lished in the 3 April 1978 *Medical World News*, Califano says "The toughest decisions I think I've had so far are the public health decisions. I reviewed that swine flu situation, and I am not sure that anybody would have made any different decisions [from those] the prior Administration made on swine flu."

A possible confusion in the Neustadt-Fineberg is that its tone in many passages implies blame for things done wrongly, although its intention, says Neustadt, is quite otherwise. "Caught in the same situation, I might well have done the same thing," says he. His narrative draws praise as well as criticism from those involved in the swine flu program. "It is a reasonably accurate description. I think he has done his damnedest to be fair and objective," says John Seal, scientific director of the National Institute for Allergy and Infectious Diseases. "The descriptive part is well done—their book is a qualified success," comments June Osborn.

The swine flu program is probably still too recent to be judged in perspective. Even if it were not the best course of action, it was at the least a rational response to an unknown risk. After the next pandemic, its good and not so good results may stand out more clearly.

—NICHOLAS WADE

NAS Saccharin Report Sweetens FDA Position, But Not by Much

A panel of the National Academy of Sciences (NAS), in a report on 4 November that offers few surprises, has concluded that the artificial sweetener saccharin poses a potential carcinogenic risk to humans, albeit a comparatively low risk. The report, which was the NAS's fifth on the sweetener since 1955, is the first by them to reach this conclusion; it also concludes for the first time that saccharin promotes the development of cancer initiated by other substances. The report calls particular attention to an alarming increase in the consumption of saccharin by children under 10 years of age, but carefully avoids any recommendations for action by the Food and Drug Administration (FDA), which commissioned the study as ordered by Congress 1 year ago.

The study does not at first blush resolve the largely political issue of whether or not the FDA should be permitted to proceed with its intended ban of saccharin. It was the FDA's announcement of the ban, which was strongly opposed by the general public, that prompted Congress to bar the action pending completion of this study and a broader Institute of Medicine (IOM) report on food safety policy, due in February 1979. Reaction to the saccharin report on Capitol Hill has largely been muted, owing in part to its release 4 days before the congressional elections. Congressional staff members have already dubbed it "OTA 2," however, after a 1977 report by the congressional Office of Technology Assessment (OTA) that reached the same conclusions. "The NAS has given us not one whit of additional help on the policy problems," said a staff member on the Senate Subcommittee on Health and Scientific Research. "It certainly doesn't clinch the debate for proponents of the ban."

Neither does the report offer any solace to the saccharin and soft drink industry, however. To the extent that the report, with the imprimatur of the NAS, is as definitive as intended, it lays to rest much of the industry's propaganda surrounding the 1977 study of saccharin by the Canadian government. That study was the third of three two-generation feeding studies to produce evidence that saccharin is carcinogenic in rats and really the only new evidence available to the NAS since its last, inconclusive report in 1974. Contrary to the industry's claim about the Canadian study, its results are not confounded by the dose levels used, by the alleged impurities of the saccharin tested, or by the use of test animals to predict a hazard for humans, the NAS panel determined. "Further studies to establish the carcinogenicity of saccharin are not needed." Short-term and single-generation saccharin studies, many of which produced negative results, are in accord with this determination because uniformly positive test findings are neither expected nor likely, said the panel, chaired by Emmanuel Farber, a pathologist at the University of Toronto, under the broader supervision of an IOM coordinating committee headed by Frederick Robbins, dean of the school of medicine at Case Western Reserve.

Additional studies were recommended in three areas: techniques for the quantitative extrapolation of animal test results to humans, the significance of in utero exposure to toxic substances, and the mechanisms of cancer promotion—each an issue of science with implications broader than the debate over saccharin itself. Current knowledge of the first of these is insufficient to predict numerically the number of human bladder cancer cases that will result from continued exposure to cancer, the NAS concluded. This is something of a slap at the FDA and the National Cancer Institute (NCI), both of which had made such predictions (the NCI had said 600 to 700 cancer cases a year would result). The NAS said the range of estimates was so broad—between 0.0007 and 3640—as to defy precision.

Children Are Particularly Vulnerable

Despite its refusal to make a precise risk assessment, the NAS did target several groups whose risk of cancer from saccharin consumption is greater than that of others. One such group is children below the age of 10 years, one-third of whom consume saccharin-containing food products. Since 1972, saccharin consumption among children in this group has jumped 160 percent, according to market data used by the NAS. Although exposure has increased for all age groups, largely because everyone has been drinking more and more soft drinks, children are particularly vulnerable in this trend. The amount they consume relative to body weight makes them the group with greatest exposure, the NAS noted. "The data which showed that 10-year-old kids are lining up and pushing 'Tab' buttons in machines all over America made a big impression on the panel," according to one of the members. "What will happen when the latency period is up?"

Also disturbing was the finding that the highest proportion of saccharin users for members of each sex falls in the 0 to 9 age group for males and the 20 to 39 age group for females. The carcinogenicity of saccharin has been found only in male rats first exposed while their mothers

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were pregnant, suggesting that in humans, potentially the most vulnerable groups—young males and women of childbearing age—are being exposed with the greatest frequency.

Predictably, the Calorie Control Council (CCC), a beverage industry trade group, assailed these findings. "The NAS dismissed the significance of studies that illustrate differences in saccharin exposure at high doses," complained Robert Gelardi, a CCC spokesman. "Also, they failed to use more reliable data on consumption that we supplied, which showed that fewer children are exposed to saccharin than the NAS said." Asked whether the CCC agreed, however, with the basic conclusion of the NAS report—that saccharin poses a potential risk of cancer to humans—Gelardi said, "in a lay sense, we disagree. In a technical sense, we acknowledge that many different substances pose a risk of cancer to humans." In the case of saccharin, he said, "the safety is evident and—as confirmed by the NAS report—the risks are hypothetical."

Lack of Benefits Data

The FDA, just as predictably, has taken the opposite tack, calling the NAS report comprehensive, objective, and thoughtful, and pulling out of it those parts that best support its own opinion. "It is particularly significant that the NAS scientists expressed concern about the exposure of children and women of childbearing age to saccharin," said FDA Commissioner Donald Kennedy, "and concluded that there are no demonstrated benefits from the use of this artificial sweetener." This last point is particularly masterful phrasing, because what the NAS concluded was that no good studies exist that demonstrate either health benefits or a lack of health benefits from saccharin use, whether by diabetics, the obese, or in foods, drugs, or toothpaste. (The risk from exposure to the amounts of saccharin in drugs and toothpaste is so small, the panel said, that the existence of any benefits may justify its use in them.) The panel did note, and the CCC emphasized in its comments, that many physicians *believe* that saccharin is useful for obese and diabetic patients. Attempts should be made to either confirm or disprove this belief, the panel recommended. Initially, the panel was inclined to state bluntly that no benefits existed, but members said that as the report proceeded through drafts the conclusions were toned down to read "there are no studies that permit an objective assessment of asserted health benefits."

Despite the absence of data on benefits, or perhaps because of it, those who support the use of saccharin are clinging to the fact that people think it is good. The American Diabetes Association (ADA), for example, responded to the NAS report on 6 November with a statement that "We believe that much subjective good from the use of nonnutritive sweeteners does accrue to those diabetic people who must avoid sugar and other sweets." At this time, the ADA continued, "we plan no change in our advice on the use of saccharin by diabetic persons . . . [and see] little justification for placing further restrictions on the use of saccharin by the American public." Ronald Kalkoff, an endocrinologist who chairs the ADA panel on saccharin and who also sat on the NAS panel, said that he did not think the NAS report and the ADA statement were contradictory. "When compared with the risks from cigarettes, coffee drinking, or other common habits, the risk from saccharin is very small," Kalkoff said. "And it does affect the quality of life for diabetics, particularly teenagers who get peer pressure to consume common foods."

It thus seems that after this round, at least, those who support either the industry or the FDA position are standing easily in their own corners. Each side is now awaiting not only the second NAS report but also the results of an epidemiological study of bladder cancer victims now being conducted by the FDA and the National Cancer Institute—awaiting the possibility that either report will deliver a knockout punch to the other side. "As it was before, we had to contend with a well-financed industry lobby against a divided scientific community, and that hasn't really changed," said one Senate staffer. "If we had to vote today, the chance of getting the congressional bar on the FDA ban lifted is still slim."

—R. JEFFREY SMITH

Librarian Turned Entrepreneur Makes Millions Off Mere Footnotes

In the spring of 1953, while working at Johns Hopkins University as an assistant librarian for an indexing project, Eugene Garfield, 27, noticed that the references at the end of a scientific paper might do more than merely acknowledge the work of another researcher. It was not long before Garfield came up with an idea for a special kind of library index. The upshot of his vision, however, has been anything but academic.

He now heads an information empire founded on the lowly footnote. He is also a millionaire.

Garfield, the man who brings you *Science Citation Index* and *Current Contents*, is the president and chairman of the board of the Institute for Scientific Information (ISI), the world's first multimillion dollar corporation to be based on providing access to scientific literature. Today the Philadelphia-based company employs more than 470 people, has offices in nine countries, has two Nobel Laureates on its board (Joshua Lederberg and Harold C. Urey), publishes three different citation indexes, and, despite predictions of financial doom when Garfield first launched the *Science Citation Index*, now has total sales of more than $15 million a year (with Garfield owning 65 percent of ISI's stock).

Though it markets more than 20 information-related services, ISI is perhaps best known for its six editions of *Current Contents* (about 40 percent of ISI's annual sales), which reproduce the contents pages from more than 5200 journals in 31 languages. Each edition is published weekly and the subscription cost is $135 per year. All together, the six editions of *Current Contents* are estimated to be read by more than 300,000 scientists. But the financial and conceptual backbone of the organization are its three indexes (about 48 percent of ISI's sales), the *Science Citation Index* (SCI), the *Social Sciences Citation Index* (SSCI), and the newly launched *Arts and Humanities Citation Index*. The SCI, for example, culls footnotes from more than 2600 scientific journals, allowing researchers to identify topic relationships missed by subject indexes and also to

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