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Feb, 1984*

House backs payments for Agent Orange exposure

Last week the House of Representatives passed a bill (H. R. 1961) that would pay some benefits to Vietnam veterans for exposure to Agent Orange, even though all of the scientific evidence is not yet in. It would provide for temporary disability or survivors' benefits for diseases that may be linked to herbicide exposure during the conflict. Specifically, it would authorize payments if the veterans showed signs of a certain liver disorder—porphyria cutanea tarda—within one year of leaving the region, or if they showed signs of soft tissue sarcoma within 20 years of leaving. The program is expected to cost \$4.7 million the first year and no more than \$6 million annually during the five years it is in effect. By that time, the \$100 million epidemiology study of the veterans—the largest ever conducted—is expected to be completed by the Centers for Disease Control. Then, sponsors say, the compensation issue will be reevaluated. The bill now moves to the Senate, which has been less active than the House on the issue.

EPA lets industry do tests on a nylon precursor

The Environmental Protection Agency seems inclined to accept industry's plan to run health-effects tests on cyclohexanone, a key intermediate for producing nylon. EPA gave a preliminary okay to the plan last month, and a final decision is expected after mid-February. Cyclohexanone is commercially important; more than 766 million lb/year are produced. The industry is coordinating work on the tests through the Industrial Health Foundation's Cyclohexanone Study Group, of Williamsburg, Va. Final reports on two key tests are due on Apr. 30.

Looking for the right test for anilines

A question the Environmental Protection Agency is wrestling with concerns the right way to set up health and environmental testing for aniline and its derivatives. While the agency has a wealth of information on exposure and release of these substances, it has been more difficult to set up the health and environmental testing. EPA thinks that one way to avoid unnecessary tests is to examine "structure-activity relationships"—in this case, testing a set of representative chemicals in several proposed subcategories: aniline, monochloroanilines and polychloroanilines, mononitroanilines and polynitroanilines, and halonitroanilines. EPA is working with the Aniline Assn. as well as with the Synthetic Organic Chemical Manufacturer's Assn. on the issue. Tests already done have persuaded EPA that an epidemiological study of workers exposed to the anilines may be needed in

light of the studies of health effects on animals. More than 613 million lb/year of aniline itself are used in the U.S. for producing isocyanates, rubber chemicals, dyes, pigments, hydroquinone, and drugs and pesticides. More action is expected from the agency in March.

ASARCO reaches a lead exposure accord

ASARCO, the United Steelworkers of America and the Occupational Safety and Health Administration last week signed an agreement outlining how the company will reduce worker exposure to lead in four primary lead smelters. The agreement, which is based on joint studies conducted by the parties, sets up specific schedules for implementing controls. Company officials estimate that the plans will be costly—possibly reaching \$7-8 million in ASARCO's Omaha, Neb., refinery operation alone over a period of years. But they also say that innovative new approaches like the negotiated lead package make a significant improvement over the traditional adversary tone that has characterized safety and health discussions about OSHA standards in general for the last few years. The four plants covered by the agreement include Omaha; the smelters in El Paso, Tex.; East Helena, Mont.; and Glover, Mo. The worker-exposure control plans call for improving ventilation, enclosing some processes or workspaces, and cleaning up more frequently. Other improvements include providing clean rooms, filled with filtered air, and mobile equipment similarly equipped, as well as periodically inspecting the worksites. Moreover, research will be conducted to develop more controls to further reduce exposures.

Ruckelshaus orders a halt on the use of EDB

Environmental Protection Agency head William D. Ruckelshaus on Feb. 3 ordered an immediate halt to the use of ethylene dibromide (EDB) as a fumigant on stored grain and as a spot fumigant on grain milling machinery. The emergency suspension is the strongest action EPA can take under law. EPA plans to recommend maximum permissible residues on grain and grain products and to set federal tolerance levels, Ruckelshaus said, "to eliminate EDB from the diet." Ruckelshaus emphasized that the public should not be alarmed. "What we're talking about here is long-term health effects," he said, citing EPA analyses that eating products containing EDB could increase cancer risk over a lifetime. No action was taken on the case of possible EDB residues in citrus, Ruckelshaus noted, because the agency needs more time to study the data and to work out the international trade problems.

URL 05005

In order to estimate the maximum potential risk of developing a tumor from exposure to 2,4,5-T containing 0.1 ppm TCDD, Dow used the very conservative "one-hit" model and upper 99% confidence limits for extrapolation from the data on rats. Since the incidence of tumors was greater in female rats in the Dow study, that frequency was used to calculate the potential for tumor formation in a female backpack sprayer. Even with this very conservative approach, the extrapolated annual risk was only 0.4 per million women who had applied 2,4,5-T each day, 5 days per week, 4 months per yr for 30 yr. In other words, there might be one tumor per 2,500,000 such female backpack sprayers per year, notwithstanding that there are probably none who fall in this category.

In contrast, what is the potential for developing cancer from exposure to known carcinogens? Based on data presented by Dr. Richard Wilson of Harvard during the 1978 OSHA carcinogen hearings (8), the relative risk for a backpack sprayer is very small compared to exposure to cigarette smoke, alcohol, saccharin, aflatoxin, chlorinated chemicals in water, and various forms of radiation.

RELATIVE RISK OF CANCER PER MILLION PEOPLE EXPOSED PER YEAR

Female backpack sprayer applying 2,4,5-T containing 0.1 ppm TCDD, 5 days per week, 4 months per yr, for 30 yr.	0.4
Smoking cigarettes	1200
Being in a room with a smoker	10
Eating and drinking	
Charcoal broiled steak, 0.25 lb per week	0.4
Water in Miami or New Orleans	1.2
Diet soda (saccharin), 1 per day	10
Milk (aflatoxin), 1 pint per day or cheese equivalent	10
Peanut butter (aflatoxin), 4 tbsp per day	40
Beer (alcohol), 1 can per day	20
Exposure to radiation	
One transcontinental flight per year	0.5
Frequent airline passenger	15
Living in Denver vs. New York	10
Average U.S. diagnostic medical X-rays	10
Living in brick vs. wood building	5
Natural background at sea level	15
Sunbathing or mountain climbing (skin cancer, curable)	5000

According to these figures, being in a room with a smoker or drinking one diet soda per day is 25 times more hazardous than 30 yr of spraying 2,4,5-T containing the maximum permissible level of 0.1 ppm TCDD; so is drinking milk, eating cheese or peanut butter, all of which may contain aflatoxins permitted by the Food and Drug Administration at levels up to 20 parts per billion. Exposure to various forms of radiation such as from traveling by air, living at high elevations, or even sunbathing is also more hazardous than being a backpack sprayer applying only 2,4,5-T for 30 yr.

RESPONSES TO THE RPAR

All responses to the RPAR are available for inspection in EPA's Federal Register office, room 401 in the east tower of Waterside Mall at 401 M Street SW in Washington, D.C. Also available are most of the 179 references cited by EPA in their risk document (PD 1) which was published in the Federal Register on April 21, 1978.

By the end of November about 2800 individual responses had been logged in and assigned by EPA to more than 2500 persons or organizations. According to Dr. William A. Wells, Acting Director of EPA's Special Pesticide Review Division, only about 20 to 40 responses are substantive and backed by data from scientific studies. The rest are only "testimonials," either from users who cite the need for continued registration and report no harm from exposure to 2,4,5-T for up to 30 yr, or from individuals who claim to have suffered harmful effects or are afraid they might if they were exposed even to spray drift. Review by Dow of all the responses on file in EPA indicates they are better than 86% in favor of continued registration of this useful herbicide.

Major respondents include Dow with 13 volumes of risk rebuttal information including copies of 158 documents or reports not cited by EPA in PD 1. Dow also submitted 8 volumes of benefits data for uses in rice, grazing lands, forests, and rights-of-way, again completely documented with copies of all cited references. Other respondents are the National Forest Products Association (NFPA) who have recently conducted an exposure study under actual field conditions to obtain more representative data than the additive "worst case" estimates used by EPA in its PD 1 for 2,4,5-T. Various user groups also responded collectively and individually, such as the National Cattlemen's Association, the National Rice Growers Association, and various Farm Bureaus. Major responses by activists were submitted by Friends of the Earth (FOE), the Environmental Defense Fund (EDF), Citizens Against Toxic Sprays (CATS), and several other coalition groups.

According to EPA's log of responses to the RPAR, only one number is assigned to letters which appear to originate from one source. For example, individual submissions from 32 foresters with firsthand experience using 2,4,5-T for up to 30 yr were all given one accession number because they all worked for International Paper Company, albeit in various locations around the country. Each of Dow's submissions during the past 7 months was listed separately under one accession number. Similarly, only one number was given to numerous submissions by Friends of the Earth under different cover letters. On the other hand, EPA curiously assigned individual numbers to each postcard or note received from various members of several families from small villages in Oregon and Arkansas. To avoid the potential for bias either way, the distribution of "for" and "against" responses reported herein is based on individual entries in EPA's log rather than according to the EPA accession numbers assigned to them.

SCIENCE/TECHNOLOGY CONCENTRATES

Science

Cancer shown to be two-step process

Researchers in the U.S. and England have shown that the transformation of normal cells into cancer cells requires at least two separate genetic changes. The findings help explain why cancer usually takes years to develop. Working independently, three research groups—led by Robert A. Weinberg at Massachusetts Institute of Technology in Cambridge, Mass., at Cold Spring Harbor Laboratory on Long Island, and Robert F. Newbold and Robert W. Oates at the Institute of Cancer Research in London, England—tried to make normal cells cancerous by introducing cellular or viral oncogenes into the cells. One group of oncogenes transformed the cells, making them proliferate in the lab instead of dying out after many generations, as most normal cells do. When these cells were exposed to any one of a second group of oncogenes, the cells became overtly cancerous, ignoring signals from surrounding normal cells to stop growing. The experiments are described in three separate papers in *Nature* [1984, 312, 602, 648 (1983)].

New ligand traps uranyl ions

A family of ligands that consist of two 1-phenylamine moieties linked together by oligoethylene oxide bridges of varying lengths "are particularly effective and selective in extracting uranyl ions from aqueous solutions into an organic phase," according to Rosangela Marchelli and coworkers from the Institutes of Organic Chemistry and General Chemistry at the University of Parma, Italy [*Angew. Chem. Int. Ed. Engl.*, 22, 563 (1983)]. The researchers find that with a 70-fold excess of ligand, 98% of the uranyl ion present in aqueous solution is extracted as either a 1:1 or 2:1 complex with the ligand. The presence of other metal cations in the solution, even in large excess, does not change the total uranyl ions extracted, and the other cations are themselves not removed from the solution. The uranyl ions can be recovered in about 90% yield from the organic phase, suggesting to the researchers that the ligands might have application in the decontamination and recovery of uranium from liquid wastes.

Aspartame raises brain phenylalanine levels

The use of aspartame in soft drinks as a replacement for saccharine may cause brain chemistry changes that will affect the mood or behavior of certain people, says Richard J. Wurtman, a physician and professor in the department of nutrition and food science at Massachusetts Institute of Technology [*New Engl. J. Med.*, 309, 1279 (1983)]. In experiments with rats, Wurtman finds that replacing glucose in food by aspartame doubles the brain levels of phenylalanine. If the rats consume carbohydrate along with the glucose or aspartame, the brain phenylalanine level

remains low. The level of brain phenylalanine, which might be perturbed by too much sugar, is lowered by drinking three soft drinks and eating a banana in the course of an afternoon. People with brain or nerve disorders or functional changes that affect levels of neurotransmitters are those with conditions such as hyperkinesia, Parkinson's disease, depression, bipolar mania, or those taking drugs that interact with plasma phenylalanine or tyrosine metabolism, such as monoamine oxidase inhibitors.

Oldest rock in world is 3.8 billion years old

Scientists at the National University, Canberra, Australia, have found the oldest rock in the world. The rock, which is a piece of zircon, is 3.8 billion years old—about 500 million years younger than the estimated age of Earth and at least 400 million years older than any other rocks dated so far. The rock was found earlier this year in a sedimentary formation in the Mount Narryer region. The dating was made by analyzing 100 grains of the mineral zircon isolated from the rocks and measuring traces of radioactive isotopes in the samples. Four of the grains showed ages in the range 4.1 billion to 4.2 billion years. The oldest previously dated rocks were from western Greenland and were estimated to date back 3.8 billion years.

Henry Taube wins Welch Award

The 1983 Welch Award in Chemistry will be given to Henry Taube, a chemistry professor at Stanford University, "for his decades of leadership and dedication" in the field of inorganic chemistry. The award, one of the more prestigious in chemistry, consists of a gold medallion and \$150,000. Taube will receive it at the Welch Foundation banquet in Houston in November. "Taube is considered to be a leading scientist in the area of inorganic reaction mechanism and has dominated the field for decades," says Jack S. Jossey, president of the foundation.

Air pollution affecting soybean yields

Air pollution is hurting soybean crop yields 15% or more, according to plant pathologist Howard E. Heggestad at USDA's Beltsville Agricultural Research Center in Maryland. Studying yield reductions caused by ozone and sulfur dioxide, USDA scientists found that at the highest level of ozone tested—0.14 ppm over a seven-hour period—soybean yields fell about 10% below those in filtered air. Sulfur dioxide at low levels (0.03 ppm) did not decrease yields, but exposure to 0.10 ppm for four hours a day reduced yields about 15%. According to Heggestad, the average ozone levels during the growing season in soybean-growing areas is 0.05 to 0.08 ppm (a seven-hour average for the sunlit part of the day). An average of 0.05 ppm for seven hours at Beltsville reduced yields 30% compared to filtered air, for soybeans grown in dry soil.

File Background Cancer

-- For 3-(3,5-dichlorophenyl)-N-(1-methylethyl)-2,4-dioxo-1-imidazolidinecarboximide and its metabolite 3-(3,5-dichlorophenyl)-2,4-dioxo-1-imidazolidinecarboximide, 60 p.p.m. in or on grapes.

-- For iprodione and its non-hydroxylated metabolites, 0.8 p.p.m. in eggs; 0.4 p.p.m. in fat, meat and meat byproducts (except kidney and liver) of cattle, goats, hogs, horses, and sheep; and 3.0 p.p.m. in kidney and liver of cattle, goats, hogs, horses, and sheep.

-- For iprodione and its non-hydroxylated and hydroxylated metabolites, 0.3 p.p.m. in milk.

The companion petition would set a food additive tolerance of 300 p.p.m. in raisins, and feed additive tolerances of 1,000 p.p.m. in raisin waste and 225 p.p.m. in dried grape pomace for residues of iprodione, its isomer 3-(1-methylethyl-N-3,5-dichlorophenyl-2,4-dioxo-imidazolidinecarboximide and its metabolite 3-(3,5-dichlorophenyl)-2,4-dioxo-1-imidazolidinecarboximide.

Amended was a Rhone-Poulenc petition which would have set a tolerance for residues of iprodione, its isomer, and its metabolite of 7.0 p.p.m. in or on lettuce (See April 13, 1983, Page 4). The crop was re-designated as "lettuce (head)" and the tolerance level was changed to 15.0 p.p.m.

Merck filed a petition to set a tolerance for thiabendazole of 0.1 p.p.m. in or on dry beans. The fungicide is 2-(4-thiazolyl)benzimidazole.

Amended was a Merck petition to set tolerances for residues of thiabendazole of 12.0 p.p.m. in or on cantaloupes; 5.0 p.p.m. in or on strawberries; and 0.5 p.p.m. in or on tomatoes (See Oct. 6, 1982, Page 12). The petition was amended to delete the proposal for tomatoes, and to increase the requested tolerance in or on cantaloupes to 15.0 p.p.m.

An EM Industries petition to set tolerances for residues of triforine of 0.01 p.p.m. in or on almonds; and 0.1 p.p.m. in or on almond hulls (See Dec. 26, 1981, Page 4) was amended to increase the requested tolerance for almond hulls to 0.2 p.p.m. The fungicide is N,N'-[1,4-piperazinediyl-bis(2,2,2-trichloroethylidene)]-bis(formamide).

Also amended was a Pennwalt petition to set tolerances for residues of thiophanate-methyl of 1.0 p.p.m. in or on cucumbers, melons, pumpkins, and squash; 5.0 p.p.m. in or on rice; 10.0 p.p.m. in or on grapes (fresh); and 15.0 p.p.m. in or on rice straw (See Sept. 1, 1982, Page 5). Deleted were the proposed tolerances for fresh grapes, rice, and rice straw. The fungicide is dimethyl-[(1,2-phenylene)bis(iminocarbonothioyl)]bis(carbamate), its oxygen analog dimethyl-4,4'-O-phenylenebis(allaphanate), and its benzimidazole-containing metabolites.

Withdrawn was a Pennwalt petition which would have established food additive tolerances for residues of thiophanate-methyl of 50.0 p.p.m. in raisins and 35.0 p.p.m. in pineapples, and feed additive tolerances of 125.0 p.p.m. in dried grape pomace and 20.0 p.p.m. in rice hulls (See Sept. 1, 1982, Page 5).

URL 05008

SHORT-TERM TESTS FOR CANCER NOT READY YET, CABINET GROUP TOLD

A background paper prepared for the Cabinet level group which is looking at toxic torts and victim compensation legislation (See June 1, Page 3) told the Cabinet Council on Legal Policy that the relevance of short-term testing for human carcinogenicity is at present "a matter of presumption."

In a lengthy discussion of the difficulties of extrapolation of bioassays in general and short-term tests specifically, the draft paper said an international collaborative program had found the short-term tests to have "variable success, much interlaboratory variation and different ability to detect different classes of carcinogens." Paraphrasing the authors of the study, F. J. De Serres and J. Ashby, the background paper said:

"... At present, the best test predicts with an accuracy of approximately 80%, with most tests having an accuracy of 60-70%. To place this in perspective, the accuracy of a prediction by flipping a coin will be 50%. Therefore, much more has to be done to make the short-term tests an adequate replacement for the chronic bioassay. The relevance to human carcinogenesis is still a matter of presumption since there has been no extensive test against human carcinogens and non-carcinogens. However, evaluating one test, the Ames assay, it was found to predict 75% of the carcinogens (28), but the test has not been evaluated against human non-carcinogens."

The document leaned heavily in a listing of carcinogens on the reports of the International Agency for Research on Cancer (See July 13, Page 2), but published also a tabulation from Lancet by W. T. Blot and J. F. Fraumeni in 1975 setting forth estimates of the "proportions of cancer deaths attributed to causes" in the U.S. The tabulation:

Proportion of Cancer Deaths in the United States Attributed to Causes^a

Factor	Percent		Cancer Deaths
	Best estimate	Range	
Tobacco	30	25-40	120,000
Alcohol	3	2-4	12,000
Diet	35	10-70	140,000
Food Additives	1	-5b-2	4,000
Sexual Behavior	7	1-13	32,000
Occupation	4	2-8	16,000
Pollution	2	< 15	8,000
Other	18		72,000

^afrom Ref. 7

^bAllowing for a possible protective effect of antioxidants.

The paper added a series of caveats, including that the approach doesn't compensate for multiple exposures, but said the estimates "remain the best ones presently possible."

OMB KILLS PMN SITE-LIMITED EXEMPTION "EXPERT REVIEW" REQUIREMENT

The Office of Management and Budget sent OTS back to the drawing boards on its long-pending proposal for exempting site-limited intermediates and some low-volume chemicals from Premanufacture Notification.

The OMB disapproval of the proposal arrived at OTS Nov. 29, although it was dated Nov. 15 -- before the PMN Significant New Use Rule comments of OMB's Christopher DeMuth drew widespread Congressional charges of "interference" (See Nov. 23, Page 20). OMB told OTS:

URL 05009

Auchter said he had not seen the memo listing the 116 "until the recent publicity brought it to my attention." He pointed out that each page of the memo said the draft bears no official endorsement and, "It should not be reproduced nor reported upon as official OSHA policy."

Charges that OSHA is planning to "eliminate the files" on the 116 are "absolutely untrue," Auchter said, adding:

the 13 years of its history, OSHA has accumulated literally hundreds of cubic feet of papers which have exceeded the storage capacity of the file cabinets in the agency's Directorate of Health Standards Programs. There was almost no control over this pile of paper the past years. OSHA had never cleaned or updated any of its health standards files. Used or inactive files were placed in boxes and containers of all types and simply pushed corners. As a result, many cubic feet of valuable agency records were misplaced, stored or otherwise improperly disposed of over the years.

Am proud that in recent months, in conjunction with the National Archives and Records Service (an agency of the General Services Administration), OSHA has conducted a major clean-up and archiving operation in the Directorate of Health Standards Programs. This resulted in the preparation of over 125 cubic feet of records for permanent, retrievable storage. These documents are awaiting transfer to the appropriate Federal Records Center. I believe, is the first time in the agency's history that the records of valuable agency health standards development have been properly achieved."

During questioning, Auchter dramatized the point, stating his Administration had opened up the closet, let some light in and stirred some dust.

The few partisan sparks of the hearing occurred as Gaydos questioned the OSHA inspection and enforcement record, asking if it wasn't fair to assume that some companies were being let off the hook by settlements. Rep. Erlenborn (R-Ill.) countered that as a former prosecuting attorney, he knew that 90% of criminal cases are handled by plea bargaining and Rep. Gaydos rejoined, "If I'm a worker, I don't want anyone plea bargaining with my life."

Gaydos asked specifically about standards for benzene, formaldehyde, toluene and 1,1,1-trichloroethane. Auchter replied that the problem has been one of documenting exposure. The standard on the last of these has been slowed, he said, because it was indicated that industry would switch to one of three more dangerous substances. On formaldehyde, he said, OSHA could not document that it was a carcinogen at or below the levels of the OSHA standard of 3 p.p.m.

Asked why he would not err on the side of protection by issuing emergency temporary standards on substances, Auchter responded, "It would be irresponsible for me to take an action I knew in my heart was illegal," an argument he used earlier in hearings on ethylene dibromide (See Sept. 14, Page 22, and separate story).

UPL 05010

ESTYLE, NON-CHEMICAL CAUSES OF CANCER POINTED OUT

A seminar held by the American Council on Science and Health in New York Oct. 4 brought from various speakers the statements, according to ACSH press releases, that:

--"Not only do our environmental health problems go far beyond those attributable to industry, but many of today's problems are trivial compared to some that have existed in the past" -- Dr. Merril Eisenbud, Director of the Laboratory for Environmental Studies, New York University Medical Center.

-- "Cancer is certainly much more talked about than it was in previous decades, but this is not in itself evidence that cancer rates among non-smokers of a given age are rising. In fact, examination of mortality data indicates that there has been no generalized increase in non-respiratory tract cancer over the past three decades. This does not, of course, guarantee that all recently introduced chemicals, pesticides, pollutants and habits are harmless. Yet, it does guarantee that to concentrate only on new environmental agents as possible causes of cancer, while discounting the role of long-established aspects of our way of life, is to ignore the possibility of preventing many common cancers"

-- Dr. Richard Peto, Reader in Cancer Studies, University of Oxford.

HEARING LIKELY TO BE REQUESTED ON SUSPENSION OF EDB FOR SOIL FUMIGATION

A hearing is expected to be requested by Great Lakes and Ethyl Corp. on the emergency suspension of the soil fumigation use of ethylene dibromide (EDB). At press time, no suspension or cancellation hearing requests had been filed with EPA (See Sept. 28, Pages 2, 15, and 25). The agency initiated emergency suspension and cancellation actions Sept. 30.

In summary, the agency: suspended the soil fumigation use which amounts to 90% of the pesticide use of EDB; cancelled, effective Sept. 1, 1984, the use as a quarantine fumigant on citrus fruits, tropical fruit and certain other fruits and vegetables; and cancelled all other uses, except some minor uses, effective in 30 days unless a hearing is requested. It is probable that the cancelled uses will not be contested.

Suspension hearing requests, if any, have to be filed this week.

Depending on results of continuing monitoring of flour, baked goods, milk, meat, poultry, and grain, the agency might ultimately take emergency suspension action against the uses of the pesticide as a spot fumigant and as a fumigant on stored grain and grain and flour milling machinery.

Minor uses retained with restricted use classification and label changes include: Fumigation of stored beehives and hive platforms to control wax moths, use on vault-stored clothing and furniture, use in USDA's Japanese Beetle control program, and termite control.

For continuing fumigation uses, protective clothing, respirators and other exposure reduction techniques are being required under interim regulations.

EPA will set tolerances for EDB per se, probably 100 p.p.b. The agency said the EDB tolerances will be set to "regulate residues of EDB which may continue in the human diet as a result of delays in these cancellation actions pending hearings, in stored commodities previously fumigated, imported foods, or from other causes."

Currently, tolerances for EDB are included as tolerances for residues of inorganic bromides, with a 125 p.p.m. total tolerance for residues of inorganic bromides in grain, resulting from use, generally, of a mixture of methyl bromide and EDB.

In about two months, Richard Johnson, Registration Division, OPP, EPA, noted last week, the agency should have enough monitoring data to decide whether to issue an emergency suspension order for the grain and milling machinery uses.

At a Sept. 30 briefing for interested parties, Johnson said the decision on the phase-out for citrus was the "toughest" aspect of the decision and that one more season of citrus use "is all we can live with" because the use presents "very serious health hazards."

URL 05011

Shore also criticized the Administration's support of legislation to permit the interstate shipment of State-inspected meat (See FOOD CHEMICAL NEWS, July 25, Page 40).

She also faulted the federal program, citing changes in inspection procedures, increased linespeeds, and lack of supervision which have resulted in an "impending public health crisis." A recent survey by the union representing meat inspectors of its members, Shore said, showed that 80% believe that the regulated industries control the federal meat and poultry inspection program.

NATURAL DIETARY ANTIOXIDANTS MAY HAVE IMPORTANT ROLE IN CANCER PREVENTION

Dietary intake of natural antioxidants, such as vitamin E, β -carotene, selenium, glutathione, and ascorbic acid, could be an important aspect of the body's defense mechanism against the great variety of natural mutagens and carcinogens contained in the human diet, Dr. Bruce N. Ames proposed in the Sept. 23 issue of Science.

Ames, Chairman of the Department of Biochemistry, University of California (Berkeley), suggested that the geographic differences in cancer rates, thought to be due mainly to life-style factors such as smoking and dietary carcinogens and promoters "also may be due in good part to less than optimum amounts of anticarcinogens and protective factors in the diet."

"Diet, which provides both carcinogens and anticarcinogens, is extremely likely to be (a) . . . major risk factor" in cancer, second only to tobacco smoking," Ames said.

Listing 16 examples of naturally-occurring mutagens and carcinogens in foods, the scientist "emphasized that no human diet can be entirely free of mutagens and carcinogens and that the foods mentioned are only representative examples."

"The human dietary intake of 'nature's pesticides' is likely to be several grams per day -- probably at least 10,000 times higher than the dietary intake of man-made pesticides," Ames pointed out, commenting: "There are health costs for the use of these natural pesticides, just as there are for man-made pesticides, and these must be balanced against the costs of producing food."

". . . Little information is available about the toxicology of most of the natural plant toxins in our diet, despite the large doses we are exposed to," he noted suggesting, "Many, if not most, of these plant toxins may be 'new' to humans in the sense that the human diet has changed drastically with historic times."

"By comparison," he said, "our knowledge of the toxicological effects of new man-made pesticides is extensive, and general exposure is exceedingly low."

"Laboratory studies of natural foodstuffs and cooked foods are beginning to uncover an extraordinary variety of mutagens and possible carcinogens and anticarcinogens," Ames noted, commenting on the following 16 examples of natural mutagens, teratogens and carcinogens in the human diet:

- (1) Safrole, estragole, methyleugenol and related compounds, present in many edible plants, such as "natural" sarsaparilla rootbeer, and black pepper, are carcinogens in rodents and several of their metabolites are mutagens.
- (2) Hydrazines, found in edible mushrooms, are carcinogens and mutagens.

- (3) Linear furocoumarins, such as psoralen derivatives, widespread in plants of the Umbelliferae family, such as celery, parsnips, figs and parsley, are potent light-activated carcinogens and mutagens.
- (4) The potato glycoalkaloids solanine and chaconine are strong cholinesterase inhibitors and possible teratogens.
- (5) Quercetin and several similar flavonoids are mutagens in a number of short-term test systems. Flavonoids are extremely widespread (daily levels close to 1 g) in the human diet.
- (6) Quinones and their phenol precursors, which can react to generate mutagens and carcinogens, are widespread in the human diet. Mutagenic anthraquinone derivatives are found in plants such as rhubarb and in mold toxins.
- (7) Theobromine, a relative of caffeine, has been shown to be genotoxic in a variety of tests, to potentiate (as does caffeine) DNA damage by various carcinogens in human cells, and to cause testicular atrophy and spermatogenic cell abnormalities in rats. Cocoa powder is about 2% theobromine and therefore humans may consume hundreds of milligrams of theobromine a day from chocolate. Theobromine is also present in tea.
- (8) Pyrrolizidine alkaloids, which are carcinogenic, mutagenic and teratogenic, are present in thousands of plant species, some of which are ingested by humans, particularly in herbs and herbal teas and occasionally in honey.
- (9) The broad (fava) bean, a common food of the Mediterranean region, contains the toxins vicine and convicine at a level of about 2 percent of the dry weight.
- (10) Allylisothiocyanate, a major flavor ingredient in oil of mustard and horseradish, is one of the main toxins of the mustard seed and has been shown to cause chromosome aberrations in hamster cells at low concentrations and to be a carcinogen in rats.
- (11) Gossypol, a major toxin in cottonseed that accounts for about 1% of its dry weight, causes pathological changes in rat and human testes, abnormal sperm, and male sterility, and appears to be a carcinogen as well.
- (12) Sterculic acid and malvalic acid are toxic cyclopropenoid fatty acids present in cottonseed oil and other oils from seeds of plants in the family Malvaceae, such as cotton, kapok, okra, and durian. Another possible source of human exposure is consumption of fish, poultry, eggs and milk from animals fed cottonseed. The toxicity of these fatty acids could be due to their ease of oxidation to form peroxides and radicals.
- (13) Leguminous plants such as lupine contain potent teratogens.
- (14) Sesquiterpene lactones are widespread in many plants and some have been shown to be mutagens.
- (15) The phorbol esters present in the Euphorbiaceae, some of which are used as folk remedies or herb teas, are potent promoters of carcinogenesis.
- (16) Alfalfa sprouts contain canavanine, a highly toxic arginine analog that is incorporated into protein in place of arginine.

In addition to these 16 examples, Ames listed coffee, alcohol, mold carcinogens, nitrite, nitrate and nitrosamines, rancid fat, and the burnt and browned material from heating protein during cooking as mutagens or carcinogens present in the human diet.

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