FINAL REPORT

"FOOD SAFETY"

by

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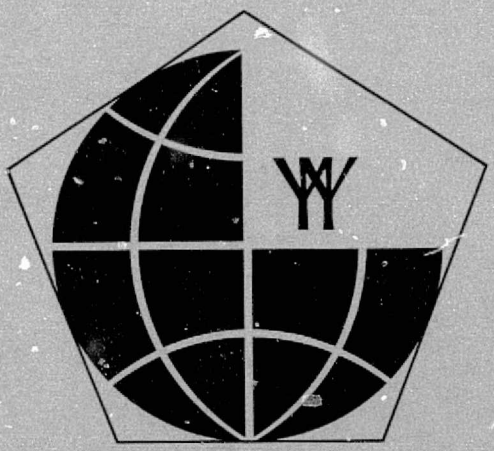

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FOOD SAFETY

I. Introduction

The human organism is impacted by three environmental contacts that may be characterized as the most intimate and important. These are air, food and water. The average adult inspires some 10-20 m^3 of air per day, and he can survive less than five minutes without some source of oxygen. The water intake is of the order of two liters per day in various forms, and the lack of water over a matter of days can be fatal. A typical food intake for an adult is about two kilograms per day (with obviously wide variations), and the organism can survive without food for weeks.

Illness induced by unsafe food is a problem of great public health significance. The incidence of food-borne illness has been placed in the range of 1-20 million cases per year. This large range of estimation is a result of the fact that most cases, being mild, are not reported to public health authorities. However, it seems clear that much human misery, generally of short-term significance, and time lost from work and other activity, is attributable to food of unsatisfactory quality.

Certainly most of the contamination resulting in unsafe food is of bacteriologic origin. This source is not under consideration in this study. This study relates exclusively to the occurrence of chemical agents which will result in food unsafe for human consumption.

The matter of food safety is of paramount importance in the mission and operation of the manned spacecraft program of the National Aeronautics and Space Administration. A mission would be seriously imperiled if an astronaut became ill at any point of the mission by virtue

of ingestion of contaminated food. Even an illness of such modest proportions as to produce slightly reduced efficiency and performance could be of the utmost seriousness. NASA's food quality assurance problems are intensified by the procurement procedures and practices for the foods to be consumed in space. Foods are prepared long in advance of the mission and stored for periods as long as two years in order that quality control practices, directed primarily at bacteriologic safety, can be observed. There is thus good reason to go beyond what is observed in terms of quality assurance practices for the general populace for the NASA situation, which can legitimately be characterized as unique.

Facilities

No special facilities were required for the execution of this study beyond those available at the School of Public Health of The University of Texas Health Science Center at Houston, augmented by the library facilities of other entities at the Texas Medical Center in Houston.

This study entailed no experimental work whatever and is based entirely upon a review of the technical literature, plus the counsel and comments of experts available to the investigators.

Personnel

The following individuals were closely associated with this effort:

Principal Investigator	Leslie A. Chambers, Ph.D. Professor of Environmental Health Sciences
Project Scientist	Stanley M. Pier, Ph.D. Assoc. Prof. of Environmental Health Sciences
Research Statistical Aid	Jane L. Valentine, M.S. Graduate Student

Ms. Valentine subsequently earned the Ph.D. degree and is now associated with The School of Public Health of The University of California at Los Angeles.

Acknowledgment

The assistance of Ms. Stephanie Norman and the entire staff of the library of The School of Public Health is gratefully acknowledged.

II. Objective and Scope

This study considers the question of food safety as related to chemical contamination. Consideration is given to those forms of chemical contamination which might lead to intoxication or other undesired effects. The matter of the adequacy of surveillance methods will be considered insofar as practicable. To the extent that data permit, criteria and standards are recommended for substances shown to be potentially harmful.

Many chemicals occur in foods. Indeed, food itself is an enormously complex mixture of chemicals. However, this study is restricted to those chemicals appearing in foods which are not the natural and normal constituents of these foods.

Chemicals occurring in foods may be characterized according to whether they are intentional or adventitious. The term intentional covers those substances which are of known composition and are added in controlled concentrations and under known conditions. Adventitious chemicals are those whose presence we may not be aware of, or whose concentration is unknown and uncontrolled.

The occurrence of chemicals in foodstuffs may be summarized as follows:

A. Intentionally used chemicals
   1. Food additives
      a. Preservatives, stabilizers and antioxidants
      b. Flavors, spices and colorants
      c. Emulsifiers
      d. Mycostatic agents

2. Cooking and preparation aids
    a. Salt
    b. Sugar
    c. Flavors, spices and colorants

B. Adventitious chemicals
    1. Incorporation during growing
        a. Heavy metals and trace elements from soil
        b. Heavy metals and trace elements from agricultural chemicals (pesticides)
        c. Chlorinated hydrocarbons and residues from pesticides
        d. Excess nitrite and nitrate from fertilizers
        e. Fungal metabolites and bacterial toxins
    2. Entry during handling or cooking
        a. Vermin control chemicals
        b. Corrosion or erosion of cooking or packaging equipment
        c. Miscellaneous chemicals from processing machinery (heat transfer and hydraulic fluids)
    3. Entry during storage of finished foods
        a. Radionuclides resulting from radiosterilization by ionizing radiation
        b. Transfer from containers and/or packages
            ..Corrosion of metal containers
            ..Leaching of plastic components

C. Chemical alteration of food components
    1. Browning pigment formation
    2. Oxidative changes
    3. Polymerization reactions
    4. Enzymatic lyses

D. Chemical toxicants occurring in foods naturally

It would obviously require a study of the most massive proportions to consider all of the aspects of the problem as outlined above. In the absence of support for such a study, it was necessary to restrict the

investigation by eliminating a number of the components. It was deemed unnecessary to consider the whole spectrum of intentionally used chemicals because these are under continuous study and surveillance by agencies of the Federal government. It was determined that consideration of the chemical alteration of food by biochemical and other processes would be impossibly complex within the scope defined by NASA. Also within the purposes of the study established by NASA, contaminants of biogenic origin were excluded. Thus, the study concentrated on trace elements, especially heavy metals, appearing in foods from any source, and pesticides.

Finally, this study is not at all concerned with the nutritional quality and characteristics of foodstuffs.

The ingestion of contaminated food can result in a wide variety of symptoms and effects, some of which are outlined in the following:

Effects of Intoxication

1. Gastroenteritic: cramps, diarrhea, vomiting, nausea, constipation, abdominal pain, etc.
2. Debilitation: vertigo, headache, weakness, malaise
3. Muscular: interference with motor performance, stiffness, prostration, spasms, lathrygenism
4. Neurological: effects on central nervous system, peripheral neurologic effects, hallucination, sensory disturbance, irritability, delerium, etc.
5. Serological: body fluid changes
6. Specific organ effects: upsets in organ function
7. Metabolic upset: interference with normal metabolism, weight loss
8. Carcinogenic/tumorogenic
9. Mutagenic/Teratogenic
10. Lethal

The effects delineated above have widely varying times of onset from the time of toxicant ingestion. A chemically induced gastroenteritis can commence in a matter of less than an hour from ingestion, whereas effects such as carcinogenesis and mutagenesis will take years or generations to be perceived. As with all toxicants, the effect is a function of the dose, the dose being a function of concentration and time.

III. Specific Contaminants

A. Metals

In order to understand the possible toxic effects of metals when contacted via the diet or other vectors, it is useful to understand the role of metals in human biochemistry.

Metals constitute a most important fraction of the biosphere as we know it, a fact that is supported partially by the compositional data provided in Table 1. It seems highly likely that this composition prevailed during most of the evolutionary process that resulted in man. Thus, it is not surprising that metals figure importantly in the composition of living matter as summarized in Table 2, which is in part reflective of the elements present during the evolutionary process.

For his life processes, man requires certain nutrients such as carbon, nitrogen and phosphorus in relatively large amounts, and others to a much lesser extent. Metals figure importantly in the latter category, and we may distinguish two general types:

1. Metals required in substantial amounts, and for which the body has a rather wide tolerance. Typical of this class are elements such as iron, sodium and potassium.

TABLE 1 (Handbook, 1968)

Metallic Composition of the Earth's Crust

Element	Content, parts per million
Iron	50,000
Sodium, Na	28,300
Potassium, K	25,900
Magnesium, Mg	20.900
Manganese, Mn	1,000
Barium, Ba	250
Chromium, Cr	200
Vanadium, V	150
Zinc, Zn	132
Nickel, Ni	80
Copper, Cu	70
Cobalt, Co	23
Lead, Pb	16
Molybdenum, Mo	15
Mercury, Hg	0.5
Cadmium, Cd	0.15

TABLE 2 (Jessop, 1970)

Elemental Composition of Living Matter

Element	Percent (weight)
Oxygen, O	76.0
Carbon, C	10.5
Hydrogen, H	10.0
Nitrogen, N	2.5
Phosphorus, P	0.3
Potassium, K	0.3
Chlorine, Cl	0.1
Sodium, Na	0.04
Calcium, Ca	0.02
Magnesium, Mg	0.02
Sulfur, S	0.02
Iron, Fe	0.01

2. Metals required in much smaller amounts, and for which the body has a quite narrow tolerance. Metals in this category include copper, manganese and cobalt. This category thus encompasses elements which are clearly essential for normal biochemical functions, but which can produce distinct toxic effects when present at higher levels.

Materials which the body requires in small or trace quantities are frequently referred to as "micronutrients". The roles of these micronutrients as presently understood are summarized in Table 3. But in terms of typical human contact with metals, we must indicate yet another category:

3. Metals for which we have not determined an essential role in the life process, and which are toxic at low levels. Elements falling into this group would include lead, mercury, cadmium and others. Of course, we must recognize that failure to define an essential role may result primarily from our imperfect understanding of life processes, and certain of those generally regarded as non-essential, whether toxic or not, may in fact fulfill an essential role at very low levels.

It is necessary to recognize the danger inherent in discussing toxicity in terms of a particular element alone. Toxic manifestations are generally a function of a given molecular configuration as well as physicochemical characteristics such as solubility, particle size, and other determinants of the degree to which a given material can intrude into the biochemical process. For example, barium is known to be a "heavy metal poison". Indeed, the ingestion of a small quantity of barium oxide could have serious consequences. On the other hand, during certain radiographic diagnostic procedures, seemingly vast quantities of barium sulfate are intentionally ingested and accepted into the organism by other routes. No toxic manifestations occur. The difference of course resides in the

TABLE 3 (Jessop, 1970)

Function of Micronutrients in Man

Element	Function
Calcium	Building of skeletal structure; essential for blood clotting and nerve and muscle function; regulates cation balance between cells and milieu; enzyme cofactor.
Magnesium	Important in ionic balance; enzyme cofactor.
Potassium	Major intracellular cation; involved in ionic balance and in maintenance of electrochemical potential across cell membranes; promotes protein synthesis.
Sodium	Major extracellular cation; important to water retention and osmotic balance; involved in cellular electrochemical processes; promotes nuclear uptake of amino acids and intranuclear protein synthesis.
Iron	Component of cytochromes, catalase, hemoglobin, myoglobin; essential for B vitamin synthesis.
Manganese	Enzyme cofactor; promotes synthesis of vitamins; affects calcium metabolism.
Copper	Required for synthesis of hemoglobin and iron-containing enzymes; enzyme component.
Zinc	Enzyme cofactor; mitotic accelerator; required for synthesis of tryptophan and carboxylase.
Cobalt	Vitamin B_{12} constituent; promotes synthesis of iron-containing pyrroles; enzyme activator.
Molybdenum	Enzyme cofactor; essential in nitrogen cycle.
Nickel	Required for insulin synthesis; enzyme activator; antianemic factor.

different solubilities of the two substances, barium oxide being highly soluble in and reactive with water, and barium sulfate being quantitatively insoluble.

For the purposes of this discussion, the classical definition of "metal" will be accepted: a class of electropositive elements that characteristically give up electrons in chemical reactions (Physical Science Today).

Man acquires his body burden of metals through his three primary environmental contacts: air, water and food. These contacts result in a buildup of metals in the human organism, with average values of such concentrations presented in Table 4.

TABLE 4 (Woolrich, 1973)
Metal Contents of "Average Man"

Metal	Content, milligrams/70 Kg man
Iron	4000-4200
Zinc	2300
Copper	72-100
Manganese	12-20
Cobalt	1.5-3
Lead	18-120
Cadmium	20-50
Mercury	13

Within this framework, it becomes possible to discuss the effects of the various metals that can be found in foods.

1. Arsenic

It is common to indict all compounds of arsenic as toxic (Smith, 1972); this is misleading. (It can be justified on the basis that almost any substance will be toxic at some concentration under some circumstances.) In fact, arsenic is a complex element. It forms compounds in two primary valence states, +3 and +5. It is also amphoteric and can form both anions and cations. There is compelling evidence that the +3 valence state of arsenic is the form of higher toxicity by a wide margin (Schroeder, 1966).

Arsenic compounds have been used beneficially over many years as chemotherapeutic agents and insecticides. Use as insecticides has resulted in contaminated foodstuffs. However the arsenicals were largely replaced years ago by the chlorinated organic pesticides. Arsenic compounds are also used as growth promoters for livestock.

Arsenic is absorbed quickly, stored in the liver and then transferred to general circulation. Acute poisoning can produce rapid or delayed symptoms, depending on the physical form of the arsenical. Chronic poisoning results in a marked loss of weight and loss of hair and skin pigmentation (Glaister, 1966).

The lowest recorded fatal dose of arsenic (form unspecified) is 2 grains (about 0.13 gram), though there have been recoveries reported after administration of doses as high as 230 grains (about 15 grams) (Glaister, 1966).

Arsenic is ubiquitous in the geosphere. Hence it occurs in the tissues of most organisms existing on the planet, including those tissues employed as foodstuffs. Typical arsenic contents of some common foods are presented in Table 5 (Schroeder, 1966). Diets rich in seafoods maximize foodborne arsenic contact (Underwood, 1973). Although the toxicity of many

TABLE 5 (Schroeder, 1966)

Arsenic Contents of Common Foodstuffs

Food	As, μg/g
Sea Food	
Haddock	2.2
Oysters	2.9
Shrimp	1.5
Meat	
Beef, stewing	1.3
Lamb Chop	0.4
Vegetables	
Wheat, Whole	0.2
Corn	0.1
Rice	0.1
Rhubarb	0.5
Tomatoes	0.4
Beverages, miscellaneous	
Tea	0.9
Cocoa	0.6
Coffee	0.0
Salt	2.7
Butter, unsalted	0.2

arsenic compounds have made the element generally suspect, there have been no reports of intoxications among those not occupationally exposed to arsenicals or in the absence of highly unusual contacts.

The most recent concern relates to the carcinogenic properties of arsenicals. In keeping with this concern, the National Institute for Occupational Safety and Health has issued a criteria document relating exposure to inorganic arsenic and adverse health effects (NIOSH, 1973). This focuses on the industrial and occupational situation in which exposures to high concentrations are most likely to be encountered. In addition, emphasis is placed on the respiratory contact.

With respect to carcinogenesis related to arsenic, there appears to be general agreement that industrial exposures to arsenicals can give rise to skin keratoses which may evolve into malignancies. However, the relationship between arsenic and other forms of carcinoma is highly equivocal (Schroeder, 1966). Efforts to produce tumors in experimental animals under controlled laboratory situations, with and without materials which have been considered as cocarcinogens, have largely been unsuccessful (Baroni, 1963).

Toxic reactions from arsenic in ordinary, uncontaminated foods and beverages are unknown (Underwood, 1973). As a precautionary matter, the World Health Organization recommends a maximum daily intake for arsenic of 0.05 mg/kg body weight.

Skylab foods are routinely analyzed for arsenic content. Data for representative foods are presented in Table 6. The actual analyses were conducted at JSC, and the detected values were converted to arsenic content in milligrams per kilogram body weight of the consumer per serving of the food item.* The data should be regarded as maxima because most of the

*These and other similar calculations are based on a 3-oz. serving for a 75 kg man.

TABLE 6

Arsenic Analysis of Skylab Foods

Food	As, ppm	Mg As/Kg body weight per serving
Grapefruit Drink (SKL-78)	<0.65	<0.007
Dried Apricots (SKL-60)	<2.3	<0.0026
Orange Drink (SKL-69)	<0.08	<0.00009
Lemon Pudding (SKL-53)	<0.27	<0.0003
Peanuts (SKL-42)	<1.4	<0.0016
Corn (SKL-5)	<1.5	<0.0017
Corn (SKL-6)	<1.5	<0.0017
Ham Spread (SKL-13A)	<3.0	<0.0034
Peanuts (SKL-45)	<1.3	<0.0015
Peanuts (SKL-41)	<1.18	<0.0013
Peanuts (SKL-40)	<1.33	<0.0015
Tuna Spread (SKL-34)	<2.36	<0.0027
Tuna Spread (SKL-32)	<2.40	<0.0027
Lemon Pudding (SKL-49)	<0.29	<0.0003
Butterscotch (SKL-25)	<0.85	<0.001
Cookies (SKL-90)	<0.46	<0.0005
Orange Drink (SKL-71)	<0.64	<0.0007
Orange Drink (SKL-72)	<0.71	<0.0008
Dried Apricots (SKL-59)	<1.48	<0.0017

values determined are in fact below the lower limit of detection for the analytical method employed. The values obtained indicate that a normal diet should keep daily arsenic intake below the WHO recommended level. Butterscotch pudding appears to be the major source of arsenic in the astronaut diet, and there should be little problem in controlling the intake of this food.

2. Beryllium

There is a vast literature relating to the toxic properties of beryllium since the recognition of the role of this element in the production of occupationally related disease. Beryllium poisoning has been observed in those who process the ore, attributable to exposure to fumes and dusts (Glaister, 1966). Beryllium disease has been characterized in a number of industries in which the element or compounds are used. It has also been observed that people living close to beryllium producing or consuming plants can be impacted to a lesser degree (Tepper, 1972; Vorwald, 1966).

It is generally held that soluble beryllium compounds have more physiologic activity than those which are insoluble in water (Tepper, 1972). In tests with rats acute lethal doses of 15, 10 and 2 mg/kg body weight were determined for beryllium fluoride, sulfate and oxyfluoride respectively. The LD_{50} values for insoluble salts were in excess of 100 mg/kg body weight (Vorwald, et al., 1966).

Beryllium has a definite affinity for bone. Soluble salts fed to poultry produced rachitic bone changes (Vorwald, et al., 1966).

There have been no reports of intoxication related to beryllium in normal, uncontaminated diets. Substantive data relating to the beryllium content of food is lacking. There are no international standards controlling the beryllium content of food.

Skylab foods are routinely analyzed for beryllium. Data for typical food items are presented in Table 7. Analyses were provided by JSC, and the beryllium contents were converted to milligrams of the element per kilogram of body weight in one serving of the particular food item.

Because there was no beryllium standard in existence, NASA requested that one be established. This was done on a highly arbitrary basis, reflecting the known toxicity of beryllium compounds under certain circumstances not related to food consumption, and with an exceedingly fragile data base. The recommended standard was 0.00005 mg Be/kg body weight/day. This is regarded as extremely conservative, possibly unreasonably so.

Inspection of the data in Table 7 will reveal that a substantial number of foodstuffs exceed the recommended acceptable daily intake. This may be correct, or it may be an artifact of the analytical method, where the limit of detection is not low enough to control the recommended standard. A better analytical method is necessary if control to the level indicated is warranted. However, it seems more reasonable to judge the previously recommended standard too restrictive, and to raise it by a full order of magnitude to a maximum of 0.0005 mg Be/kg body weight/day in the face of a total lack of evidence that current levels of beryllium consumption, whatever they may be, are producing any adverse health effects.

3. Boron

Boron is an essential element for plant life. Consequently, there is a high concentration of this element in many plants used for food. Concentrations as high as 25-50 ppm (dry weight) have been noted for legumes, with fruits and vegetables only slightly below this range at 5-20 ppm.

The total dietary intake of boron is at issue, with a wide range of values being reported in the literature. The most widely accepted value

TABLE 7

Beryllium Analysis of Skylab Foods

Food	Be, ppm	Mg Be/Kg body weight per serving
Grapefruit Drink (SKL-78)	<0.026	<0.00003
Dried Apricots (SKL-60)	<0.09	<0.0001
Orange Drink (SKL-69)	<0.03	<0.00003
Lemon Pudding (SKL-53)	<0.01	<0.00001
Peanuts (SKL-42)	<0.05	<0.00006
Corn (SKL-5)	<0.059	<0.00007
Corn (SKL-6)	<0.062	<0.00007
Ham Spread (SKL-13A)	<0.12	<0.00001
Peanuts (SKL-45)	<0.053	<0.00006
Peanuts (SKL-41)	<0.05	<0.00006
Peanuts (SKL-40)	<0.051	<0.00006
Tuna Spread (SKL-34)	<0.09	<0.0001
Tuna Spread (SKL-32)	<0.10	<0.0001
Lemon Pudding (SKL-49)	<0.01	<0.00001
Butterscotch (SKL-25)	<0.04	<0.00005
Cookies (SKL-90)	<0.02	<0.00002
Orange Drink (SKL-71)	<0.03	<0.00003
Orange Drink (SKL-72)	<0.03	<0.00003
Dried Apricots (SKL-59	<0.06	<0.00007

is in the range of 3 mg/day (Zook, 1965) based on analyses of 4200 calorie diets. This caloric intake is obviously somewhat high, the data being based on the diets of high school boys. An even higher value of about 5 mg B/day can also be found (Tipton, 1970), though most of the other reported values are below the two cited.

Some boron compounds are known to be toxic. Borates act as central nervous system depressants and can produce necrosis of the gastrointestinal tract as well as renal tubular dysfunction. Boric acid appears to be among the most toxic of the common boron compounds. One teaspoonful has caused death. On the other hand, a woman given an injection of 600 ml of 2.5% H_3BO_3 recovered. Many instances of death in children due to accidental poisoning with boric acid have been described (Glaister, 1966).

There are no reports of intoxication by boron compounds through normal food contacts. This probably relates to the fact that boron in food is rapidly absorbed and excreted (Underwood, 1971).

There is no standard for the content of boron in foods. In response to a specific request from NASA, a standard of 0.04 mg B/kg body weight/day was recommended. For a 70 kg man, this would permit a daily intake of 2.8 mg boron, which is below the reported typical daily intake. There is no evidence that this typical daily intake results in adverse health effects.

Skylab foods are routinely subjected to analysis for boron. Data supplied by JSC for typical foods are presented in Table 8. The analytical results, obtained at JSC, were converted to intakes per serving. Only two foods, dried apricots and dry roasted peanuts, seem to present even a prospect of reaching the acceptable daily intake for boron. Consequently, excessive consumption of these foods should be avoided. This caution is

TABLE 8

Boron Analysis of Skylab Foods

Food	B, ppm	Mg B/kg body weight per serving
Grapefruit Drink (SKL-78)	0.88	0.001
Dried Apricots (SKL-60)	22.4	0.025
Orange Drink (SKL-69)	1.64	0.0019
Lemmon Pudding (SKL-53)	1.42	0.0016
Peanuts (SKL-42)	11.6	0.0132
Corn (SKL-5)	1.54	0.0017
Corn (SKL-6)	1.54	0.0017
Ham Spread (SKL-13A)	1.37	0.0016
Peanuts (SKL-45)	5.76	0.0065
Peanuts (SKL-41)	17.8	0.02
Peanuts (SKL-40)	9.43	0.011
Tuna Spread (SKL-34)	0.68	0.0008
Tuna Spread (SKL-32)	1.60	0.0018
Lemon Pudding (SKL-49)	1.59	0.0018
Butterscotch (SK1-25)	1.20	0.0014
Cookies (SKL-90)	0.19	0.0002
Orange Drink (SKL-71)	3.51	0.004
Orange Drink (SKL-72)	2.20	0.0025
Dried Apricots (SKL-59)	15.45	0.018

almost unnecessary, inasmuch as the recommended standard is probably so conservative that consumption very much in excess of the recommended limit would likely be entirely safe.

4. Cadmium

No role has been defined for cadmium in the physiological or biochemical functioning of the human organism. Consequently, most of the interest in cadmium concerns its toxic properties.

Cadmium is broadly distributed in the environment. It occurs at low levels in essentially all foods and beverages used by man (Schroeder, 1965).

Cadmium is a component of tobacco used for cigarettes and other tobacco products. Some cadmium is carried to the smoker in the smoke, with the impact being dependent upon the depth of inhalation (Friberg, 1971).

There is some disagreement concerning the total daily intake of cadmium. One estimate (Schroeder, 1970) placed the intake at 160 μg/day, but this is believed to be high. In 1968, a "market basket" study was run in which 82 food items were analyzed for cadmium. As a result of this investigation, the daily intake was placed at about 26 μg (Duggan, 1969). Food probably accounts for most of the daily intake of cadmium. Data for cadmium contents of foods (for Britain) are presented in Table 9 (Elton, 1973).

The high toxicity of cadmium has been known for some time and it is viewed as a significant occupational hazard (Anderson, 1966). Brief inhalations of high concentrations of cadmium compounds when in the form of finely divided particles can produce severe and often fatal pulmonary

TABLE 9 (Elton, 1973)

Cadmium Contents of Common Foodstuffs

Food	Cd, µg/g
Meats	
Beef kidney	0.5
Beef	0.1
Chicken liver	0.1
Cereals	
Flour, whole meal	0.1
Bread, white	0.0
Fruits and vegetables	
Cabbage	0.1
Carrots	0.1
Onions	0.0
Potatoes	0.1
Sea Foods	
Crab, canned	3.8
Sardines	0.2
Beverages	
Coffee, instant	0.1
Milk	0.0

changes. A fatal dose is probably less than 2500 min.-mg/m^3, which is equivalent to an exposure of 5 mg/m^3 for eight hours (Friberg, 1971). Exposures of this magnitude would be restricted to occupational situations.

Acute cadmium intoxication causes a series of symptoms, mostly of a respiratory nature. These symptoms include dyspnea, cough, fever, followed by swelling and hyperplasia of bronchiolar lining cells, leading to chronic pneumonitis (Anderson, 1966). This symptomology again would be a consequence of the inhalation of cadmium fumes or dusts.

Both chronic and acute poisoning have been encountered when food has been prepared or stored in containers coated with cadmium. As with other metals the effect is most pronounced with acidic foods and upon prolonged storage. However, cadmium intoxication has been reported when food was in contact with refrigerator shelving plated with cadmium (Glaister, 1966).

The carcinogenic properties of cadmium are at issue. One view (Fassett, 1972) holds that cadmium and cancer in man are not associated. Another view maintains that although the relationship between cadmium in the environment and human cancer is equivocal, cadmium is more significantly related to cancer than any other trace metals (Berg, 1972). Other research (Furst, 1971) results indicate cadmium to be carcinogenic as the element and its oxide and sulfide and other soluble salts.

Considerable research has been expended on the relationship between cadmium and cardiovascular disease, especially hypertension. There is considerable logic in studying the role of metals in hypertension because a surprising number of antihypertensive drugs have the common characteristic of being able to bind transition and related trace metals (Perry,

1972). Cadmium is an especially likely candidate for an association with hypertension because of the affinity of this element for the kidney, and the finding of parallel trends for the incidence of hypertension and renal cadmium for different populations around the world (Perry, 1972). Studies have shown that cadmium levels in organs and tissues are very low at birth, rising to a value in excess of 10 mg renal cadmium for the average adult.

Evidence for the relationship between cadmium and hypertension was obtained in a study of 117 subjects without hypertension who died accidentally, and comparing these with 17 hypertensives who died under similar circumstances, i.e., not due to the hypertension condition. (All of these were Americans.) The non-hypertensives had significantly lower renal cadmium levels (based on kidney ash) than the hypertensives (Schroeder, 1965). However, other studies (Morgan, 1969) failed to disclose a similar relationship between cadmium in organs and hypertension or other cardiovascular diseases. The association is further eroded by the fact that workers occupationally exposed to cadmium do not show a higher incidence of hypertensive disease (Carroll, 1966).

In a recent epidemiologic study of the relation between cadmium in drinking water and deaths from arteriosclerosis, no correlation was found. This study involved a varied population in Houston (Valentine, 1973). Again opposite data are available. In 28 American cities, death rates for all types of heart disease except rheumatic were significantly correlated with the cadmium content of the urban air (Carroll, 1966).

The issue of the relationship between cadmium and cardiovascular disease will obviously require further study.

Cadmium has been implicated as the causative agent in Itai-Itai (Japanese for Ouch-Ouch) Disease, which has been significant in Japan.

The condition is characterized by severe pain in bones and joints, a series of metabolic abnormalities and multiple skeletal fractures. A high case fatality rate was experienced. The disease was attributed to environmental pollution from industries producing or using cadmium, but other factors, including other environmental contaminants have not been excluded (Fassett, 1972).

There have been no reports of cadmium intoxications involving uncontaminated foods. No standard for cadmium limits in food has been promulgated. In response to a specific request from NASA, a standard was recommended at 0.003 mg Cd/kg body weight/day. For a 75 kg man, this would permit a consumption in the range of 200 µg/day, which is at the upper range of the reported normal daily intakes.

It has been the practice to analyze Skylab foods for cadmium and typical values are presented in Table 10. Most foods are very low in this element, though an inordinate consumption in a single day of dried apricots and tuna spread might permit reaching the recommended maximum. This conclusion is provisional, because all of the analytical results are below the lower detection limit of the method. Thus, it may be concluded that if consumption as low as the proposed standard is warranted, a better analytical method must be employed for certain of the foods. However, it is most probably that the standard proposed is so conservative as to be entirely adequate.

5. Chromium

Chromium represents another example of an element whose toxicologic properties are very much a function of chemical composition. The element itself is essentially inert. Compounds of chromium are widely distributed in the environment and fairly abundant. Chromium is amphoteric, forming

TABLE 10

Cadmium Analysis of Skylab Foods

Food	Cd, ppm	Mg Cd/kg body weight per serving
Grapefruit drink (SKL-78)	<0.26	<0.0003
Dried Apricots (SKL-60)	<0.9	<0.001
Orange Drink (SKL-69)	<0.3	<0.0003
Lemon Pudding (SKL-53)	<0.1	<0.0001
Peanuts (SKL-42)	<0.5	<0.0005
Corn (SKL-5)	<0.059	<0.00007
Corn (SKL-6)	<0.062	<0.00007
Ham Spread (SKL-13A)	<0.12	<0.0001
Peanuts (SKL-45)	<0.053	<0.00006
Peanuts (SKL-41)	<0.5	<0.0006
Peanuts (SKL-40)	<0.5	<0.0006
Tuna Spread (SKL-34)	<0.90	<0.001
Tuna Spread (SKL-32)	<1.0	<0.001
Lemon Pudding (SKL-49)	<0.10	<0.0001
Butterscotch (SKL-25)	<0.40	<0.0005
Cookies (SKL-90)	<0.18	<0.0002
Orange Drink (SKL-71)	<0.30	<0.0003
Orange Drink (SKL-72)	<0.28	<0.0003
Dried Apricots (SKL-59)	<0.60	<0.0007

both anions and cations. More important, compounds of chromium exist in two primary valence states, +3 and +6. There is general agreement that trivalent chromium compounds are of little toxicologic significance (Underwood, 1971), whereas compounds of chromium in the hexavalent oxidation state are of considerable importance (Smith, 1972).

Essentially all of the problems associated with contact with chromium exist in the industrial situation. Exposure to chromic acid mist, a combination of chromic oxide dust and sulfuric acid in an aerosol form produces severe respiratory irritation and serious attack on the nasal septum (NIOSH, 1973). It has also been known for some time that chromium compounds are likely to produce severe cases of dermatitis, again in the occupational situation (NIOSH, 1973).

In general, symptoms of excessive dietary intake of chromium in man are unknown. The known instances of intoxication are restricted to exposure to airborne chromium or to chromium applied directly to the skin (NAS, 1974).

Chromium is generally accepted an as essential trace element for humans (NAS, 1974), although the evidence is equivocal (Underwood, 1971). Because of the widespread distribution of the element, it is found in many foods and water supplies. Typical chromium contents of common foodstuffs are shown in Table 11 (Schroeder, 1962). It is obvious that concentrations are quite low. There is considerable disagreement as to the total daily intake from normal diets. One estimate based on actual determinations of typical diets (Tipton, 1970) sets the daily intake for adult males at 230 µg/day. A typical Canadian diet is said to provide about 282 µg/person/day, with an extraordinarily narrow range of 281-283 µg/person/day (Meranger, 1972). A 1966 survey of Type A school lunches

TABLE 11 (Schroeder, 1962)

Chromium Contents of Common Foodstuffs

Food	Cr, ug/g
Condiments	
Pepper, black	3.7
Thyme	10.0
Salt	0.0
Dairy Products	
Milk, whole	0.0
Eggs	0.2
Butter	0.2
Cheese	0.1
Meat	
Beef chuck	0.1
Lamb chop	0.1
Chicken breast	0.3
Sea Food	
Lobster, digestive gland	0.3
Clams	0.4
Scallop	0.1
Vegetables	
Potato, white	0.0
Beans, Navy	0.1
Lentils	0.1
Carrots	0.0
Lettuce	0.1
Fruits	
Peach	0.0
Pear	0.0
Tomato	0.0
Grains and cereals	
Corn meal	0.1
Corn oil	0.5
Flour, wheat	0.0
Rice	0.1
Cigarettes	0.4

served to sixth graders in 300 schools was found to provide 19 μg/person/meal, with a range of nine to 88 μg Cr in the lunch meal. The U.S. Public Health Service recommended standards for drinking water is 0.05 ppm Cr^{+6}.

The most substantive issue regarding chromium contact relates to the carcinogenic properties of hexavalent chromium. Again, the problem has been restricted to the industrial situation where the primary contact is respiratory.

The literature discloses no basis for concern relating to the chromium content of foods. Neither is there any reason to undertake a routine analysis of foods for this element.

6. Cobalt

Cobalt has been identified as a component of all living matter. The principle biological role of cobalt is as a constituent of Cobalamine--Vitamin B_{12} (Jessop, 1970). Indeed, the weight of evidence indicates that cobalt is active physiologically in higher animals only when it is incorporated as Vitamin B_{12} or one of the cobamide derivatives (O'Dell, 1972). The major enzymes requiring Vitamin B_{12} are methylmalonyl-Co A mutase, methyl tetrahydrofolate oxido reductase, homocysteine methyltransferase and ribonucleotide reductase (Davies, 1972).

Cobalt has a powerful stimulating effect upon red blood cell production, though there is no evidence that the element is essential for erythropoiesis in man (Best, 1966). However, it has long been known that cobalt deficiency in sheep and cattle causes severe anemia (Anderson, 1966). Because of the known ability of cobalt to stimulate erythrocyte production, it has been used in the treatment of refractory anemias, frequently with toxic side effects (Davies, 1972). Because of this, cobalt therapy for pernicious anemia has largely been abandoned.

Cobalt deficiency in humans is not known, leading to the inference that the requirement for this element must be quite low (Mertz, 1972). The typical daily intake has been estimated in the range of 0.015-0.16 mg (Spivey Fox, 1972). A dietary intake closer to 0.1 mg/day has been determined for the typical Canadian diet (Meranger, 1972).

Cobalt may have an indirect involvement in iodine metabolism, and thus may have some role in the development and/or prevention of goitre (Davies, 1972).

Cobalt has been established as the etiologic agent in a series of instances of severe cardiac failure (cobalt cardiomyopathy) in persons consuming large amounts of beer, when these beers were treated with soluble cobalt salts for the stabilization of the froth or "head", entirely for esthetic reasons. The cobalt contents of the offensive beers were in the range of 1.2-5 ppm. This finding is at variance with the fact that up to 300 mg of cobalt salts daily has been used therapeutically without cardiotoxic effects. The inference is that there is some synergism between the cobalt and alcohol or other component of the beverages in the reported beer-related cardiomyopathy (Underwood, 1973).

The oral intakes of cobalt necessary to produce significant polycythemia approximate 200 to 250 ppm Co in the total diet. This is many times that which could be obtained by any reasonably normal diet.

There appears to be no issue of intoxication associated with the cobalt content of food. Skylab foods have not been routinely analyzed for this element, and there is no basis for a recommendation that any such practice be initiated.

7. Copper

Copper has been identified in all living organisms (Jessop, 1970). It has been known since at least 1928 that copper deficiency can produce a severe anemia (Hart, 1928) as well as lesser symptoms such as the graying of hair (Anderson, 1966).

Copper is essential in a number of important proteins, including cerebrocuprein I, erythrocuprein, hemocuprein, hepatocuprein and mitochondrocuprein. It is also essential to a number of enzymes, including ceruloplasmin, tyrosinase, amine oxidase, cytochrome C oxidase, uricase and dopamine B-hydrosylase (Davies, 1972). Flavoproteins in general require copper (as well as other metals) for proper functioning. For many invertebrates, copper is the key metal component of the respiratory pigments (Jessop, 1970).

The involvement of copper in so many vital biochemical systems results in serious deficiency diseases when the dietary intake of the element is inadequate. The disorders of copper deficiency include anemia, vascular abnormalities, depigmentation of hair (usually the first indication of deficiency), difficulty in parturition, abnormalities of bone formation, myocardial fibrosis, demyelination and disturbances of gastrointestinal function.

Copper is also believed to act as a catalyst in some stage of hemoglobin synthesis, though it does not enter into the structure of hemoglobin itself (Best, 1966).

The dietary intake of copper in the western world is variously placed at 3-5 mg/day (Davies, 1972) or 1-4 mg/day (Spivey Fox, 1972). Actual dietary assays show a value of 2.9 mg/day for adult American males (Tipton, 1970) and 2.2 mg/day for the typical Canadian (Meranger, 1972).

The extent of absorption by the human organism is 5-10%, though some claim absorptions as high as 40%. The main absorption area is considered to be the upper reaches of the small intestine. Most of the ingested copper is excreted in the feces. The average adult human body contains in the range of 100 to 150 mg of copper, concentrated in the hair, skin, liver, muscle and lung, with the muscle being the main repository (Davies, 1972). The circulating blood normally contains 0.1-0.5 mg of copper (Best, 1966).

A pathological condition in which excessive copper is deposited in the brain, skin, liver, pancreas and myocardium is known as Wilson's Disease (Davies, 1972). This is not associated with copper intake.

The recommended daily dietary requirement for copper has been placed at 2 mg. This requirement is almost certainly met by most normal diets. However, copper deficiency diseases have been reported in several countries around the world, as well as in this country when feeding on unusual special diets is the case. This is especially prone to happen with infants being fed special and highly restricted diets.

It has been observed that serum copper levels can rise significantly in a number of acute and chronic infections. These changes can be of considerable diagnostic and prognostic significance. The mechanism and possible functions of these serum copper changes are not understood (Weinberg, 1972).

Copper intoxication can result from the contact of food or water with copper vessels. Severe gastroenteritis can result, which is in many cases confused with bacterially-induced distress. Cases of contamination have been reported from sources as diverse as tea prepared in and served from a copper vessel (Glaister, 1966), alcoholic beverages mixed in a copper shaker (Wyllie, 1967) and even water standing for an extended period in

copper vessels (Nicholas, 1968). The effect of copper leaching from vessel into food is most pronounced with acidic foods (Ross, 1955), a condition that exists for many other metals.

A number of epidemiologic studies have failed to disclose any association between copper and cancer in man (Furst, 1971). Indeed, there is some evidence from animal experimentation that copper may help to protect against cancer. Possible mechanisms suggested are an inhibition of the action of the carcinogenic agent, potentiation of the activity of anticancer agents and the actual inhibition of tumor growth. The anticancer activity of copper in humans is highly equivocal (Pories, 1972). It is generally considered that extraneous exposures to copper are of little biological consequence relative to normal levels of this element in all living organisms (Vinogradov, 1953). The occurrence of copper in common foods is shown in Table 12. Copper has a marked affinity for lipids, and the highest concentrations are found in tissues high in phospholipids (Schroeder, 1966).

A dietary concentration of 200 ppm of copper in the total diet on a dry basis is probably acceptable for prolonged periods, which is about twenty times the normal dietary intake (Underwood, 1973). There are no chronic degenerative disorders in man associated with copper (Underwood, 1971).

The copper content of foods used in the manned space program does not appear to be an area for concern. However, because of the possibility of chemical gastroenteritis with excessive concentrations, it appears to be advisable to avoid the use of copper vessels for the preparation and/or storage of food. The recommendation is especially important with respect to low pH foods.

TABLE 12 (Schroeder, 1966)

Copper Contents of Common Foodstuffs

Food	Cu, µg/g
Sea Foods	
Clams	3.3
Oysters	137.0
Kippers	1.7
Shrimp	3.4
Meats	
Beef liver	11.0
Lamb chop	7.1
Chicken	2.0
Dairy Products	
Egg yolk	2.4
Milk, whole	0.2
Butter, salted	3.9
Vegetables	
Peas	0.5
Turnip	1.8
Carrots	3.4
Pepper, green	0.7
Cucumber	0.5
Asparagus	0.4
Fruits	
Apple	1.4

TABLE 12 (Schroeder, 1966) cont'd

Food	Cu, µg/g
Grains	
Wheat, whole	2.5
Corn	0.5
Rye	4.1
Rice	0.5
Oils and Fats	
Lard	3.0
Lecithin, animal	26.4
Corn oil	2.2
Nuts	
Peanuts	7.8
Almond	14.1

No basis exists at this time for any routine surveillance program relating to the copper concentration in Skylab foods.

8. Lead

No essential function for lead in human biochemistry has been determined. Rather, lead has long been regarded as a ubiquitous, cumulative, protoplasmic poison (Anderson, 1966).

Lead exerts its most significant toxic effects on the nervous system, the hematopoietic system and the kidney. Effects on the nervous system include motor disturbances, sensory disturbances and ultimately major brain damage. In the hematopoietic system, lead interferes with the synthesis of heme. One of the first signs of lead intoxication is the appearance of increased amounts of delta-aminolevulinic acid in the urine (and serum), indicating a block to porphyrin synthesis. Later lead interferes with the incorporation of iron into heme. Finally, lead produces renal tubular dysfunction, leading to many secondary effects (Goyer, 1972).

Lead intoxication is a progressive process. Early signs include anemia, followed by a variety of behavioral disturbances, and then acute abdominal colic. Colic develops at a level of systemic lead such that the blood lead reaches and exceeds 80 μg/100 g whole blood. This blood lead level has generally been accepted as the threshold for indicating clinical lead intoxication, or plumbism. As lead contact continues, acute encephalopathy ensues, characterized by convulsions, coma, respiratory arrest and death (Goyer, 1972). At a level of lead intoxication below that producing colic, a pigmentation of the oral mucosa occurs. A line of deep blue pigmentation appears at the junction of teeth and gums caused by the formation and precipitation of lead sulfide (PbS) at that site (Anderson, 1966).

Data have been developed suggesting an association between environmental lead pollution and mental health. In one study, it was found that nearly half of a group of mentally retarded children had blood levels of lead above the maximum level of 36 µg/100 g blood found in a control group of normal children (Bryce-Smith, 1972). However, another study (Miller, 1970) found no association between elevated blood lead levels in children and mental deficiency.

Normal man is in "lead balance", in that intake and excretion are virtually identical. Extensive studies (Kehoe, 1961) have also shown the adaptability of man to increasing lead contacts, at least at reasonable levels.

Of the total daily intake of lead of some 300 µg, about 90% comes via food and water, and 10% in the air breathed. This disparity is overcome somewhat by the fact that only about 10% of the lead is absorbed via the gastrointestinal tract, compared with 25-40% of the pulmonary contact (USPHS, 1966). An actual food intake of just over 100 µg/day has been determined for the Canadian diet (Meranger, 1972).

Lead has not generally been regarded as a carcinogen, but some work suggests a possible role (Boyland, 1962). Epidemiologic studies testing an association between lead in drinking water and a variety of neoplasms showed a significant positive correlation between lead levels and kidney cancer mortality and deaths from all lymphomas and all leukemias (Berg, 1972). Much more work must be done to test this association.

Another interesting association is that areas in Scandinavia which are low in environmental lead show a low incidence of multiple sclerosis (Armstrong, 1971).

The ubiquity of lead results in the appearance of compounds of this element in most foodstuffs. As previously noted, this contact is man's primary involvement with lead. Table 13 presents some typical lead analyses of common foods (Schroeder, 1961).

No foods are notably high in lead. The lead contents of common food appears not to have changed significantly over at least 20 years of surveillance (Schroeder, 1961).

The lead contents of foods can be somewhat subject to environmental contamination. Crops grown in areas subject to lead contamination, i.e., near smelters or heavily-travelled highways, will incorporate lead that is deposited in the soil. Vegetables can thus have elevated lead levels. Should such crops be used as forage by farm animals, this lead contamination can be carried into milk or meat obtained from such animals.

The recognized systemic toxic properties of lead, whether ingested or inspired, has resulted in the recommendation of international standards. The World Health Organization recommends a maximum daily intake of 0.005 mg Pb/kg body weight. This standard is considered to have considerable margin of safety.

A practice of analyzing Skylab foods for lead has been observed. Analytical data provided by JSC, which have been converted to intake per serving, are presented in Table 14. Of the food data provided, only corn, ham spread, tuna spread and dried apricots show significant concentrations of lead. Thus, excessive consumption of these foods should be avoided. As in other cases, this statement must be considered in light of the fact that the standard is undoubtedly extremely conservative, and that the analytical data are below the detection limit and thus represent maxima.

TABLE 13 (Schroeder, 1961)

Lead Contents of Common Foodstuffs

Food	Pb, µg/g
Condiments	
Salt	0
Sugar	0.2
Baking powder	1.5
Yeast, dry	1.2
Sea Food	
Shrimp, fresh	0.5
Lobster claw meat	2.5
Clams	0.2
Anchovies	0.9
Swordfish	0.2
Haddock	0.3
Meat	
Beef chuck	0.2
Lamb chop	0.2
Pork chop	0.2
Egg	0.2
Grains	
Wheat, crushed	1.4
Flour	0.5
Rye, seed	0.2
Rice, polished	0.1

TABLE 13 (Schroeder, 1961) cont'd

Food	Pb, µg/g
Vegetables	
Potatoes, white	0.1
Kale (organically grown)	1.3
Spinach	0.2
Beans, string	0.0
Beans, red kidney	0.2
Tomato	0.0
Fluids	
Milk, whole	0.0
Cola	65 µg/liter
Cigarettes	24.0

TABLE 14

Lead Analysis of Skylab Foods

Food	Pb,ppm	Mg Pb/kg body weight per serving
Grapefruit drink (SKL-78)	<0.39	<0.0004
Dried Apricots (SKL-60)	<1.4	<0.0016
Orange Drink (SKL-69)	<0.48	<0.0005
Lemon Pudding	<0.16	<0.0002
Peanuts (SKL-42)	<0.83	<0.0009
Corn (SKL-5)	<0.88	<0.0010
Corn (SKL-6)	<0.89	<0.0010
Ham Spread (SKL-13A)	<1.8	<0.0020
Peanuts (SKL-45)	<0.80	<0.0009
Peanuts (SKL-41)	<0.71	<0.0008
Peanuts (SKL-40)	<0.80	<0.0009
Tuna Spread (SKL-34)	<1.42	<0.0016
Tuna Spread (SKL-32)	<1.44	<0.0016
Lemon Pudding (SKL-49)	<0.17	<0.0002
Butterscotch (SKL-25)	<0.51	<0.0006
Cookies (SKL-90)	<0.27	<0.0003
Orange Drink (SKL-71)	<0.38	<0.0004
Orange Drink (SKL-72)	<0.43	<0.0005
Dried Apricots (SKL-59)	<0.90	<0.001

9. Manganese

Manganese has been found in all living matter (Jessop, 1970). The element concentrates in the divalent state, Mn^{+2}, in the cell mitochondria (Davies, 1972).

Manganese has been shown to be required for the proper functioning of flavoproteins (Jessop, 1970). The element also exerts a catalytic effect on hemoglobin synthesis, but the effect is less pronounced than in the case of copper (Best, 1966). Manganese also appears to be involved in the synthesis of cholesterol (Davies, 1972). The metal is a constituent of liver arginase and pyruvate, and is a cofactor in many enzymes. Manganese is essential to arginase and alkaline phosphatase activity in the liver.

Manganese deficiency in humans has not been documented. However, in experimental animals, a manganese-deficient mother will produce defective offspring, a higher mortality rate, and osseous defects in surviving animals (Anderson, 1966). There has been a suggestion that manganese deficiency may be related to a progressive neurological disorder known as Amyotrophic Lateral Sclerosis (Hopps, 1971). However, magnesium may also be involved in this condition.

The intake of manganese by human has been estimated in the range of 2 to 7 mg/day. Actual dietary assays have shown values of about 6.0 mg/day for adult American males (Tipton, 1970) and just over 4 mg/day for the typical Canadian diet (Meranger, 1972). Inasmuch as human deficiency has not been documented, it must be concluded that the minimum daily intake of 2 mg is in excess of the minimum daily requirement (Mertz, 1972). The body pool of manganese has been estimated at 12-20 mg, with most of the element concentrated in the bones, liver, pancreas, kidney and pituitary. Only a small proportion of the ingested manganese, probably less

than 5%, is normally absorbed (Davis, 1972). Table 15 presents some data on the manganese contents of common foods (Schroeder, 1966).

There is some possibility that there is a link between excessive manganese intake, or a disturbance in manganese metabolism, and diseases such as rheumatoid arthritis and Parkinson's Disease (Davies, 1972; Hopps, 1971).

Manganese may reduce the activity of certain bacillus strains in animals, but there are no data concerning this phenomenon in man (Weinberg, 1972).

Manganese intoxication has been restricted to instances in which the respiratory system is the route of contact. Food has not been implicated as an intoxication pathway. Manganese accumulation occurs in a very few human beings, and it is not known whether such excesses produce disease states (Schroeder, 1966).

In sum, it may be said that manganese is held to be among the least toxic of trace elements to mammals, including man (Underwood, 1971). Manganese toxicity in man arising from excessive intakes of this element in foods has never been reported (Underwood, 1973).

Skylab foods were not routinely analyzed for manganese as part of any surveillance program. There appears to be no need to do so.

10. Mercury

There is no known beneficial role for mercury in human physiology. The toxicity of mercurials has been known for many years, and individuals throughout history have been dispatched by means of mercury compounds.

Any consideration of mercury toxicity must be specific to the chemical nature of the toxicant. Elemental merucry is probably innocuous by ingestion. However, the pure element poses a hazard by inhalation

TABLE 15 (Shroeder, 1966)

Manganese Contents of Common Foodstuffs

Food	Mn, μg/g
Grains	
Wheat flour	5.2
Bread, white	1.8
Corn meal	2.1
Rice, brown	1.4
Macaroni	10.6
Dairy Products	
Milk, whole	0.2
Butter	1.0
Cheese, Swiss	1.3
Eggs	0.5
Meat	
Beef liver	0.2
Beef, wasting	0.1
Pork chop	0.3
Chicken	0.2
Sea Food	
Oysters	0.1
Halibut steak	0.1
Fruit	
Orange	0.4
Peach	1.0
Raisin	4.7
Vegetables	
Beans, green	0.2
Carrots	1.6
Spinach	7.8
Asparagus	0.3
Cucumber	0.1
Condiments and beverages	
Pepper, black	47.5
Coffee, Ground	20.7
Tea, leaves	275.6

because of its volatility, which is extraordinarily high for a metal. Mercury at 20 C has a high enough vapor pressure to produce an equilibrium concentration in air that is more than 130 times the industrial maximum allowable concentration of 0.1 mg/m^3 (D'Itri, 1972). Mercuric chloride ($HgCL_2$), known as corrosive sublimate, is highly toxic by virtue of producing corrosion of the intestinal tract. On the other hand, mercurous chloride (Hg_2Cl_2) has been used medicinally over many years and is relatively non-toxic (Goldwater, 1972).

The toxic effects of mercurials are generally a function of solubility, and more specifically, the ability to combine with sulfhydryl (-SH) groups in biochemically important enzymes and proteins (Anderson, 1966).

The principle manifestations of acute mercury poisoning are stomatitis and digestive upset. Extensive renal injury will accompany a heavy dose (Anderson, 1966).

Chronic mercurialism primarily involves the central nervous system, leading to serious and frequently permanent damage. The symptomology of chronic mercury poisoning includes progressive anemia, gastric disorders, salivation, metallic taste in the mouth, inflammation and tenderness of gums and tremors. Teeth blackening and loss result from poisoning by some mercury compounds. Renal complications are common. Extensive behavioral changes can also occur (Glaister, 1966). Organomercury compounds, i.e., compounds containing a carbon-mercury bond, are enormously more toxic than the inorganic compounds by virtue of being able to penetrate the brain and attack the central nervous system. There is also a possibility that these organomercurials can attack the membranes of cells, significantly altering the permeability of the membrane (Goldwater, 1972).

Interest in the environmental mercury problem was stimulated by the experience in Japan which gave rise to the characterization of Minimata Disease (D'Itri, 1972). A chemical plant bordering Minimata Bay employed an inorganic mercury compound as a catalyst for a process, not realizing that the process was resulting in the conversion of the catalyst to an organomercurial. Over many years, large numbers of people were being made ill, exhibiting symptoms that were eventually recognized as mercury poisoning. It was finally determined that the organomercurial was being concentrated in marine animals that constituted the dietary staple of the local population, resulting in chronic exposure and gradual intoxication.

A similar situation occurred in Sweden, in which mercury poisoning was experienced by a population eating fish which had become contaminated by an organic mercury compound that had been used as a pesticide and which washed into the local waters (D'Itri, 1972).

Mass poisonings from organic mercury compounds have been experienced in Iraq and Guatemala (Goldwater, 1972), Pakistan and Yugoslavia (Wallace, 1971). Most recently, 144 cases of alkylmercury poisoning occurred in Ghana due to the ingestion of maize which had been treated with ethylmercuric chloride. Twenty of the cases ended fatally (Derban, 1974).

The problem has even been encountered in this country. An impoverished family in New Mexico experienced three cases of mercurialism, from mild to severe, subsequent to the consumption of pork which had been fed on grain treated with organomercury compounds (Storrs, 1970).

The generally held view is that inorganic mercury compounds are absorbed readily through the lungs and gastrointestinal tract, but poorly through the skin. On the other hand, organic mercurials are absorbed efficiently via any of the three possible contacts (Wallace, 1971).

Mercury is present in many foodstuffs, as evidenced by the data in Table 16, which pertains particularly to foods surveyed in the United Kingdom. Fish tend to show the highest values, which is an observation that has been made for essentially all areas in which surveys have been conducted. Some variations exist, especially where industrial operations producing mercury discharges to water ways might result in higher concentrations in fish taken from those waters.

A survey in England (Elton, 1971) disclosed that the ingestion of mercury by the average consumer was something less than 10 μg/day, probably close to 7-8 μg/day. Persons with an inordinately high seafood diet would show somewhat higher intakes. A typical Canadian diet has been assayed at a mean mercury intake of 10 μg/day, with an extreme of twice that value (Merenger, 1972).

The biological half life for mercury has been found to be 70-90 days for the whole body, and 40-70 days for mercury in the circulating blood (Elton, 1971).

The World Health Organization has recommended a limit of zero for the acceptable daily intake of mercury. This is obviously impossible, so a practical limit of 0.02-0.05 ppm of the total diet has been suggested.

Some data concerning an acceptable daily intake can be derived from the Swedish experience with mercury poisoning. Persons were observed in that country who had eaten fish containing up to 6.7 ppm Hg. Assuming a daily intake of about 150 g/day of fish, this would be equivalent to an ingestion of about 1 mg of mercury, an intake that resulted in no detectable clinical illness. Applying the commonly used safety factor of 10, this suggests an acceptable daily intake of 0.1 mg Hg/day (Wallace, 1971).

TABLE 16 (Elton, 1971)

Mercury Contents of Common Foodstuffs

Food	Hg, μg/g
Dairy Products	
Milk	0.0
Cheese	0.2
Eggs	0.0
Meats	
Beef	0.0
Pork	0.0
Fish	
Tuna, canned	0.2
Salmon, canned	0.1
Shellfish	0.1
White fish	0.1
Cereals	
Bread	0.1
Flour	0.0
Breakfast cereal	0.2
Vegetables	
Potatoes	0.0
Green vegetables	0.1
Onions	0.1
Miscellaneous	
Pickles	0.4
Sugar	0.0
Spices	0.1

Some support for this suggestion is afforded by animal feeding experiments which provided an acceptable daily intake level, with a 10:1 safety factor, in the range of 0.06 to 0.12 mg/day for mercury.

Skylab foods were analyzed for mercury, and the data supplied by JSC were converted into intakes per serving. These data are presented in Table 17. Most foods are low in this element, with tuna salad spread, dried apricots, peanuts and ham spread showing the highest levels. Consumption of these foods would result in exceeding the ADI. However, because this has a large safety factor, it would not be expected to produce any problems for the consumers of these products. This statement should be qualified somewhat by the recognition that mercury compounds differ so widely in their toxic properties. If all of the mercury present were in the form of methyl mercury or other organomercurials, the matter would be more worrisome than if the mercury compounds were of the far less toxic inorganic variety.

11. Nickel

Nickel is regarded as being among the less toxic of the trace metals. It is found in many human tissues, and the analytical data for tissues obtained at various ages suggest that it is not cumulative. Standard man contains about 10 mg total nickel distributed through body tissues (Schroeder, 1962).

Poisoning by nickel compounds is very rare. Some of the water-soluble salts are toxic if injected directly into the blood stream (Smith, 1972). Overall, the toxicity of nickel salts for mammals is low, though high concentrations of salts can act as gastrointestinal irritants (Schroeder, 1962). The low toxicity on oral ingestion is attributed to poor absorption (Underwood, 1973). Rats were fed nickel

TABLE 17

Mercury Analysis of Skylab Foods

Food	Hg, ppm	Mg Hg/kg Body Weight per Serving
Grapefruit-drink (SKL-73)	<0.65	<0.0007
Dried Apricots (SKL-60)	<2.3	<0.0026
Orange Drink (SKL-69)	<0.80	<0.0009
Lemon Pudding (SKL-53)	<0.27	<0.0003
Peanuts (SKL-42)	<1.4	<0.0016
Corn (SKL-5)	<1.5	<0.0017
Corn (SKL-6)	<1.5	<0.0017
Ham Spread (SKL-13A)	<3.0	<0.0034
Peanuts (SKL-45)	<1.3	<0.0015
Peanuts (SKL-41)	<1.18	<0.0013
Peanuts (SKL-40)	<1.33	<0.0015
Tuna Spread (SKL-34)	<2.36	<0.0027
Tuna Spread (SKL-32)	<2.40	<0.0027
Lemon Pudding (SKL-49)	<0.29	<0.0003
Butterscotch (SKL-25)	<0.85	<0.001
Cookies (SKL-90)	<0.46	<0.0005
Orange Drink (SKL-71)	<0.64	<0.0007
Orange Drink (SKL-72)	<0.71	<0.0008
Dried Apricots (SKL-59)	<1.48	<0.0017

salts at levels of 250, 500 and 1000 ppm per day for three to four months without toxic manifestations (Underwood, 1971).

The essentiality of nickel for the human organism is at issue (Underwood, 1971).

Nickel is known to be an irritant and a toxicant in the industrial situation. Many forms of the element encountered industrially produce a severe dermatitis known as "nickel itch" in exposed workers. Nickel workers also appear to have excessive rates of pulmonary and nasal cancers (Smith, 1972).

Nickel carbonyl [$Ni(CO)_4$], is among the most toxic substances known, and is also highly correlated with pulmonary cancer (Glaister, 1966; Smith, 1972). Extreme precautions must be observed when this compound might be present. It has even been suggested that nickel carbonyl can be generated in burning cigarettes, nickel being present in tobacco.

The nickel contents of some typical foods are summarized in Table 18. The element is very common in vegetables and vegetable products, and much lower in meats. The total daily intake has been estimated at 300-600 mg Ni/day (Schroeder, 1962).

The literature discloses no citations of intoxication stemming from consumption of ordinary, uncontaminated foodstuffs. No standard exists for the control of this element in foods. However, at the request of NASA, a standard of 0.004 mg Ni/kg body weight/day was suggested. For the typical 75 kg average man, this would permit an intake of 300 μg Ni/day, which is at the lower end of the reported normal daily intake.

Skylab foods have been analyzed for nickel, and typical data are summarized in Table 19. Analytical data were provided by JSC and converted to intakes per serving. Of the foods available, only lemon pudding exceeds

TABLE 18 (Schroeder, 1962)

Nickel Contents of Common Foodstuffs

Food	Ni, µg/g
Condiments	
Salt	0.4
Pepper, black	3.9
Baking powder	13.4
Sea Food	
Oyster	1.5
Clams	0.6
Sardines	0.2
Swordfish	0.0
Meats	
Lamb chop	0.0
Egg	0.0
Beef	0.0
Grains	
Wheat	0.2
Bread, whole wheat	1.3
Wheat flour	0.3
Vegetables	
Potato	0.6
Peas	0.4
Lettuce	0.1
Fluids	
Milk	0.0
Tea	7.6
Cocoa	5.0

TABLE 19

Nickel Analysis of Skylab Foods

Food	Ni, ppm	Mg Ni/kg Body Weight per Serving
Grapefruit Drink (SKL-78)	0.65	0.0007
Dried Apricots (SKL-60)	1.27	0.0014
Orange Drink (SKL-69)	0.21	0.0002
Lemon Pudding (SKL-53)	8.52	0.0097
Peanuts (SKL-42)	1.42	0.0016
Corn (SKL-5)	<0.059	<0.00007
Corn (SKL-6)	<0.062	<0.00007
Ham Spread (SKL-13A)	<0.12	<0.0001
Peanuts (SKL-45)	0.82	0.0009
Peanuts (SKL-41)	1.27	0.0014
Peanuts (SKL-40)	1.30	0.0015
Tuna Spread (SKL-34)	<0.09	<0.0001
Tuna Spread (SKL-32)	<0.10	<0.0001
Lemon Pudding (SKL-49)	0.07	0.00008
Butterscotch (SKL-25)	0.31	0.0004
Cookies (SKL-90)	0.14	0.0002
Orange Drink (SKL-71)	0.14	0.0002
Orange Drink (SKL-72)	0.17	0.0002
Dried Apricots (SKL-59)	0.33	0.0004

the recommended intake. However, the recommended standard is so conservative as to make it unnecessary to recommend elimination of this food item.

Private communication with JSC personnel indicated that drinking water is collected and stored in nickel vessels in some of the space vehicles. The water thus handled has been reported to contain as much as 7 ppm Ni. This possible source of significant amounts of nickel in the diet of the astronauts should receive further consideration.

12. Selenium

Selenium has been established as an essential element in human biochemistry. Poisoning by selenium has not been reported in human subjects, though selenium intoxication in other animals has been thoroughly documented (Underwood, 1971). The minimum dietary level at which selenium will accumulate in tissues of animals and possibly produce toxicity is generally set at 3-4 ppm of the total diet. It is difficult to envision any human diets that could even approach this level (Underwood, 1973).

Some data relating to the selenium contents of common foods are presented in Table 20 (Morris, 1970). These data must be viewed with some caution because the selenium contents of foodstuffs are highly subject to the area in which these foods were obtained. This factor is primarily a reflection of the uneven geochemical distribution of this element. Because of the volatility of many selenium compounds, there is substantial loss of natural selenium from foods in the course of the cooking process (Underwood, 1971).

Selenium has been alleged to be carcinogenic in rats, but protective against cancer in humans. These data are inconclusive (Underwood, 1971).

TABLE 20 (Morris, 1970)

Selenium Contents of Common Foodstuffs

Food	Se, µg/g
Vegetables	
Carrots	0.0
Corn	0.0
Garlic	0.3
Tomatoes	0.0
Grains and Cereals	
Barley	0.6
Bread, white	0.3
Rice, polished	0.3
Dairy Products	
Egg	0.2
Cheese	0.1
Milk	0.0
Meats	
Beef	0.3
Pork	0.1
Chicken	0.1

There is no standard for the control of selenium in foods. NASA requested that one be proposed. An acceptable daily intake of 0.002 mg Se/kg body weight was suggested, admittedly on the basis of the barest minimum of data. Very likely, this is extremely conservative, though it is difficult to support this or any other value.

The proposed standard would permit an intake of 0.14 mg/day Se for the 70 kg man. One reference (Underwood, 1973) suggests the minimum dietary level which might produce toxicity as being around 3-4 ppm in terms of the total diet. For a total food intake of 2 kg, this would entail ingestion of about 3 mg Se. Thus, the proposed standard is conservative by a factor of about 20. It would thus seem possible to increase the acceptable daily intake by a factor of about two with an entirely suitable margin of safety remaining. However, there is very little more basis for an acceptable daily intake of 0.004 mg Se/kg body weight than there is for the original proposal of 0.002 mg.

Skylab foods have been analyzed for selenium content and summary data are presented in Table 21. The analytical results, supplied by JSC, have been converted to intakes per serving. It can be seen that ham spread and dried apricots approach the original proposal, but that other foods are low in selenium. It must again be considered that we are operating below the detection limit of the selenium analysis method, and the true value may be very much lower.

13. Titanium

Titanium is one of the more abundant elements in the lithosphere, generally appearing with aluminum. It therefore appears in most growing plants, though titanium contents are low because of the relatively low efficiency of absorption of the element.

TABLE 21

Selenium Analysis of Skylab Foods

Food	Se, ppm	Mg Se/kg Body Weight per Serving
Grapefruit Drink (SKL-78)	<0.39	<0.0004
Dried Apricots (SKL-60)	<1.4	<0.0016
Orange Drink (SKL-69)	<0.48	<0.0005
Lemon Pudding (SKL-53)	<0.16	<0.0002
Peanuts (SKL-42)	<0.83	<0.0009
Corn (SKL-5)	<0.88	<0.0010
Corn (SKL-6)	<0.89	<0.0010
Ham Spread (SKL13A)	<1.8	<0.002
Peanuts (SKL-45)	<0.80	<0.0009
Peanuts (SKL-41)	<0.71	<0.0008
Peanuts (SKL-40)	<0.80	<0.0009
Tuna Spread (SKL-34)	<1.42	<0.0016
Tuna Spread (SKL-32)	<1.44	<0.0016
Lemon Pudding (SKL-49)	<0.17	<0.0002
Butterscotch (SKL-25)	<0.51	<0.0005
Cookies (SKL-90)	<0.27	<0.0003
Orange Drink (SKL-71)	<0.38	<0.0004
Orange Drink (SKL-72)	<0.90	<0.0005
Dried Apricots (SKL-59)	<0.90	<0.001

Little is known relating to the titanium contents of human foods or typical daily intakes. There are no standards defined for the control of the titanium content of foods. There are no toxicity problems identified as attributable to exposure to low levels of this element or its compounds.

A request was issued by NASA that an acceptable daily intake be defined for titanium. With absolutely no basis, the level of 0.004 mg Ti/kg body weight/day was proposed. This was deemed to be conservative, though it was not even possible to conjecture what margin of safety might be involved.

Skylab foods have been analyzed for titanium contents, and typical data are presented in Table 22. The analytical data were supplied by JSC and these were translated to intakes per serving.

It is immediately obvious that all foods, except for tuna spread, are very low in titanium. There is no readily apparent explanation for the extremely high value of greater than 1000 ppm observed in the two samples of the tuna product. Neither natural nor contamination sources suggest themselves. All foods conform to the proposed standard except for tuna, though it must be emphasized again that the standard proposed is entirely arbitrary. In light of the unusually extreme result for tuna spread, these determinations must be viewed as suspect.

14. Vanadium

Vanadium is another of the elements that is both amphoteric and capable of existing in multiple valence states. The major valence states of vanadium are V^{+5} and V^{+3}. The pentavalent state is generally regarded as the more toxic (Smith, 1972). However, vanadium is not especially toxic to man. No toxic effects were noted when human subjects were fed ammonium

TABLE 22

Titanium Analysis of Skylab Foods

Food	Ti, ppm	Mg Ti/kg Body Weight per Serving
Grapefruit Drink (SKL-78)	0.34	0.0004
Dried Apricots (SKL-60)	1.13	0.0013
Orange Drink (SKL-69)	0.28	0.0003
Lemon Pudding (SKL-53)	0.38	0.0004
Peanuts (SKL-42)	0.28	0.0003
Corn (SKL-5)	0.73	0.0008
Corn (SKL-6)	0.31	0.0004
Ham Spread (SKL-134)	<0.12	<0.0001
Peanuts (SKL-45)		
Peanuts (SKL-41)	0.51	0.0006
Peanuts (SKL-40)	0.40	0.0005
Tuna Spread (SKL-34)	>1,000	>1.135
Tuna Spread (SKL-32)	>1,000	>1.135
Lemon Pudding (SKL-49)	0.41	0.0005
Butterscotch (SKL-25)	0.24	0.0003
Cookies (SKL-90)	0.12	0.0001
Orange Drink (SKL-71)	0.17	0.0002
Orange Drink (SKL-72)	0.28	0.0003
Dried Apricots (SKL-59)	0.87	0.001

vanadyl tartarate at concentrations of 4.5 to 18 mg vanadium per day, though subjects receiving the higher concentrations experienced some gastrointestinal distress (Underwood, 1971).

A normal adult "average man" will contain 10 to 25 mg total vanadium, mostly in the bones, teeth and adipose tissue. The dietary intake has been estimated at one to four milligrams per day (Underwood, 1971).

Vanadium is recognized to have some offensive or toxic properties in industrial situations. Vanadium pentoxide, V_2O_5, is irritating to the mucosa and is a pulmonary irritant generally. There is also some evidence that the element can act as a cholinesterase inhibitor. Vanadium has also been implicated in the production of cardiac disease when vanadium is a component of airborne particulates (Smith, 1972).

There are no reports of foodborne vanadium resulting in any form of human intoxication. Consequently, there are no standards promulgated for the limitation of this element in foods. Nonetheless, NASA requested the suggestion of an acceptable daily intake value for vanadium, and the level of 0.01 mg V/kg body weight/day was proposed. This value is rather arbitrary. However, based on this standard, the 75 kg average man would be limited to the ingestion of 0.75 mg V per day, compared with an estimated average intake of 1-4 mg/day as previously noted. Thus, the proposed standard is conservative.

Vanadium analyses were performed on Skylab foods, and summary data are provided in Table 23. Analytical results supplied by JSC were converted into intakes per serving. It is obvious that all foods are quite low in vanadium, and there appears to be no problem in meeting the proposed standard. However, this statement should not be taken to indicate that the proposed standard has more than an arbitrary basis and that it has to be met.

TABLE 23

Vanadium Analysis of Skylab Foods

Food	V, ppm	Mg V/kg Body Weight per Serving
Grapefruit Drink (SKL-78)	<0.026	<0.00003
Dried Apricots (SKL-60)	<0.09	<0.0001
Orange Drink (SKL-69)	<0.03	<0.00003
Lemon Pudding (SKL-53)	<0.01	<0.00001
Peanuts (SKL-42)	<0.05	<0.00006
Corn (SKL-5)	<0.059	<0.00007
Corn (SKL-6)	<0.062	<0.00007
Ham Spread (SKL-13A)	<0.12	<0.0001
Peanuts (SKL-45)	<0.053	<0.00006
Peanuts (SKL-41)	<0.05	<0.00006
Peanuts (SKL-40)	<0.05	<0.00006
Tuna Spread (SKL-34)	<0.29	<0.0003
Tuna Spread (SKL-32)	<0.10	<0.0001
Lemon Pudding (SKL-49)	<0.01	<0.00001
Butterscotch (SKL-25)	<0.04	<0.00005
Cookies (SKL-90)	<0.02	<0.00002
Orange Drink (SKL-71)	<0.03	<0.00003
Orange Drink (SKL-72)	<0.03	<0.00003
Dired Apricots (SKL-59)	<0.06	<0.00007

B. Pesticides

Pesticides cover a category of economic poisons of major importance to modern agriculture. The broad rubric pesticides encompasses a family of chemicals categorized according to the target organisms the chemical is designed to control. Probably the most important type is insecticides, intended for the control of insect pests. Herbicides serve to control the growth of undesirable plants - weeds - which are competitive with the desired crop for soil nutrients and water, and which could also complicate crop harvesting and processing. The control of fungal diseases which can destroy crops or reduce yield is accomplished by fungicides. Insect pests while still in the larval or soil-living stage are frequently controlled by fumigants. Rodents are capable of consuming vast amounts of harvested crops such as grains, and these grains in storage may be protected by rodenticides.

Pesticides are available and applied in all physical states. The fumigants are generally gaseous, this property being optimal for penetration of the soil matrix. The other varieties may be applied in the solid form, in solution and in suspension. In most instances, the pesticidally active chemical is a small proportion of the total formulation, generally less than 10%.

Pesiticide utilization dates back at least 2000 years. Prior to World War II, inorganic compounds and natural products were most widely used. Many of the inorganics, i.e., lead arsenate, remained in the area in which they were deposited for many years. Consequently, the issue of environmental persistence is by no means a new one, though it was largely ignored until recently.

Pesticidal persistence has two dimensions, one useful and one possibly detrimental. Persistence in the activity sense is highly desirable. This permits an application of the chemical to perform the intended purpose for an extended period, obviating the need for frequent application. This can be of paramount importance when the issue is that of insect disease vector control in underdeveloped areas where frequent application is difficult or impossible.

Environmental persistence is the issue that has precipitated actions with respect to pesticidal chemical choices that may have been ill-advised. This issue relates to the acknowledged stability of certain of the chemical agents in the environment, enabling the chemical to move through the various ecologic trophic levels with instances of concentration or magnification. This issue will not be dealt with further in this report.

The major categories of modern pesticides are two: chlorinated organics and organophosphates. These are identified in Table 24. The chlorinated organic era began during World War II with dichlorodiphenyltrichloroethane, the famous DDT. This agent spurred the development of many others. DDT represents the epitome of a desirable insecticide in that it has a high order of toxicity toward the target species, and a very low order of toxicity to non-target species, including man. The agent is also highly persistent, with respect to both activity and the environment.

The organophosphates (and thiophosphates) are direct descendents of the neurotoxic war gases (G-agents) developed by the Germans during World War II. They are highly toxic toward the target species, but also highly toxic toward unintended species, including man. The persistence of the organophosphates in both senses is much lower than for the chlorinated organics.

TABLE 24

PESTICIDE CONTAMINANTS

Pesticide	Toxic Level[1]	Effect
Aldrin: 1,2,3,4,10,10-hexachloro-1,4-4a, 5,8,8a-hexahydro-1,4-endo-exo-5, 8-dimethanonaphthalene.	5-500 mg/Kg	Neurological effect on central nervous system, with convulsions; specific organ effects - mild and transient injuries of kidney (edema of tubular epithelium) and liver (small foci of central lobular necrosis) have been described; gastroenteritic - nausea and vomiting.
Dieldrin: 1,2,3,4,10,10-hexachloro-6,7-epoxy-1,4,4a,5,6,7,8,8a-octahydro-1, 4-endo-exo-5,8-dimethanonaphthalene.	5-500 mg/Kg	Neurological effect on central nervous system, with convulsions; specific organ effects - mild and transient injuries of kidney (edema of tubular epithelium) and liver (small foci of central lobular necrosis) have been described; gastroenteritic - nausea and vomiting.
Endrin: 1,2,3,4,10,10-hexachloro-6,7-epoxy-1,4,4a,5,6,7,8,8a-octahydro-1, 4-endo-endo-5,8-dimethanonaphthalene.	5-50 mg/Kg	Neurological effect on central nervous system, with convulsions and hallucinations; gastroenteritic - nausea.
Heptachlor: 1,4,5,6,7,8,8-heptachloro-3a,4,7, 7a-tetrahydro-4,7-endomethanoindene.	50-500 mg/Kg	Neurological effect on central nervous system, with convulsions; specific organ effect - possible liver damage as late manifestation.
DDT: 2,2-bis (p-chlorophenyl)-1,1,1-trichloroenthane.	50-500 mg/Kg	Neurological effect on central nervous system, the cerebellum and higher motor cortex appear to be the chief sites of action - convulsions are also present; specific organ effect - pulmonary edema; gastroenteritic - vomiting and delayed emesis and/or diarrhea.
DDD,TDE: 2,2-bis (p-chlorophenyl)-1,1-dichloroethane	500-5 gm/Kg	Neurological effect on central nervous system, with convulsions which are less frequent than in DDT poisoning.

TABLE 24

PESTICIDE CONTAMINANTS (Cont'd)

Pesticide	Toxic Level	Effect
Methoxychlor: 2,2-bis (p-methoxyphenyl)-1,1,1-trichloroethane	500 mg-5 gm/Kg	Neurological effect on central nervous system.
BHC, lindane: 1,2,3,4,5,6-hexachlorocyclohexane	50-500 mg/Kg	Neurological effect on central nervous system, with convulsions; gastroenteritic - nausea and vomiting; debilitating - headache; specific organ effect - respiratory failure.
Toxaphene:	500 µg-5 mg/Kg	Gastroenteritic - salivation and vomiting; neurological - convulsions; specific organ effect - respiratory failure.
Fenthion: O,O-Dimethyl O-(4-(methylthio)-m-tolyl) phosphorothioate	50-500 mg/Kg	Similar in effect to parathion.
Diazinon: O,O-Diethyl O-(2-isopropyl-4-methyl-6-pyrimidyl) phosphorothioate	50-500 mg/Kg	Metabolic upsets - cholinesterase inhibitor
Malathion: O,O-dimethyl S-(1,2-dicarbethoxy-ethyl) phosphorodithioate.	50-500 mg/Kg	Metabolic upsets - low anti-cholinesterase potency; gastroenteritic - nausea, vomiting, abdominal cramps, diarrhea and excessive salivation. Possibly debilitating - headache, giddiness, and vertigo. Neurological - effect on central nervous system with convulsions. Specific organ effect - paralysis of respiratory muscles, excessive secretion of respiratory tract mucus.

TABLE 24

PESTICIDE CONTAMINANTS (Cont'd)

Pesticide	Toxic Level	Effect
Methyl parathion: O,O-Dimethyl-O-p-nitrophenyl phosphorothioate	5-50 mg/Kg	Metabolic upsets - low anti-cholinesterase potency; gastroenteritic - nausea, vomiting, abdominal cramps, diarrhea and excessive salivation. Debilitating - headache, giddiness, and vertigo. Neurological - effect on central nervous system with convulsions, and coma; specific organ effects - respiratory effects with difficulty in breathing, excessive secretion of saliva, and/or respiratory tract mucus, respiratory arrest arising from failure of the respiratory center, paralysis of respiratory muscles or intense broncho-constriction.
Parathion: O,O-Diethyl-O-p-nitrophenyl phosphorothioate	Less than 5 mg/Kg	Gastroenteritic - nausea, vomiting, abdominal cramps, diarrhea and excessive salivation. Debilitating - headache, giddiness, and vertigo. Neurological - effect on central nervous system with convulsions and coma; respiratory effects - difficulty in breathing, excessive secretion of saliva and of respiratory tract mucus, oronasal frothing, cyanosis, pulmonary rates. Lethal - due to respiratory arrest arising from failure of the respiratory center, paralysis of respiratory muscles, intense broncho-constriction, or all three. Metabolic upsets - cholinesterase inhibitor.
2,4-D: 2,4-dichlorophenoxyacetic acid	50-500 mg/Kg	Gastroenteritic - nausea, vomiting and diarrhea. Neurological - central nervous system effects - lack of motor function.

TABLE 24

PESTICIDE CONTAMINANTS (Cont'd)

Pesticide	Toxic Level	Effect
2,4,5-T: 2,4,5-trichlorophenoxyacetic acid	500 mg-5 gm/Kg	Gastroenteritic - nausea, vomiting and diarrhea. Neurological - central nervous system effects - control of motor function.
2,3,6-TBA: 2,3,6-trichlorobenzoic acid	500 mg-5 gm/Kg	Specific organ effect - lung congestion, and kidney inflammation.
Simazene: 2-chloro-4,6-bis (ethylamino)-S-triazine.	500 mg-5 gm/Kg	Possibly specific organ effects - increased respiratory rates; possibly muscular effects - muscular spasms or stiff walk.

[1]Toxicity levels taken from Clinical Toxicology of Commercial Products, 3rd edition, The Williams and Wilkin Company, Baltimore, 1969.

The manner of use of pesticides enables intimate contact with foods during the growing process. Pesticides are sprayed onto crops and onto and into the soil in which they are growing. Some incorporation into the plant tissue is thus possible. Animals consuming such crops have intimate contact with the contaminating chemicals, and these chemicals and their residues may be incorporated into those portions of livestock used as food by humans.

Rain and irrigation results in runoff from agricultural areas into streams and other waterways. Pesticides are thus suspended or dissolved in the receiving water. Organisms, both plant and animal, growing in these waters can thus contact the contaminants and again incorporate these chemicals into their tissues, which may ultimately reach man.

Most of the generally used pesticides are organic, hence lipophilic. There is thus a strong tendency for the pesticides to concentrate in the fatty tissues of organisms in the water rather than to remain suspended in the relatively inhospitable water phase. This concentration or "manification" is most pronounced in the aquatic system. It is found very little in the terrestrial system, i.e., in growing plants.

A survey of pesticide levels in food was conducted by review of the literature. (Pesticide levels in food appear to be affected by cooking and processing methods and thus will differ from residues found in uncooked foods.) Some typical residues in human foods are given in Table 25 (Edwards, 1970). Current values would likely be lower by virtue of changed insecticide use patterns.

Cooking methods have been found to affect pesticide residue levels in food. The effect of commonly employed cooking methods and of heating

TABLE 25 (Edwards, 1970)

Pesticide Residues in Human Foods

Food	Residue, ppm			
	DDT	γ BHC	Heptachlor	Aldrin
Fruit	0.012	t	---	0.003
Grain, cereal	0.005	0.008	0.002	t
Leafvegetable	0.025	t	---	t
Rootvegetable	0.008	---	---	---
Eggs	0.02	t	t	---
Milk	0.13	0.01	0.03	t
Meat	0.28	0.017	0.01	---

on DDT-containing chicken tissue was investigated. All cooking and heating methods employed resulted in the conversion of DDT to DDD. The treatments did not significantly alter the concentration of DDE. Frying or steaming resulted in greater pesticide residue losses from tissues than baking or heating in closed containers. Losses in residue concentrations were reported to be greatest in cooking procedures involving leaching of fat.

A study concluded that broccoli plants showed mean losses after cooking of 9, 34, 8 and 7% respectively, for plants harvested 1, 2, 3, and 4 days after Malathion application.

Commercial processing has been found to have an effect on pesticide residues in food. In one study, tomatoes grown on field plots were treated with Aldrin and Dieldrin at three levels. After harvesting, the tomatoes were processed by commercial procedures and residues were determined in samples taken from various points in the processing operation. It was found that commercial canning and processing juicing operations removed 80% of the Aldrin and Dieldrin residues.

A question was posed concerning the possible effects of pesticide residues, generally dieldrin, in Skylab foods. These residues were measured to be in amounts below 0.5 part per million, and generally below 10 parts per billion.

The World Health Organization has considered human intakes of pesticides and pesticide residues and has recommended the following Acceptable Daily Intake (ADI) values:

Pesticide	ADI, mg/kg Body Weight
Dieldrin & Aldrin	0.0001
DDT	0.01
BHC	0.0125
Heptachlor	0.0005

As with all ADI values, these may be assumed to be safe or "zero effect" limits.

Although dieldrin is generally recognized as being more toxic to warm blooded mammals than DDT, a considerable tolerance appears to exist. One study (Hunter, 1967, 1969) involved feeding dieldrin to 13 human volunteers in amounts of 10, 50 or 211 micrograms daily for prolonged periods. Throughout 18 months of feeding, no signs of ill health were recognized in any of the subjects; neither were there any clinical signs of abnormalities. The body burdens of individuals receiving 50 μg of dieldrin daily were four times those of the general population. Subjects receiving the 211 μg daily dose showed body burdens about 10 times normal.

Adipose tissue samples taken from U.S. residents not having occupational exposure to dieldrin show dieldrin concentrations averaging around 0.2 ppm, with a significant range around the mean (Edmundson, 1968).

The situation with respect to DDT is of even less concern. Despite quite general appearance of DDT and derivatives thereof in foodstuffs and the environment, there appears to be little issue of human morbidity associated with DDT. A key study (Laws, 1967) involved men with 11 to 19 years of contact with DDT in a facility manufacturing the insecticide. Adipose tissue of these subjects analyzed 38-647 ppm DDT, compared with an average of about 8 ppm for the general population without such occupational exposure. The daily DDT intake of the industrial subjects was estimated to be in the range of about 18 mg per day, compared with about 0.04 mg per day for the general population. None of the heavily exposed population manifested any demonstrable ill effects.

In 1969 the dietary intake of pesticides was estimated (Barney, 1969) to be 0.8 μg/kg body weight for DDT and related compounds, 0.08 μg/kg body weight for dieldrin and 0.004 μg/kg body weight for endrin.

Other, more limited studies, have described long term ingestion of DDT in gram quantities without ill effects.

Analysis of adipose tissue samples from subjects in the less developed nations where gross overuse of DDT is frequently the case indicate significantly higher DDT contents, but still without ill effects (Edwards, 1970).

Quite beyond the systemic toxic effects of pesticides, both acute and chronic, an issue has been raised regarding the carcinogenic and tumorigenic properties of the chlorinated hydrocarbons. Laboratory experiments have shown the development of neoplasms in the case of DDT, dieldrin and BHC (Walker, 1973). Special concern has been evinced with regard to the carcinogenicity of dieldrin and aldrin (Davis, 1962). Although laboratory studies have shown neoplasm development at high levels of administration, frequently by unusual means and generally in susceptible strains of experimental animals, there have been no reports of any such phenomena in human populations. Nonetheless, the Environmental Protection Agency has advocated the banning of dieldrin and aldrin, an action that has found considerable opposition (O'Brien, 1973).

No data currently exist which point to the development of tumors or carcinomas from food containing trace quantities of pesticides or their residues.

In summary, a review of the literature concerning pesticides and pesticide residues in foods has disclosed the following:

1. For the United States, the most broadly distributed pesticide residue is dichlorodiphenyltrichloroethane (DDT) with significant amounts of

dieldrin also involved. Depending on the location, quantities of chloridane and heptachlor can also be found. The "mix" of pesticide residues outside of the United States is somewhat different, reflecting the different use pattern. The quantity of DDT far out-weighs all others and this may be expected to decline as DDT is displaced by other pesticides.

2. Pesticide residues found in typical foods and potable water supplies remain substantially below current levels of concern.

3. Terrestrial plants, including human and animal food crops, when grown in soil contaminated with chlorinated pesticides can incorporate pesticides in the plant tissues. This is a highly variable matter from one type of plant to another. Root crops appear to be most prone to incorporation of pesticides because the water-insoluble pesticides carried in ground water will tend to concentrate the organic growing tissues. When fields growing food crops are sprayed for pest control, the quantity of pesticide remaining with the food can be minimized by insuring adequate time between spraying operations and harvesting of the crop. Pesticides will remain adherent to plants after spraying, but this can be removed by adequate washing.

4. Marine organisms can extract pesticides from the water phase, again because of the lipophilic nature of the chlorinated pesticides. Several species of vertebrates tend to concentrate pesticide residues to levels substantially above the total environmental level.

5. Terrestrial plants for the most part do not exhibit the "magnification" phenomenon or concentration of pesticides from the soil in which grown to the same extent as the aquatic environment because of the single-link food chains. Some aquatic plants can concentrate pesticides.

6. Vertebrates tend to concentrate ingested pesticides in their fatty tissues.

7. To date, there have been no instances reported of harm to normal, healthy humans resulting from the ingestion of food or water showing traces of pesticide residues. Where morbidity or significant mortality has been experienced, it has been associated with ingestion of food items grossly contaminated with DDT by emaciated individuals, or starvation resulting in consumption of adipose tissue and consequent mobilization of pesticide residues stored therein. There have been instances of intoxication with phosphate insecticides such as Parathion, but these occurred through direct contact rather than ingestion.

IV. Analytical Methods for Food Contaminants

In view of the low levels of acceptable daily intakes established for certain of the food contaminants, notably heavy metals, it is clear that the analytical techniques now employed, atomic absorption spectrophotometry and optical emission spectroscopy, are not uniformly acceptable by virtue of some relatively high limits of detection. Accordingly, a review was made of possible other analytical methodologies.

For the trace elements arsenic, cadmium, mercury, nickel, selenium, thallium, titanium and vanadium, neutron activation analysis appears to offer advantages over atomic absorption spectrophotometry. In the case of cadmium, both methods appear satisfactory. If future studies indicate a need for an order of magnitude improvement in detection limit for cadmium, a technique such as atomic fluorescence spectroscopy should be considered. For lead, atomic absorption is to be preferred. The permissible levels of boron permit a relatively free choice among methods.

Limits of detection data by atomic absorption spectrophotometry (AAS) and neutron activation analysis (NAA) are shown in Table 26 (Equipment suitable for the analysis of foods by NAA is available to Texas A&M University.)

With respect to the pesticides and pesticide residues, continued use of gas chromatographic analysis is the best prospect, with some refinement of techniques. NAA has been adapted to the analysis of chlorinated pesticide residues, but the technique becomes less useful when the material being analyzed contains chlorine from other than the pesticide residue. This would be expected to be the case for many of the foods which contain salt.

TABLE 26

ANALYTICAL METHODS

LIMITS OF DETECTION

Element	[1] AAS, ppm	[2] NAA, µg
Arsenic	0.2	$1\text{-}3 \times 10^{-4}$
Beryllium	0.002	Not detected
Boron	6.	Not detected
Cadmium	0.005	4.9×10^{-3}
Lead	0.01	1-3
Mercury	0.5	$1\text{-}3 \times 10^{-3}$
Nickel	0.005	$4\text{-}9 \times 10^{-3}$
Selenium	0.5	$1\text{-}3 \times 10^{-3}$
Thallium	Not detected	$4\text{-}9 \times 10^{-2}$
Titanium	0.2	$1\text{-}3 \times 10^{-2}$
Vanadium	0.04	$1\text{-}3 \times 10^{-4}$

[1] Atomic Absorption Spectrophotometry

[2] Neutron Activation Analysis

Recognizing the inadequacy of presently used methods, several discussions were held with key personnel of the Activation Analysis Research Laboratory at Texas A&M University. This installation represents what is generally regarded as the most advanced facility for neutron activation analysis, NAA. NAA is under consideration as an alternative analytical method for some of the key trace elements of concern. Complete information concerning the possible applicability of NAA was obtained by means of a visit to AARL.

The AARL facility includes three sources of activation: a 14 mev accelerator (fast neutrons), a cyclotron and a nuclear reactor. The cyclotron provides a variety of charged particles rather than neutrons. In effect, the reactor offers the best method of activation, providing a flux of about 10^{13} neutrons/cm^2/sec. Many samples can be irradiated simultaneously, and vacuum is not required. The accelerator does not afford a suitable activation method, and also permits only a single irradiation at a time. The cyclotron requires sample exposure in high vacuum or sealed ampoules, and also permits only a single irradiation at a given time, and the cost is substantially higher than with the other methods.

A variety of detectors is available for the actual analysis, and the selection of the proper instrument is important. The detector can influence the lower limit of detection.

For the elements of interest to the Skylab program, following in Table 27 are the best values obtained for the lowest limit of detection expressed as micrograms of element:

TABLE 27

Limits of Detection by Neutron Activation Analysis

Element	Detection Limit, μg
Arsenic, As:	0.0015
Beryllium, Be:	not reported
Boron, B:	not applicable
Cadmium, Cd:	0.0039
Lead, Pb:	200
Mercury, Hg:	0.083
Nickel, Ni:	0.18
Selenium, Se:	0.013
Thallium, Ti:	not reported
Titanium, Ti:	0.04
Vanadium, V:	0.00038

Where the sample irradiated amounts to one gram, the above values are also the detection limits in parts per million. The lower limit of detection can be improved by increasing the sample size, but this has a practical limit of about 20 grams. Thus, the above detection limits in terms of parts per million might be improved by a factor of about 20.

The above values must be regarded as ideal, and detection limits are degraded by having elements in combination where one might overwhelm another. A particularly offensive element is sodium, which tends to mask others in their ability to be detected at low concentrations. This problem can be circumvented by suitable adjustments in means and time of irradiation and means and times of counting, especially with respect to delaying counting to permit the decay of one element to low activity rates so that

another may be detected. To a degree, this means that complex samples can require considerable study before analytical techniques can be optimized.

AARL has gained some experience with foods, notably citrus fruits and cattle forage. Many elements other than the above are detectable to low levels.

AARL does not offer a routine analytical service. However, samples have been analyzed under contract. AARL is quite eager to cooperate with NASA-MSC, if for no other reason than the fact that their installation was made possible largely by funding from NASA.

V. Statistical Sampling for Food Quality Assurance

Consideration of the food sampling problem was undertaken. The sampling scheme for food packages presently being used at NASA gives a 10% chance of accepting 6.94 percent defectives for a lot size of 10,000 at an acceptable quality level (AQL) of 0.40 percent. This probability of acceptance of such a percent of defectives is unacceptable for consideration in the sampling of foods. It was therefore undertaken to provide a a more rigorous sampling plan.

The sampling plan used by NASA is that given in MIL-STD-105D and involves the use of inspection level S-4 of Table 28. This inspection level is not as stringent a level as the general inspection levels I, II, and III. It was felt that with an extension of Table 28, a more stringent sampling scheme could be obtained. To compute the desired sample size, the binomial and hypergeometric distributions were employed. The computed sample sizes by both methods for 10%, 5% and 1% chance of accepting defective lots at a particular AQL level are given in Tables 28 and 29.

This study was presented September 16, 1971 to a group meeting at NASA to review Skylab Food Microbiology Inspection procedures and specifications.

As another aspect of the food quality assurance program, statistical evaluation of the data on trace metals for Orange Juice Drink (samples SKL-71 and 72) was undertaken. Statistical treatment involves comparing of two populations means μ_1 and μ_2, on the basis of samples from these populations. If we are willing to assume a priori that $\sigma_1^2 = \sigma_2^2 = \sigma^2$, the t-distribution can be applied to the problem of testing the significance of, and obtaining confidence intervals for, the difference $= \mu_1 - \mu_2$ of

Table 28. Sampling Plan (Normal Inspection)
Computed by
Binomial Distribution

Sample Size Code Letter	Lot Size	p (In Percent Defective)	Required Sample Size for Given P_a [a] 10%	5%	p (In Percent Defective)	Required Sample Size for Given P_a [a] 10%	5%
E	50	4	34 (68%)	39 (78%)	4	34 (68%)	39 (78%)
F	90	2.5	61 (67%)	70 (77%)	4	39 (40%)	47 (52%)
G	150	1.5	85 (56%)	99 (66%)	2.5	63 (42%)	76 (51%)
H	280	1.0	141 (50%)	167 (60%)	1.5	108 (39%)	132 (47%)
J	500	0.65	229 (46%)	275 (55%)	1.0	227.27 (45%)**	210 (42%)
K	1,200	0.40	588.24 (49%)	.036 (86%)	0.65	344.83 (29%)	448.62
L	3,200	0.25	909.09 (28%)	1,182.73 (37%)	0.40	588.24 (18%)	765.29
M	10,000	0.15	1,428.57 (14%)	1,858.57 (19%)	0.25	909.09 (9%)	1,182.73
N	35,000	0.10	2,500 (7%)	3,252.5 (9%)	0.15	1,428.57 (4%)	1,858.57

a Percent of lots expected to be accepted with given p

* Sample size greater than 50% of lot size

** Percentage of lot size

Table 28. Sampling Plan (Normal Inspection)
(cont'd) Computed by
Binomial Distribution

Sample Size Code Letter	Lot Size	p (In Percent Defective)	Required Sample Size for Given P_a[a] 10%	5%	p (In Percent Defective)	Required Sample Size for Given P_a[a] 10%	5%
E	50	4	34 (68%)	39 (78%)	4	34 (68%)	39 (78%)
F	90	4	39 (40%)	47 (52%	4	39 (40%)	47 (52%)
G	150	4	56.50 (37%)**	73.50 (49%)	4	56.50 (37%)	73.50 (49%)
H	280	2.5	90.91 (33%)	118.27 (42%)	4	56.50 (20%)	73.50 (26%)
J	500	1.5	151.52 (30%)	197.12 (39%)	2.5	90.91 (18%)	118.27 (24%)
K	1,200	1.0	227.27 (19%)	295.68 (25%)	1.5	151.52 (13%)	197.12 (16%)
L	3,200	0.65	344.83 (11%)	448.62 (14%)	1.0	227.27 (7%)	295.68 (9%)
M	10,000	0.40	588.24 (6%)	765.29 (8%)	0.65	344.83 (3%)	448.62 (5%)
N	35,000	0.25	909.09 (3%)	1,182.73 (3%)	0.40	588.24 (2%)	265.29 (0.8%)

a Percent of lots expected to be accepted with given p

* Sample size greater than 50% of lot size

** Percentage of lot size

Table 29. Sampling Plan (Normal Inspection)
Computed by
Binomial Distribution

Sample Size Code Letter	Lot Size	p (In Percent Defective)	Required Sample Size for Given P_a[a] 1%	p (In Percent Defective)	Required Sample Size for Given P_a[a] 1%
E	50	4	*	4	*
F	90	2.5	82 (91%)	4	73 (81%)
G	150	1.5	122 (81%)	2.5	99 (66%)
H	280	1.0	210 (75%)	1.5	174 (62%)
J	500	0.65	353 (71%)	1.0	283 (56%)
K	1,200	0.40	1079 (89%)	0.65	957 (79%)
L	3,200	0.25	*	0.40	1,176.47 (37%)
M	10,000	0.15	2,857.44 (29%)**	0.25	1,818.18 (18%)
N	35,000	0.10	5,000 (14%)	0.15	2,857.14 (8%)

a Percent of lots expected to be accepted with given p

* Sample size greater than 50% of lot size

** Percentage of lot size

Table 29. (cont'd) Sampling Plan (Normal Inspection) Computed by Binomial Distribution

Sample Size Code Letter	Lot Size	p (In Percent Defective)	Required Sample Size for Given P_a [a] 1%	p (In Percent Defective)	Required Sample Size for Given P_a [a] 1%
E	50	4	*	4	*
F	90	4	73 (81%)	4	73 (81%)
G	150	4	75 (50%)	4	75 (50%)
H	280	2.5	*	4	112.99 (40%)**
J	500	1.5	*	2.5	181.81 (36%)
K	1,200	1.0	454.55 (38%)	1.5	303.03 (25%)
L	3,200	0.65	689.66 (22%)	1.0	454.55 (14%)
M	10,000	0.40	1,176.47 (12%)	0.65	689.66 (7%)
N	35,000	0.25	1,818.18 (5%)	0.40	1,176.47 (3%)

a Percent of lots expected to be accepted with given p

* Sample size greater than 50% of lot size

** Percentage of lot size

means of two populations assumed to be normally distributed. Here we are using σ^2 to be defined as the variance of population.

Results from the above statistical evaluation of data supplied by NASA are presented in Table 30. It was found that differences between averages of two samples of orange juice drink are significant for elements Boron, Nickel, Titanium. Other elements could not be compared due to the lack of sensitivity of instrumental methods employed.

If indeed the sample was a split one the statistical treatment should not have resulted in a significant difference. By the fact that significance was found it must be inferred that analytical methodologies are in error either due to the analysts involved or instrumental error.

TABLE 30
COMPARISON OF FOOD SAMPLE MEANS

Food	Element	t - Values Calculated	To .975	Significance
Orange Juice Drink	Boron	8.5958	2.7764	Yes
	Nickel	300	2.7764	Yes
	Titanium	366	2.7764	Yes

VI. Sterilization of Space Foods by Ethylene Oxide and Propylene Oxide

A variety of gaseous sterilants have been applied for the destruction of microbial life on materials, including foods, which are too sensitive for sterilization by heat or ionizing radiation. The most popular of these is ethylene oxide (EO) followed by propylene oxide (PO). The technique of gaseous sterilization was extensively studied at the Ft. Detrick Biological Warfare Laboratory during and after World War II (Chambers, 1971). The Food and Drug Administration has ruled on the suitability of the method for the sterilization of foods destined for human and animal consumption.

All of the gaseous fumigants fall into chemical category of alkylating agents. They are especially reactive toward protein amino acids containing -NH and -SH linkages. Reactions with -OH groups in carbohydrates also occur readily. These reactions afford means of attack on living matter, and this is believed to be the mechanism of microbial destruction, i.e., alteration of DNA and/or RNA. However, the reaction is by no means specific toward microorganisms.

Ethylene oxide has been used to inhibit the growth of molds, yeasts, bacteria (Lawrence, 1968) and viruses (Ginsberg, 1950).

Some concern regarding the suitability of foods sterilized by menas of ethylene oxide (or propylene oxide) was occasioned by the finding that rats failed to grow when fed special diets which had been treated with ethylene oxide (Hawk, 1955).

The U.S. Food and Drug Administration has adapted a strong position against wide use of EO for food sterilization. The agent has been approved only for the sterilization of spices, walnuts and copra (Lawrence, 1968). The major reason is related to the tendency of EO to destroy the nutritional

value of foods, notably the B vitamins and a fairly broad range of amino acids (Windmueller, 1959). This could produce a situation of nutritional deficiency if the foods thus sterilized are significant or the major sources of the nutritional component. In cases where only a small portion of the diet is EO treated, this consideration assumes lesser importance.

Starches have been demonstrated to undergo ethoxylation upon treatment with EO (Gordon, 1959). For the most part, the ethoxylated derivatives have been shown to be eliminated after ingestion without apparent harm. However, detailed feeding experiments to detect the impact of possibly toxic derivatives have not been conducted.

Another factor of toxicological concern is that EO sterilization results in ethylene glycol residues on treated foods. This results from the simple reaction of EO with water. Where high chlorine contents are involved, such as with foods high in salt (NaCl), some ethylene chlorohydrin is also formed. Both of these are regarded as toxic to humans.

PO appears to manifest fewer undesirable side effects and has been approved for the sterilization of a slightly wider spectrum of foods, including fruits. Starch, but not whole potatoes, is approved for PO sterilization by FDA. Reactions still occur, but the matter of propylene glycol residues is of minimal concern because propylene glycol is an approved food additive.

Comparing EO and PO, the former is substantially more effective in terms of the destruction of microbiological life per unit quantity of sterilant. In some cases, only EO will result in complete sterilization though PO will achieve a reduction of microbial contamination to very low levels.

The physical and chemical properties of EO and PO must be considered in the application of these agents for sterilization of foods.

Both EO and PO are flammable. The flammability limits in air are 3.6 to 100% (by volume) for EO and 2.1 to 21.5% for PO. EO is also explosive. Thus, care must be used in conducting the sterilization process.

Both gases are toxic. An industrial hygiene standard of 50 ppm maximum has been recommended for EO; the value for PO is 100 ppm (ACGIH, 1972). There is also some evidence that the two gases, especially EO, have mutagenic and carcinogenic properties.

Materials sterilized with the gaseous fumigants and the packages in which they are contained can retain some of the agent absorbed on or dissolved in the solid matter. The gas is slowly released on standing. Sufficient material can be retained to produce burns when such material comes into contact with moist skin. This problem can be acute with EO. Good practice requires that the sterilized items be allowed to stand for sufficient time to permit release of the sterilant before use.

The literature review and discussions with acknowledged experts in this field results in the following summary. Sterilization by means of propylene oxide, if realizable, would be preferred to sterilization with ethylene oxide. The use of ethylene oxide would probably be acceptable in terms of the effects on the foods if only a small portion of the diet were involved. If wider use of EO sterilization were resorted to, some diet supplementation with vitamins, especially the B vitamins, would be desirable. The generation of toxic materials by means of gaseous sterilization would probably be of minimal significance (Kaye, 1971).

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