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Report to the Ranking Minority Member, Committee on Foreign Relations, U.S. Senate

September 1990

FOOD TAMPERING

FDA's Actions on Chilean Fruit Based on Sound Evidence

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GAO

United States
General Accounting Office
Washington, D.C. 20548

Human Resources Division

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September 6, 1990

The Honorable Jesse Helms
Ranking Minority Member
Committee on Foreign Relations
United States Senate

Dear Senator Helms:

In March 1989, the U.S. Embassy in Chile received warnings that Chilean fruit destined for the United States had been poisoned with cyanide. As a result, the Food and Drug Administration (FDA) increased its inspection of Chilean fruit and, on March 12, 1989, found grapes that contained cyanide. The grapes were found on a Chilean vessel that had arrived in Philadelphia. Based on this finding, fruit imports from Chile were suspended for 5 days, beginning March 13, while FDA developed a more comprehensive inspection program for Chilean fruit. On March 17, the suspension was lifted and all Chilean fruit that passed FDA's inspection was allowed to enter U.S. markets.

In May 1989, you expressed concern about the justification for FDA's actions given their reported substantial economic impact and asked us to review several issues relating to FDA's discovery of cyanide in Chilean grapes. In general, your request focused on the adequacy of the evidence FDA used to support its decision that resulted in the temporary suspension of Chilean fruit imports to the United States.

As agreed with your office, we assessed whether FDA, in taking its actions on Chilean fruit,

- used proper laboratory tests and procedures, including adequately safeguarding fruit samples;
- complied with the law and FDA regulations pertaining to adulterated food products; and
- consulted with other federal agencies and affected parties before arriving at its decisions.

Results in Brief

We found that FDA's discovery of cyanide in Chilean grapes was based on generally accepted tests that were conducted properly. Based on its finding, FDA acted within its legal authority to suspend imports of Chilean fruit, and, although not required by law, FDA made its decision after consulting with other federal agencies and affected parties,

including the Departments of State and Agriculture, and representatives of the Chilean government and food industry.

We did not identify any studies addressing the economic impact of FDA's actions on the U.S. economy. Representatives of the Chilean fruit industry estimated that FDA's actions cost the Chilean economy at least $333 million. We did not review the industry's cost estimate and, therefore, cannot express an opinion on its reliability. However, Chilean fruit exports to the United States in 1990, a year after the poisoning incident, reached an all time high, indicating that exports to the United States and other countries have not been seriously affected by the incident.

Background

The Federal Food, Drug, and Cosmetic Act requires that foods distributed and sold in the United States be pure and wholesome, safe to eat, and produced under sanitary conditions. It prohibits the importation of any food that contains a poisonous or other harmful substance that may pose a health risk. Under the act and applicable regulations, FDA has been delegated responsibility from the Secretary of Health and Human Services for ensuring that imported food products it regulates meet the requirements of the act. The U.S. Customs Service shares responsibility for regulating imported foods in that it controls the entry of all imported products into the United States. Imported foods that fail to meet the requirements of the law are detained at the entry location and must be brought into compliance, destroyed, or removed from the United States.

The United States is the largest single market for Chilean fruit. In the 1990 season, about 56.5 million crates of Chilean fruit were sold in the United States. About 70 percent of Chile's fruit shipments to the United States arrive at Philadelphia.

On March 2, 1989, an unidentified person called the U.S. Embassy in Santiago, Chile, claiming to have poisoned fruit with cyanide that was being shipped to the United States and Japan. The Department of State told us that the Japanese Embassy and the Chilean Exporters Association in Chile also received a similar threat. The caller to the U.S. Embassy did not specify the type(s) of fruit poisoned or the vessel(s) on which the fruit was shipped. The Department of State notified the Customs Service, which, in turn, notified FDA of this threat on March 3. As a precaution, that same day, the Customs Service ordered the detention of all Chilean fruit while it consulted with FDA. That hold was lifted on March 6, after FDA initially concluded the threat was a hoax. On March 7, FDA began conducting experiments on fruits injected with cyanide. On

March 8, the U.S. Embassy in Chile received a second telephone call that Chilean fruit had been poisoned and, consequently, FDA increased its inspections of Chilean fruit at U.S. seaports. On March 10 and 11, three ships containing Chilean fruit arrived in the United States. By March 12, FDA had examined about 1,200 crates of fruit when an FDA investigator found three unusual-looking grapes in a crate unloaded from a ship (the Almeria Star) docked in Philadelphia. FDA's Philadelphia laboratory analyzed a grape sample and found it contained cyanide.

FDA did not allow fruit from the Almeria Star to enter the country. Also, it suspended Chilean fruit imports while it worked with other federal agencies and Chilean representatives to develop an examination plan to further increase inspections of fruit from Chile. The suspension lasted for 5 days until FDA and Chilean representatives agreed on a plan to inspect Chilean fruit imports and release fruit that passed inspection. Although, on March 17, FDA was notified of a third telephone threat in Chile, no additional contaminated fruit was found, and import inspections returned to normal by mid-April 1989.

Although a June 1990 study by the Chilean Exporters Association reported a $333 million loss to the economy of Chile, there has been no independent assessment of the actual impact.[1] The Association reported that this loss was due to lost revenue and extraordinary costs resulting from the tampering incident. The Association defined lost revenue as the difference between the value of fruit that Chile expected to export in 1989 and the amount actually exported. Extraordinary costs include costs to destroy fruit denied entry into the United States, interest and financing costs for loan extensions and other methods used to finance continued operations, increased inspection and security costs, and miscellaneous expenses.

Figure 1 shows the chronology of key events during the course of the tampering incident. More detailed information is in appendix IV.

[1] We did not verify the Association's study and, therefore, cannot express an opinion on it.

Figure 1: Chronology of Events During the Chilean Fruit Incident (March 1989)

Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
			1	**2** First threat telephoned to U.S. embassy	**3** Customs detains Chilean fruit and notifies FDA	**4** Customs consults with FDA
5	**6** Customs lifts hold on most fruit; FDA begins to examine 10% of large fruit	**7** FDA begins cyanide experiments	**8** Second threat telephoned to U.S. embassy	**9**	**10** FDA decides to examine all other Chilean fruit[a]	**11** *Almeria Star* arrives in Phila.; FDA begins examination[b]
12 FDA discovers cyanide in grapes from *Almeria Star*	**13**	**14**	**15**	**16**	**17** FDA notified of third telephone threat	**18** Industry begins visual examination of grapes under FDA supervision
	FDA suspends fruit imports and develops an examination plan					
19	**20**	**21**	**22** Industry begins visual examination of pears and nectarines	**23**	**24** Industry begins visual examination of most other fruits	**25**
26	**27**	**28**	**29**	**30**	**31**	
			Industry reduces frequency of examinations[c]			

[a]Bound from Chile, the Spring Desire arrives at Philadelphia at 9 00 a m , and the Kriti Rex arrives at Los Angeles at 5 00 p m., at 6 00 p m , FDA decides to inspect 2 percent of all other fruit

[b]Almeria Star left Chile on February 27, 1989, travelled non-stop to Philadelphia and arrived 13 days later on March 11

[c]FDA resumed normal inspection levels on April 14, 1989

Objectives, Scope, and Methodology

The objectives of our review were to assess (1) the appropriateness of FDA's laboratory testing of fruit, (2) the legal propriety of FDA's actions related to Chilean fruit, and (3) the extent to which FDA consulted with others regarding its proposed action on fruit imports. We also agreed to

summarize any studies we identified on the economic impact of FDA's actions on the U.S. and Chilean economies.

In conducting our review, we interviewed and obtained information from officials of FDA, including the former FDA Commissioner; the Customs Service; the U.S. Department of Agriculture; the Federal Bureau of Investigation (FBI); the State Department; the Chilean Exporters Association; and import firms.

We used four outside consultants to evaluate the adequacy of FDA's testing and sample protection methods and to assess the reliability of FDA's findings. The Association of Official Analytical Chemists (the principal authority on analytical chemical methods) assisted us in identifying potential consultants. The consultants reviewed all of the pertinent information related to the tests performed by FDA's Philadelphia laboratory. They reviewed experimental studies conducted by FDA and others, and accompanied us in interviewing Chilean fruit industry scientists. The consultants also interviewed FDA staff, including the analysts who performed the tests that found cyanide contamination in a sample of grapes. One of the consultants prepared a draft report on the review of FDA's testing and sample protection methods. The draft report was reviewed by the other three consultants. The consultants' findings are contained in appendix V.

To evaluate FDA's measures to safeguard the fruit sample found to contain cyanide, we reviewed the adequacy of FDA's sample identification and protection procedures. In addition, we sought the views of the FBI and the consultants we hired on this matter.

To determine whether FDA's actions were consistent with applicable law and regulations, we reviewed court decisions and administrative decisions interpreting the applicable statutes.

We performed our work between October 1989 and April 1990 in accordance with generally accepted government auditing standards. The results of our work are summarized below and discussed more fully in appendixes I through III.

FDA's Laboratory Testing and Sample Protection Were Proper

After the suspension of Chilean fruit imports, controversy arose over FDA's handling of the situation. In particular, several news stories and the Chilean fruit industry accused FDA of improperly conducting its laboratory tests and of mishandling fruit samples. We found, however, after extensively evaluating FDA's laboratory testing procedures that FDA used proper testing methods and adequately protected fruit samples from being mishandled while in its possession. The laboratory tests and findings were the basis for FDA's actions on Chilean fruit imports.

FDA used two widely accepted tests and conducted them in accordance with sound scientific methods. One test, referred to as a cyantesmo test, was initially done to screen the fruit for cyanide. In the instance where this test identified cyanide, FDA conducted a second test, called the chloramine-T test, to confirm the initial test results and to quantify the amount of cyanide remaining in the fruit. To help assure that any cyanide present in the grapes or other fruit would not be lost during testing, FDA modified the chloramine-T test. The need for this modification was based on FDA's experience with cyanide that had been placed in another food product. FDA's modified test yielded a valid finding that cyanide was present in the grape sample.

Both our review and the FBI's investigation of the incident found that the samples sent to FDA's laboratory for testing were adequately protected against mishandling and contamination.

FDA's Actions Were Consistent With Its Legal Authority

Upon finding grapes from the Almeria Star that contained a small amount of cyanide, FDA denied entry to the ship's fruit; warned the public not to eat Chilean fruit; increased inspections of subsequent Chilean fruit shipments and fruit already in cold storage; and recommended that retail outlets and wholesalers remove Chilean fruit from distribution. FDA's actions were consistent with the Federal Food, Drug, and Cosmetic Act, which requires that imported food be denied entry to the United States when examination, sampling, or other evidence indicates that the food appears to be adulterated. The act also allows FDA to issue public warnings if an imported food presents a health hazard. Although the level of cyanide detected in the grapes was not in itself sufficient to cause illness, FDA determined that there was a distinct possibility that other fruit could also be contaminated and could result in serious illness or death.

FDA Consulted With Others on Its Proposed Actions

The Federal Food, Drug, and Cosmetic Act does not require FDA to consult with other agencies in determining whether an imported food product appears to be adulterated. Nor does the act require consultation on how to remedy the problem.

Nevertheless, after determining that Chilean fruit aboard the Almeria Star was adulterated, FDA consulted with officials from several federal agencies, the Chilean government, and the fruit industry about the tampering incident and actions needed to protect public health and lessen the impact on Chile. The federal agency officials either agreed with FDA's proposals or deferred any decision regarding Chilean fruit imports to FDA.

The primary focus of FDA's consultations with the Chilean government and fruit industry officials was to develop an examination plan to inspect Chilean fruit and allow fruit that passed inspection to enter the market. On March 17, 1989, FDA and the Chileans agreed on an examination plan that called for industry-hired inspectors operating under FDA supervision to examine 5 percent of all Chilean fruit; both fruit coming into and fruit in cold storage in the United States that was shipped after February 20, 1989. Since no further cyanide contamination was found, FDA discontinued the increased inspection program on April 14, 1989.

As agreed, we did not obtain written agency comments on the report, but discussed it with FDA and officials of the Department of State, the Department of Agriculture, the Customs Service, and the FBI. Where appropriate, we incorporated their comments into the report.

Unless you publicly announce its contents earlier, we plan no further distribution of this report until 30 days after its issue date. At that time, we will send copies to cognizant congressional committees; the Secretary of Health and Human Services; and the Director, Office of Management and Budget. We will also make copies available to others upon request.

This report was prepared under the direction of Mark V. Nadel, Associate Director, National and Public Health Issues, who may be reached on (202) 275-6195. Other major contributors are listed in appendix VI.

Sincerely yours,

for Edward A Glensmore

Lawrence H. Thompson
Assistant Comptroller General

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Abbreviations

FBI	Federal Bureau of Investigation
FDA	Food and Drug Administration
GAO	General Accounting Office
HHS	Department of Health and Human Services

FDA's Laboratory Testing and Sample Protection Were Appropriate

FDA's actions that resulted in the temporary suspension of Chilean fruit imports have been the subject of much controversy. This controversy centered on whether FDA procedures and testing were appropriate to detect cyanide contamination of the fruit. We found that FDA used two widely accepted cyanide detection tests, properly protected the samples against contamination, conducted the tests in accordance with appropriate scientific principles, and accurately analyzed the results. Thus, we believe FDA inspections and laboratory testing procedures provided a reasonable scientific basis for the subsequent actions it took on Chilean fruit.

Alleged Improprieties of FDA's Laboratory Procedures

On March 12, 1989, FDA inspectors at the Tioga Fruit Terminal in Philadelphia identified three suspicious-looking grapes and sent them to FDA's Philadelphia laboratory for testing and analysis. FDA determined that a sample of two of the grapes contained cyanide. Subsequently, several allegations were made by the news media and the Chilean fruit industry that the laboratory tests were not properly conducted and analyzed. The specific allegations were that FDA:

- used inappropriate tests to determine the presence of cyanide in grapes;
- inappropriately modified a test, thereby invalidating the test's results;
- did not promptly record test results; and
- did not exercise adequate control to protect fruit samples against contamination.

Additionally, it was alleged that cyanide could not be injected into grapes and other fruit in Chile and be retained in the fruit after the 13 day trip to the United States, thereby implying that the grapes were contaminated in the United States.

FDA Used Proper Test Methods and Procedures to Detect Cyanide

FDA's Philadelphia laboratory used two different tests—the cyantesmo and chloramine-T tests—to detect and confirm the presence of cyanide in the sample of suspicious-looking grapes. Both tests are widely used and accepted within the scientific community for detecting cyanide in food. The cyantesmo test is a screening test that FDA initially used to detect the cyanide in the fruit. The test uses a specially treated paper strip that turns blue when it reacts with hydrogen cyanide gas, indicating the presence of cyanide.[1]

[1] An acid is added to fruit samples to convert cyanide that may be in samples into hydrogen cyanide gas.

FDA performed cyantesmo testing on approximately 75 suspicious-looking fruit samples from the Almeria Star during March 11 and 12, 1989. A sample of grapes from that ship showed a positive reaction to the cyantesmo test, indicating the presence of cyanide. A second FDA analyst immediately repeated the test on this sample and obtained the same positive reaction.

To confirm the initial finding and to quantify the amount of cyanide in the grapes, FDA used the chloramine-T test. This test chemically converts cyanide to a substance that absorbs light at a specific wavelength. It determines the amount of cyanide in the fruit by measuring the quantity of light absorbed with a spectrophotometer.

Based on the results of the chloramine-T test, the sample of two grapes contained approximately 0.51 parts per million of cyanide (approximately 0.003 milligrams in a sample weighing 6 grams). This quantity is well below a fatal dose.[2] However, because hydrogen cyanide is a gas, an indeterminate amount of the poison was unavoidably used up in preparing and conducting the cyantesmo test. Thus, the amount of cyanide measured by the chloramine-T test was less than the amount that was actually present in the sample before testing. Because the Federal Food, Drug, and Cosmetic Act prohibits the importation of any food product that appears to be adulterated, FDA was mainly concerned with determining whether any fruit had been poisoned rather than in determining the precise amount of poison present.

FDA's Modification of Test Was Appropriate

At the time of the tampering incident, FDA had no published procedures for conducting a chloramine-T test to detect cyanide in fruit. However, FDA did have published procedures for conducting the chloramine-T test on other products, including a laboratory bulletin on conducting the test to detect cyanide in tea. That procedure called for heating the sample solution (distillation) to release cyanide gas. But, in preparing the grape sample for the chloramine-T test, the FDA analyst modified the procedure by separating grape solids from the liquid through centrifugation rather than using the distillation method. The analyst made the modification based on the Philadelphia laboratory's recent experience involving testing for cyanide in another food product. The laboratory had found that distilling samples containing known quantities of cyanide resulted in significant loss of the poison, while centrifugation

[2]Estimates of a fatal dose of cyanide for a human range from about 10 to 200 milligrams, depending on the person's age and weight.

resulted in less cyanide being lost. Accordingly, the FDA analyst centrifuged the grapes to remove the grape particles rather than risk losing the cyanide from the small sample of two grapes through distillation. A subsequent FDA laboratory experiment confirmed that using a centrifuge was an acceptable method to prepare fruit samples for chloramine-T analysis. In our view, the modification was appropriate, did not distort the test results, and yielded a valid finding that the sampled grapes contained cyanide.

Test Results Were Promptly Recorded

FDA procedures require that laboratory worksheets be completed as tests are performed. For this case, the FDA analysts who performed the tests completed the worksheets on March 15, 1989, 3 days after performing the tests on the sample found to contain cyanide. FDA officials said that the worksheets were not completed sooner because the analysts continued to perform tests on additional fruit samples from the same crate that contained the poisoned grapes. Our review of the worksheets confirmed these statements.

In our view, the 3-day delay in completing the worksheets did not invalidate the test results because other evidentiary documents were maintained by FDA and recorded immediately. Portions of the laboratory worksheets and other records that were prepared on March 12, 1989, the same date the poisoned grapes were found, support FDA's finding of cyanide. These documents included:

- a log of cyantesmo test results, which included an entry noting the positive cyanide finding;
- a photograph of the first cyantesmo paper strip, which had been placed in a laboratory flask with the sample and which showed a positive reaction to cyanide;
- two cyantesmo paper strips showing a color change (indicating cyanide) mounted on a laboratory worksheet; and
- the chloramine-T test graph produced by the spectrophotometer and the worksheet prepared by the analyst who performed the test.

Sample Accountability and Protection Were Adequate

FDA's laboratory procedures manual establishes requirements for protecting and maintaining proper accountability for samples of domestic food products. Among other things, the manual requires that all samples taken for examination be individually marked and transfers of the samples be recorded. The manual does not specify that the same procedures are to be used for import samples, but it does require that the laboratory

performing the analysis establish a written procedure to account for import sample integrity and continuity of handling.

The Philadelphia laboratory's written procedures to account for and protect import samples are similar to FDA's requirements for domestic foods. The procedure for inscribing identifying marks on crates of inspected fruit was modified slightly in the case of the Chilean fruit imports; however, adequate accountability and protection was maintained over fruit that was inspected and tested. We were able to track the sample that subsequently tested positive for cyanide from the time it was assigned a sample number at the dock in Philadelphia until it arrived at the FDA laboratory. We did not find any serious deficiencies in the chain of custody for the sample at various points in the process. The FBI also looked at this process and found the chain of custody to be adequate to protect the integrity of the sample.

FDA visually examined about 1,200 crates of fruit from the Almeria Star on March 11 and 12, 1989. FDA's Philadelphia district director said that because the inspectors were examining many crates FDA did not mark each crate examined as provided for in its procedures. Instead, if an inspector found fruit that appeared unusual, the procedure was to take the entire crate to an inspection table, leaving the suspicious-looking fruit on top. Another inspector was responsible for placing the fruit in a plastic bag and assigning a sample number both to the suspicious fruit and the crate from which it came. Periodically, another FDA employee transported the collected samples to FDA's Philadelphia laboratory. The laboratory maintained a log of samples sent from the dock and entered the chemical test results in the log. In our view, the modification to the crate-marking procedure had no effect on the validity of the cyanide finding or the origin of the poisoned grapes, because only Chilean fruit from the Almeria Star was being inspected at the time of the cyanide discovery.

We also assessed the adequacy of the chain of custody for the sample of grapes that tested positive for cyanide. We were able to trace the custody of the sample from the point FDA assigned it a sample number at the dock all the way through the testing process. Among other things, FDA documents identified:

- the FDA staff who assigned the sample number and who transferred the sample from the dock to FDA's Philadelphia laboratory;
- the FDA analysts who performed the laboratory tests; and

- the FDA representative who took a portion of the sample of the contaminated grapes to FDA's Elemental Analysis Research Center in Cincinnati, Ohio, for further analysis.[3]

FDA's Philadelphia laboratory had retained, as of June 1990, part of the sample of grapes used in the chloramine-T test.

The FBI told us that it was also able to reconstruct the custody of the sample when it conducted its investigation into the incident, and found it to be adequate.

Studies Show Cyanide Can Be Injected Into Fruit and Retained

Since the March 1989 finding of cyanide in Chilean grapes, FDA and other researchers have conducted several studies on the effects of cyanide on fruit. The objectives were to determine (1) whether cyanide can be injected into grapes and other fruit, (2) the amount that can be injected, and (3) the extent to which fruit can retain cyanide over time. Some studies also observed whether and to what extent fruit containing cyanide changed appearance over time.

Although the studies' methodologies and results differ significantly, they all showed that grapes and other fruit can be injected with cyanide. When analyzed over time periods ranging from 4 hours to 16 days after injection, grapes showed retention levels of cyanide ranging from less than 1 percent to over 9 percent of the quantity of cyanide injected. However, there was no clear relationship between the amount of cyanide injected and the percentage of cyanide retained nor with the time periods when the analysis was conducted. The studies showed that some fruit injected with lesser amounts of cyanide retained more cyanide after a given period of time than the same type of fruit injected with larger amounts of cyanide. The studies also showed that some grapes and other fruit appeared normal for 2 weeks or more after injection before they began to change color, form, or texture. Key findings of some of the studies follow.

[3]This center specializes in forensic analysis of several different kinds of products regulated by FDA, including foods.

- Studies performed by FDA's Center for Food Safety and Applied Nutrition and FDA's Elemental Analysis Research Center showed that some poisoned fruit, when refrigerated, retained cyanide at levels comparable to those found in the grapes tested by FDA's Philadelphia laboratory. Some fruit also retained their normal appearance for up to 16 days. (Fruit on the Almeria Star was refrigerated during its 13-day voyage to Philadelphia.)
- A 1989 study performed at the University of Chile indicated that the same variety of grapes found contaminated in Philadelphia, when refrigerated, generally retained a fresh-looking appearance for at least 2 weeks after a 50-milligram injection of cyanide per grape. Other fruit also appeared normal for extended periods after being poisoned with large amounts of cyanide. However, the study makes no mention of the amounts or percentages of cyanide the fruit retained.
- A study by other Chilean researchers on the retention rates of cyanide concluded that because cyanide naturally dissipates rapidly from grapes after injection, the contaminated grapes found in Philadelphia almost certainly must have been injected not more than 4 hours before FDA's tests. This study was done on grapes that were not refrigerated. However, a study conducted by the University of California at Davis for the Chilean Exporters Association contradicts this theory. Although the second study's focus was on whether cyanide could migrate from injected grapes to neighboring ones, the reported results indicate that grapes that absorbed cyanide through migration retained the cyanide for as long as 21 days. The study did not indicate whether or not the grapes injected with cyanide were refrigerated.

FDA's Actions Consistent With Law and Regulations

The Federal Food, Drug, and Cosmetic Act provides the basic statutory authority governing the treatment of imported food products. FDA's policies for dealing with product tampering are specified in its Regulatory Procedures Manual. FDA's actions to (1) temporarily suspend Chilean fruit imports, (2) issue a public health warning, (3) deny entry to the fruit on the Almeria Star, and (4) conduct increased inspections of Chilean fruit imports were consistent with FDA's statutory authority and regulations. In addition, FDA's actions were consistent with the actions it has taken on other incidents involving tampering threats against imported foods.

Based on its legal authority, its experience with tampering incidents, results of its laboratory testing, and experimental data showing that fruit could be injected with cyanide and appear normal for certain periods, FDA had adequate justification for the actions it took regarding Chilean fruit.

Law Prohibits Poisoned Food From Entering the United States

Section 801 of the Federal Food, Drug, and Cosmetic Act provides that imported food products that appear to be adulterated are to be denied entry into the United States. A product is adulterated if it contains an added poisonous substance that may render it harmful to health. For imported food, the owner of a product that appears to be adulterated has three options: destroy the product, remove it from the United States, or bring it into compliance with the law. In an instance of cyanide poisoning, the product cannot be brought into compliance; thus, it must be destroyed or shipped out of the United States.

Under section 705 of the act, FDA can disseminate information on foods that pose an imminent danger to public health. FDA's Regulatory Procedures Manual is consistent with the act and includes requirements for (1) investigating tampering threats or incidents, (2) notifying state and foreign governments when FDA has found an adulterated product, and (3) instituting product recalls or market withdrawals of adulterated foods. The manual also requires FDA to evaluate the potential health hazard caused by a tampering threat or incident.

Once FDA determined that some fruit on the Almeria Star contained cyanide, FDA:

- refused to admit any of the ship's fruit. FDA did this because (1) tampering was the only possible explanation for the presence of cyanide in the fruit and (2) other fruits may have been poisoned but might not

have been detectable without laboratory analysis of all the fruit, which would have destroyed it;

- notified state health departments and other countries that also imported Chilean fruit (including Canada, Japan, and European countries) of the cyanide finding;
- recommended that U.S. retail outlets remove Chilean fruit from distribution and that consumers refrain from eating Chilean fruit they had purchased;
- increased inspections of incoming Chilean fruit and fruit in cold storage warehouses; and
- prepared a health hazard evaluation report. The March 1989 report noted that FDA tests showed enough cyanide could be injected into fruit to cause injury or death. Because the incident involved deliberate tampering rather than accidental adulteration, the report concluded that FDA could not estimate with any degree of certainty the chances that other shipments might also have been tampered with.

In sum, the actions FDA took subsequent to discovering cyanide in a sample of Chilean fruit were consistent with its statutory authority and procedures for dealing with imported foods that appear to be adulterated.

FDA's Actions Consistent With Actions Taken in Similar Incidents

Between 1984 and 1989, FDA investigated about 3,800 tampering threats and incidents. FDA officials said that the Chilean fruit incident was the largest tampering incident FDA has investigated because the threat did not specify the type(s) of fruit poisoned or the vessel(s) on which the fruit was being shipped, as had been done in some other tampering incidents. It was also the first occasion that FDA found an imported food product that had been tampered with actually arriving in the United States. Thus, FDA had no exact precedent to guide its investigation of this incident. However, FDA's actions on the Chilean fruit were consistent with its actions on two earlier tampering incidents.

One 1985 incident involved tea. An unknown person sent a letter to the U.S. Embassy in Sri Lanka claiming that tea bound for the United States had been poisoned with cyanide. Similar to its actions on Chilean fruit, FDA (1) refused entry of Sri Lankan tea into the United States, (2) developed a test to detect cyanide in tea, and (3) increased its examinations of Sri Lankan tea for cyanide. After receiving no additional threats nor finding cyanide in tea that was sampled, FDA lifted its ban on Sri Lankan tea imports 4 months after denying entry.

The second incident occurred in 1978 when terrorists contaminated with metallic mercury a shipment of Israeli oranges bound for Germany and the United States. Oranges unloaded in Germany were found to contain mercury. When the remainder of the shipment arrived in the United States, FDA performed visual examinations and conducted other tests on 77,000 oranges. FDA did not find mercury in any of the inspected oranges. After detaining the shipment for 4 days, while tests were being conducted, FDA released it for distribution to markets.

FDA Consulted With Others Before Acting

The Federal Food, Drug, and Cosmetic Act does not require FDA to consult with other federal agencies in determining that an imported food product appears to be adulterated and, thus, poses an imminent danger to health. Nor does the act require FDA to consult with other agencies on how to remedy the problem.

Nevertheless, after determining that Chilean fruit aboard the Almeria Star was adulterated, FDA consulted with several federal agencies regarding proposals to confront the danger. Before taking action on March 13, 1989, the FDA Commissioner contacted the Secretary of Health and Human Services and the Office of the President on the proposed actions. Both HHS and the Office of the President supported the Commissioner's proposals. Additionally, FDA consulted with the Departments of State and Agriculture and the Customs Service. Because FDA is the primary public health agency for dealing with these situations, these agencies deferred any decisions regarding the fruit to FDA and made no recommendations to FDA for dealing with the tampering incident.

U.S. Agencies Consulted With Chilean Interests

Additionally, FDA consulted with the Chilean Foreign and Agricultural Ministers, the Chilean Ambassador, and representatives of the Chilean Exporters Association and the American Produce Association. The main focus of these consultations was to devise an inspection plan for Chilean fruit and release any fruit that passed inspection. The Chilean representatives made recommendations to FDA concerning the proposed plan. They recommended that FDA examine 1 to 2 percent of the shipments because of the time and expense of performing more extensive examinations. However, FDA believed this inspection level was too low. FDA's statistical calculations showed that a 10-percent inspection level was necessary to provide a sufficient level of confidence that any additional tainted fruit would be found.

The State Department helped to convince the Chilean representatives of the need to inspect more fruit than what Chile proposed. Ultimately, FDA and the Chilean government agreed on a 5-percent inspection level for incoming fruit and fruit in storage. This level was based on the time and cost of performing inspections and the ability to inspect, store, and transport incoming fruit and fruit already in cold storage waiting to be inspected.[1] FDA concluded that this level of inspection would be sufficient to detect contaminated fruit because of the other actions it had

[1] FDA had used about 100 staff days over a 4-day period to inspect slightly more than 3 percent of the fruit on the Almeria Star.

taken to safeguard consumers, including denying entry to fruit on the Almeria Star and recommending the removal of Chilean fruit from retail outlets. The Chilean government also agreed to provide additional security and perform fruit inspections in Chile.

Chronology of Events Relating to Poisoning of Chilean Fruit

This chronology details the key events during the course of the Chilean fruit tampering incident. For discussion purposes, we have organized the chronology by the time periods during which key decisions were made.

March 2 to 7, 1989

On March 2, 1989, an unidentified person called the U.S. Embassy in Santiago, Chile, claiming to have injected cyanide into fruit destined for the United States and Japan. The caller said that his purpose was to draw attention to the poor living conditions of Chilean workers. The U.S. Embassy notified the Department of State of the threat. The State Department then notified the Customs Service, which in turn notified FDA.

Customs ordinarily clears Chilean fruit for entry into the United States in advance of its arrival and does not detain it at the port of entry for inspection. Although the Department of State thought the threat was a hoax, the Customs Service, as a precaution, placed a temporary hold at ports of entry on new arrivals of Chilean fruit shipments on March 3 and notified FDA of its action. As the threat posed a potential public health problem, FDA took lead responsibility for the investigation based on the provisions of the Federal Food, Drug, and Cosmetic Act and an agreement with Customs. After meeting with representatives of the Chilean government and the Chilean fruit industry, FDA concluded that the threat was a hoax and, on March 6, requested Customs to lift the hold on most Chilean fruit imports. As a precaution, on March 6, FDA also began to visually examine 10 percent of large Chilean fruit. On March 7, FDA began conducting laboratory experiments on the feasibility and effects of poisoning fruit with cyanide.

March 8 to 10

On March 8, 1989, the U.S. Embassy in Chile received a second telephone call that essentially repeated the first threat and insisted that the threat was not a hoax. On March 9, the State Department notified FDA of the second threat. Although the Department believed this threat was also a hoax, as a precaution, FDA, on March 10, decided to visually inspect 1 to 2 percent of all Chilean fruit imports. U.S. Department of Agriculture personnel who examine and grade the quality of incoming fruit provided guidance to FDA inspectors on the types of defects that were normal in fruit (such as staple or nail holes and blemishes).

March 11 to 17

On the morning of March 11, 1989, the vessel Almeria Star arrived in Philadelphia. This was the first ship containing Chilean fruit to arrive in the United States subsequent to FDA's decision to visually examine 1 to 2 percent of the fruit. FDA began inspecting the fruit on Almeria Star on March 11. Allegations were made that FDA targeted the Almeria Star to the exclusion of other arriving vessels containing Chilean fruit, implying that FDA had been "tipped" as to where the poisoned fruit could be found. However, we found no evidence to support this allegation. On March 10, 1989, two other ships carrying Chilean fruit had arrived in Philadelphia and Los Angeles before FDA decided to inspect all Chilean fruit. FDA subsequently examined about 4 to 5 percent of the fruit from those ships that was being held in cold storage warehouses. None of the fruit examined from these two ships contained cyanide, and FDA released the fruit for distribution.

The inspection of fruit from the Almeria Star consisted of FDA inspectors judgmentally selecting pallets of fruit from different growers and shippers. Each pallet contained approximately 100 crates of fruit. Under this procedure, once a pallet was selected, inspectors examined every piece of fruit in every crate from the pallet. Fruit with abnormalities, such as softness or an apparent injection mark, was sent to FDA's Philadelphia laboratory for analysis. By March 12, FDA inspectors had visually examined about 1,200 crates of fruit (less than 1 percent of the cargo) and FDA's Philadelphia laboratory had analyzed about 75 suspicious-looking samples; one of the samples, consisting of two grapes, tested positive for cyanide. Upon analysis, FDA found the grapes contained about 0.003 milligrams of cyanide.

FDA's Philadelphia district office immediately notified FDA headquarters of the positive cyanide finding. After the FDA Commissioner was notified by FDA headquarters, on March 13, he interviewed the FDA chemists who performed the tests regarding the testing methodology and results. The Commissioner interviewed the chemists to satisfy himself that the testing had been performed properly. He also obtained the preliminary results of FDA's laboratory experiments, which showed that some fruits injected with cyanide retained the poison and still appeared edible several days later. Based on this evidence and after consultation with HHS, the Commissioner requested Customs to temporarily suspend all Chilean fruit imports. In addition, the Commissioner recommended the removal and destruction of all Chilean fruit in retail outlets because of the impracticality of attempting to inspect the large volume of fruit already in the distribution chain. The Commissioner also warned consumers not to eat any Chilean fruit they had purchased. FDA was concerned that

more fruit from the Almeria Star might be contaminated but escape FDA detection. Because of this and the impracticality of inspecting the entire cargo of approximately 365,000 crates of fruit, FDA denied entry to the entire shipment of fruit on that vessel.

FDA then began to work with representatives of several federal agencies, including other components of the Department of Health and Human Services, State, and representatives of the Chilean government and the fruit industry to develop a plan to inspect Chilean fruit. The former FDA Commissioner told us that FDA's strategy in developing the inspection plan was to return Chilean fruit that passed inspection to the market as rapidly as possible. On March 17, FDA announced its inspection plan. The plan called for different inspection levels based on when the fruit was shipped to the United States. Under the plan, industry-hired inspectors under FDA supervision would examine 1 percent of fruit shipments made on or before February 20, 1989. Shipments made after that date would be inspected at a 5-percent level. Additionally, security and inspection levels in Chile would be increased.

Also, on March 17, FDA was notified that a third telephone threat had been received by the U.S. Embassy in Chile.

March 18 to April 14

During this period, industry inspectors continued to examine arriving Chilean fruit shipments and fruit still in warehouses. About 650 temporary workers hired by industry performed the inspections. Since no further cyanide contamination was found, by March 29, FDA began to reduce the inspection levels. By April 14, FDA discontinued the increased inspection program.

Review of FDA Testing Procedures Used to Determine Cyanide in Chilean Fruit—Consultants' Report to GAO

Consultants

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Questions GAO Furnished to Four Consultants

Listed below are the questions we asked the consultants to address. The consultants report on their findings follows.

I. Did FDA Use Generally Accepted Tests to Detect Cyanide?

FDA's Philadelphia laboratory used cyantesmo and chloramine-T tests to detect the presence of cyanide in Chilean grapes and other fruit. As we understand, the specially treated paper used in the cyantesmo test changes color when acid is added to a sample containing cyanide. The chloramine-T test uses a spectrophotometer to quantify the amount of cyanide in a liquid by measuring the intensity of the liquid's color.

(1) Are these two tests generally considered by experts to be acceptable screening methods to detect cyanide?

(2) Are there any other tests or other methods that would have produced more reliable results or been more appropriate to use in a situation such as this one? If so, please describe these methods and the advantages over the tests FDA used.

In regard to the cyantesmo test that FDA used to initially screen fruit:

(1) Would the cyantesmo test detect any poison or harmful substance other than cyanide?

(2) Would the presence of other substances, whether harmful or not, produce a reaction that could cause the cyantesmo paper to change color and possibly distort the test results (i.e., produce a false positive)?

(3) Conversely, could other substances make the cyantesmo paper less likely to change color (i.e., produce a false negative)?

(4) Would sulfite, which was used in the packing in the Chilean fruit crates, affect the cyantesmo test? (See section on "Effect of Sulfite on Cyantesmo Paper" in FDA's Laboratory Information Bulletin (LIB) 3352 which is included with the enclosures.)

FDA's Laboratory Information Bulletins 3029, 3352, and 3383, (enclosed) describe procedures used by FDA laboratories for conducting chloramine-T tests in tea, use of cyantesmo paper to detect cyanide in fruit, and the extraction of cyanide from fruit. These bulletins are disseminated to FDA's field laboratories for consideration in future testing.

(1) Are these procedures reasonable or appropriate? If not, please describe the proper methods for conducting the tests versus the methods described by FDA.

FDA's LIB 3029 describes a chloramine-T test to detect cyanide in tea that used a distillation method. In the grape incident, the FDA analyst substituted centrifuging for distillation. According to FDA, both methods provide accurate test results, but the centrifuging method is quicker.

(1) Is it appropriate or reasonable to substitute centrifuging for distillation when conducting chloramine-T tests? If not, please explain why it is not and the extent, if any, centrifuging affects the chloramine-T test results?

II. Did FDA Properly Conduct the Testing and Correctly Analyze the Results?

FDA believes that the cyantesmo and chloramine-T tests and analysis performed by its Philadelphia laboratory were done in accordance with established scientific principles and standards. However, other chemists cited in news stories contend that FDA's work was seriously flawed. Specifically, the critics have cited the following as problems with the FDA tests:

- FDA did not retain part of the samples for future analysis;
- FDA improperly modified the chloramine-T test procedure by using the centrifuge instead of distillation;
- The cyantesmo test is not conclusive and only indicates the possibility of the presence of cyanide or other contaminants;

- The chloramine-T test indicated such a low level of cyanide present that it was inconclusive;
- FDA's test overstated the amount of cyanide present (the chloramine-T test should have shown 0.28 ppm of cyanide present in the grapes, compared to FDA's 0.51 ppm result); and,
- The grapes may have been contaminated accidentally in the FDA lab, based on calculations done by the University of California after injecting 160 micrograms of cyanide into a grape and then conducting a chloramine-T test.

(1) Are the criticisms of FDA's testing valid?. If the criticisms are legitimate, describe the impact of any testing deficiencies on FDA's tests of Chilean fruit.

Considering your overall assessment of FDA's testing of the Chilean fruit, do you believe there were any deficiencies in the testing that could have materially affected the outcome?

III. Was FDA's Research on Contamination of Fruit With Cyanide Conducted in Accordance With Appropriate Scientific Principles?

FDA's Center for Food Safety and Applied Nutrition conducted laboratory studies in March and April 1989 on the effects of contaminating fruit with cyanide. The purpose of this research was to determine (1) whether fruit would retain cyanide after it is injected, (2) how cyanide affected the appearance of the fruit, (3) how rapidly the cyanide dissipated, and (4) whether existing methods to detect cyanide were reliable.

(1) To what extent did FDA's research results serve as a valid indicator of the effects of cyanide on fruit?

1. Introduction

The prime task of the consultants was to assess whether the FDA used appropriate analytical procedures in testing cyanide-contaminated Chilean fruit. The GAO provided a list of questions which were to be specifically addressed by the consultants and included in their report. Although the consultant team was assembled primarily to evaluate analytical chemical procedures used by FDA, it was also asked by the GAO to comment on sampling procedures, documentation and any other matters that may have influenced the analytical results obtained by FDA. The consultants did not address the issue of criminal tampering of the grapes. This report contains the findings of the consultant team and represents their unanimous opinion.

2. Procedure

The GAO sent to each consultant a file containing substantial background material relating to all aspects of the cyanide-Chilean fruit incident. This included detailed copies of FDA analytical results, descriptions of testing procedures, supplementary studies by FDA's Center for Food Safety and Applied Nutrition (CFSAN) and press articles related to the incident.

Each consultant independently reviewed the information, then met in Philadelphia on 13 and 14 February 1990 with GAO project evaluators and FDA-Philadelphia personnel. On 13 February 1990, the consultants were fully briefed by GAO evaluators on all aspects of the cyanide-Chilean fruit incident and were given additional documents to consider as part of the evaluation. On 14 February 1990, the consultants interviewed FDA-Philadelphia staff (and F. Fricke, FDA, Cincinnati) who were directly involved in the analysis of Chilean fruit for cyanide.

3. Findings

Part A. Responses to GAO Questions

I. Did FDA Use Generally Accepted Tests to Detect Cyanide?

A. The consultants agreed that the FDA did use generally accepted chemical tests to detect cyanide in fruit. The two tests used by FDA, namely the cyantesmo strip and the chloramine-T spectrophotometric method are based on classical chemical reactions. The cyantesmo strip test is based on the reaction of hydrogen cyanide gas (HCN) (generated by acidification of the sample) with iron salts impregnated in a paper strip to form a blue complex, Prussian Blue. Analytical applications of this reaction date back to at least 1947 (A.O. Gettler and L. Goldbaum, Anal. Chem. 19, 270 (1947)). The reaction is very selective for HCN. Reducing agents may interfere by causing a reduced response to HCN, possibly leading to false negatives if the CN levels were close to the detection limit. Sulfite, as SO_2, for example, was shown by FDA to cause a reduced response to HCN. Halides such as chloride, bromide and iodide do not interfere. Thiocyanate (SCN), another type of cyanide does not produce a response because it is not volatile upon acidification.

The chloramine-T test involves a series of chemical reactions with cyanide (CN) in solution to yield a magenta (purplish-red) colored dye. Cyanide first reacts with chloramine-T to produce cyanogen chloride which in turn reacts with pyridine to yield a dialdehyde. The dialdehyde reacts

with barbituric acid to produce the magenta colored polymethine dye. This product absorbs light at a specific wavelength in the visible spectrum. The color (visible absorption) of the final solution is measured using a colorimeter or spectrophotometer. Analytical applications of this reaction date back to at least 1947 (J. Epstein, Anal. Chem. 19, 273 (1947)). This reaction is also rather selective. However, nitrite at 25 parts per million or greater may lead to a slight increase in intensity of the color formed and might even yield a false positive if present in very large concentrations. Also, thiocyanate reacts in a similar manner as CN. Reducing agents, particularly sulfite, may cause a reduction in color formation. This could lead to false negatives if CN levels were near the detection limit and sulfite (for example) levels were high enough. (J.C.L. Meeussen, E.J.M. Temminghoff, M.G. Keizer and I. Novozamsky, Analyst 114, 959 (1989)). Variations of the chloramine-T method have been used successfully to determine CN in soybean products, cassava, industrial waste waters, milk or blood at sub- parts per million concentrations.

The consultants are of the opinion that the reactions involved in both the cyantesmo test and the chloramine-T spectrophotometric method are well known and have been used successfully for a variety of sample types over many years. In applying any analytical procedure to a new sample type, it is imperative to analyze reagent blanks, sample blanks, standard CN solutions and spiked blanks (sample and reagent blanks with known amounts of CN added). These analyses are required to determine possible interferences, both positive and negative, as well as detection limits and linear range if quantitation is required. Both of these tests are considered acceptable for screening fruit provided that blanks and spikes are regularly analyzed as mentioned above. The information provided to the consultants clearly indicated that the FDA carried out all necessary method tests before and during the application of the procedures to grapes.

Other colorimetric tests for CN (picric acid, phenophthalein, copper acetoacetate) may have worked as well as those used by FDA, but they offer no particular advantages. Methods involving specific ion electrodes, gas chromatography-mass spectrometry, flow injection analysis, titration or ion chromatography all require more sample preparation or specialized equipment. In addition, the reliability of the newer methods has not been fully evaluated.

B. Use of the Cyantesmo Test for Screening Fruit

(1) As far as the consultants are aware, from the literature and from personal experience (J. Fleming, consultant) no other known poison gives a positive result with the cyantesmo test as employed by the FDA.

(2) There are no known substances (especially in grapes) which would yield a false positive CN value with the cyantesmo test as employed by the FDA. Because the test strip does not come into direct contact with the acidified sample in the flask, non-volatile anions such as thiocyanate and nitrate which might yield a positive value if the test strip were actually immersed in the sample liquid, do not interfere.

Independent experience by the Virginia Division of Consolidated Laboratory Services confirms the appropriateness of the cyantesmo test. After accounts of the cyanide-Chilean fruit incident were reported by the news media, Virginia Department of Agriculture received a complaint about grapes that had made a consumer sick. Inspectors followed up on this complaint and collected white and red Chilean grapes from complainant's grocery store. Approximately 3 pounds of red grapes and approximately 3.5 pounds of white grapes were submitted to Consolidated Labs for tampering analyses on March 16, 1989. Janet Fleming, consultant, independently analyzed these grapes by a very similar method to FDA's. Each grape was visually examined and any suspicious grapes were microscopically examined. One red grape and one white grape each had a slight puncture mark. Both were crushed and screened for cyanide by cyantesmo strips and were found to be negative. Along with the suspect grapes, control (normal) white and red grapes and spiked grapes at 2 and 3 parts per million cyanide levels were also tested. Control grapes were negative and spiked grapes tested positive. Virginia has utilized these same screening procedures (visual, microscopic and cyantesmo) for suspected food tampering cases for several years and has found these to be appropriate.

(3) It has been shown in the literature and from FDA studies that sulfite (as SO_2) clearly can have a negative effect on CN detection with several types of colorimetric CN tests. Most other substances that have been shown to interfere, do so only to a lesser extent and then only in solution. There are no reports in the literature on volatiles other than SO_2 that would cause false negatives in the test as performed by the FDA.

(4) Sulfite has been shown in the literature to be one of the major interferants in the colorimetric determination of CN by either the Prussian Blue (cyantesmo test strip) or chloramine-T reaction. Its effect is to inhibit color formation in both tests which could lead to false negatives. The FDA studies on the effect of sulfite on the cyantesmo test clearly showed that sulfite at the maximum permitted level on grapes, 10 parts per million, could have a negative effect on results at 1 parts per million CN or less. If sulfite were present in the grape sample that was found to be positive, the true value for CN would likely have been higher than that estimated by the tests used by FDA. The procedures used in the sulfite studies carried out by FDA conform to standard analytical practices (i.e. analyzing samples with and without sulfite at different concentration levels and observing the effects on CN determination). The FDA did not test for sulfite in the bunch of grapes associated with the two positive grapes. It is conceivable that very low levels of CN were present from migration but may not have been detectable if sulfite were present.

C. Comments on FDA Laboratory Information Bulletins 3029, 3352 and 3383

The FDA Laboratory Information Bulletin 3029 describes a colorimetric procedure using chloramine-T for the determination of CN in tea. The FDA modified this procedure for the determination of CN in grapes. The major change was to omit the distillation step used for tea and, instead, to centrifuge the samples to remove suspended matter so that a portion of the clear liquid could be tested using the chloramine-T reaction. The consultants have no difficulty in accepting this change. Modifications of methods for specific applications is commonplace in analytical chemistry and is done for a variety of reasons. However, with any modification or application of an existing method to a new type of sample (eg. grapes instead of tea) an evaluation must be performed to prove that the modifications are acceptable for that particular analysis. The FDA used an accepted analytical approach and showed that omission of the distillation step had no effect on the determination of CN in grapes at levels greater than ca 0.2 parts per million. This was done by analyzing blank (non-contaminated) grapes and grapes injected with CN.

Laboratory Information Bulletin 3352 describes work done by CFSAN on the evaluation of the cyantesmo strip for the determination of CN in various fruits. The procedure requires 30-40 grams of fruit which are placed in a glass jar and mashed. Sulfuric acid is added to acidify the sample causing the release of HCN gas if CN is present in the sample. A strip of cyantesmo paper is suspended over the sample (not touching)

and the lid is immediately placed tightly on the jar. A positive response to HCN is indicated by the paper changing to a blue color.

CFSAN studied a variety of fruits and observed negative results for all uncontaminated fruit. Positive results were found with crushed pits of nectarines and peaches which are known to contain an organic type of CN which can yield HCN upon addition of sulfuric acid. (J. Fleming, consultant, has evaluated this same procedure for a variety of food commodities and found no false positives. Crushed apple seeds, also known to contain an organic type of CN, yielded HCN upon addition of acid and gave a positive test with the cyantesmo paper strip). The CFSAN studies with sulfite and old cyantesmo paper strips were carried out using proper analytical procedures. The results obtained for the sulfite studies agree well with similar reports in the literature on the negative effects of sulfite on CN determinations.

Laboratory Information Bulletin 3383 describes a rapid sample preparation procedure which omits the distillation step of Bulletin 3029 (method for CN in tea using chloramine-T). It employs centrifugation for fruit samples. From the results presented, the centrifugation step is more than adequate for CN determination in the fruits studied (CN could be detected at levels down to 0.006 parts per million or less). These results agree with those obtained by the FDA Philadelphia laboratory and the FDA Cincinnati laboratory (Fricke) for grapes, using the same method. However, rather than using only 587 nanometers wavelength of light, the Philadelphia and Cincinnati laboratories scanned the whole visible wavelength range (spectra) to better observe the absorbance maximum at 587 nanometers and to observe the shape of the spectra which provides additional qualitative information for identification purposes. This is good analytical chemistry.

All of the above studies were carried out under the principles of good laboratory practice and were appropriate to the work carried out by the FDA Philadelphia laboratory on the Chilean grapes. The studies described in Bulletins 3352 and 3383 confirm that the work carried out by the Philadelphia laboratory was indeed valid.

D. Substitution of Centrifugation for Distillation by the FDA in Grape Sample Preparation

As mentioned in section C above, the consultants have no difficulty in accepting this substitution. FDA studies with blank (uncontaminated)

grapes and a variety of other fruit (FDA laboratories in Philadelphia, Cincinnati and CFSAN in Washington) all showed that the centrifugation was adequate. It is faster than the distillation and requires less sample, both of which were prime requirements during the Chilean grape crisis. In addition, previous experiments by analysts at the FDA Philadelphia laboratory using spiked yogurt samples showed that the distillation procedure yielded reduced recoveries of CN. This also was a factor in not using the distillation procedure for the grape samples.

II. Did FDA Properly Conduct the Testing and Correctly Analyze the Results?

A. Overall, and considering the circumstances, the consultants found the FDA work to be very thorough and carried out with care. Many suspicious samples were photographed before analysis. Upon finding the CN-positive grape sample, as indicated by two cyantesmo strip tests and the chloramine-T test, efforts were made to determine if it was a false positive. These included analyzing the SO_2 pad, stamped ink label, the paper label and even the photographic film used to photograph the samples.

(1) The FDA did retain part of the suspect grapes. The consultants were shown the remainder of the original extract (made basic with sodium hydroxide) which tested positive twice by the cyantesmo test and positive by the chloramine-T method. Also FDA has retained the remaining half of the third grape (which had a white ring around a small slash or slice mark) in Cincinnati.

The analyst who did the tests on the three suspect grapes chose two for analysis and retained the third for use later. Two grapes were chosen in order to have enough material for the analysis. This also would yield an average CN value for the two grapes. Considering that only three grapes were available, the consultants feel that the selection of two grapes for the test was appropriate. The third grape remained untouched (not mashed nor acidified) for later analysis. The question of whether only one grape should have been used for analysis is not important in light of the results found. It is clear that at least one of the grapes contained measurable CN.

(2) As described above (sections C and D), the modifications to the chloramine-T method were done using proper analytical procedures. The modifications were evaluated using reagent blanks, blank (uncontaminated) samples, spiked (injected) samples and several different types of fruit.

(3) The cyantesmo test involves a selective reaction for CN. The color change strongly indicates the presence of CN in the samples. The chloramine-T test was performed on a portion of the same extract to confirm the results obtained by the first test. Because uncontaminated grapes yield negative CN values for both tests, the only conclusion that can be drawn is that the positive results are due to contamination (deliberate or otherwise) with a CN-containing substance. As mentioned in section A, the two different tests used by FDA are very selective for CN. No other substances (that do not contain CN) cause false positives in both of these tests.

(4) The level of CN determined in the positive grapes by the chloramine-T test was about 8 times higher than the minimum quantity detectable with the test (assuming the detection limit was 3x the level of the blank grape). The CFSAN studies (FDA Bulletin 3383) found a minimum detectable level of 0.006 parts per million CNin the fruits examined. This detection limit is about 80 times less than the 0.51 parts per million detected in the positive grapes by the FDA Philadelphia Lab. These results indicate that the 0.51 parts per million level determined in the positive sample was a definite, unambiguous positive result.

(5) The consultants could find no evidence from the calculations and raw data provided by FDA that the concentration of CN should have been 0.28 parts per million instead of 0.51 parts per million. The quantitation was based on a comparison of the results of the test solution (grape extract) to a standard solution containing a known quantity of CN. The calculated value was corrected by subtracting the spectrophotometer reading from a known blank grape sample. The difference is attributed to "added" CN. Parts per million were calculated by dividing the amount of CN found by the weight of grapes taken for the analysis. The consultants' own calculations confirmed that 0.51 parts per million is the correct result.

(6) Independent studies by the University of California suggest that the grapes which tested positive for CN must have been accidentally contaminated with CN by FDA within 4 hours of analysis. Their conclusion is based on the appearance of the contaminated grapes, the levels of CN found and the results of their own time studies on deliberately contaminated (injected) grapes.

The consultants questioned FDA personnel in detail on exactly how their analyses were carried out and how standards and spiked samples were included in the analytical procedures. They indicated that the analyses

were done "assembly-line" fashion. The positive sample was the only positive found in a series of samples analyzed at that time. The likelihood of contamination from the atmosphere appears remote since more than one sample would have been affected. Also, HCN has a very characteristic odor and would have easily been detected in the air if it were present. The odor of HCN was noticed by four different analysts from the one positive sample upon acidification, but not with any other of the approximately 1000 grape samples analyzed during the crisis). Spiked samples and standards were prepared by a different analyst in a fumehood in a different location from where the inspection samples were analyzed. Thus, the likelihood of contamination from inadvertent sample spiking appears remote. After each individual analysis glassware was thoroughly cleaned, rinsed and dried in an area remote from the analytical laboratory before reuse. Contamination from this source also appears remote. The consultants found that good analytical practice was followed throughout the analyses. The FDA analysts were fully aware of the potential for accidental contamination and took appropriate steps to avoid it.

Studies similar to those carried out by the University of California were independently performed by CFSAN in Washington and FDA in Cincinnati (Dr. Fricke). All studies indicated that CN levels decreased with time when injected into fruit. However, in the studies by CFSAN and FDA, Cincinnati, CN was detected in the grapes up to 21 days after injection. While these studies showed significant variation among individual injected grapes, it appears that there is an initial rapid decrease in CN by the end of the first day followed by a much lower rate of decomposition or even a levelling off up to 21 days (similar results were observed for CN-treated apples and plums, by J. Lawrence consultant). Also, studies by the University of California have shown that CN apparently can migrate (presumably as HCN, which is volatile) to other grapes and be detected for up to 21 days. The CN on these grapes apparently does not affect their appearance after that length of time.

Fruit, such as grapes, injected with CN, showed within a certain period of time, visible signs of deterioration of quality (dehydration, browning near injection point). However, the rate of visual degradation in quality of the grape s was not uniform in the studies. The CFSAN studies were carried out by injecting very large quantities of CN into grapes (up to 18 milligrams per grape). Their results indicated that some injected grapes showed no change in appearance after 2 days of storage at room temperature and up to 6 days when refrigerated. The studies by Dr. Fricke (where lower amounts of CN were injected) also showed that some

grapes injected with CN (160-1000 micrograms) lasted up to 16 days without significant degradation.

All of these studies show that some injected grapes can retain their original appearance for a much longer period of time than others. It is somewhat difficult to relate these studies to the results found by the Philadelphia lab with the positive grapes during the crisis for several reasons. First, the grapes analyzed during the crisis were "young" grapes sampled immediately upon arrival in the U.S. The studies by FDA and University of California may have been done using grapes that were picked at a later date or stored for longer periods and thus may have been "riper" than the samples analyzed in the crisis. Secondly, the variability in results is an indication that all grapes do not necessarily react in the same way to CN injection. Thirdly, the variability in how the samples were injected (depth and volume of injection, exactly where in the grape the injection was made, size of needle used, type of solution injected: eg. acidic, basic, containing other substances in addition to CN) could affect the results. (It is even conceivable that juice may have been withdrawn from the CN positive grapes before injections with CN to minimize the leakage from the fruit.) Fourthly, the crisis samples were stored in the presence of sulfite pads, the purpose of which was to prevent degradation and likely browning of the grapes. (Sulfite is a known inhibitor of browning of fruits and vegetables.) These conditions would likely minimize the visual changes that might have been induced by CN injection.

In summary, the studies carried out by FDA and the University of California showed that some grapes can be visually changed in a short time by CN injection while others are much more resistant, retaining a good appearance for up to 16 days depending upon levels of CN injected, freshness of the grapes and storage conditions. Also, CN has been shown to remain in injected grapes for up to 21 days. The grapes analyzed in Philadelphia during the crisis were very fresh, stored under mainly refrigerated conditions prior to analyses and were in the presence of sulfite pads. Under these conditions it is possible that the grapes could have been injected with CN 2-3 weeks before analysis by FDA.

Based on all the evidence examined, the consultants disagree with the University of California conclusions that the grapes must have been contaminated with CN within 4 hours prior to analysis.

B. After an examination of all documents made available to the consultants, and interviews with personnel directly involved in the discovery

of CN in the two suspect grapes, the consultants believe that there were no deficiencies in the testing that could have materially affected the outcome (see details presented in other sections of this report).

III. Was FDA's Research on Contamination of Fruit with Cyanide Conducted in Accordance with Appropriate Scientific Principles?

(1) The consultants found no significant deficiencies in the chemical methods used by FDA (CFSAN and the Cincinnati Lab) to study the effects of CN on grapes and other fruit. The results indicated that CN can have an effect on the appearance of fruit which is dependent on time, temperature, quantity of CN injected and ripeness of the fruit. (See detailed comments in Part A section II A of this report.)

(2) The studies by FDA and other research groups (University of California, and others sponsored by the Chilean interests) have addressed a number of issues concerning different aspects of CN contamination. All of the studies used either potassium or sodium cyanide to inject into the grapes. However, there are other cyanide containing substances that could have been injected (e.g. amygdalin or other cyanogenic glycosides). It may be useful to carry out injection studies with these types of compounds to observe degradation of CN and the visual quality of the grapes with time. Also, a detailed study on the storage of grapes in the presence of SO_2 pads may contribute information relating to the effect of SO_2 on the stability of CN in the grapes and to the change in visual appearance with time.

Part B. Additional Consultants' Comments Interviews With FDA Analysts

The consultants questioned in some depth the FDA analysts who tested the CN positive grapes. The analysts explained that they had extensive experience with the cyantesmo test and the chloramine-T test and, in fact, performed about 1000 tests on yogurt samples immediately before the Chilean grape crisis. All analysts knew and understood the basic principles involved in the analyses and carried out the necessary analytical tests to ensure that any modifications to existing procedures were valid. The consultants were impressed with their competence.

The consultants questioned the analysts on the discrepancy between results of the Philadelphia lab and the later test carried out by Dr. Fricke of the Cincinnati lab several hours later on the same sample. It was learned that upon addition of sodium hydroxide to the grape sample (to prevent loss of HCN), the color of the liquid changed from purplish

(acidic or neutral) to pale green. The pale green mixture was transported to Cincinnati by H. Miller. However, upon arrival, Mr. Miller remarked that the color of the sample was again purplish, possibly indicating a return to acidic (or neutral) conditions. Under these circumstances, any remaining CN may have been lost as HCN during transit or possibly have reacted further with sample constituents reducing the amount remaining for analysis by the Cincinnati lab to below their detection limit. The consultants have no difficulty in accepting this possibility. Basic pH was used to prevent volatile HCN formation by converting it to water soluble, non-volatile CN ion. This is normal procedure to prevent the loss of volatile acidic substances. However, studies carried out since the grape crisis have shown that even in basic solution CN may decompose significantly in a few hours (University of California study and experience of J.F. Lawrence, consultant).

Sampling and Documentation Procedures

The consultants briefly discussed the sampling procedure used by FDA to obtain samples of grapes from the suspect shipment. The sampling approach was considered appropriate for the detection of deliberate CN contamination in the fruit. However, the consultants did not study the background statistical criteria used by FDA to select the sampling procedure.

The consultants found no significant flaws in the chain of custody documentation or procedures used by the FDA. Some of the documentation and lab reports were not clearly presented but all essential information concerning sample labelling, transport from one person to the next, lab testing and results of tests were documented. The consultants found no errors or omissions that would have had an impact on the results obtained by the FDA Philadelphia laboratory.

Conference Call With Representatives of the GAO and Chilean Interests

The consultants participated in a conference call on 16 March 1990 to discuss, in particular, recent findings by the University of California related to CN in grapes. These included migration of CN and the efficacy of cyantesmo testing. Some discussion also centered on the effect of sulfite on the analyses and differences between distillation and centrifugation in the chloramine-T test. The following are some comments.

a) Migration of Cyanide

It appears that CN may migrate from injected berries to nearby fruit. The migration seems to involve conversion of CN to volatile HCN which escapes and may adsorb onto the surfaces of other grapes. Direct contamination of neighbouring berries by contact with liquid from the injected berries is also possible. The degree of contamination via migration would likely depend upon the quantity of CN injected into the grapes and the storage conditions. If only small quantities were initially injected, the amount of CN migrating might not be detectable by the cyantesmo or chloramine-T tests.

b) Efficacy of Cyantesmo Testing

The studies by the University of California showed that results by the cyantesmo test are affected by the quantity of CN injected into the grapes and the length of time the grapes are stored. This does not appear unusual and would be expected knowing the behavior of CN in injected fruit. In some cases, the second cyantesmo tests were more positive than the first ones. It is not known why this occurs.

c) Comparison of Centrifugation and Distillation

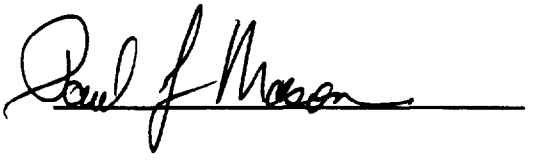
No research has been done on a direct comparison of the centrifugation method with distillation for injected grapes. It is possible that recoveries and detection limits of CN could be different depending upon how CN is held in the samples. Sulfite can cause CN losses in the distillation procedure (C.H.P. van Eeden and A.W.J. de Jong, Z. Lebensm. Unters. Forsch. 181, 412 (1985)). However, overheating (charring) during distillation might lead to CN formation from natural constituents (I. Thompson and R.A. Anderson, J. Chromatogr. 188, 357 (1980)), thus yielding false positives. On the other hand, heating of CN in a food matrix could cause a loss of CN by its accelerated reaction with food components. The likelihood of these occurring can only be determined by analyzing reagent blanks, sample blanks and spiked sample blanks.

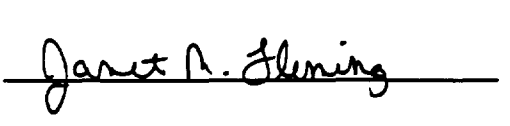
4. Conclusion

The consultants are of the opinion that the FDA did find CN in the two grapes during the grape crisis. After interviewing FDA personnel and reviewing all available information from the crisis and the results of many studies carried out after the incident, the consultants believe that a false positive reading is extremely unlikely. The overall conclusion on the injection studies is that CN can persist in grapes for at least three

weeks, depending upon quantities injected, condition of the grapes and storage conditions. The visual appearance of some fruit may only be minimally affected by CN injection (again depending upon quantity injected) while that of others may be more affected. The analytical methods used by the FDA were scientifically sound. Their analytical procedures were carried out under good laboratory practice and their staff were fully familiar with CN testing. Overall, the consultants could find no significant error or omission in the FDA work that would have had an impact on their findings.

Signatures of Consultants:





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