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Nitrosamines in Bacon: a Case Study of Balancing Risks

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Synopsis

Nitrite has been used for centuries to preserve, color, and flavor meat. Today, about 10 billion pounds of cured meat products are produced annually, accounting for some one-tenth of the American food supply. Regulators became concerned about the safety of using nitrite in the early 1960s when studies showed the presence of carcinogenic nitrosamines in cured meat products. In the early 1970s, a study at the Massachusetts Institute of Technology implicated nitrite itself as a carcinogen. As studies have raised concern over the safety of nitrite, regulators have had to weigh the potential risk from

cancer against nitrite's proven role in protecting consumers from deadly food poisoning bacteria.

Today there is little scientific support for the theory that nitrite is a direct carcinogen. To deal with the nitrosamine problem, the U.S. Department of Agriculture (USDA) lowered the permissible amount of nitrite in cured meats to that level considered necessary for botulism protection. Regulators, however, found it necessary to take additional steps with bacon because nitrosamines were found consistently in fried bacon samples. In addition to lowering the amount of nitrite that could be added to "pumped bacon" (cured by injecting liquid curing agents in the pork belly), USDA required the addition of nitrosamine inhibitors and began an intensive monitoring program in processing plants to ensure that fried bacon did not contain confirmable nitrosamines. The cooperative effort between Government and industry resulted in the virtual elimination of confirmable nitrosamines in pumped bacon by 1980.

USDA is continuing its efforts to reduce nitrite in meats wherever possible. It is involved in active research programs in the Federal Government, academia, and industry.

THE USE OF NITRITE TO CURE MEAT dates back thousands of years. Every year, about 10 billion pounds of meat products are cured with nitrite. These products—including such traditional items as bacon, ham, and hot dogs and other sausages—account for about one-tenth of the American food supply.

Nitrite serves an important function in addition to coloring and flavoring the meat. It inhibits the growth of *Clostridium botulinum* spores and the formation of its

toxin. The toxin causes botulism, a rare but often fatal form of food poisoning.

Responsibility for regulating nitrite is divided between the Food Safety and Inspection Service of the U.S. Department of Agriculture (USDA) and the Food and Drug Administration (FDA) of the U.S. Department of Health and Human Services. Acting under authority of the Federal Meat Inspection Act, USDA formally approved the addition of nitrite to meats as a curing agent in

1925. Thus, this use had a "prior sanction" when Congress passed the Food Additives Amendment to the Food, Drug, and Cosmetic Act in 1958. The amendment places strict safety requirements on additives not approved or "sanctioned" before the amendment was passed. Therefore, nitrite and other previously sanctioned substances are not subjected to the same scrutiny as a food additive first entering the marketplace.

U.S. food laws, however, have always provided authority to take action against any substance proven to be an adulterant. This authority was used in the late 1970s when a study indicated that nitrite may act as a direct carcinogen (1). Before I discuss in detail the role of nitrite in the formation of nitrosamines, I would like to put in perspective the matter of nitrite per se as a potential carcinogen.

The MIT Study

In the late 1970s, concern about the safety of nitrite went beyond its role in the formation of nitrosamines to the safety of nitrite itself. In 1975, an FDA-sponsored study of nitrosamines developed evidence to suggest that nitrite, when fed alone to rats, produces malignant lymphoma. This evidence led FDA to award a contract for a much larger study to determine whether continuous lifetime exposure of laboratory rats to nitrite causes cancer. The study was conducted at the Massachusetts Institute of Technology by Dr. Paul Newberne.

Newberne's findings, submitted to FDA in the spring of 1978, implicated nitrite itself as a carcinogen (1). The findings, however, were clouded by controversy over the methodology and conclusions. USDA and FDA experts examined the test results and also awarded a contract to an independent group of pathologists to review the Newberne study.

After the thorough review, the agencies issued a joint statement on the nitrite study on August 19, 1980 (Washington, D.C., USDA news release No. 1649-80). It stated that "the 1978 study contained insufficient evidence to support a conclusion that nitrite induced cancer in the laboratory animals." "There is no basis for action to remove nitrite from foods at this time," the agencies concluded.

The National Academy of Sciences, in its December 1981 report on the health effects of nitrite, agreed, stating that "evidence does not indicate that nitrite acts directly as a carcinogen in animals." However, the Academy investigators called for further animal testing, with attempts to distinguish between the types of carcinogenic activity found (2).

The question of the direct carcinogenicity of nitrite has again been raised in a recently published study conducted by Dr. William Lijinsky of the National Cancer

Institute (3). Before the USDA can use this study as the basis for regulatory action, the findings will have to undergo intensive scrutiny by the scientific community. That review has already begun, with scientists from FDA and USDA reviewing Lijinsky's protocol and results.

Current regulatory efforts, however, have been focused on the formation of nitrosamines, which are known carcinogens. There is continuing concern about the formation of nitrosamines when nitrite combines with the amines available in meat to form nitrosamines.

Early Concerns About Nitrosamines

Regulators first became concerned about nitrite in the early 1960s, when studies indicated that nitrosamine contamination of foods preserved with nitrite caused an outbreak of hepatotoxicosis in mink and sheep in Norway (4,5). In the late 1960s, various studies indicated that nitrosamines were present in a number of foods, including cured meats and cheeses. Although several volatile nitrosamines were found, N-nitrosopyrrolidine—a known potent carcinogen—was found consistently in cooked bacon at concentrations as high as 100 parts per billion (ppb) (6).

In October 1969, meat industry scientists met with the Assistant Secretary of Agriculture to discuss the possible existence of a nitrosamine problem in cured meats in the United States. The following year USDA and FDA formed a group to coordinate agency activities and define research needs. This led to the scheduling of a cooperative research program funded by industry with active participation by USDA, FDA, and industry. The research was spurred on by a 1971 market survey revealing nitrosamines in the parts per billion range in cured meat products.

With concern over the potential danger of nitrosamines growing, consumer groups petitioned the USDA in 1972 to ban or greatly reduce nitrite in cured meats. As grounds for the nitrite curb, the petition cited the detection of nitrosamines in a variety of products and evidence that nitrosamines form in vivo in some mammalian species (Wellford, H., Shuck, M., Center for Science in the Public Interest: Petition to amend Section 318.7, February 9, 1972).

The USDA denied the petition, citing a lack of convincing evidence showing any hazard from the use of nitrite at the levels permitted, while evidence did support nitrite's role in the prevention of botulism. The Department also cited its need for more data from its continuing research program before a final determination could be made (Lyng, R.: Response to petition, August 11, 1972).

A major step in controlling nitrosamines in cured meat products followed a 1973 finding by Canadian Department of Agriculture researchers of nitrosamines in spice

cure premixes (premixed combinations of spices and agents used to cure pork bellies). The USDA confirmed the findings and banned these premixes.

In 1973, the Secretary of Agriculture appointed an expert panel to assess the public health significance of the nitrosamine question and to determine if alternate methods of processing cured meats were available. At its fourth meeting, in July 1974, the panel submitted three major recommendations to the Secretary of Agriculture.

The expert panel sought to limit the use of nitrite wherever it was not essential for protection against botulism. The recommendations generally called for:

- elimination of *nitrate* in most products, because nitrite is actually the curing agent, and residual nitrite could be better controlled in this manner;
- limiting the level of nitrite added to most products to 156 parts per million (ppm); and
- lowering the permitted level of residual nitrite in various products to reflect what is achievable with advanced technology.

Action on bacon, fermented sausage products, and dry-cured products was deferred, pending additional research data (USDA, Animal and Plant Health Inspection Service Expert Panel on Nitrites and Nitrosamines, minutes, July 15, 1974).

The Secretary of Agriculture accepted the recommendations, publishing a proposed regulation in November 1975 that incorporated them. The proposal also prohibited nitrite in infant and junior foods (7).

Nitrosamines in Fried Bacon

The 1975 proposal by the USDA went farther than the expert panel had suggested; the proposal included rules on the use of nitrite in "pumped bacon" (cured by injecting liquid curing agents in the pork belly), using data collected by the USDA that year. The Department was concerned about growing evidence that fried bacon posed a special problem. Various studies continued to show nitrosamines in bacon even after USDA banned spice cure premixes. The heat normally used to fry bacon to its desired crispness—approximately 340° F—resulted in the formation of nitrosamines in the fried bacon (7). Although nitrosamines are not found consistently in all cured meat products in which nitrite is an additive, nitrosopyrrolidine has been confirmed repeatedly in fried bacon (8).

In its 1975 proposal, the Department recognized this unique problem, noting that "greater efforts need to be directed toward the removal of nitrosamines from bacon." The regulation proposed limiting the nitrite in the solution used to cure bacon to 125 ppm and requiring that 550 ppm of sodium ascorbate or erythorbate be

included because of their ability to inhibit the formation of nitrosamines. Ascorbic acid retards, but does not totally eliminate, the formation of nitrosamines. The Department called on the industry to accelerate its studies exploring processing changes that would prevent nitrosamine formation in bacon (7).

In October 1977, USDA gave industry 90 days to provide "data demonstrating whether the use of nitrates and/or nitrites in the production of bacon results in the formation of carcinogenic nitrosamines during its ordinary processing and/or preparation for eating." Deadlines were also given for submitting data on several other groups of cured products for which the Department had limited information (10). Data that were submitted indicated that the nitrosamine problem was generally limited to bacon, most other products being free of nitrosamines when cooked.

In February 1978, the expert panel issued its final report. The panel recommended the reduction of nitrite levels in all products, the use of sodium ascorbate or erythorbate in bacon to minimize nitrosamine formation, and the use of these nitrosamine inhibitors in other cured products for 2 years while more data are collected (11).

In May 1978, on the basis of USDA and industry data, USDA issued a final regulation, reducing the level of nitrite that could be used in curing bacon from 200 ppm to 120 ppm and requiring that the nitrite be used in combination with 550 ppm of sodium ascorbate or erythorbate. The regulation also contained a significant policy statement. In a major step to ensure the protection of the public health, the Department stated that cooked pumped bacon could not contain confirmable levels of nitrosamines (12).

At the same time, USDA proposed further decreasing the level of nitrite in bacon to 40 ppm, used in combination with 0.26 percent potassium sorbate. USDA tests showed that this method of curing bacon resulted in less nitrosamine formation and provided protection against botulism. Sorbate is used in a variety of products and had not been shown to cause adverse effects in toxicity tests. However, the use of potassium sorbate was later ruled out because it caused allergic reactions in some people handling and tasting the fried bacon during taste tests conducted by USDA taste panels (13). Subsequently, several reactive products formed by the combinations of sorbate and nitrite at low pH and high temperatures were found to be mutagenic (14). Today, USDA still enforces the levels required by the May 1978 regulation—120 ppm of nitrite used with 550 ppm of sodium ascorbate or erythorbate.

Nitrosamine Monitoring Program

The USDA took forceful steps to ensure that bacon was in compliance with the new regulations. From the

available data, USDA concluded that the danger of "preformed" nitrosamines, which form in a cured meat product before it is eaten, was limited to bacon. Bacon is a staple in some 60 percent of U.S. households, and there are estimates that bacon eaters consume an average of 3 pounds of cooked bacon a year. USDA saw a critical need to ensure the safety of this popular product.

In December 1978, USDA began an extensive three-phase monitoring program for all pumped bacon produced, nearly 99 percent of all bacon. In the monitoring phase, bacon samples from statistically selected plants are analyzed each week by the thermal energy analyzer technique. If the nitrosamine level is shown to be at or above 17 ppb, the confirmation phase begins. Bacon produced by the plant is resampled and analyzed by the gas-liquid chromatography-mass spectrometry procedure. If the procedure confirms the presence of nitrosamines above 9 ppb, all bacon in the plant is retained. All lots retained must be tested and found free of confirmable levels of nitrosamines before being marketed.

The intent of the program has not been to stop production, but rather to produce bacon that meets USDA requirements. Plants can correct their procedures to reduce nitrosamines from the time a presumptive positive is found until the end of the confirmatory phase. After a plant changes its procedures, five consecutive lots must be in compliance before routine monitoring resumes at the plant.

The monitoring program is a model cooperative effort that has worked well. USDA has offered technical assistance to plants with potential problems. Industry has responded by tightening its quality control over bacon production. The result: nearly all pumped bacon was free from confirmable levels of nitrosamines within 1 year of the start of the three-phase monitoring program.

In October 1980, USDA was able to modify its sampling plan so that frequency of sampling was based on the plant's record of compliance with the regulations. A plant with a history of producing bacon within compliance is sampled as seldom as twice yearly, and a plant with a poor compliance record may be sampled as often as six times per year.

The success has continued over the years. Out of the 241 plants monitored during 1982, only six had violative samples confirmed by gas-liquid chromatography-mass spectrometry. Nearly 1,000 samples were analyzed that year, with nitrosopyrrolidine confirmed in only 0.62 percent.

Current Efforts to Lower Nitrite

USDA feels confident that the problem with nitrosamine formation in bacon has been controlled effectively. However, there is still some concern over in vivo

formation of nitrosamines after ingestion of nitrite and the finding of nitrosamines at low levels that cannot be confirmed. Therefore, it has been the policy of USDA to reduce nitrite in cured meat products to the extent possible without compromising botulism protection.

The U.S. meat industry has been very cooperative with the USDA on these issues. In fact, the American Meat Institute petitioned the Department on August 30, 1983, to reduce the amount of nitrite used in pumped bacon from 120 ppm to 100 ppm. The group cited a 1982 study by Hauschild that concluded that selective reductions in nitrite could be made safely (15). USDA is currently reviewing the petition.

The National Academy of Sciences has supported USDA's efforts. In its 1981 report on the health aspects of nitrite, the Academy urged the USDA to continue its search for alternatives to the use of nitrite. "No new agent or combination of agents should be substituted for nitrite until adequate testing has ensured that it does not present a hazard to human health" (2).

In its 1982 report on nitrite alternatives, the second part of its study, the Academy's investigators identified several promising substitutes for nitrite, but concluded that further research is needed before they could be widely used. Alternatives include treating meat with ionizing radiation to kill bacteria, inhibiting the growth of *Clostridium botulinum* bacteria by adding other harmless bacteria that produce lactic acid, and adding bacterial inhibitors. Until alternatives can be used, the Academy recommended that the best way to reduce health risks is to add nitrosamine-inhibiting ascorbate, alpha-tocopherol, or both to bacon (16).

The USDA has been active in seeking a nitrite substitute or alternative method of curing that will further reduce the risk of nitrosamines. There are numerous USDA studies underway following the recommendations made by the National Academy of Sciences.

Conclusion

The use of nitrite to preserve, color, and flavor meat has a long history. Recent scientific studies led regulators to review carefully the use of nitrite to protect consumers of cured meat products from a carcinogenic risk. The potential risk from cancer had to be weighed against nitrite's proven role in protecting consumers from a deadly food poisoning bacterium. Today there is little scientific support for the theory that nitrite is a direct carcinogen.

Analysis of data collected narrowed the problem of preformed nitrosamines to fried bacon. The USDA took regulatory action to lower the amount of nitrite added to pumped bacon, require the addition of nitrosamine inhibitors, and prohibit the presence of confirmable nitro-

samines in fried bacon. A cooperative effort between Government and industry resulted in the virtual elimination of confirmable nitrosamines in pumped bacon.

USDA continues to press ahead with its program to reduce nitrite in meats wherever possible. Toward this end, its research program is active with the Federal Government, academia, and industry.

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Abstract

Use of Epidemiology and Clinical Toxicology to Determine Human Risk in Regulating Polychlorinated Biphenyls in the Food Supply

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Because it was published in Regulatory Toxicology and Pharmacology, the paper is given here in abstract. See Regulatory Toxicology and Pharmacology 3: 252-274 (1983) or contact Frank Cordle, Epidemiology and Clinical Toxicology Unit, Bureau of Foods, Food and Drug Administration, HFF-108, 200 C St., SW, Washington, D.C. 20204.

Polychlorinated biphenyls (PCBs) became a national problem in 1971 when several incidents of accidental contamination of food were reported. Extensive efforts were successfully undertaken by the Food and Drug Administration (FDA) to reduce the residues of PCBs in food. However, the PCB levels in several species of

freshwater fish have raised concern about PCB residues from environmental contamination. This concern prompted a reassessment of the human risk involved in consumption of such fish. The best evidence that a chemical may produce adverse health effects in humans is provided by adequate epidemiologic data confirmed or supplemented by data from valid animal tests.

Traditionally, when regulatory agencies have used the results of animal toxicology experiments to evaluate hazard and predict hypothetical safety for humans, "safety factors" such as 1 to 10 or 1 to 100 have been used. The size of the safety factor and the potential exposure to a chemical are the result of a properly informed scientific judgment. More recent efforts have used a combination of human and animal data and a variety of mathematical models to determine risk. The human epidemiology data and animal toxicity data of PCB exposure are reviewed, as well as risk assessment in general. Specific examples of risk assessment are presented in which animal data are extrapolated to humans, based on several levels of human exposure to PCBs in fish.