

]]]]]]]] U.S. Expected to Lift Ban On Cyclamate []]]]]]
Sweetener Harmless, Most Experts Say
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Federal health officials, who banned the artificial sweetener cyclamate 20 years ago in the midst of one of the biggest health scares of the 1960s, are now widely expected to reapprove it, possibly this year. Once accused of causing everything from bladder cancer to birth defects, cyclamate is now widely thought to be harmless.

``I have no reluctance in saying that with cyclamate we made a mistake,' said Robert Scheuplein, acting director of the office of toxicological services for the FDA's Center for Food Safety and Applied Nutrition.

A group of monkeys at the National Cancer Institute provides evidence of the mistake. Each of them has been fed the amount of cyclamate that would sweeten 30 cans of diet soda every day, five days a week, for the past 17 years.

In February, the institute issued its first progress report: the monkeys are doing just fine.

After two decades of legal and regulatory controversy, scores of cancer and toxicology studies and heated scientific debate, the jury on cyclamate is in.

The agency's reversal on cyclamate promises to add to the growing public debate about how government health officials evaluate potential health risks. According to scientists and industry officials involved in the controversy, the evidence exonerating cyclamate was available years ago and the fact that the agency took two decades to concede its mistake shows how large a role politics can play in decisions presented as scientific.

Even some government officials concede that the long and often bizarre story of the chemical is an example of how a system designed to separate real from imagined risks broke down.

Cyclamate was one of the world's most widely used artificial sweeteners when, in the late 1960s, its safety became a matter of

public concern. In 1969, following the completion of a study by a New York laboratory showing that some rats with cyclamate pellets implanted in their bladders were developing tumors, the FDA restricted the sale of the chemical. The following year, under pressure from Congress, the agency banned it entirely.

From the beginning, the ban was controversial. Referring to the ``farcical progress'' of the cyclamate veto ``bandwagon,'' the British scientific journal Nature ridiculed that FDA decision, calling the evidence indicting cyclamate ``about as solid as candy floss.''

One problem, for example: The method of surgically implanting cyclamate pellets in rats -- as opposed to feeding them the chemical -- was one the National Academy of Sciences had rejected that same year as not analogous to the way humans are exposed to cyclamate.

Over the next few years, 10 more experiments were conducted on rats, seven on mice, one on hamsters, one on beagles, and two on monkeys -- all in an attempt to replicate the original New York study. None could. The scientist who headed up the one damning experiment renounced it. Numerous countries that had followed the U.S. lead on banning cyclamate reapproved it.

The FDA, however, stood firm. In 1980, seven years after the manufacturer of cyclamate, Abbott Laboratories, filed for reapproval of cyclamate, the agency emphatically denied the request. Only today, seven years after Abbot filed again for reapproval, after two dozen long-term cancer studies, more than 70 experiments looking for genetic damage, hundreds of other toxicological studies, and exhaustive and positive reviews of the chemical by the National Cancer Institute and the National Academy of Sciences, is the FDA apparently comfortable with reapproving the chemical.

According to many of the scientists and industry officials involved with cyclamate, the FDA's long delay in acknowledging the new evidence raises troubling questions about the way in which the agency assesses suspected carcinogens.

One concern is over the way that politics -- not science -- appeared to play the lead role in the evaluation of cyclamate.

``The matter was taken out of the hands of the scientists here and handled by attorneys.'' said Scheuplein of the agency's 1980 decision not to reapprove the sweetener. ``Meetings were not held. Things were not pursued. Work was not done. The people who were involved at the time were inadequate to the job.''

``It was just politics,'' said Elizabeth Weisberger, the now

retired assistant director for chemical carcinogens at the National Cancer Institute. ``Once the decision was made, no one wanted to reverse it. It would have meant a loss of face.''

In a strongly worded letter to the FDA after the 1980 decision, the American Statistical Association said the arguments used to reject cyclamate amounted to an ``extreme misrepresentation of our professional methodology'' and routinely used methods ``foreign to everything that is taught in the statistics profession.''

``We strongly encourage you to have the appropriate professionals prepare a new statement that correctly expresses the statistical principles that are involved in this issue,'' the latter said. ``This new statement is needed to avoid the ridicule of knowledgeable scientists including those in your organization. FOR THESE REASONS WE BELIEVE THAT A REVISION MUST BE PUBLISHED IN THE FEDERAL REGISTER AS A CORRECTION. [emphasis is theirs]''

The group's arguments centered on interpretation of what statisticians call ``p'' values, a measure of the probability that an experimental result could have happened by chance and not because of the thing being tested, cyclamate in this case, alone. The p value is calculated from the size of the experimental and control groups. Typically scientists do not accept results as statistically significant if there is greater than a 5 percent chance that the observed differences between two groups could be a chance occurrence.

In the 1980 cyclamate decision, however, the FDA routinely interpreted as significant experiments with high p values, including one study with very few tumors where the chances of a spontaneous tumor development was 20 percent.

What the agency's actions reflected, according to many within the scientific and regulatory community, is the extreme conservatism that public and congressional pressure has demanded from the FDA on issues involving cancer risk.

According to the FDA's congressional mandate, for example, the agency is not allowed to approve any substance that is known to cause cancer in animals. The effect of this, though rarely invoked explicitly by the agency, has been to turn mouse and rat studies into a ``gold standard'' for carcinogenicity, even though new scientific evidence has increasingly cast doubt on whether giving mice or rats massive doses of a chemical is actually an effective way of predicting the cancer-causing potential of the same compound in humans.

In the case of cyclamate, many scientists and regulators say that holding the sweetener to such a standard made it impossible to overturn the FDA's prior decision to ban.

[The following is not part of the original article.]

Edith Efron. The Apocalypitics: How Environmental Politics Controls What We Know About Cancer. New York: Simon & Schuster, Inc., 1984.

William R. Havender. Of Mice and Men: The Benefits and Limitations of Animal Cancer Tests. New York: American Council On Science and Health, August 1984.

Lester B. Lave, et al. ``Information Value of the Rodent Bioassay'', Nature 336, p. 631-633 (15 December 1988). (``Tests for human carcinogens using lifetime rodent bioassaysays are expensive, time-consuming and give uncertain results. For most chemicals such tests are not cost-effective.'')

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