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Chemical Week

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Needed in cancer controversy: facts

SOCMA meeting agrees that all the facts must be presented to those making ultimate benefit-risk decisions and that absolute safety is unlikely to be ever achieved

"There is too much confusion now. The public has to be told what causes cancer so they won't be misled by such hogwash as charges that Mississippi River water can cause cancer because it has three parts per billion of chloroform." That is the task the chemical industry faces, says John Weisburger, research vice-president of the Naylor Dana Institute.

Weisburger and other cancer experts and toxicologists had much to say at a seminar on chemicals and cancer, sponsored by the Synthetic Organic Chemicals Manufacturers Assn. in Atlanta last week. And they generally agreed that the emotional issue of cancer and chemicals overflows with fact and fiction and that the chemical industry has a long, hard road to travel to get all the facts before those who must make the ultimate benefit-risk decisions.

There also was general acceptance of the often stated estimate that links up to 90% of cancers with environmental factors. The cancer experts and toxicologists put exposure to manufactured chemicals at the bottom of the list of environmental causes—behind life style factors, such as diet and smoking, and a category classified as "virus causes." But the picture often appears to have been distorted by hysteria and statistical projections of limited data that don't stand up to scientific scrutiny. The big question that was asked: When the chemical industry presents its data is it merely talking to itself?

Robert C. Barnard of Cleary Gottlieb, Steen & Hamilton, counsel to SOCMA, said the industry must realize that it faces an increasing responsibility to ensure that the administrative procedure of regulation "makes sense, is capable of dealing with the facts and arrives at a sensible appraisal. And that means having the willingness to get in and fight on the legislative front, the administrative front and, if necessary, the courts."

Controlling Diet: Naylor Dana's Weisburger said, "Diet controls will do more to control causes of cancer in the U.S. than any banning of chemicals." He

noted, for example, that colon cancer is linked to fat intake. The colon-cancer rate is high in the U.S., where 45% of dietary calories are in the form of fat, and low in Japan, where only 15% of calories come from fats.

He also pointed out that stomach cancer has decreased since 1930, while lung cancer has risen sharply—now comprises one-fourth of the 360,000 yearly cancer deaths in the U.S.

Weisburger "guesses" that of the 600,000 yearly cancer incidents, 5,000 could be allocated to occupational hazards, 60,000 to unknown or viral causes and the remainder to life-style factors. But he told the audience that "there is no excuse for occupational cancer in 1976."

Chemical Cause: The action of chemical carcinogens is based on an electrophilic reaction in which the positively charged molecule of the compound attaches to the negative charge on the deoxyribonucleic acid (DNA) molecule of the tissue. This leads to a breakdown of the DNA and possible uncontrolled reaction.

So-called "ultimate carcinogens" don't need metabolic reactions before attacking DNA. But they can be stopped short of this destructive path by entrapment with nucleophilic agents (charged compounds that tie up the carcinogen's positive charge). Chemical carcinogens, according to Weisburger, require metabolic activation before they can attack the DNA. But



ANIMAL TESTING is the only means now available for screening possible carcinogens.

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the reaction can be modified by species strain, age, sex and diet of the host. "If there is any hazard from a chemical carcinogen, an older person should be employed because the metabolism is slower and there is better detoxification, Weisburger says.

On the other hand, the body's immune system diminishes with age, leading to higher cancer incidence in older people, says John J. Costanzi, director of the cancer center at the University of Texas Medical Branch (Galveston).

"We're all developing cancers constantly, but the body's T-cell system is constantly killing them," Costanzi says. Cancer patients have depressed immune systems and a lower ability to kill cancerous cells. The white blood cells (lymphocytes) in the T-cell system are influenced by hormones in the thymus gland. Some day research may make it possible to use the E-rosette test of the immune system to determine why a particular host is a victim of cancer, Costanzi adds.

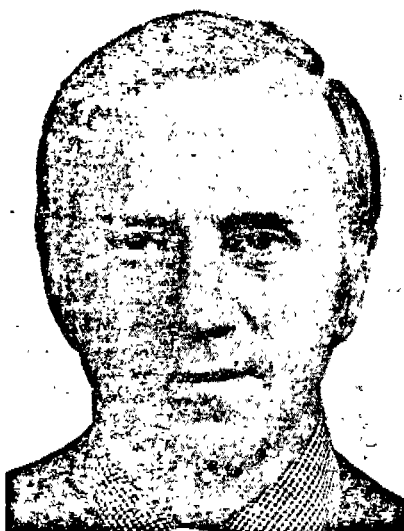
Test Data: At present epidemiological data and large-scale animal testing must be used to indicate a material's possible carcinogenicity. Researchers at the University of California have found a correlation of up to 90% between mutagenic testing of bacteria and known carcinogens. Weisburger sees the technique as a possible prescreening method, but says, "Not all carcinogens are mutagenic."

Alexander Munn, industrial medical officer for ICI, calls the technique "so artificial in so many ways its only purpose is in seeing if more testing is needed."

And in animal testing, extremely high exposures often are necessary to obtain quick results. "Translation of the data to predict the hazard of low-level exposure is presumptuous guesswork at best," says Perry J. Gehring, director of Dow's toxicology research laboratory.

Experimentation at Dow has shown that when the body's elimination systems for some carcinogens become overloaded (e.g., with high doses), the carcinogens can't be eliminated. In the case of vinyl chloride monomer, the primary (respiratory) elimination system is overwhelmed as the exposure concentration is increased. At concentrations exceeding 220 ppm., the secondary (digestive) elimination system becomes the predominant path.

Dealing with Definitions: Meanwhile, government agencies seem to be fumbling for cancer definitions. The Environmental Protection Agency developed nine principles that became 17 for car-



DOW'S GEHRING: 'Predicting hazard of low-level exposure is presumptuous guesswork.'

cinogen determination. They have been used in pesticides hearings to translate test data into evidence of carcinogenicity. But EPA hasn't felt too secure in using the principles and the National Cancer Advisory Board is developing a new set.

At the SOCMA seminar Raymond Harbison, assistant professor of pharmacology and biochemistry at Vanderbilt Medical Center, read a letter of Jan. 20 from the Society of Toxicology to EPA that "put the agency on notice for what we consider to be its irresponsible acts in publishing the principles of carcinogenicity."

Harbison pointed out that neither animal research nor epidemiology have been particularly useful in discovering cancer hazards to humans, and he asserted that it is impossible "to promulgate hard and fast rules for identifying chemicals as carcinogens at this time."

And he warned that the chemical industry must not be misled into oversimplifying the causes of cancers or the chemical mechanisms that induce cancer. "There are no quick and easy screening tests at this time," he said.

And there probably will always be some risk. As ICI's Munn puts it: "Absolute safety is unlikely to ever be achieved. Safe is not synonymous with zero risk. The real issue is: Does the use of the compound constitute a carcinogenic risk? It is not whether the compound is carcinogenic."

And the big question is whether fuller disclosures and additional data by the chemical industry can bring this point home to those who must make the decisions.

Spending going up

The U.S. chemical industry is planning a 6.7% spending hike for domestic plants and equipment in 1976, says the Commerce Dept. Latest estimates of business spending were gathered by Commerce's Bureau of Economic Analysis. The department's data are not adjusted for cost changes.

On a seasonally adjusted annual rate basis, Commerce pegs chemical industry estimated spending at \$6.31 billion in first-quarter 1976, \$6.56 billion in the second quarter and \$6.87 billion in the second half.

These figures compare with annual rate spending in 1975 of \$6.29 billion in the first quarter, \$6.46 billion in the second, \$6.40 billion in the third and \$5.89 billion in the fourth.

Actual expenditures by chemical firms: \$1.42 billion during the first quarter, \$1.66 billion in the second and \$3.59 billion in the second half. Last year the industry spent \$1.42 billion in the first quarter, \$1.63 billion in the second, \$1.52 billion in the third and \$1.68 billion in the fourth. Total 1976 estimated spending of \$6.67 billion compares with actual payouts of \$6.25 billion in 1975, \$5.69 billion in 1974.

Projected 1976 spending for all U.S. industries is \$120.1 billion, a 6.5% boost over the previous year. Spending in 1975 of \$112.8 billion was, in turn, 0.3% above 1974 outlays.

Commerce notes, however, that its data do not take into account price changes. It says that respondents to a survey conducted near the end of 1975 indicated that capital goods prices rose 12% in 1975 and are expected to go up 10% this year. That means that despite the increases in outlays, investment in real terms may have declined more than 10% last year and may drop 3% this year.

Pipeline delay likely

Canadian National Energy Board hearings on construction of a pipeline to carry natural gas from Alaska's North Slope may be in for some delay following a Supreme Court ruling that disqualified Chairman Marshall Crowe.

The hearings began last October and were adjourned early in February for the court hearings. In a five-to-three decision the court agreed with three public interest groups that there is danger Crowe might be biased in the matter because he had once been a member of the board of Canadian Arctic Gas (CAG), one of the

Chloroform ban due

The Food and Drug Administration will ban all use of chloroform in medicine and toothpaste this week, according to a well-informed industry source. The move comes in response to the recent National Cancer Institute report showing that the substance caused cancer in mice and to a lawsuit initiated by a Ralph Nader group aimed at forcing FDA to ban the products.

The NCI rodent experiments showed a high incidence of liver cancer among mice fed high doses of chloroform, and a lower incidence at lower feeding levels. Kidney tumors were also seen in the test animals.

FDA's cough and cold medicine over-the-counter advisory committee has recommended that chloroform in such preparations be reduced drastically, to 0.4%. That recommendation was based on a review of NCI data. In addition, the committee said that chloroform has no value as an expectorant, only as a flavor agent.

The lawsuit, filed last week in federal district court in Washington by Public Citizen, Inc., sought to force FDA to ban medicines and toothpaste containing the substance.

In addition, Sidney Wolfe, director of the Health Research Group, wrote a letter last week to Health, Education and Welfare Secretary David Mathews requesting a ban and recall. Wolfe's group had petitioned FDA for a ban on uses of the substance earlier this year based on knowledge of the NCI report (*CW*, Jan. 14, p. 19).

Drop in new ideas

Innovation in the chemical industry has gone downhill since the late 1960s, according to a study sponsored by the National Science Foundation and conducted by Gellman Research Associates. In 1968 the chemical, electrical, mechanical and instrument industries accounted for 80% of all industrial innovations, NSF reports. Those sectors account for only 66% now.

The innovation rate of the petroleum, rubber, fabricated metals and transportation industries has increased.

Although small firms had been considered most fertile for novel ideas, Gellman indicates that the largest companies (more than 10,000 employees) have increased their rate of innovation. Small-company innovation has dropped from about 50% to less than 40%, while big firms jumped from 35% in 1959 to 45%.

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companies seeking to build the pipeline.

One of the groups that challenged Crowe, Committee for Justice and Liberty Foundation, is now asking that the hearings begin again with a new panel.

Before being named NEB chairman in October 1973, Crowe was president of government-owned Canada Development Corp., which he represented on CAG's board. The groups opposing his chairmanship of the pipeline hearings said he might have already made up his mind on some of the issues. They noted that as the committee chairman Crowe would have had to judge some of the decisions he and other CAG directors made in preparing a pipeline application.

CAG says it still expects NEB to rule by next fall on competing applications. The company has proposed a \$10-billion line from Prudhoe Bay to U.S. and Canadian markets by way of the Mackenzie Delta, and Foothills Pipe Lines wants to build a \$4.6-billion line from the delta, mainly for Canadian markets.

Gulf Canada has already awarded an engineering and design contract for a plant to gather and process 300 million cu.ft./day of gas in the area for delivery to one of the two proposed pipelines.

Enrichment by laser

Exxon Nuclear applied to the Nuclear Regulatory Commission last week for permission to build and operate an experimental facility to test the feasibility of uranium enrichment by laser. If approval is given, the company expects to begin construction in 1977, start up the first phase in 1978-1979. The unit will be located at Exxon's nuclear installation in Richland, Wash. Estimated first-phase costs: \$15 million.

The test facility would use a patented laser isotope-separation technique developed by Jersey Nuclear-Avco Isotopes—a joint venture owned 80% by Exxon and 20% by an Avco Corp. subsidiary, Avco Everett Research Laboratory (*CW Technology Newsletter*, Aug. 14, 1974). The plant will be operated on behalf of this joint firm.

Noting that domestic uranium enrichment at present is performed only in large gaseous-diffusion plants owned and operated by the government, Exxon maintains that the laser technique holds the potential for significantly reducing the cost of uranium enrichment.

R. L. Dickeman, Exxon Nuclear president, cautioned, however, that "the ultimate practical feasibility and economics of the technique remain to be fully de-

fined and demonstrated before it definitely could be considered competitive with alternative existing methods of uranium enrichment."

On a related topic, Exxon Nuclear says it is not yet ready to announce a possible site for a \$1-billion gas-centrifuge enrichment plant it proposed last year (*CW*, July 30, 1975, p. 11).

Arco spinoff on

Saskoil, a Saskatchewan government company, has purchased the province's assets of Atlantic Richfield Canada for about \$23 million, subject to a final agreement. The arrangement was unveiled a week after it was disclosed that negotiations for the sale of all of Arco's Canadian assets to Petro-Canada, state-owned oil company, were under way.

The Saskoil deal calls for the transfer of all of Arco's production, transmission facilities, land holdings and easements in Saskatchewan, including oil production of about 2,800 bbls./day, approximately 400,000 acres and a small amount of gas production and gathering facilities.

Arco's proposed sale to Petro-Canada of 100% of the Canadian subsidiary's common shares included a price tag of \$400 million, now reduced by \$23 million. Under terms of the deal, Petro-Canada has a 90-day option, which expires June 1. Petro-Canada says it had been aware of the Saskoil talks, and "actively encouraged" them. It adds that at no time were Arco's Saskatchewan interests the subject of negotiation with Petro-Canada.

An Arco official says the move out of Canada is part of an already stated goal of becoming a "self-sufficient operator" in the U.S., and he notes that increases in Canadian royalties and taxes plus Canada's reduction in allowable exports played a part. Revenues from the deals will go for "U.S. investment opportunities," he says, which could mean increasing cash resources to finance North Slope activities. But the Arco official notes the company is "looking for opportunities in the lower 48."

More Shaheen Developments: Also in Canada last week, the Newfoundland Supreme Court began bankruptcy hearings involving a Shaheen Natural Resources refinery at Come-By-Chance, brought by Ataka & Co.'s subsidiary, Atlantic Trading, which claims it is owed \$21 million by the refinery's operators. Shaheen lawyers had obtained a restraining order in New York forbidding a bankruptcy action by Atlantic Trading.



OCCIDENTAL PETROLEUM'S BAIRD will avoid petrochemical area's cyclical swings.

Oxy avoids cycles

Occidental Petroleum last week told analysts in Chicago its chemical expansion plans do not include entry into petrochemicals.

And Alco Standard (Valley Forge, Pa.) says it expects a 15% sales growth this year in the proprietary fertilizer products of its Synthane Group.

Joseph E. Baird, president of Occidental, is "not terribly optimistic" about petrochemicals because it is even more capital intensive than the fertilizer business and subject to similar cycles. But he says Oxy will substantially expand its chemical and coal operations, believes earnings from Hooker Chemicals should be up moderately in 1976.

Oxy's capital spending plans in 1976 will approximate 1975's \$496 million, he says, while earnings are projected to drop substantially in first-quarter 1976, from \$73.8 million in the year-ago quarter. He sees an over-all gain in performance in 1976.

Ray B. Mundt, president of Alco, projects a 10% earnings increase this year over 1975's \$31-million net income on \$939.6 million in sales.

He says Synthane Companies, a chemicals rubber and plastics operation, expects sales and earnings hikes of 20% or more for the year to be fueled by gains in areas such as proprietary formulated fertilizer products. This operation also produces pesticides, water-treatment chemicals, and epoxy adhesives. Synthane's revenues in the fiscal year ended Sept. 30, 1975, were \$105 million. Alco also distributes containers and paper.

Unsure on cyclamates

A special review by the National Cancer Institute concludes that there is no adequate evidence that cyclamates cause cancer in rats. Furthermore, an NCI committee, in its final report issued last week, could reach no conclusion on the cancer-causing potential in humans.

The final 200-page report, delivered to Food and Drug Commissioner Alexander Schmidt, corresponds to a preliminary view given earlier this year (*CW*, Jan. 21, p. 17). The study was undertaken a year ago by NCI at FDA's request. The committee did say, however, that its extensive review of cyclamates data had raised a number of concerns, including the higher rates of all types of tumors in cyclamate-fed animals.

Abbott Laboratories, which has been persistent in its efforts to get FDA to overturn the six-year-old ban, says the NCI review "should satisfy FDA." The agency, however, was taking a far more sober view. "Care should be taken not to add to speculation that an FDA decision on cyclamate is imminent," it emphasized. FDA will evaluate the report, along with all other data, including the possibility of cyclamates' relationship to hypertension and effects on reproductive systems of animals.

Cancer-link inquiries

An arsenic-based pesticide may have played a role in four deaths in Wisconsin caused by a rare liver cancer. And a study of cosmetic talc preparations found concentrations of 2-20% of asbestos fibers, also linked to cancer, in nine of 19 products tested.

These findings were disclosed last week by researchers working with Dr. Irving Selikoff at the laboratory of environmental sciences at Mount Sinai Hospital (New York).

Dr. Henry A. Anderson, who specializes in internal and occupational medicine, says the Marshfield Clinic (Marshfield, Wis.) reported to the Federal Center for Disease Control (Atlanta) four deaths caused by the rare cancer since July 1974. A recent inquiry by Representative David R. Obey (D., Wis.) into the case prompted a request that Mount Sinai join the study because of its previous investigation of cases of the disease among polyvinyl chloride plant workers (*CW*, Feb. 25, p. 41).

Anderson notes that the early findings are based on interviews with survivors, who said the men had mixed an arsenic-

based insecticide by hand before applying the chemical by hand-pump sprayers. It appears that the pesticide used was calcium arsenate, he says, but adds that the laboratory does not have materials to analyze. Actual levels of the pesticide in the workers are still to be determined from tissue tests.

Anderson adds he might seek data on the pesticide from Allied Chemical, which halted production of arsenical acids at its Race Street plant in Baltimore in 1974, and any other producers.

Talc Cited: Researchers involved with the talc study, begun in 1973 and completed six months ago, say their findings of asbestos indicate that the Food and Drug Administration should look at talc products again to determine whether they are safe for human use. Asbestos has been linked with a rare form of chest and abdominal cancer, and previous talc studies at Mount Sinai discovered that talc used to coat short-grained rice may also contain asbestos.

Test results showed levels of 8% or more of asbestos in several products, the researchers say. Included: Sterling's ZBT Baby Powder with baby oil, Colgate's Cashmere Bouquet Body Talc, Pfizer's Coty Division's Coty Airspun Face Powder; and two discontinued products—Kendall Co.'s Bauer & Black Baby Talc and McKesson's Rosemary Talc.

But FDA says results of its 1975 survey of 76 commercial cosmetic talc products did not find asbestos.

Chemical jobs up

Chemical industry employment rose nearly 0.6% in February, seasonally adjusted, to 1.031 million, compared with 1.025 million the month before, the Labor Dept.'s Bureau of Labor Statistics reported last week. BLS noted also that there were over-the-month employment gains in 64% of the 172 industries in the nonagricultural payroll employment category, helping to raise over-all U.S. employment nearly 0.2%, to more than 86.3 million from almost 86.2 million the month before.

On an unadjusted basis, chemical jobs increased about 0.5%, to 1.022 million from about 1.017 million in January. This was also above the more than 1.015 million employed in February 1975.

Most chemical process categories posted gains for the month: rubber and plastic products, to 616,000 from 613,000 in January; textile mill products, to 961,000 from 958,000; and paper and allied products, to 669,000 from 664,000.