of milled products of irradiated grains.

### 3.6 Quality of food to be irradiated

As a general principle, the process of irradiation should be applied only to those foods that meet appropriate standards of quality before irradiation. The need to affirm this principle arose when the attention of the Committee was drawn to a problem that could arise from irradiation of food contaminated with fecal matter (see section 10.6). In this case, irradiation would probably destroy the common bacterial indicators of fecal contamination, as well as the enteric pathogens, but

---

[1] Further information on this point is given in document WHO/FAD/75.3, which is obtainable on request from Food Additives, World Health Organization, 1211 Geneva 27, Switzerland.

pathogenic viruses that may also be present would probably not be destroyed. It is important, therefore, to establish the hygienic quality of foods *before* irradiation if there is any reason to suspect fecal contamination.

### 3.7 Technological aspects of irradiated food

As part of the technological assessment of irradiated foods, cognizance should be taken of the possible consequences of irradiation for the secondary uses that will be made of the food. For example, if irradiation of wheat produced changes in gluten, this would affect the quality of bread, pasta and noodles prepared from it ; however, in this instance, the level of irradiation accepted by the Committee for wheat falls well below that at which gluten is appreciably degraded.

## 4. RADIATION CHEMISTRY

The Committee endorsed the recommendations made by the 1974 WHO consultation group[1] concerning the desirability of chemical studies to provide data for the evaluation of irradiated food. However, if the toxicological data are adequate for acceptance of an irradiated food, radiation chemistry studies will not be required as a condition for acceptance.

The analyses of radiolytic products that have been carried out so far have removed much of the previous uncertainty about the validity of extrapolating from one food to another in arriving at an evaluation of the consequences of irradiation (see section 2.3). A previous Expert Committee (*30*) questioned the validity of using toxicological data obtained with foods subjected to higher doses of irradiation than would be used in practice. The objection was based on the theoretical consideration that high doses of radiation might destroy radiolytic products that were formed at low doses. However, the experimental evidence that has since accumulated indicates that the concentrations of radiolytic products generally increase in proportion to radiation dosage until they reach a plateau with radiation doses of about 10 kGy (1 Mrad) (*25*).

It may be concluded, therefore, that when no significant toxic effects have been obtained with a food treated with a high dose of radiation, there will be no effect when the same food is treated with a lower dose

---

[1] The report of the consultation group (document FAD/75.3) is available on request from Food Additives, World Health Organization, 1211 Geneva 27, Switzerland.

of radiation. It is not such a straightforward matter to extrapolate from data on foods treated with high doses of radiation that do produce toxic effects ; this is because it is not yet possible to give an assurance that *all* the radiolytic products having possible toxicity have been identified and because the biological dose/response relationships of even the known radiolytic products have not been determined with precision. Therefore there is still a need at present for a certain degree of toxicological testing to establish with confidence the safety of irradiated foods. However, the general principle of radiation chemical reactions, as revealed by analytical studies, will reduce considerably the extent to which toxicological testing is needed and will simplify the testing procedures.

In recent years, a considerable number of irradiated foods have been analysed chemically in detail. Most of the radiolytic products that have been identified are also found in various non-irradiated foods (*6*, *17*, *18*). The concentrations formed by radiation with doses of up to 60 kGy (6 Mrad) are generally less than 1 mg/kg (*17*, *19*, *25*). The major radiolytic products, such as carbon dioxide, methane, and hydrogen, are tolerable at considerably higher concentrations. The concentrations of radiolytic products that are formed by doses *below* 10 kGy (1 Mrad) are so low that their reliable identification is possible only in simple food materials such as starch, crystalline sugar, and pure fats.

The evidence so far obtained from radiation chemistry indicates that no acute toxicological effects will occur with irradiated foods. There remains, however, the possibility that more subtle long-term effects (e.g., carcinogenesis, mutagenesis) may occur. Most compounds with such effects either possess an electrophilic reactivity or are metabolized into compounds with such reactivity. In addition, autoxidizable compounds that yield peroxides possibly present a hazard. Considering from these viewpoints the chemical structure of the minor radiolytic products that have been identified, and the low concentrations at which they occur, there are no grounds for suspecting that they represent an actual hazard in irradiated foods.

Studies on the radiation chemistry of proteins, carbohydrates, and lipids have shown that these major food constituents react in uniform ways. This allows the prediction of the major radiolytic products that are likely to be present in more complex foods (*33*), though caution must be exercised in this respect.

It thus appears that the radiolytic products detected in the wide range of foods and individual food constituents that have been studied so far do not pose any toxicological hazards in the concentrations at which they have been detected. It is envisaged that radiation chemical investigations will eventually provide sufficient data (when taken in conjunction with findings from toxicological, nutritional and microbiological investigations) to facilitate greatly the evaluation of irradiated foods (5).

## 5. NUTRITIONAL ASPECTS

Irradiation, like certain other food-processing techniques, results in physicochemical changes in the product that may alter not only its organoleptic properties, and therefore consumer acceptance, but also its nutrient composition. Because of wide differences in the chemical constitution of different foods, the nature and extent of these changes may depend on the kind of food subjected to irradiation and on the irradiation dose. It is therefore important to :

(1) examine the changes that occur in the nutrient content of foods following irradiation ;

(2) determine whether the bio-availability of nutrients is in any way altered ; and

(3) establish whether changes, if they do occur, would have possible adverse nutritional consequences.

Relatively small changes in nutrient composition or bio-availability in foods that are consumed in considerable amounts in habitual diets may acquire nutritional significance, whereas similar changes in foods that are eaten only in small quantities would be less likely to affect nutritional balance. Thus, alterations in the nutritional quality of meat and fish, where these foods constitute a major part of the diet, would be more serious than changes in foods like papaya, mushroom, and strawberry. In several developing countries, large population groups obtain a very high proportion of several nutrients from a single food source (e.g., wheat, rice, or millet).

Generally, foods are irradiated in the raw state and stored for varying periods of time before they are cooked and consumed. Storage and cooking are among the factors known to result in loss of nutrients, depending on the type and duration of storage and the method of cooking. The extent to which irradiation may contribute to those losses deserves examination. Nutritional evaluation of irradiated foods should be carried out, when feasible, on foods as they are actually consumed.

The data available to the Committee do not indicate any significant deficiency in the nutritional quality of the irradiated foods that are evaluated in this report. However, as irradiation becomes more important as a process for the preservation of foods, it is likely that an increasing proportion of the diet will consist of irradiated foods. In assessing the wholesomeness of such a diet, it will be necessary to ensure that there is no cumulation of deficit of constituents that are lost as a result of irradiation.

## 6. MICROBIOLOGICAL ASPECTS

The Committee noted a number of technical terms that have been used to describe microbiological aspects of the processing of foods by irradiation (*8*). It was decided not to use these terms in this report, but they are listed and explained in Annex 1 for the convenience of those reading the literature on this subject.

The microbiology of irradiated foods can be considered only by regarding irradiation as a process. As with other processes (e.g., heating), the resulting microbiological changes depend on the nature of the product, its microflora, the dose of radiation, and the subsequent conditions of storage (*11*, *13*, *26*). Accordingly, each system requires separate consideration.

With high-dose irradiation, aimed at achieving commercial sterility of the food, no public health problems can be foreseen, provided the process is effective (*12*, *13*, *16*). However, at lower doses the microorganisms that survive irradiation may give rise to public health problems. The Committee reaffirmed the statement made by an FAO/IAEA group of consultants (*34*) that : " The microbiological problems of low- and intermediate-dose irradiation of food are not unique to this treatment. Virtually the same problems arise with several authorized and widely used preservation methods that do not lead to complete sterility."

The Committee reviewed a number of publications of international agencies (*7*, *28*, *30*, *34*) and the comments made on them by Member States. It also reviewed more recent data from selected studies. From these sources five areas of concern were identified that are considered in the following sections.

### 6.1 Storage temperature

It has been recommended that irradiated perishable foods be stored at 0°C. However, the Committee came to the conclusion that no single storage temperature can properly be recommended. To delay spoilage, perishable foods require storage at low temperatures, whether they have been irradiated or not. When organisms that constitute significant public health risk may be involved, the temperature that will achieve effective control should be specified ; this may be above the minimum temperature at which growth can occur. Appropriate storage temperature will thus differ from food to food. In irradiated fish, *Clostridium botulinum* type E is the likely hazard, but its growth can be controlled by storage at 3°C (*23*). In grain, aflatoxin-producing *Aspergillus* strains present a possible hazard, but they do not grow and form toxin below 10°C in moist systems (*4*) or even below 20°C in systems with a low water content (*20*). Some foods require no control of temperature during storage, whether they have been irradiated or not.

### 6.2 Viruses

Regarding the effect of irradiation on foodborne viruses, the following statement (*27*) seems valid :

> No evidence has been found that irradiation can increase the virulence of any virus present in food and since radiation in moderate dose is able to destroy at least some viruses it is reasonable to expect that the irradiation of food will diminish, and certainly not enhance, any hazard, slight though it may be, that already exists from the transmission to man through food of any infective virus responsible for ill health.

Subsequent research has confirmed that significant degrees of inactivation result from radiation treatments such as are envisaged (*9*, *14*, *24*), and a search for radiation-induced mutants revealed nothing of significance (see Annex 2).

### 6.3 Packaging

In those cases where the integrity of the package is critical, it must be remembered that irradiation may affect the chemical and physical properties of the packaging material and may thereby influence the microbiology of the food (*15*). However, doses of less than 10 kGy (1 Mrad) have little effect on packaging materials (*1*).

### 6.4 Enhanced pathogenicity

*Virulence*. There is some evidence that the pathogenicity of infectious organisms is diminished by irradiation (*10*, *12*). No evidence is known of increased pathogenicity following irradiation. There is no evidence of a problem resulting from growth, in the alimentary tract, of bacterial mutants that have survived non-sterilizing doses of radiation. If such a problem existed, it would probably have been detected in animals fed irradiated foods, because these animals are examined specifically for histological and gross pathology.

*Toxin-production*. The majority of investigations have demonstrated that irradiation decreases toxin production (*12*). In a few laboratory experiments, increases in toxin production have been reported after irradiation with doses of 1–5 kGy (100–500 krad), but the conditions did not correspond to those encountered in commercial practice. Handling of the food after irradiation must be such as to preclude outgrowth of toxin-producing organisms, as is required if the food is not irradiated.

### 6.5 Enhanced radiation resistance

Radiation-resistant variants have been produced under laboratory conditions that are not representative of the conditions prevailing in industry. These variants tend to be more selective with respect to conditions of growth than are the non-irradiated parent organisms (*12*, *21*).

The possibility that resistant forms may develop emphasizes the importance of good manufacturing practice and identification of critical control points (*2*). Similar concerns arise with food processes other than irradiation, such as heating (*3*, *22*).

## 7. TOXICOLOGICAL ASPECTS

The Committee emphasized that the responsibility for selecting the types of test to be carried out to establish the safety of irradiated foods rested on the investigators. It was therefore inappropriate to draw up strict protocols, but the Committee reiterated the necessity for following the generally accepted guidelines for adequate toxicological testing.

### 7.1 Diets used in toxicological testing

#### 7.1.1 *Experimental diets*

The Committee recommended that before any extensive study is started on irradiated food preliminary investigations should be performed to ensure the suitability of the test diet for use in later experiments. Such preliminary studies should aim at determining the maximum amount of food in question that can be incorporated in the animal diet without impairment of optimum growth, survival, and reproduction of the animals.

The maximum amount of the food will depend on its physical nature and nutritional quality and, as was shown by the data on onions and mushrooms considered by the present Committee, will be limited by the presence of natural constituents of foods that exert toxicologically significant effects when they are fed at high levels in the diet.

### 7.1.2 *Control diets*

The Committee noted that the irradiation of prepared feed for laboratory animals is becoming an increasingly common practice. Concern was expressed about the possible effect of irradiated feed on control groups used in toxicological testing. Such an effect might obscure differences that would have been discerned if a non-irradiated feed had been used.

The Committee was not aware of any published account, based on experience with long-established animal colonies, comparing basic biological data on the animals before and after the introduction of irradiated feed. Examples of the type of data required include mortality, morbidity, growth rate, haematology, tumour incidence, and reproductive capacity. To the extent that such data could be provided, they could be taken into account in the general assessment of the safety of irradiation as a process for the preservation of foodstuffs.

## 7.2 Toxicological studies

Continuing progress in methodology has resulted in modifications of traditional procedures, such as the introduction of transplacental exposure in long-term studies. However, the Committee emphasized that adequate data obtained prior to the introduction of these modifications were still acceptable for evaluation.

The Committee considered that the traditional multigeneration studies extending over three generations in one species should normally suffice for evaluation. If the results are inconclusive, the studies must be repeated in another species. Similarly, if teratological findings are equivocal, additional experiments will be required.

The Committee agreed with the views set forth in the reports of two WHO scientific groups (*31*, *32*) that no single test system can be expected to detect and characterize all mutagenic agents. The use of several tests is thus advisable.

### 7.3 Relevance of test materials to food as consumed by man

In testing for potential toxicity (and in other biological testing, such as for nutritional quality) it is necessary to establish that the material being tested corresponds to the food product that will be consumed in the diet.

#### 7.3.1 *Extracts of irradiated foods*

The administration by gavage of a water-ethanol extract of irradiated raw potatoes to mice resulted in mutagenic effects. The Committee regarded these findings as an interesting contribution to radiation toxicology that may stimulate further chemical work to determine the nature of the mutagenic principle(s). However, the findings are not of direct relevance to the safety evaluation of irradiated potatoes since the mutagenic effect was only obtained if the extract was prepared within a few hours of irradiation. Similar extracts from potatoes that had been stored for 40 days after irradiation were not mutagenic. Furthermore, boiling freshly irradiated potatoes before preparing the extract eliminated the mutagenic effects.

#### 7.3.2 *Reduction of water content of irradiated foods*

A number of toxicological studies were carried out on foods that were dried after irradiation. Thus, strawberries were freeze-dried and onions were dried by heating.

With strawberries, the freeze-drying was necessary to preserve the material for use in long-term feeding experiments. This procedure raised two questions that were considered by the Committee. The first was the relevance of findings obtained with the stored material to the intake of strawberries by man, which is generally within one week of irradiation. On this count, the Committee considered that the radiolytic products likely to be present in the strawberries at the time of their ingestion by man would be stabilized in the freeze-dried material. The second was the possibility that the removal of constituents with a high vapour pressure may have altered the toxicological properties of the irradiated strawberries. It was concluded that this did not distort the findings since short-term studies with whole strawberries and with the volatiles had also been carried out, and these revealed no toxic effects.

The use of heat-dried onions similarly raised the question of the loss of volatile components that may have exerted toxic effects. However, cooking results in a loss of volatile components similar to that produced by heat-drying, and a further safeguard is provided by the fact that raw onions are not normally consumed in large amounts. Consequently, the effects of irradiation on the volatile components was not regarded as a significant factor in the safety evaluation. Nevertheless, the Committee considered that it is desirable for further work to be carried out on the nature and biological properties of the volatile components that are lost from irradiated onions during heat-drying and recommended that these components be compared with those lost during cooking and with those lost from non-irradiated onions by heat-drying and cooking.

### 7.3.3 *Time after irradiation*

Biological effects of possible toxicological significance were obtained with freshly irradiated potatoes and wheat (see section 9.1) but the effects were absent after storage. This reinforces the need to test the food as it is consumed by man.

### 7.3.4 *Radiation dose and processing conditions*

Because the radiation dose varies to some extent between samples treated under practical conditions in a food irradiation plant, it is recommended that the food to be used in feeding studies should be exposed to a radiation dose at least as high as the maximum dose likely to be encountered in commercial practice (see section 3.1). Furthermore, certain physical properties such as the water content of the irradiated material, the availability of oxygen, the temperature, and the storage conditions after irradiation should approximate to those that will prevail in commercial practice.

## 7.4 Observations in man and extrapolation from animal studies to man

The Committee was aware of the usefulness of adequate observations in man but noted the limitations inherent in the accepted scope of human experimentation. The Committee recognized the existence of the general problem of extrapolation to man of data obtained in experimental animals. Nevertheless, the absence of toxicologically significant effects from all relevant animal studies on an irradiated food and on related foods may be taken as indicative of the safety of the irradiated food for consumption by man.

# 8. METHOD OF EVALUATION

## 8.1 Categories of acceptance

A previous Expert Committee (*30*) decided in 1969 to adopt three categories of acceptance broadly similar to the types of acceptance that had been prescribed for food additives in 1967 (*29*). The present Committee found that, in dealing with the irradiated foods on its agenda, it was sufficient to have only two categories of acceptance, defined as follows.

*Unconditional acceptance*. Acceptance granted when adequate data are available for the unequivocal establishment of the wholesomeness of the irradiated product.

*Provisional acceptance*. Acceptance granted when additional testing is required to establish the wholesomeness of the irradiated product for lifetime use by man but when there are sufficient existing data to indicate that no hazards to health would arise from consumption of the irradiated product in the diet over the period that would elapse before the additional testing was carried out and the findings were evaluated. It is recommended, therefore, that a provisional acceptance should remain in force until the new data are evaluated by a future FAO/IAEA/WHO Joint Expert Committee.

The Committee chose the term " provisional " for the second category of acceptance to avoid the implications that have become attached to the terms " temporary " and " conditional " in respect of the acceptance of food additives. Moreover, the major determinant of acceptance of food additives is the toxicological evaluation, whereas the categories of acceptance for irradiated food are based on the concept of wholesomeness, which implies not only safety from the toxicological point of view but freedom from microbiological hazard and adequacy of nutritional quality.

The acceptance granted to an irradiated food is always subject to revision when further data become available. This is so regardless of whether the food has been granted unconditional or provisional acceptance.

## 8.2 Further work recommended

In granting a provisional acceptance, the Committee has in all cases specified the " further work required ". This implies a mandatory requirement in the sense that failure to accomplish the work or to submit the data for evaluation could result in revocation of the provisional acceptance. It is envisaged that evaluation of the required work would normally lead to an unconditional acceptance for the irradiated food, unless the data fail to provide adequate evidence of its wholesomeness.

In some cases, the Committee has stated that there is " further work *desired* " in respect of certain irradiated products that have been granted either unconditional or provisional acceptance. This does not imply that acceptance will be revoked if the work is not carried out ; rather, it is an expression of the opinion of the present Committee that the results of the desired work would provide a more comprehensive view of the biological consequences of ingestion of irradiated food.

### 8.3 Irradiated foods for which acceptance has not been granted

In some cases, the Committee has not been sufficiently satisfied with the available data to warrant even the provisional acceptance of certain irradiated foods.

However, it is recognized that the benefits likely to accrue from the processing of these foods by irradiation merit the encouragement of further testing to allow their eventual acceptance.

## 9. RE-EVALUATION OF IRRADIATED WHEAT, POTATO, AND ONION

### 9.1 Irradiated wheat (*Triticum* species) and ground wheat products

*Purpose of irradiation*

To control insect infestation in stored wheat and in ground wheat products.

*Irradiation data*

| | |
|---|---|
| Dose range | 0.15–1.00 kGy (15–100 krad). |
| Type of radiation | gamma rays from $^{60}$Co or $^{137}$Cs ; or fast electrons of up to 10 MeV energy. |

*Microbiological aspects*

To be acceptable for storage or irradiation, wheat and ground wheat products must have a water content sufficiently low to prevent the growth of microorganisms. Under these circumstances there is no known public health hazard of microbial origin.

If, through incorrect storage, the water content is raised, a growth of toxin-producing fungi might conceivably create a significant health hazard. Some laboratory reports suggest that irradiation may lead to enhanced toxin formation by these fungi ; in view of this possibility, irradiated wheat must be stored in such a way as to prevent mould outgrowth (as is also the case with non-irradiated wheat). However, recently developed data indicate that the regrowth of fungi on irradiated wheat is slower than on non-irradiated wheat and that toxin-producing fungi are more susceptible than other fungi to irradiation. Some pathogenic organisms may be introduced into wheat during grinding but they do not ordinarily grow in the product if it is properly stored and irradiation may kill some of them. Even if the conditions of subsequent storage are not ideal, no microbiological problems are likely to arise from the ingestion of irradiated wheat and ground wheat products.

### *Nutritional aspects*

Wheat constitutes the staple diet for large population segments in many countries. A major proportion of several nutrients such as protein, carbohydrates, vitamins of the B complex group, and minerals is derived from this single item of food.

Within the range of radiation doses to be used, no appreciable changes are produced in the total moisture, ash, nitrogen, protein, fat, and carbohydrate content of wheat. The protein nutritive value of whole wheat and of wheat gluten, including the lysine content, is unaltered by irradiation within the range of the technical specification. Irradiation does not alter the nutrient composition of bread baked from wheat, even when the wheat has been stored for a period of 12 months after irradiation. The requirement of the 1969 Joint Expert Committee (*30*) that data be provided on this point has therefore been met.

Following irradiation within the technological range, vitamin E in wheat is stable, and the concentrations of the B complex vitamins do not show much change except for thiamine, which may be lost to some extent. But even this loss is unlikely to affect the vitamin supply significantly. It is concluded that irradiation with doses falling within the range of the technological specification does not impair the nutritional qualities of wheat and ground wheat products.

### *Toxicological aspects*

The additional investigations considered by the Committee meet the requirements of the 1969 Joint Expert Committee (*30*).

Extensive toxicological data are now available from long-term reproduction and mutagenicity studies. The Committee noted the increase in frequency of polyploid cells reported in certain investigations on several species fed freshly irradiated wheat. However, no increase in polyploidy was seen when wheat stored for 12 weeks after irradiation was used. Since irradiated wheat is usually stored for longer than 12 weeks, no problems are likely to arise in practice. Furthermore, in studies carried out by other investigators, no increase in the frequency of polyploidy was observed even when using wheat stored for as short a period as 24 hours after irradiation. It would be desirable to investigate further the factors that may be involved in the increase in the incidence of polyploidy produced by irradiated wheat. The significance of the observations on polyploidy are not clear since the range of incidence of polyploidy varies considerably between normal groups of the same species of animal, and the toxicological implications of an increased incidence of polyploidy are not understood.

For the evaluation of safety based on the principles enunciated in the report (section 2.3), it was considered reasonable to take into account the radiation chemical studies on various starches and the absence of adverse effects in feeding studies with irradiated maize starch. In addition, the data on rice and potatoes (both high starch foods) were taken into account.

Toxicological data do not indicate any health hazard resulting from the consumption of irradiated wheat and ground wheat products.

*Evaluation*

Unconditional acceptance of wheat and ground wheat products irradiated for the purpose of disinfestation with a maximum radiation dose of 1 kGy (100 krad).

### 9.2 Irradiated potato (*Solanum tuberosum*)

*Purpose of irradiation*

To inhibit sprouting during storage.

*Irradiation data*

| | |
|---|---|
| Dose range | 0.03–0.15 kGy (3–15 krad). |
| Type of radiation | gamma rays from $^{60}$Co or $^{137}$Cs; or fast electrons of up to 10 MeV energy. |

### *Microbiological aspects*

No special microbiological problems of public health significance are known to be associated with irradiated potatoes.

### *Nutritional aspects*

Potatoes form an important part of the diet in many countries. The important nutrients that they supply are carbohydrates, ascorbic acid, and niacin. Following irradiation, the concentration of total carbohydrates shows only small changes, although there is an immediate increase in the free sugar content. Some changes occur in the concentration of free amino acids without any alterations in the amino acid make-up of the protein. With doses of 0.1 kGy (10 krad), losses in ascorbic acid do not exceed 15% and subsequent loss during storage is not accentuated. Thiamine and riboflavin contents remain unaltered. Experimental studies on a variety of animal species have shown that the nutritional quality of diets containing irradiated potatoes (as much as 18% dry weight) is no different from that of diets containing similar amounts of non-irradiated potatoes. It would appear that the nutritive value of potatoes is essentially unchanged by irradiation.

### *Toxicological aspects*

Long-term studies in two rodent species have shown that the inclusion of irradiated potatoes in the diet does not induce any adverse effects. One long-term study reported statistically significant changes in ovary size, but this was not associated with any abnormal histopathological findings. Moreover, extensive reproduction studies in mice and rats revealed no abnormalities as a result of ingestion of cooked irradiated potatoes nor did they produce any evidence of mutagenic potential.

For the evaluation of safety based on the principles enunciated in section 2.3, it was considered reasonable to take into account the radiation chemical studies on various starches and the absence of adverse effects in feeding studies with irradiated maize starch, irradiated wheat, and irradiated rice.

The toxicological data do not indicate any health hazards from ingestion of irradiated potatoes, and the requirements of the 1969 Joint Expert Committee (*30*) for the provision of adequate reproduction and long-term studies have been met.

*Evaluation*

Unconditional acceptance of potatoes irradiated for the purpose of controlling sprouting with a maximum radiation dose not exceeding 0.15 kGy (15 krad).

### 9.3 Irradiated onion (*Allium cepa*)

*Technological purpose of irradiation*

To inhibit sprouting during storage.

*Irradiation data*

| | |
|---|---|
| Dose range | 0.02–0.15 kGy (2–15 krad). |
| Type of radiation | gamma rays from $^{60}$Co or $^{137}$Cs; or fast electrons of up to 10 MeV energy. |

*Microbiological aspects*

No special microbiological problems of public health significance are known to be associated with irradiated onions.

*Nutritional aspects*

Few population groups consume onions habitually in large amounts, and the contribution of onions to total nutrient intake is small. Hence changes in the concentration of nutrients in onions following irradiation may be relatively unimportant. Irradiation of onions within the range of the technical specification has little effect on their ascorbic acid content or on the subsequent loss of the vitamin during storage. No consistent changes occur in the total sugar content and reducing sugars.

There is no evidence to show that ingestion of irradiated onions in the amounts usually consumed has any adverse nutritional effects.

*Toxicological aspects*

Onions are known to contain natural constituents causing haemolysis and anaemia with consequential splenic enlargement and haemosiderin deposition. The 1969 Joint Expert Committee was unable to evaluate the results of earlier experiments (in which high levels of onions were fed to several species) because of interference from nonspecific effects. New data from long-term studies on mice and rats revealed no excessive mortality, despite the reduction in group size as a result of interim sacrifices, and produced no evidence of carcinogenic effects. A one-year study in rats at a lower feeding level gave no evidence of any adverse chronic toxic effects. These findings, together with the radiation chemical studies, tend to exclude the possibility of a carcinogenic potential of irradiated onions.

The statistically significant changes in the weights of ovaries and testes observed when irradiated onions were fed to mice in a reproduction study were not associated with abnormal histopathological changes or deleterious effects on reproduction. The changes in organ weights were therefore not regarded as being of consequence for human health. However, in subsequent long-term rat studies, special attention should be paid to the ovaries and testes.

The occurrence of fused costal cartilages in the $F_3$ progeny of the mouse reproduction study was not considered to be significant because too few controls had been used and not enough information had been available on the natural incidence of the phenomenon in the particular mouse strain used. The repeat experiment revealed no similar abnormalities in the three generations examined.

The toxicological data do not indicate any health hazard arising from ingestion of irradiated onions.

*Evaluation*

Provisional acceptance of onions irradiated for the purpose of controlling sprouting with a maximum radiation dose of 0.15 kGy (15 krad).

*Further work required by 31 December 1979*

Multigeneration reproduction study in rats at feeding levels below that causing biological changes due to the biologically active substances naturally present.

## 10. NEW EVALUATIONS

### 10.1 Irradiated chicken (*Gallus domesticus*)

*Purpose of irradiation*

(*a*) To prolong storage life of
(*b*) To eliminate pathogenic microorganisms from
eviscerated chicken stored below 10°C.

*Irradiation data*

| | |
|---|---|
| Dose range | for purpose (*a*) to reduce microbial spoilage, 2–7 kGy (200–700 krad). |

| | |
|---|---|
| | for purpose (*b*) to reduce the number of pathogenic microorganisms, 5–7 kGy (500–700 krad). |
| Type of radiation | gamma rays from $^{60}$Co or $^{137}$Cs; or fast electrons of up to 10 MeV energy. |

*Microbiological aspects*

The known foodborne microbial pathogens of public health significance occurring in chicken are the salmonellae, *Clostridium perfringens*, and *Clostridium botulinum*. The specified radiation doses are likely to reduce salmonellae contamination by a factor of about 10 000. It is important that the irradiated product be handled in such a way as to prevent recontamination and that the temperature of subsequent storage be sufficiently low (10°C) to control regrowth from any surviving salmonellae.

Substantial proportions of the incident *Clostridium* spores in chicken are likely to remain viable after irradiation, but temperatures that will control regrowth of salmonellae should suffice to control clostridia as well.

The lowest temperatures necessary to delay spoilage should be used, but in no case should this temperature exceed 10°C. Where proper refrigeration is practised, no microbiological public health problems are likely to arise from the ingestion of irradiated chicken.

*Nutritional aspects*

No changes in the protein nutritive value have been seen with doses up to 7 kGy (700 krad). On storage, however, there was an increase in the peroxide value of the fat.

Data on changes in vitamins following irradiation are conflicting. Thiamine losses in chicken, as in other foods, are a function of radiation dose, storage time, and temperature. Where chicken is not a major source of meat-derived thiamine, the small changes that may occur have no nutritional implications.

*Toxicological aspects*

Long-term studies in two rodent species, a three-generation reproduction study in rodents, and a one-year study in the dog have failed to reveal any adverse findings associated with the ingestion of irradiated chicken. The absence of abnormalities in the offspring of rats and mice in the multigeneration studies indicates the absence of teratological or mutagenic potential.

The toxicological data do not indicate any health hazard resulting from the ingestion of irradiated chicken.

*Evaluation*

Unconditional acceptance of chicken irradiated for the purpose of reducing microbiological spoilage or of reducing the number of pathogenic microorganisms at a maximum radiation dose of 7 kGy (700 krad).

## 10.2 Irradiated fresh cod (*Gadus morhua*) and redfish (*Sebastes marinus*) intended for evisceration

*Purpose of irradiation*

(*a*) To reduce microbial spoilage of packaged or unpackaged fish refrigerated at or below 3°C.

(*b*) To reduce the number of pathogenic microorganisms in packaged or unpackaged fish refrigerated at or below 3°C.

*Irradiation data*

| | |
|---|---|
| Dose range | 1.0–2.2 kGy (100–220 krad). |
| Type of radiation | gamma rays from $^{60}$Co or $^{137}$Cs ; or fast electrons of up to 10 MeV energy. |

*Microbiological aspects*

Consideration is restricted to fresh teleost fish. At the time they are caught, fish taken from the deep ocean are far less likely to harbour organisms pathogenic for man than are fish caught near the shore. At the time of irradiation, the native microflora of the fish will have been modified by handling and by any other process that may have been applied.

No microbiological problems of public health significance are likely to result from irradiation of fresh fish that is stored at or below 3°C, whether packaged or not.

*Nutritional aspects*

Fish is a good dietary source of protein, B vitamins, and iodine. It is less important as a source of fat and of vitamins A and D. Radiation doses of 1.0–2.2 kGy (100–220 krad) do not appreciably change the organoleptic properties of fish.

The amino acid content of fish does not change after irradiation. The protein quality of a variety of fish, including cod, haddock, and flounder, is unaltered even by doses of the order of 10 kGy (1 Mrad).

The fat content of fish varies with species and season. Data on changes in the lipid profile of fish after irradiation are scanty and their provision is desirable.

No significant changes in the concentrations of thiamine, riboflavin, niacin, pyridoxine, and $B_{12}$ have been found after irradiation with a dose of 3 kGy (300 krad). After doses of 6 kGy, between 47% and 94% of the thiamine can be lost. However, even with these high doses, other B complex vitamins are not destroyed to any significant extent. The nutritive value of irradiated fresh fish intended for evisceration remains essentially unchanged after irradiation with the technically specified doses.

*Toxicological aspects*

Short-term studies in mice, rats, and dogs have been carried out either on mixed eviscerated cod (a non-fatty fish) and redfish (a fatty fish) or on other fish varieties. They do not reveal any evidence to suggest that feeding of irradiated fish causes any deleterious effects. Some of the studies are still incomplete. Only the mixed cod and redfish material has been adequately tested in the rat in long-term, multigeneration reproduction, dominant lethal, and cytogenetic studies. Earlier long-term studies on other fish varieties were inadequate in design and number of animals used per group, but they did not indicate any adverse effect.

A number of studies on other varieties of fish are in progress but none is sufficient in itself to support acceptance. However, when these studies are completed a subsequent Committee may wish to consider the total information when evaluating the wholesomeness of teleost fish in general.

There is also a need for data on irradiated fish liver and roe in order to evaluate the wholesomeness of these commodities after irradiation of the whole fish.

The toxicological data do not indicate any health hazard resulting from ingestion of the flesh of irradiated cod and redfish.

*Evaluation*

Provisional acceptance of cod and redfish eviscerated after irradiation for the purpose of reducing microbiological spoilage and the number of pathogenic organisms at a maximum radiation dose of 2.2 kGy (220 krad).

*Further work required by 31 December 1979*

Results of the various studies that are in progress.

### *Addendum on microbiological aspects of irradiated dried fish*

The purpose of irradiation of this product is disinfestation. Clearly the product must be handled so as to prevent reinfestation. It is assumed that the product, dried with or without salt, is microbiologically stable. It must not be allowed to concentrate moisture. There will then be no need to store it at a temperature other than that usual for normal (non-irradiated) dried fish. No microbiological public health problems are likely to arise from the ingestion of irradiated dried fish.

## 10.3 Irradiated mushroom (*Agaricus campestris* var. *bisporus*)

### *Purpose of irradiation*

To retard opening of the cap (rupture of the veil) in cultured mushrooms, thereby increasing shelf-life and reducing losses in quality and value of the product.

### *Irradiation data*

| | |
|---|---|
| Dose range | 0.25–3.00 kGy (25–300 krad). |
| Type of radiation | gamma rays from $^{60}$Co or $^{137}$Cs; or fast electrons of up to 10 MeV energy. |

### *Packaging*

If packaged mushrooms are irradiated, care must be taken to maintain aerobic conditions in the package.

### *Microbiological aspects*

It has previously been suggested that there are no public health problems of a microbiological nature associated with irradiated mushrooms. However, it has recently been shown that, in fresh mushrooms experimentally inoculated with *Clostridium botulinum* spores and stored in airtight packages, outgrowth and production of botulinum toxin result. Since *C. botulinum* spores may survive on irradiated mushrooms it seems that both irradiated and non-irradiated mushrooms should be packaged in such a way as to maintain aerobic conditions. No microbiological public health problems are likely to arise from the ingestion of irradiated mushrooms.

### *Nutritional aspects*

There is virtually no information regarding changes in the nutrient composition of mushrooms following irradiation. In view of the relatively small amounts in which they are consumed, any changes that may occur will be unimportant from the nutritional point of view.

*Toxicological aspects*

In short-term feeding experiments with high dietary levels in the rat and the dog a number of adverse effects were observed.

It was difficult to differentiate between the effects produced by irradiated mushrooms and those produced by non-irradiated mushrooms. Any effects due to irradiation were thus undetectable. The long-term study in rats has been carried out with small numbers of animals per group and cannot be regarded as adequate evidence of absence of carcinogenic or other adverse effects. The reproduction studies and the teratogenicity study in rats do not reveal any statistically significant adverse effects that could be related with certainty to the radiation dosages employed. No data from specific mutagenicity tests are available.

It was recognized that mushrooms are in a different category from major staple foods. The testing requirements to establish a satisfactory basis for acceptance of the wholesomeness of irradiated mushrooms may be less stringent than those for staple foods.

*Evaluation*

Not possible with the data provided.

## 10.4 Irradiated papaya (*Carica papaya*)

*Purpose of irradiation*

To control insect infestation in papaya and to improve its keeping quality by delaying ripening.

*Irradiation data*

| | |
|---|---|
| Dose range | 0.5–1.0 kGy (50–100 krad). |
| Type of radiation | gamma radiation from $^{60}$Co or $^{137}$Cs should be used in order to secure deep enough penetration to kill insects at the centre of the fruit. |

*Microbiological aspects*

No direct microbiological investigations are available. However, the natural microflora on papaya surfaces does not normally include pathogenic organisms, and the total number of microorganisms can be expected to be relatively low owing to the washing and drying practices employed prior to irradiation. The range of storage temperatures commonly encountered for papaya would also tend to limit the possibility of significant microbial outgrowth. The same hygienic control and handling practices are required for irradiated fruit as are commonly employed for the non-irradiated product. No microbiological public health problems are likely to arise from the ingestion of irradiated papaya.

### *Nutritional aspects*

Papaya is a rich source of two nutrients : beta carotene and ascorbic acid. Irradiation of green or three-fourths-ripe papaya with 0.25–0.75 kGy (25–75 krad) may lead to the loss of up to 24% of its ascorbic acid content, but the irradiation of ripe fruit has little effect on vitamin content. Data on changes in the beta carotene content of papaya are not available. Communities that depend on this fruit as an important source of the two vitamins are most unlikely to make use of papayas as a marketed commodity, which is the way the irradiated fruit is handled. Losses in ascorbic acid and beta carotene due to irradiation are unlikely to have nutritional effects on people who consume the irradiated fruit since they are likely to obtain these two vitamins from other food sources. The irradiation of papaya poses no nutritional problems.

### *Toxicological aspects*

The available short-term, long-term, and reproduction studies in mice and rats and the short-term tests in dogs are adequate and reveal no evidence of deleterious effects attributable to irradiated papaya. The host-mediated assay revealed no mutagenic activity. The results of reproduction experiments in the dog cannot be evaluated because of the known difficulties experienced with this type of test. Similarly the isolated adverse findings in some of the dog progeny, taken in conjunction with all other evidence, cannot be judged as related to the ingestion of irradiated papaya.

The toxicological data do not indicate any health hazard resulting from ingestion of irradiated papayas.

### *Evaluation*

Unconditional acceptance of papaya irradiated for the purpose of disinfestation with a maximum radiation dose of 1 kGy (100 krad).

## 10.5 Irradiated rice (*Oryza* species)

*Purpose of irradiation*

To control insect infestation in stored rice.

*Irradiation data*

| | |
|---|---|
| Dose range | 0.1–1.0 kGy (10–100 krad). |
| Type of radiation | gamma rays from $^{60}$Co or $^{137}$Cs; or fast electrons of up to 10 MeV energy. |

*Microbiological aspects*

To be acceptable for storage or irradiation, rice must have a water content sufficiently low to prevent growth of microorganisms. Under these circumstances there is no known public health hazard.

If through incorrect storage the water content were raised, growth of toxin-producing fungi might conceivably create a significant health hazard. Some laboratory reports suggest that irradiation may lead to enhanced toxin production by these fungi, and in view of this possibility irradiated rice must be stored in such a way as to prevent mould outgrowth. The same consideration applies to non-irradiated rice. However, more recent data indicate that toxin-producing fungi are more susceptible than are other fungi to irradiation and that toxin-producing aspergilli require higher water content for growth than do other aspergilli, in which case the toxin-producing species are likely to be overgrown by the other species. Even if the conditions of subsequent storage are not ideal, no microbiological problems are likely to arise as a result of irradiation of rice.

*Nutritional aspects*

Like other cereals, rice constitutes a staple food for large segments of the population in several continents. A major proportion of several nutrients therefore comes from rice.

The available data show that irradiation has no detectable effect on the nitrogen content, free amino acid concentration, and amino acid profile of rice protein. Following storage, free fatty acid levels increase in both non-irradiated and irradiated rice, but the increase appears to be greater in irradiated samples.

Riboflavin content is not altered within the range of radiation doses specified above, although higher doses cause losses. Studies on the effects of irradiation on the thiamine content of rice are limited. More data on this aspect are desirable since there is considerable loss of thiamine during traditional cooking methods employed in certain countries. The extent of losses due to irradiation may become relevant when rice is a staple item of the diet and a major source of thiamine.

*Toxicological aspects*

The only short-term study in mice that has been adequately performed revealed no adverse effects from the ingestion of irradiated rice. Other studies were considered inadequate either because of the small number of animals per group or because only a few variables were examined. A long-term feeding study in rats is in progress and interim reports do not appear to indicate any significant adverse effects arising from the irradiation of rice. A multigeneration teratogenicity study and a mutagenicity study have been performed in mice. Both these studies are adequate, and neither reveals any deleterious effect.

For the evaluation of safety, based on the principles enunciated in this report (section 2.3), it was considered reasonable to take into account the irradiation chemical studies in various starches and the absence of adverse effects in the feeding studies with irradiated maize starch, irradiated wheat, and irradiated potatoes.

Toxicological data do not indicate any health hazard resulting from the ingestion of irradiated rice.

*Evaluation*

Provisional acceptance for rice irradiated for the purpose of controlling insect infestation at a maximum radiation dose of 1 kGy (100 krad).

*Further work required by 31 December 1979*

Results of the long-term study in rats and the study in monkeys that are now in progress.

### 10.6 Irradiated strawberry (*Fragaria* species)

*Purpose of irradiation*

To prolong the storage life of fresh strawberries by partial elimination of spoilage organisms.

*Irradiation data*

| | |
|---|---|
| Dose range | 1–3 kGy (100–300 krad). |
| Type of radiation | gamma rays from $^{60}$Co or $^{137}$Cs; or fast electrons of up to 10 MeV energy. |

### *Microbiological aspects*

From the microbiological standpoint, strawberries have not ordinarily presented public health problems. However, outbreaks of gastrointestinal disease have recently been recorded among consumers of strawberries that had been irrigated with sewage-polluted water. Such strawberries can be identified, and rejected, on the basis of bacteriological tests for fecal indicators. If these strawberries were irradiated, the bacterial indicators and any bacterial enteric pathogens would probably be destroyed, but the viruses that are likely to be present would not. Therefore, if there is reason to suspect contamination, bacteriological tests should be carried out before irradiation. No microbiological problems are likely to arise from the ingestion of irradiated strawberries of good hygienic quality.

### *Nutritional aspects*

The nutritive value of strawberries lies predominantly in their high ascorbic acid content. Irradiation within the specified range of doses does not significantly reduce the ascorbic acid concentration. The irradiation of strawberries raises no nutritional problems.

### *Toxicological aspects*

Investigations with preparations of irradiated strawberries included adequate short-term and long-term studies in rats, and two-year studies in chickens and dogs. These showed that feeding various frozen or freeze-dried preparations of irradiated strawberries caused no adverse effects significantly different from those produced by the ingestion of similar preparations of non-irradiated strawberries. The observed deleterious effects occurred randomly in various control and test groups and were not related to the administration of irradiated material. The small number of animals used in the dog study and the large individual variations in the variables examined render statistical evaluation difficult. *In vitro* mutagenicity tests show no evidence of mutagenic activity, and the tumour incidence in the long-term rat study showed no significant differences between the group fed irradiated strawberries and the group fed non-irradiated strawberries.

Strawberries are normally consumed within one week of irradiation, but freeze-dried strawberries were used in the feeding studies. Since radiation chemical studies indicate that radiolytic products are stabilized by freeze-drying, the results of these feeding studies are considered relevant to the toxicological assessment of fresh irradiated strawberries.

In addition, studies performed with strawberry *purée* showed no adverse effects. The volatile substances from irradiated and non-irradiated strawberries have been examined for mutagenic potential with negative results. Toxicological data do not indicate any health hazard resulting from ingestion of irradiated strawberries.

*Evaluation*

Unconditional acceptance for strawberries irradiated for the purpose of prolonging storage life with radiation doses up to a maximum of 3 kGy (300 krad).

## 11. FUTURE RESEARCH

In addition to the "further work required" on specific irradiated foods for which provisional acceptance was granted (sections 9.3, 10.2 and 10.5), the Committee recommends that work be carried out in the following areas to increase general knowledge about the consequences of food processing by irradiation and to facilitate future evaluations:

(1) Further identification of radiolytic products and, where appropriate, determination of their toxicity (see section 2).

(2) Collection and scrutiny of data from long-established animal colonies for possible changes in basic biological data that may have resulted from the use of irradiated laboratory feed (see section 7.1).

(3) Comparison of the losses of nutritional value produced by irradiation with those produced by other processes and by storage, and the effect of combinations of irradiation and other processes on the nutritional value (see section 5).

(4) Comparison of the toxicological properties of volatile components of irradiated and non-irradiated foods (see section 7.3.2).

(5) Chemical, nutritional, and toxicological studies on the radiolytic products of lipids, with reference to peroxide and epoxide formation and *cis-trans* isomerization (see section 10.2).

## 12. RECOMMENDATIONS

Since there is need for further research on the irradiation of a number of foods and on related matters and since the results of such work will be forthcoming, the Committee recommended that FAO, IAEA, and WHO should give consideration to the establishment of an intersecretariat mechanism for keeping under constant review the progress being made in the field of food irradiation and for convening further meetings of experts to evaluate data at appropriate times.

In view of advances of knowledge in the field of food irradiation, the Committee suggested that future evaluations of the wholesomeness of individual irradiated foods should take into consideration all relevant data obtained from tests on analogous irradiated foods and on representative food constituents.

## REFERENCES

1. Agarwal, S. R. & Sreenivasan, A. *Journal of food technology*, **8** : 27–37 (1972)
2. Baumann, H. E. *Food technology*, **28**(9) : 30–34 (1974)
3. Corry, J. E. L. & Roberts, T. A. *Journal of applied bacteriology*, **33** : 733–737 (1970)
4. De Waart, J. et al. *Alimenta*, **13** : 35–43 (1974)
5. Diehl, J. F. & Scherz, H. *International journal of applied radiation and isotopes*, **26** : 499–507 (1975)
6. Drawert, F. In : *Proceedings of the International Colloquium on the Identification of Irradiated Foodstuffs, Karlsruhe, 24–25 October 1973*. Luxembourg, Commission of the European Communities, Directorate-General Scientific and Technical Information and Information Management, 1974, pp. 109–124 (EUR 5126)
7. FAO Atomic Energy Series, No. 6, 1966
8. Goresline, H. E. et al. *Nature (London)*, **204** : 237 (1964)
9. Heidelbaugh, D. & Giron, D. J. *Journal of food science*, **34** : 239–241 (1969)
10. Idziak, E. S. & Incze, K. *Applied microbiology*, **16** : 1061–1066 (1968)
11. Ingram, M. *International journal of applied radiation and isotopes*, **6** : 105–109 (1959)
12. Ingram, M. *Microbiology of foods pasteurised by ionising radiation*. Karlsruhe, International Project in the Field of Food Irradiation, 1975 (Technical Report Series IFIP–R 33)
13. Ingram, M. & Roberts, T. A. Microbiological principles in food irradiation. In : *Food irradiation*. Vienna, International Atomic Energy Agency, 1966, pp. 267–285
14. Johnson, C. D. *In vitro* experiments on the radiosensitivity of foot-and-mouth disease virus and other animal viruses to the direct effect of X-irradiation. In : *Elimination of harmful organisms from food and feed by irradiation : proceedings of a panel, Zeist, 12–16 June, 1967*. Vienna, International Atomic Energy Agency, 1968, pp. 65–69
15. Killoran, J. J. *Radiation research reviews*, **3**(4) : 369 (1972)

16. Matsuyama, A. Present status of food irradiation research in Japan with special reference to microbiological and entomological aspects. In : *Radiation preservation of food : proceedings of an international symposium, Bombay, 13–17 November 1972.* Vienna, International Atomic Energy Agency, 1973, pp. 261–278

17. Merritt, C., Jr. *Radiation research reviews,* **3** : 353–363 (1972)

18. Nawar, W. W. In : Elias, P. S. & Cohen, A. J., ed. *Radiation chemistry of basic food components.* Amsterdam, Elsevier (in press)

19. Nawar, W. W. & Balboni, J. J. *Journal of the Association of Official Analytical Chemists,* **53**: 726 (1970)

20. Northolt, M. D. et al. *Journal of milk and food technology,* **39** : 170–174 (1976)

21. Parisi, A. N. & Antoine, A. D. (In press)

22. Peterson, A. C. & Gunnerson, R. E. *Food technology,* **28**(9) : 37–44 (1974)

23. *Preservation of fish by irradiation.* Vienna, International Atomic Energy Agency, 1970

24. Sullivan, R. et al. *Applied microbiology,* **26** : 14–17 (1973)

25. Taub, I. A. et al. *Journal of food science,* **41** : 942–944 (1976)

26. Thornley, M. J. & Ingram, M. *International journal of applied radiation and isotopes,* **14** : 45–48 (1963)

27. United Kingdom, Ministry of Health, Committee on Medical and Nutritional Aspects of Food Policy. *Report of the Working Party on Irradiation of Food.* London, H.M. Stationery Office, 1964, p. 29, para. 121

28. WHO Technical Report Series, No. 316, 1966

29. WHO Technical Report Series, No. 383, 1968

30. WHO Technical Report Series, No. 451, 1970

31. WHO Technical Report Series, No. 482, 1971

32. WHO Technical Report Series, No. 546, 1974

33. Elias, P. S. & Cohen, A. J., ed. *Radiation chemistry of basic food components.* Amsterdam, Elsevier (in press)

34. *Report of an FAO/IAEA Consultants' Meeting on Microbiological Aspects of Food Irradiation, 16–19 December 1974, Vienna.* (Document available on request from Food Preservation Section, International Atomic Energy Agency, A-1011 Vienna, P. O. Box 590, Austria.)

# Annex 1

## TERMS USED IN RADIATION MICROBIOLOGY

*Radappertization.* Treatment of food with a dose of ionizing radiation sufficient to reduce the number and/or activity of viable microorganisms to such a level that very few, if any, are detectable by any recognized bacteriological or mycological testing method applied to the treated food. The treatment must be such that no spoilage or toxicity of microbial origin is detectable no matter how long or under what conditions the food is stored after treatment, provided it is not recontaminated.

*Radicidation.* Treatment of food with a dose of ionizing radiation sufficient to reduce the number of viable specific non-spore-forming pathogenic bacteria to such a level that none is detectable in the treated food when it is examined by any recognized bacteriological testing method.

*Radurization.* Treatment of food with a dose of ionizing radiation sufficient to enhance its keeping quality by causing a substantial reduction in the numbers of viable specific spoilage microorganisms.

The terms radappertization, radicidation and radurization replace the designations Type I, II, and III respectively, as defined in the report of the Joint FAO/IAEA/WHO Expert Committee on the Technical Basis for Legislation on Irradiated Food.[1, 2]

---

[1] GORESLINE, H. E. ET AL. *Nature (London)*, **204**: 237 (1964).

[2] FAO Atomic Energy Series, No. 6, 1966; WHO Technical Report Series, No. 316, 1966, p. 27.

## Annex 2

# UNLIKELIHOOD OF MUTAGENIC EFFECTS OF RADIATION ON VIRUSES [1]

The possibility that gamma rays might produce mutations in foodborne viruses that were not inactivated was suggested several years ago.[2] The results of unpublished studies on the mutagenesis of enteroviruses by gamma rays carried out at the Food Research Institute of the University of Wisconsin during the years 1966–69 are given below.

Four enteroviruses were selected as models : poliovirus 1 (strain CHAT), coxsackievirus A-9 (strain Bozek), coxsackievirus B-2 (undesignated strain), and echovirus 6 (strain D'Amori). These were treated with gamma radiation from $^{60}$Co in doses of 2–5 kGy (200–500 krad).

Four genetically controlled properties of the viruses were studied. These properties and their significance for public health are as follows.

(1) *Serotype*. A change in antigenicity as a result of irradiation may result in loss of existing immunity against a virus, and existing vaccines against it would no longer be effective.

(2) *Neurotropism*. An irradiated virus might acquire the ability to infect the central nervous system of a subsequent host.

(3) *Replication at increased temperature and acidity*. A radiation-induced increase in the ability of a virus to replicate under these conditions may be associated with increased pathogenicity and virulence.

(4) *Host species specificity*. Irradiated viruses might acquire the ability to infect species other than their normal hosts.

Selection tests were performed on each irradiated virus type, for each of the four properties, under conditions that would favour any variants over the parent type. Most tests gave negative results, and only a few variants were found during the 3-year study. Coxsackievirus A-9 showed two presumptive changes in an irradiated derivative : some of the virus reacted less avidly with antiserum against the parent strain and some

---

[1] Prepared by Professor D. O. Cliver, Food Research Institute and Department of Bacteriology, University of Wisconsin, Madison, WI, USA.

[2] CLIVER, D. O. Viruses and rickettsia in foods and the possible role of radiation preservation. In : *Radiation preservation of foods*. Washington, DC, National Academy of Sciences/National Research Council, 1965 (Publication 1273), pp. 269–274.

appeared to have acquired the ability to replicate in swine cells.[1] Neither of these changes was definitive. The antigenic variant was still neutralized by homologous antiserum, but more antiserum was required. The lots of swine cell culture in which the irradiated virus could replicate all seemed to contain an adventitious swine virus, which may have been serving as a " helper ".

The study was intended to determine whether viruses contaminating foods, when exposed to levels of irradiation that might be used in processing such foods, are likely to mutate in ways that are significant to public health. While the viruses irradiated may not have been representative of all foodborne viruses, the weight of evidence indicates that significant virus mutations are unlikely.

---

[1] Cliver, D. O. & Anders, R. J. *Nature (London)*, **218** : 187–188 (1968).

WHO publications may be obtained, direct or through booksellers, from:

| | |
|---|---|
| ALGERIA | Société nationale d'Edition et de Diffusion, 3 bd Zirout Youcef, ALGIERS. |
| AUSTRALIA | Mail Order Sales, Australian Government Publishing Service P.O. Box 84, CANBERRA A.C.T 2600; *or over the counter from* Australian Government Publications and Inquiry Centres at 113 London Circuit, CANBERRA CITY; 347 Swanston Street, MELBOURNE; 309 Pitt Street, SYDNEY Mr. Newman House, 200 St. George's Terrace, PERTH; Industry House, 12 Pirie Street, ADELAIDE 156–162 Macquarie Street, HOBART — Hunter Publications, 58A Gipps Street, COLLINGWOOD Vic. 3066. |
| AUSTRIA | Gerold & Co., I. Graben 31, VIENNA 1. |
| BANGLADESH | WHO Representative, G.P.O. Box 250, DACCA 5 — The Association of Voluntary Agencies P.O. Box 5045, DACCA. |
| BELGIUM | Office international de Librairie, 30 avenue Marnix, BRUSSELS — Subscriptions to *World Healt* only: Jean de Lannoy, 112 rue du Trône, 1050 BRUSSELS. |
| BRAZIL | Biblioteca Regional de Medicina OMS/OPS, Unidad de Venta de Publicaciones, Caixa Postal 20.381, Vila Clementino, 01000 SÃO PAULO, S.P. |
| BURMA | *see* India, WHO Regional Office. |
| CANADA | *Single and bulk copies of individual publications (not subscriptions):* Canadian Public Health Association, 1335 Carling Avenue, Suite 306, OTTAWA, Ontario, Canada K1Z 8N8. *Subscriptions:* Subscriptions orders, accompanied by check made out to the Royal Bank of Canada, Ottawa, Account World Health Organization, should be sent to the World Health Organization, P.O. Box 1800, Postal Station B, OTTAWA, Ont. K1P 5R5. Correspondence concerning subscriptions should be forwarded to the World Health Organization, Distribution and Sales, 1211 GENEVA 27, Switzerland. |
| CHINA | China National Publications Import Corporation, P.O. Box 88, PEKING. |
| COLOMBIA | Distrilibros Ltd, Pio Alfonso Garcia, Carrera 4a, Nos 36-119, CARTAGENA. |
| CZECHOSLOVAKIA | Artia, Smecky 30, 111 27 PRAGUE 1. |
| DENMARK | Ejnar Munksgaard, Ltd, Nørregade 6, COPENHAGEN. |
| ECUADOR | Libreria Cientifica S.A., P.O. Box 362, Luque 223, GUAYAQUIL. |
| EGYPT | Nabaa El Fikr Bookshop, 55 Saad Zaghloul Street, ALEXANDRIA. |
| EL SALVADOR | Libreria Estudiantil, Edificio Comercial B No 3, Avenida Libertad, SAN SALVADOR. |
| FIJI | The WHO Representative, P.O. Box 113, SUVA. |
| FINLAND | Akateeminen Kirjakauppa, Keskuskatu 2, HELSINKI 10. |
| FRANCE | Librairie Arnette, 2 rue Casimir-Delavigne, 75006 PARIS. |
| GERMAN DEMOCRATIC REPUBLIC | Buchhaus Leipzig, Postfach 140, 701 LEIPZIG. |
| GERMANY, FEDERAL REPUBLIC OF | Govi-Verlag GmbH, Ginnheimerstrasse 20, Postfach 5360, 6236 ESCHBORN — W. E. Saarbach, Postfach 1510, Follerstrasse 2, 5 COLOGNE 1 — Alex. Horn, Spiegelgasse 9, Postfach 3340, 62 WIESBADEN. |
| GREECE | G. C. Eleftheroudakis S.A., Librairie internationale, rue Nikis 4, ATHENS (T. 126). |
| HAITI | Max Bouchereau, Librairie "A la Caravelle", Boite postale 111-B, PORT-AU-PRINCE. |
| HONG KONG | Hong Kong Government Information Services, Beaconsfield House, 6th Floor, Queen's Road, Central, VICTORIA. |
| HUNGARY | Kultura, P.O.B. 149, BUDAPEST 62 — Akadémiai Könyvesbolt, Váci utca 22, BUDAPEST V. |
| ICELAND | Snaebjørn Jonsson & Co., P.O. Box 1131, Hafnarstraeti 9, REYKJAVIK. |
| INDIA | WHO Regional Office for South-East Asia, World Health House, Indraprastha Estate, Ring Road, NEW DELHI — Oxford Book & Stationery Co., Scindia House, NEW DELHI: 17 Park Street, CALCUTTA 16 (Sub-agent). |
| INDONESIA | M/s Kalman Books Services Ltd, Jl. A. Yani, P.O. Box 3105, JAKARTA. |
| IRAN | Iranian Amalgamated Distribution Agency, 151 Khiaban Soraya, TEHERAN. |
| IRELAND | The Stationery Office, DUBLIN 4. |
| ISRAEL | Heiliger & Co., 3 Nathan Strauss Street, JERUSALEM. |
| ITALY | Edizioni Minerva Medica, Corso Bramante 83-85, TURIN; Via Lamarmora 3, MILAN. |
| JAPAN | Maruzen Co. Ltd. P.O. Box 5050, TOKYO International, 100-31. |
| KENYA | The Caxton Press Ltd, Gathani House, Homa Bay Road, P.O. Box 41742, NAIROBI. |
| KUWAIT | The Kuwait Bookshops Co. Ltd. Thunayan Al-Ghanem Bldg, P.O. Box 2942, KUWAIT. |

Price: Sw. fr. 6.—

Prices are subject to change without notice.