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Report to the Ranking Minority Member
Committee on Government Operations
House of Representatives

June 1993

HOSPITAL STERILANTS

Insufficient FDA Regulation May Pose a Public Health Risk

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Human Resources Division

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June 14, 1993

The Honorable William F. Clinger, Jr.
Ranking Minority Member
Committee on Government Operations
House of Representatives

Dear Mr. Clinger:

This report is in response to a January 17, 1992, request from Congressman Frank Horton, former Ranking Minority Member of the House Committee on Government Operations, asking our office to review the regulatory actions of the Environmental Protection Agency (EPA), Food and Drug Administration (FDA), and Federal Trade Commission (FTC) that resulted in the termination of sales of Sporicidin International, Inc., products. Sporicidin International manufactured sterilants and disinfectants that were used to clean medical instruments. Because such sterilants and disinfectants are considered to be medical devices, he asked us to also review FDA's regulation of such products.

The results of our work are summarized below and discussed more fully in appendixes I and II. Our scope and methodology are discussed in appendix III.

Results in Brief

EPA and FDA acted correctly in halting the sale of Sporicidin Cold Sterilizing Solution and disinfectants in December 1991. FTC acted appropriately in stopping false and deceptive advertising of the sterilant. These products were designed to protect patients from serious infections that can result when unsterile instruments are used to treat them. However, Sporicidin Cold Sterilizing Solution did not effectively sterilize medical instruments, and the company had been marketing its products without FDA's prior authorization and failed to register its products, as required by law. Also, FDA inspections found there were significant violations of good manufacturing practices regarding cleanliness and recordkeeping.[1]

Although FDA took proper action against Sporicidin International, its overall regulation of other manufacturers of hospital sterilants and disinfectants has been inadequate. In this regard, only a few sterilant and

[1]Manufacturers are required to comply with FDA regulations, which prescribe current good manufacturing practice for devices, to prevent production of defective products. See 21 C.F.R. part 820. This part describes the methods to be used in, and the facilities and controls used for, the manufacture, packing, storage, and installation of all finished devices intended for human use to assure that such devices will be safe and effective.

disinfectant manufacturers have registered their products with FDA, and few of the hundreds of products have been authorized for marketing by FDA, as required by law.

Background

Hospital sterilants and disinfectants are used to clean medical instruments.[2] According to the Centers for Disease Control and Prevention (CDC), about 5 percent of all hospital patients acquire an infection while hospitalized. Hospital-acquired infections prolong hospital stays, increase patient care costs, and in some instances cause death. Research has linked some infections, including fatal ones, to contaminated endoscopes and other medical instruments.[3] Interest in the efficacy of sterilants and disinfectants has also increased because of the growing number of acquired immune deficient patients, who are highly susceptible to infections.

Hospital sterilants and disinfectants are regulated by several federal agencies. Because hospital sterilants and disinfectants are used to destroy harmful bacteria and other organisms EPA regulates them as pesticides. It is EPA's responsibility to register all pesticides and approve them as safe and effective before they can be marketed. FDA regulates them as medical devices because they are used on medical instruments. Before a hospital sterilant or disinfectant can be marketed, FDA requires manufacturers to submit a premarket notification containing evidence supporting the safety and efficacy of the device. FTC is responsible for guarding against false or deceptive product advertising, including hospital sterilants and disinfectants.

In December 1991, FDA seized and halted the marketing of Sporicidin International's sterilant and disinfectant products because it determined that the company had not complied with legal and regulatory requirements for selling these products. EPA estimated that Sporicidin International represented 21 to 25 percent of the hospital disinfectant market. In announcing the seizure of the five Sporicidin products, FDA's Commissioner said that sterilizing and disinfecting agents are supposed to protect patients from contact with harmful microorganisms. He said FDA

[2]A sterilant is intended to destroy or eliminate viruses and all living bacteria, fungi, and their spores. A disinfectant is intended to destroy or inactivate one or more major species of bacteria, such as tuberculosis bacteria.

[3]An endoscope is a medical instrument that is inserted in a hollow organ, such as the rectum, to visually examine its interior.

will not tolerate products that would permit the transmission of disease from one patient to another.

Also, EPA took joint action with FDA against the company to stop the sale of its cold sterilizing solution. FTC brought action requiring Sporicidin International to correct advertising for Sporicidin Cold Sterilizing Solution because it charged that the company falsely advertised the effectiveness of this product.

Regulatory Agencies Had a Valid Basis for Actions Taken Against Sporicidin International

A competitor's complaint to FTC that Sporicidin products were unfairly marketed led to investigations by FTC and subsequently by FDA and EPA of Sporicidin International's manufacturing and marketing activities. FTC's investigation of the complaint, which included a review of advertisements and marketing material for Sporicidin Cold Sterilizing Solution, found that the company falsely advertised the effectiveness of the product.

Based on FTC's finding, FDA and EPA initiated their own investigations of Sporicidin products. FDA found that the products were not manufactured according to its standards and that Sporicidin Cold Sterilizing Solution was not an effective sterilant for medical instruments. EPA, through tests conducted for it by FDA, also found that Sporicidin's Cold Sterilizing Solution was ineffective.

Moreover, Sporicidin International advised us that it had been marketing its products for about 14 years. However, the company had not submitted premarket notifications to FDA for most of its products before they were marketed. Although the company contends it was not aware of FDA's requirement for premarket notifications, in 1983 it submitted a notification and obtained FDA's authorization to market a disinfectant for a hemodialysis device.

FDA's inspections of the two contractor facilities that manufactured Sporicidin products found significant problems. For example, at one facility: the manufacturing site was "very dirty"; product ingredients were not accurately measured; two sets of records were maintained, inconsistently listing different ingredients used in manufacturing particular products; and there was no assurance that the manufacturing equipment, also used to make a rug shampoo, was properly cleaned before it was used to produce sterilants and disinfectants.

FDA's laboratory tests found that Sporicidin's sterilant did not work as the manufacturer claimed. When the sterilant was used according to its labeling, it failed to kill all the microorganisms in the samples tested. Several other independent studies (see p. 13) also found that Sporicidin sterilant or other products with similar chemical ingredients were ineffective as a hospital sterilant or disinfectant when used according to their labeling.

Sporicidin International Disagrees With the Actions Taken Against Its Products

Sporicidin International does not believe that EPA, FDA, or FTC had an adequate basis for their actions against its products. The company submitted to us written comments that are contained in appendix IV. The comments and our response to them are discussed beginning on page 17.

Overall FDA Regulation of Hospital Sterilants and Disinfectants Has Been Inadequate

Although FDA took proper action against Sporicidin International for not complying with pertinent laws and regulations, in general the agency's regulation of hospital sterilants and disinfectants has been inadequate. The agency is responsible for assuring that hospital sterilants and disinfectants are safe and effective before they are marketed; however, its regulation of these products does not provide such assurance.

To market hospital sterilants and disinfectants, a company must first provide a premarket notification to FDA showing that its products are safe and effective in killing harmful microorganisms. Because hospital sterilants and disinfectants are considered medical devices, FDA is also required by law to inspect a company's manufacturing facilities biennially to assure that the products are manufactured in accordance with prescribed good manufacturing practices.

During our review, we discovered that FDA has been aware for at least the past 3 years, based on information it received from EPA, that sterilant and disinfectant manufacturers had not registered with FDA. Nevertheless, FDA has allowed many hospital sterilants and disinfectants to be marketed without assurance that they are safe and effective. The EPA information showed that EPA had registered 59 sterilants for sale by 24 companies and had registered about 1,200 hospital disinfectants for sale by about 330 companies.[4] While clearly the 59 sterilants are medical devices, FDA has not

[4]Some of the 330 companies also manufacture sterilants.

reviewed the 1,200 disinfectants registered by EPA to determine what number of them are intended for use with medical devices.[5]

As of April 1993, FDA had authorized the sale of only 16 products—3 sterilants and 13 disinfectants. FDA authorized these products on the basis of a premarket notification to FDA in which the manufacturers claimed the products were substantially equivalent to a similar product that was already on the market. FDA officials told us that FDA, for the most part, had not sought premarket notifications from manufacturers because it did not have enough staff to review them. Notwithstanding its limited resources, we believe that FDA should devote more attention to these products because ineffective products can pose a serious public health risk.

Recently, FDA tested the efficacy of 26 sterilants for EPA. Based on completed or partially completed results, 5 products failed or are expected to fail, 7 passed or are expected to pass, and 14 are still pending. FDA tested nine of the same products for its own regulatory purposes; five failed or are expected to fail, and four passed or are expected to pass.

In addition to submitting a premarket notification to FDA for their products, manufacturers, according to law, must also register their products and companies with FDA. Although EPA provided information to FDA indicating that more than 300 companies were registered by EPA to sell hospital sterilants and disinfectants, only 5 companies were registered with FDA as of April 1993.

FDA is also required to inspect manufacturers' facilities biennially. However, it was not until 1990 that FDA began inspecting the facilities of the manufacturers of hospital sterilants and disinfectants because of the rising numbers of hospital infections and the growing number of immune deficient patients. Between October 1990 and December 1992 FDA inspected manufacturing facilities for 23 companies and found serious deficiencies at over 50 percent of them. As a result, FDA seized the products of two companies, one of which was Sporicidin International. FDA's district offices that inspected four other manufacturing facilities recommended their products also be seized because the manufacturers did not comply with good manufacturing practices. However, FDA had not made a decision on these recommendations as of March 1993. Two other manufacturers voluntarily discontinued marketing their products after FDA's inspections found a deviation from good manufacturing practices

[5]The number of products that are actually being sold could not be ascertained from FDA or EPA. Neither agency maintained this information.

and an instance of product misbranding. The remaining four manufacturers were issued warning letters by FDA.

FDA's testing of hospital sterilants is another area that might benefit from increased management attention. Currently, EPA and FDA continue to have many of the same hospital sterilants tested separately by FDA for efficacy because EPA does not have laboratory facilities. By coordinating its testing with EPA's, FDA could make more efficient use of its limited resources.

In recent years, FDA has taken action to improve its regulation of sterilants and disinfectants. In 1990, FDA developed a strategy to inspect manufacturing facilities, test the efficacy of hospital sterilants and some disinfectant products, and enforce compliance with requirements for premarket notifications. Additionally, after we discussed the problems concerning the regulation of hospital sterilants and disinfectants with FDA officials, they expressed a willingness to contact manufacturers to advise them of the need to comply with the requirements for marketing their products.

FDA does not plan to review the 1,200 disinfectants identified by EPA to determine if they are used with medical devices. Therefore, FDA will not have identified all disinfectants that should be regulated by FDA to determine whether they are safe and effective. Moreover, FDA has not developed a strategy to ensure that future manufacturers who produce hospital sterilants and disinfectants obtain FDA authorization before they market them.

Recommendations to the Commissioner of FDA

We recommend that the Commissioner of FDA

- develop a plan to identify all manufacturers of sterilants and disinfectants and ensure that they comply with the law.
- devise a strategy to ensure that in the future sterilants and disinfectants are not marketed without FDA's prior authorization.
- develop procedures, in coordination with EPA, that would satisfy the requirements of both agencies for testing hospital sterilants and disinfectants to avoid unnecessary duplication of product testing.

Unless you publicly announce its contents earlier, we plan no further distribution of this report until 10 days after its issue date. At that time, copies of this report will be sent to appropriate congressional committees

and subcommittees, the Secretary of Health and Human Services, the Administrator of the Environmental Protection Agency, the Commissioner of the Food and Drug Administration, the Chairman of the Federal Trade Commission, and other interested parties. It also will be made available to others on request.

If you have any questions regarding this report, please call me at (202) 512-7123. Other major contributors are listed in appendix V.

Sincerely yours,

Mark V. Nadel

Mark V. Nadel
Associate Director, National and
Public Health Issues

Contents

Abbreviations

AOAC	Association of Official Analytical Chemists
APA	Administrative Procedures Act
CDC	Centers for Disease Control and Prevention
EPA	Environmental Protection Agency
FDA	Food and Drug Administration
FTC	Federal Trade Commission
GAO	General Accounting Office

Basis for Actions Taken Against Sporicidin International Appears Valid

The Food and Drug Administration, Environmental Protection Agency, and the Federal Trade Commission had adequate basis for sanctions they imposed in December 1991 against Sporicidin International. FDA ordered Sporicidin International to stop selling and distributing its Sporicidin Cold Sterilizing Solution and seized all Sporicidin sterilants and disinfectants based on FDA laboratory tests that showed the cold sterilizing solution was not effective as a sterilant, and the products were marketed without FDA's authorization. Additionally, while not a basis for the sanctions, FDA inspections showed the products were not manufactured according to FDA good manufacturing practices.

EPA also suspended the sale of the Sporicidin Cold Sterilizing Solution based on separate FDA laboratory tests conducted for EPA that showed the product was not effective. FTC filed a complaint seeking a preliminary injunction against the company because it found that the company falsely advertised the effectiveness of the Sporicidin Cold Sterilizing Solution.

Regulatory Responsibilities of FDA, EPA, and FTC

Because FDA has classified hospital sterilants and disinfectants as medical devices, the Federal Food, Drug, and Cosmetic Act requires a manufacturer to obtain FDA's authorization before marketing its product. To obtain this authorization, a manufacturer must submit to FDA at least 90 days before marketing a product a premarket notification indicating that the product is safe and effective when it is used according to its labeling. Products marketed without FDA's authorization are considered to be adulterated and misbranded and are subject to seizure.

EPA is responsible under the Federal Insecticide, Fungicide, and Rodenticide Act for registering all pesticides before they are marketed. EPA may register a pesticide only if it determines that the product is effective when used according to its labeling, without causing an undue risk to health and the environment. A pesticide manufacturer is required to provide EPA evidence of its product's safety and efficacy.

FTC has responsibility under the Federal Trade Commission Act to safeguard the public by preventing the dissemination of false or deceptive advertisements of products. Companies, however, are not required to submit advertising material to the FTC for prior approval.

Sporicidin Products Failed FDA Inspections and Laboratory Tests and Were Marketed Without FDA Authorization

On December 13, 1991, FDA ordered Sporicidin International to stop selling and distributing Sporicidin Cold Sterilizing Solution. FDA seized the total line of Sporicidin sterilant and disinfectant products because it determined that they were adulterated and misbranded based on their ineffectiveness and failure to receive authorization from the agency. FDA's actions appear valid because (1) FDA's inspections of the products' manufacturing facilities showed that the manufacturing process did not comply with good manufacturing practices, (2) the product failed FDA's efficacy tests, and (3) the company did not obtain FDA's authorization before marketing its products as required by law.[1] Marketing a product under these conditions violates laws and regulations that could result in seizure of the product and/or injunction against the manufacturer.

Sporicidin International's products were designed to sterilize or disinfect medical devices, such as surgical instruments, dental equipment, and endoscopes, without heating them. Because the products did not rely on heat to accomplish their intended purpose, they were cold sterilants and disinfectants. They were sold in the form of a solution, spray, and towelette.

Manufacturing of Sporicidin Products Did Not Comply With FDA Standards

The Federal Food, Drug, and Cosmetic Act requires FDA to inspect facilities of medical device manufacturers at least every 2 years.[2] In December 1990, FDA inspected the facilities that manufactured Sporicidin products. These products were manufactured by two companies under contract with Sporicidin International. One contractor, located in Baltimore, Maryland, also manufactured rug shampoos. The other contractor was located in Jonesborough, Tennessee. FDA's inspections found that these contractors' manufacturing processes did not comply with FDA's manufacturing standards.

These inspections were initiated after a Sporicidin competitor complained to FTC that the Sporicidin disinfectant was unfairly marketed. The complaint charged that a manufacturer of medical instruments recommended that its instruments be cleaned only with Sporicidin's disinfectant. As part of its investigation of the complaint, FTC staff reviewed advertisements and marketing material that Sporicidin

[1]The Federal Food, Drug, and Cosmetic Act provides that when a party intends to market, significantly modify, or change the use of a medical device, the party must submit a premarket notification to FDA 90 days before marketing the device.

[2]Every manufacturer registered with FDA is subject to inspection at least once every 2 years. The inspection covers the methods, facilities, and controls used in manufacturing, packaging, and storing medical devices. It also identifies the essential elements the quality assurance program requires.

International prepared and concluded that Sporicidin's efficacy claims for its cold sterilizing solution were false and deceptive. FTC staff shared its findings with FDA and EPA. As a result, FDA and EPA initiated their own investigations of Sporicidin products.

FDA's January 1991 inspection report for the contractor's manufacturing facility in Maryland cited 29 deficiencies. The inspection found, among other things, that (1) product ingredients were not weighed accurately, (2) two sets of records were maintained, each showing that different ingredients were used in manufacturing the products, (3) the manufacturing site was "very dirty," and (4) the manufacturer did not have procedures or records to show whether the equipment used to make a rug shampoo was properly cleaned before it was used to produce sterilants and disinfectants.

FDA's January 1991 inspection report for the Tennessee manufacturing facility stated, in part, that (1) the contractor did not have written quality assurance procedures and did not have its quality assurance procedures audited as required, (2) manufacturing equipment was not protected against filth, (3) several production lots were not tested as required to assure the accuracy of the products' ingredients, and (4) the contractor did not maintain records to show whether newly purchased product ingredients met the specifications for the product.

In January 1991, FDA notified Sporicidin International of the inspection results of the Maryland and Tennessee facilities. Because Sporicidin International did not correct the deficiencies found during the inspections of the Maryland and Tennessee facilities, FDA issued a regulatory letter to Sporicidin International on April 16, 1991.[3] In response to the letter, Sporicidin International advised FDA on May 6, 1991, that (1) the company was making internal changes at the two contractors' facilities to correct the deficiencies noted during the inspections and (2) company representatives had visited the contractors' facilities to evaluate the progress of the corrective actions being taken at them.

FDA also notified the Maryland and Tennessee contractors of the inspection results in January 1991. The Maryland contractor stopped manufacturing Sporicidin products in May 1991. The Tennessee contractor promised to take corrective action. FDA conducted a follow-up inspection

[3]A regulatory letter is issued to advise a company to take prompt action to correct deficiencies in its manufacturing practices. It warns a manufacturer that noncompliance could result in seizure of the property or injunction actions.

in December 1991 to determine whether the Tennessee contractor had made any corrections. FDA found that the corrections had not been made.

Sporicidin Product Did Not Meet FDA's Laboratory Test for Efficacy

During its inspection of the Maryland manufacturing facility, FDA collected samples of Sporicidin Cold Sterilizing Solution and tested the efficacy of the solution in the agency's Minneapolis laboratory. FDA's test found that the solution was not effective as a hospital sterilant when used according to its labeling (in a diluted form of one part of Sporicidin to seven parts of water or 1:8 dilution).

FDA tested four diluted samples of the Sporicidin Cold Sterilizing Solution and four undiluted samples of the solution. All samples were taken from newly opened bottles. FDA used the Association of Official Analytical Chemists (AOAC) testing protocol for sporicidal germicides.[4] For a sporicidal product to be used as a sterilant, as defined by AOAC and FDA, it must destroy all viruses and all bacteria, fungi, and their spores. In short, no sporicidal growth can be tolerated.

The labeling for the Sporicidin Cold Sterilizing Solution claimed that the diluted product would destroy all microorganisms after 8 hours of exposure to the product. The four diluted samples were tested and all failed the test at the 1:8 dilution. Sporicidal growth occurred on 196 of 480 carriers (41 percent) after 8 hours of exposure to the product in the diluted form, and growth occurred in 204 of 480 carriers (43 percent) after 10 hours of exposure to the product.[5] In addition, two of the four undiluted samples also failed the test. Sporicidal growth occurred in 13 of the 480 carriers (2.7 percent) after being exposed to Sporicidin for 6-3/4 hours.

Independent studies also showed that Sporicidin, which is a glutaraldehyde-phenol solution, and other products similar to it, are ineffective as hospital sterilants or disinfectants. A Canadian study showed Sporicidin in its diluted form to be ineffective against mycobacterium tuberculosis.[6] An Italian study that used the AOAC test procedures showed

[4]AOAC is an association of scientists from government, industry, and academia that helps develop and endorse standard methods of analysis for evaluation of substances subject to regulatory statutes. In 1957, AOAC developed a sporicidal-test method to determine a germicide's efficacy as a sterilant.

[5]Carriers are either small cylinders called "penicylinders" or suture loops. They are used to simulate the surface on which the product would be used, such as a medical instrument. The cylinder or suture loop is contaminated with spores the product is supposed to destroy and then used to assess the effectiveness of the product.

[6]M. Best, and others, "Efficacies of Selected Disinfectants Against Mycobacterium Tuberculosis," Journal of Clinical Microbiology, October 1990, pp. 2234-39.

Sporicidin when diluted was an ineffective sterilant against bacillus subtilis spores.[7] This study also showed that Sporicidin failed the AOAC-test protocol at a 1:8 dilution when the carriers with attendant spores were exposed to the Sporicidin solution for 24 hours, considerably longer than the 8 hours required by its labeling. A state health department also found the use of a diluted-glutaraldehyde phenate disinfectant was ineffective in sterilizing endoscopes. The health department found the disinfectant was "associated with heavy growth" of pseudomonas species on 17 of 39 endoscopes tested.[8]

The labeling for Sporicidin International's sterilizing solution claimed that the diluted solution could be reused for 30 days. However, a 1987 independent study of another glutaraldehyde-phenol solution (similar to Sporicidin) whose labeling also claimed a 30-day reuse life found that under heavy use in the diluted form it lost efficacy much sooner than 30 days, probably owing to the high dilution.[9]

Sporicidin Products Were Marketed Before Obtaining FDA's Authorization

With one exception, Sporicidin International did not obtain FDA's authorization before marketing its products as required by law. In 1983, FDA authorized marketing of a Sporicidin disinfectant solution for hemodialysis devices. Although FDA authorized this solution as a disinfectant for a single medical device, the hemodialysis device, Sporicidin International marketed its product as a sterilant for other medical devices without FDA's prior authorization. FDA later found that the sterilant that had been marketed for several years did not adequately sterilize medical instruments.

Since FDA removed Sporicidin products from the market in December 1991, FDA has authorized the sale of Sporicidin disinfectant towelettes, spray, and solution as intermediate-level disinfectants.[10] FDA authorized the marketing of these three products in early 1993 after the company provided FDA evidence of their safety and efficacy as disinfectants. FDA and Sporicidin International have agreed that before

[7]M. Fitsurra, and others, Department of Hygiene, University of Perugia, Perugia, Italy, "What About the Sporicidal Activity of Gluteraldehydes?" Presented at Second International Conference of the Hospital Infection Society on September 2-6, 1990, London, England.

[8]Ebenezer Israel, M.D., Department of Health and Mental Hygiene, State of Maryland, "Survey on Disinfection of Endoscopes," April 12, 1990.

[9]R.A. Robinson, and others, "A Suspension Method to Determine Reuse Life of Chemical Disinfectants During Clinical Use," Applied and Environmental Biology, Jan. 1988, pp. 158-164.

[10]FDA considers an intermediate-level disinfectant to be a germicide that kills all microbial pathogens, except bacterial endospores, when used according to labeling.

Sporicidin Cold Sterilizing Solution can be marketed as a sterilant, Sporicidin International will need to demonstrate to FDA through scientific evidence that that product meets FDA's efficacy standards for sterilants. As of April 22, 1993, FDA had not authorized any Sporicidin products for use as a sterilant.

EPA Finds Sporicidin Sterilant Ineffective

On December 13, 1991, EPA ordered Sporicidin International to stop the sale of Sporicidin Cold Sterilizing Solution because EPA determined the solution was not effective as a sterilant. EPA based its determination on the results of laboratory tests conducted by FDA for EPA, under an interagency agreement, that showed that the Sporicidin solution failed to perform as a sterilant when used in accordance with the labeling instructions.[11] FDA tested samples of the Sporicidin solution collected by EPA. FDA used AOAC's testing protocol for these tests.

Four diluted samples and one undiluted sample of Sporicidin Cold Sterilizing Solution were tested. The four diluted samples were tested and all of them failed at the 1:8 dilution. Spore growth occurred on 442 of 960 carriers (46 percent) after being exposed to the solution for 8 hours. Spore growth occurred on 503 of 960 carriers after 10 hours of exposure to the diluted solution. The test showed the undiluted sample destroyed the spores on all but one of the 240 carriers that were used in the test after being exposed to Sporicidin for 6-3/4 hours.

Based on the test results, in addition to its order to discontinue the sale of the sterilant, EPA assessed Sporicidin International a penalty of $430,000 because the product's labeling claims regarding its efficacy were false and misleading because the product did not perform as its labeling indicated. EPA's order and penalty applied only to the Sporicidin Cold Sterilizing Solution and not to other Sporicidin products.

However, because Sporicidin International has changed the labeling on some of its other products in response to FDA's complaints, the new labeling on these products will have to be approved by EPA before the products can be marketed again. As of April 1993, EPA had not approved the labeling changes for those products, and Sporicidin International had not met EPA's requirements to market the Sporicidin Cold Sterilizing Solution. To demonstrate the efficacy of its solution, the company contracted with an independent laboratory in July 1992 to test the solution

[11]EPA does not have laboratory facilities to test sterilants and disinfectants. Therefore, in September 1990, EPA entered into an agreement with FDA to test the efficacy of hospital sterilants.

in accordance with the EPA's requirements for efficacy. In February 1993, Sporicidin International had the laboratory terminate the test because of a lack of testing protocol, according to an official of the laboratory.

FTC Determined Sporicidin Advertising Was False and Deceptive

As noted previously, FTC's investigation was triggered by a competitor's complaint that a manufacturer of medical instruments recommended that its instruments be cleaned only with a diluted Sporicidin solution. The medical instrument manufacturer claimed the Sporicidin Cold Sterilizing Solution diluted at a 1:16 ratio was an effective high-level disinfectant for cleaning the manufacturer's medical instruments.[12] After obtaining information from various sources including FDA, EPA, and CDC, FTC staff was concerned that many of the efficacy claims made by the medical device manufacturer and Sporicidin International were false or deceptive.

On December 13, 1988, FTC staff requested Sporicidin International to provide information and documents to support the efficacy claims for the sterilizing solution. Later, in December 1988 and in January and February 1989, Sporicidin International provided the information and documents to FTC. The data the company provided did not, in FTC's opinion, support the efficacy claims for the solution. Later, in August 1989, the medical instrument manufacturer discontinued promoting the use of Sporicidin products to disinfect its products, and advised Sporicidin International of this fact. Sporicidin International, however, did not change its labeling.

On December 13, 1991, FTC filed a complaint in court to seek a preliminary injunction against Sporicidin International for false and unsubstantiated advertisements of Sporicidin Cold Sterilizing Solution. However, on February 4, 1993, the FTC Commissioner agreed to a settlement with Sporicidin International, which included a permanent injunction against the company barring it from making further unsubstantiated representations as to its product's safety and efficacy.

[12]Centers for Disease Control and Prevention defines a high-level disinfectant as a sterilant that kills all harmful microorganisms. In other words, the same formulation of a high-level disinfectant can accomplish sterilization if the exposure time (soaking) is long enough.

Sporicidin International Disagreed With Basis for Regulatory Actions

In commenting on a draft of our report, Sporicidin International disagreed with the basis for the actions taken against the company by FDA, EPA, and FTC. With respect to the three specific problems—product efficacy, manufacturing practices, and marketing authorization—that the agencies found with Sporicidin products, the company

- took exception with the validity of the AOAC test that was used to assess its product's efficacy,
- stated that the manufacturing deficiencies were not part of the basis for FDA's sanctions and that the deficiencies were corrected, and
- implied that although it did not have FDA's authorization to market its sterilant, its products had been registered with EPA since 1976 and, therefore, they were approved for marketing.

Validity of AOAC Test

Sporicidin International contended that the AOAC Sporicidal Test that FDA used to assess the efficacy of Sporicidin Cold Sterilizing Solution is unreliable. To support its contention, the company referred to (1) an EPA Federal Register notice and (2) transcripts of a court hearing involving another company in which EPA and the court were purported to have said the AOAC test was not valid for testing the efficacy of sterilants. However, we believe that neither the Federal Register notice nor the court transcripts that Sporicidin International provided to us support the company's contention.

Sporicidin International stated that EPA considers the test to be unreliable, inconsistent, and nonreproducible and cited an EPA Federal Register notice to support its statement. The Federal Register notice, however, did not say that EPA believes the AOAC test is faulty. The notice stated that questions have been raised about the AOAC test by some sources outside of EPA, and the notice solicited proposals for a research study to address allegations that the test lacks reliability and reproducibility.

EPA awarded a contract to the University of Ottawa for the study. The study is expected to be completed in September 1996. EPA officials told us that Sporicidin International had misrepresented EPA's position on the AOAC test. Additionally, EPA officials said that EPA will continue to use the AOAC test because it has no reason to believe the test is unreliable. AOAC concurred with EPA that the test is valid for its purpose.

Regarding its contention that a court has determined that the AOAC test is not valid, Sporicidin International stated that a U.S. district court judge

had found essentially identical test results involving another company's sterilant product "not valid," and the company further stated that the "judge found EPA's reliance on the FDA lab's performance of the test to be legally arbitrary and capricious." The court in this case was reviewing a motion for a restraining order "to prevent further government publication and release of information relating to the alleged failure of plaintiff's products in April 1991 tests."

According to the transcript excerpt provided to us by Sporicidin International, the judge did not make any determinations regarding the validity of the AOAC test. The judge stated: "I do not - and I wish to be clear - address in any respect and as I indicated a number of times through the course of the hearings, whether the AOAC test should or should not be used by the EPA in discharge of its regulatory function." However, because there was no documentation to determine whether FDA followed good laboratory practices in testing this one product, the judge stated that EPA in deciding to publish the test results arbitrarily and capriciously failed to adequately review the test protocol from the April 1991 test. Because the judge's comments applied only to the performance of a particular test on a specific product and not to the validity of the AOAC test in general, his opinion would not apply, as Sporicidin claims, to the tests that were performed on the Sporicidin product.

Problems With Manufacturing Practices

Sporicidin International noted that the manufacturing deficiencies cited in FDA's inspection reports of Sporicidin's manufacturing facilities were not an issue in FDA's sanctions that included seizure of the company's products. While the manufacturing deficiencies were not cited in the seizure actions, one purpose for the inspections was to collect the product samples that FDA used for its efficacy tests. FDA officials told us that FDA had considered including the manufacturing deficiencies in its basis for the sanctions taken against the company. FDA officials said, however, that the laboratory tests showing that the company's sterilant was ineffective and the lack of a premarket authorization were sufficient to support FDA's actions against the company.

Sporicidin International said that the company and its contract manufacturers took actions to correct the manufacturing deficiencies that FDA found in its inspections. The company also complained about dual regulation by FDA and EPA and stated that EPA inspected the manufacturing facilities during the past 14 years.

Since each agency regulates hospital sterilants and disinfectants under different legislative authority and for different purposes, there is a potential for some overlap between the two agencies' regulation of these products. However, we are not aware of any EPA inspections of the contractor's manufacturing facilities to determine compliance with good manufacturing practices. Nor did Sporicidin International provide us with EPA inspection reports or information on the results of any EPA inspections. EPA officials told us that EPA has not inspected the manufacturing facilities for Sporicidin products nor does it have authority to inspect manufacturing facilities to determine compliance with good manufacturing practices. The EPA officials said that EPA visited the manufacturing facilities for Sporicidin products only to collect product samples to test.

Regarding the assertion that the manufacturers corrected the deficiencies found during FDA inspections, Sporicidin International did not provide us any inspection reports or other documentation to show that the deficiencies were corrected. In fact, as noted earlier, FDA's follow-up inspection at one manufacturing facility found that the deficiencies were not corrected, and the manufacturer at the other facility voluntarily stopped producing Sporicidin product, obviating the need for a follow-up inspection.

Lack of Premarket Authorization

Sporicidin International acknowledges that it did not have FDA's authorization to market its cold sterilizing solution. However, the company points out that FDA is allowing other companies to market hospital sterilants and disinfectants without FDA's premarket authorization. This deficiency in FDA's regulation of these products is discussed in appendix II of this report.

Although it has not had FDA's authorization to market its sterilizing solution, Sporicidin International notes that its products have been registered with EPA for marketing since 1976. The company notes that on December 12, 1991, 1 day before its products were seized, EPA sent Sporicidin International a notarized letter stating the products could be sold and marketed in the United States. Also, the company points out that since 1983 it has had an FDA authorization to market a disinfectant for hemodialysis devices.

Sporicidin products have been registered with EPA, as the company claims. Also, the company stated that in 1977 EPA tested its sterilant product using

the AOAC testing protocol and the product passed the test. At that time, EPA tested the product in an undiluted form rather than in the diluted form its current labeling recommends for usage of the product. When Sporicidin Cold Sterilizing Solution was tested in 1990 in a 1:8 dilution form in accordance with its labeling it was found ineffective as a sterilant (see p. 15). Based on this finding, EPA took action to stop the sale of the cold sterilizing solution. EPA officials explained to us that although a product's sale is restricted, its registration is not revoked. Once the problems with the product are corrected the sale restriction is lifted and it can be sold again.

EPA admitted that it made an error when it provided the December notarized letter to Sporicidin International. The responsibilities for registering products and for regulating their safety and efficacy rest in two different EPA units—registration and compliance units. An official in the registration unit told us that companies often request notarized letters to validate that their products are in fact registered with EPA for various business reasons. EPA routinely provides the letter if there are no regulatory actions pending against the products. The official said that the December letter was issued in response to a request from Sporicidin International without first checking with the compliance unit to determine whether any actions were pending against the company. This EPA official told us that the two units have taken measures to coordinate with each other to avoid similar situations in the future.

Since 1983, when FDA authorized a Sporicidin disinfectant to be marketed for hemodialysis devices, Sporicidin International changed the labeling on the product to claim that the disinfectant could also be used as a sterilant for other medical instruments, such as endoscopes. In 1983 the labeling directed that the product be diluted with water at a ratio of 1:35 (one part Sporicidin to 34 parts water). Later, the company changed the labeling stating the product could be used as a disinfectant at a reduced dilution ratio of 1:16 and as a sterilant at a dilution ratio of 1:8. These labeling changes required the company to obtain a new authorization from FDA to market its product, which Sporicidin International failed to do.

Although a company is registered with EPA, the registration is not a substitute for FDA's premarket authorization for hospital sterilants because each agency's requirements differ. In part, FDA requires manufacturers to demonstrate the safety and efficacy of their products under conditions that simulate actual use. This requirement is to assure that residues from the sterilant do not remain on the medical instruments after they are

sterilized. Such residues could pose a risk to a patient. EPA's efficacy requirements can be met with tests that are performed under laboratory conditions, which do not involve use of the sterilant on medical instruments.

Other Sporicidin International Comments

Other Sporicidin International comments and our evaluations of them are presented below.

- The company stated that Sporicidin products have been on the market for about 14 years and that there have been no reported illnesses or infections resulting from the use of these products.

  Although there may not be any reported incidents of illness associated with the use of a product, a product is considered adulterated if, as in the case of Sporicidin International's Cold Sterilizing Solution, it is marketed without FDA's authorization, it does not perform as its labeling claims, or it is manufactured under conditions that could cause it to become adulterated. Because adulterated products, by definition, are considered to pose a risk to the public health, they are subject to regulatory action on this basis alone, without the need to show reported incidents of illness or infection.

- Sporicidin International said that it had responded to FDA's request for information on the company's submission for premarket authorizations for its disinfectants since October 1990 and that FDA authorized the sale of the disinfectants in February 1993, 14 months after the company's operations were suspended, without changes in their ingredients.

  The products' ingredients may not have changed, but the products' labeling changed in 1983 when FDA authorized marketing a Sporicidin disinfectant product for hemodialysis devices. Once a product's labeling is changed, a company must obtain a new authorization from FDA before it markets the product with the new labeling.

  Sporicidin International made a labeling change that expanded the use of its disinfectant. In addition to hemodialysis devices, the revised product labeling claimed it could be used for other medical devices and instruments, such as endoscopes. To obtain a new authorization Sporicidin International must show that its disinfectant is safe and effective when used in accordance with its revised labeling. Notwithstanding the information that the company may have provided to

FDA since December 1991, it had not been able to adequately demonstrate to FDA's satisfaction that the disinfectants performed as claimed in its new labeling until February 1993.

- Sporicidin International disagreed with FTC's conclusion that the company claimed that its high-level disinfectant at a diluted ratio of 1:16 was a sterilant. The company stated that FTC's conclusion was erroneous because the company never made that claim, and it has letters from CDC saying it is a high-level disinfectant.

  Because Sporicidin International entered into a settlement with FTC after the complaint was filed, the FTC's complaint was never finally adjudicated. Sporicidin International agreed, without admitting to any violation of law, to stop making any representations that, among other things, the cold sterilizing solution when diluted 1:16 can be used as a high-level disinfectant. Therefore, the accuracy of the charges has never been determined. The product that Sporicidin International stated is a high-level disinfectant is the same product it marketed as a cold sterilizing solution. The basic difference between its use as a sterilant and disinfectant depends on its rate of dilution, and the length of time it remains in contact with an instrument. At a dilution ratio of 1:8 the company claims its cold sterilizing solution is a sterilant, and at 1:16 it is a disinfectant. Sporicidin International did not provide any evidence showing that CDC considered the Sporicidin Cold Sterilizing Solution to be a high-level disinfectant when diluted 1:16. The CDC letters the company provided to us did not mention anything about the effectiveness of Sporicidin products in a diluted form.

- Sporicidin International stated that EPA, FDA, and CDC have different and conflicting definitions for hospital germicides, which causes confusion for industry in attempting to conform to government regulations.

  The differing ways the three agencies define disinfectants might cause some confusion. EPA defines a disinfectant differently than FDA and CDC, whose disinfectant definitions are similar. However, EPA, FDA, and CDC define sterilants the same way and, therefore, their definition for sterilants should not cause confusion to the industry. The three agencies require a sterilant to kill all harmful microorganisms, including their highly resistant spores. FDA and EPA took action against the company because they determined that the company's cold sterilizing solution did not meet the agencies' efficacy requirements for sterilants. And FDA took action against the company's disinfectants because they were marketed without FDA's

authorization. Neither FDA's nor EPA's definition for disinfectants was a basis for any actions taken against Sporicidin International. EPA did not take action against the company regarding its disinfectants.

- Sporicidin International stated that "each agency requires different tests, has its own standards and its own philosophies."

  Each of the three agencies has a distinct statutory mission to protect different aspects of the public interest. The standards and testing procedures adopted by FDA and EPA reflect their separate responsibilities. FTC is authorized to halt companies from making false, misleading, and deceptive advertising representations affecting commerce. EPA is charged under the Federal Insecticide, Fungicide, and Rodenticide Act to regulate disinfectant products regarding their chemical composition, hazards associated with use of the product, and effectiveness claims against specific microorganisms. FDA has responsibility under the Medical Device Amendments Act of 1976 to regulate medical devices intended for human use to ensure their safety and effectiveness.

- Sporicidin International complained that FDA requires the company to conduct specific testing in order to obtain FDA's authorization to market its sterilant; but EPA refuses to allow shipment of product samples to laboratories for the FDA testing and has proposed a $30,000 fine on the company for sending samples to laboratories.

  EPA would have allowed Sporicidin International to ship products to laboratories for testing if it met certain conditions. EPA proposed the fine in a complaint it issued alleging Sporicidin International shipped products to laboratories without complying with those conditions.

  EPA's Stop Sale, Use, or Removal Order provides that all quantities of Sporicidin Cold Sterilizing Solution covered by the order shall not be sold, used, or removed except as provided in the order. The order states that failure to comply with it will constitute a violation of the Federal Insecticide, Fungicide, and Rodenticide Act and subject the company to applicable penalties prescribed in the law. On March 26, 1992, EPA advised Sporicidin International and Sporicidin International's attorney that EPA would vacate the order to allow "removal (that is, shipment) of new batches of Sporicidin Cold Sterilizing Solution for the purpose of testing," provided certain information, including the information on the composition and supplier of raw material and the formulation of specific ingredients, was first provided to EPA. Sporicidin International told us they

could not comply with EPA's order before testing since the specific ingredients in Sporicidin Cold Sterilizing Solution would not be known to them until the laboratory testing was performed.

The purpose of the required laboratory test is to verify that the product's actual ingredients are the same as those the company claims are in the product. Shipping new batches of its product for laboratory testing would have been permitted if the company first provided EPA information on ingredients and the sources of the raw materials for the product it intended to ship for testing. Although the company knew what ingredients it used to formulate its product, it did not provide EPA the required information and shipped batches of the product contrary to EPA's requirement.

In a July 27, 1992, letter to EPA, Sporicidin International requested an opportunity to address EPA's view that the company may have violated the stop sale order. In the letter, the company noted that the order and EPA's March 26 letter were based on the premise that the company would formulate new batches of buffer (a product ingredient) for any testing; however, it decided to test batches with existing buffer solution. The company further noted that it was "quite clear that 'to ship the product to the laboratory violates the EPA Order.'" On September 4, 1992, Sporicidin International advised EPA that it had made shipments of Sporicidin Cold Sterilizing Solution to six laboratories for testing. The company had not complied with the conditions in the stop order before shipping the products. On October 14, 1992, EPA issued a complaint against the six shipments of the cold sterilizing solution in which EPA proposed a $5,000 penalty for each shipment for a total of $30,000.

- Sporicidin International stated that the FDA laboratory that performed the test for EPA did not follow good laboratory practices and quality assurance or quality control.

We did not review the practices followed by the FDA laboratory because we did not have the expertise to conduct such a review. FDA laboratory officials told us that the laboratory follows the practices of its Quality Assurance Program. The company's allegation concerning the laboratory was based primarily on the views of two consultants who reviewed FDA laboratory records at the request of the company. Based on the records they reviewed, the consultants concluded that the laboratory did not comply fully with good laboratory practices. However, both consultants stated that they were unable to determine whether the results and

conclusions of the FDA laboratory study were valid. The copies of the consultants' reports and statements that Sporicidin International provided to us did not indicate whether they reviewed the laboratory's Quality Assurance Program.

- Sporicidin International stated that our report refers to several irrelevant, refuted, or fictitious tests.

  In our report, we refer to four studies in which the Sporicidin sterilant or products containing ingredients that are similar to the Sporicidin sterilant were tested. To support its comment, Sporicidin International provided us with a critique of several papers and articles that apparently question the efficacy of the Sporicidin sterilant. The critique done by a consultant at the request of Sporicidin International's attorneys took exception with the conclusions of the papers and articles. The critique addressed only one of the four studies we refer to in this report. Further, the study that the consultant critiqued was published in a professional journal that subjects studies to peer review to assess the reasonableness of their methodology and the credibility of their results. Sporicidin International did not provide any specific comments regarding the other three studies.

- Sporicidin International suggested that FDA based its seizure action against its products on an "unofficial 'Guidance' document" issued 1 month after the seizure action and that issuance of the guidance did not comply with Administrative Procedures Act (APA) requirements for obtaining public notice and comment on regulations.

  FDA's seizure action was not based on the guidance issued in January 1992 (which superseded earlier 1986 guidance) but, among other things, on Sporicidin's failure to fulfill the requirements for registering and listing medical devices as required by statute and by 21 C.F.R. Part 814, regulations published and promulgated in 1977 after public notice and an opportunity by interested persons to comment (42 Federal Register 42520, Aug. 23, 1977).

  In our opinion, it is not clear that the "unofficial 'Guidance' document" would be subject to APA. APA requires an agency to follow notice and comment procedures when it promulgates regulations pursuant to statutory authority that are intended to have the force and effect of law, are substantive, and which affect individual obligations. Issuances that merely clarify or explain an existing rule or statute are not subject to APA notice and comment procedures.

- Sporicidin International alleged that the travel of certain FDA and CDC employees in the United States and abroad, with costs paid by a major competitor, Johnson & Johnson, constitutes a clear appearance of conflicts of interest, particularly in that these same individuals are directly involved in the enforcement action against Sporicidin International.

  Department of Health and Human Services employees are permitted by statute to accept payment for travel and subsistence expenses from nongovernment entities to attend meetings or perform advisory services concerning Department functions or activities. The authority to approve the acceptance of such travel expenses is formally delegated from the Secretary to the heads of major organizations of the department or higher authorities. Some travel expenses of the CDC official in question were paid by Johnson & Johnson as statutorily authorized. CDC did not, however, take any enforcement action against Sporicidin International. While FDA did bring an enforcement action against Sporicidin International, none of the travel expenses of the FDA official in question were paid by Johnson & Johnson.

FDA's Program to Regulate Hospital Sterilants and Disinfectants Has Been Inadequate

Although the Food and Drug Administration is responsible for ensuring that hospital sterilants and disinfectants that are used for medical devices are safe and effective in killing harmful microorganisms before they are marketed, its regulation of these products does not provide such assurances.

As previously discussed, before hospital sterilants and disinfectants can be marketed, manufacturers must submit to FDA a premarket notification. A premarket notification must contain evidence that the products are safe and effective or otherwise substantially equivalent to a similar product already marketed. Manufacturers must also register their establishments and list their products with FDA.

Generally, manufacturers have not been complying with these requirements. Notwithstanding the FDA Commissioner's stated concern in December 1991 about the health risks associated with ineffective hospital sterilants and disinfectants, FDA has done little to regulate these products.

More specifically, FDA has not enforced the requirement that manufacturers submit premarket notifications and register their products. FDA has had information from the Environmental Protection Agency indicating that many companies are manufacturing hospital sterilants and disinfectants for sale. Moreover, FDA's inspections of manufacturers' facilities have been limited. FDA is required to periodically inspect a manufacturer's facilities to make sure the products are manufactured in compliance with FDA's regulations for good manufacturing practices. Without effective regulation, FDA has insufficient basis for assuring the public that these products are safe and effective.

FDA Has Not Authorized Most Products

Information we obtained from FDA shows that as of February 1993, 24 companies have registered with EPA to sell 59 hospital sterilants that are subject to FDA regulation. These include 36 liquid sterilants and 23 ethylene oxide gas sterilants.[1] An EPA official advised us that about 330 companies have registered with EPA to sell about 1,200 disinfectants. FDA has not reviewed the 1,200 disinfectants registered with EPA to determine what number of them are intended for use with medical devices.

[1]The 23 ethylene oxide gas sterilants are subject to both FDA and EPA regulation. However, since at least 1980, EPA has assumed responsibility for regulating these products. FDA's 1980 final rule on regulating ethylene oxide gas sterilizers noted that FDA and EPA had been discussing the regulation of ethylene oxide gas sterilants and would develop a memorandum of understanding concerning each agency's responsibility for the regulation of the device. Until the memorandum is published, EPA will continue to be responsible for regulating the gas sterilant. As of February 23, 1993, a memorandum of understanding had not been prepared.

Information FDA provided to us showed that as of April 22, 1993, 23 companies had submitted premarket notifications for 26 sterilants and 23 disinfectants. FDA has authorized 16 of these products for marketing—3 sterilants and 13 disinfectants. Of the remaining 33 products: FDA did not authorize the sale of 1 product, the manufacturer of another product withdrew its premarket notification, and FDA deleted premarket notifications for 5 other products because the manufacturer did not provide required information on time. FDA had not completed its review of 26 products as of April 22.

According to EPA, hospital sterilants are widely used in hospitals on medical and surgical instruments and equipment and are most "crucial" to infection control. Hospital disinfectants are considered important to infection control. EPA reassessed its policy for regulating sterilants and disinfectants and developed a plan to test products that are registered.

The plan provides that EPA will test all sterilants, as well as any disinfectants that claim to be a tuberculocidal. The policy change was influenced by existing information, including laboratory data and data in scientific journal articles, that suggested some products were not efficacious, and a GAO report that pointed out that EPA's disinfectant program did not provide assurance that registered disinfectants were effective.[2]

The burden for filing a premarket notification rests with the manufacturer. FDA has relied on manufacturers to voluntarily comply with this requirement. In our view, FDA should identify manufacturers of hospital sterilants and disinfectants. FDA then has the responsibility under the Federal Food, Drug, and Cosmetic Act to pursue those manufacturers that it knows are manufacturing products for sale requiring FDA's prior authorization. EPA provided information to FDA on the 59 sterilants that were registered with EPA. Recently FDA has tested the efficacy of 26 of the 59 sterilants for EPA. Five products failed, or are expected to fail, 7 passed, and the results of the remaining 14 were pending as of April 2, 1993.

FDA advised us that it also tested the efficacy of nine sterilants for its own purposes. FDA reported that based on completed or partially completed tests four products passed or are expected to pass the test and five failed or are expected to fail. (Nine products were included in the products FDA tested for EPA and the results for them were the same—three passed, one failed, and the results of five are pending).

[2]Disinfectants: EPA Lacks Assurance They Work (GAO/RCED-90-139, Aug. 30, 1990).

An FDA official told us that EPA also had provided FDA with a list of registered manufacturers 3 years ago. However, the official said that FDA had not reviewed the list to identify manufacturers that produce hospital sterilants and disinfectants that should be regulated by FDA.

Other FDA officials told us that for the most part FDA had not sought premarket notifications from manufacturers because it did not have enough staff to review them. These officials said that FDA already reviews about 5,000 premarket notifications for premarketing medical devices annually. They believed that the FDA staffing allocated to review these premarket notifications did not allow for any significant increase in work load.

In 1990, FDA developed a plan to monitor hospital sterilants and disinfectants. The plan called for (1) inspecting facilities that manufacture sterilants and disinfectants, (2) obtaining and analyzing samples of such products, and (3) requesting manufacturers to submit premarket notifications for their products. However, the scope of the plan was limited to 22 of the 59 sterilants that were registered with EPA and only 24 disinfectants. An FDA official told us that the lack of FDA resources limited the plan's scope.

In January 1993, FDA requested labeling information from about 350 manufacturers about their products. This information is expected to help FDA determine what, if any, action manufacturers need to take to comply with requirements for the manufacture and sale of their products. An FDA official told us he did not know how many manufacturers responded, but he believed that most of the firms replied to the agency's request. FDA expects to begin analyzing the replies after mid-1993, when the agency anticipates having more staff resources available.

Most Manufacturers Had Not Registered With FDA

Of the more than 300 manufacturers of sterilants and disinfectants registered with EPA, only 5 manufacturers had registered and listed their products with FDA as of April 1993. Every manufacturer of a hospital sterilant or disinfectant must register its establishment and list its products with FDA each year. Like the premarket notification requirement, primary responsibility for registration rests with the manufacturer.

Although it is a manufacturer's responsibility to comply with the registration requirements, FDA, which is responsible for ensuring that medical devices are safe and effective, should seek compliance from

known manufacturers who have not registered. However, FDA has done little to determine which manufacturers should be registered.

FDA Had Made Limited Inspections of Manufacturers' Facilities

Although FDA is required to inspect the facilities of all sterilant and disinfectant manufacturers biennially, it has not inspected the facilities of most manufacturers. Although only five companies had registered with it, FDA had identified additional manufacturers from other sources. Based on this information, FDA inspected 23 of the more than 300 sterilant and disinfectant manufacturers between October 1990 and December 1992. Inspections are important to ensure that products are manufactured in accordance with FDA's prescribed good manufacturing practices.

Of the 23 manufacturers it inspected between October 1990 and December 1992, FDA found deficiencies at about 50 percent of them. Two manufacturers had deficiencies that were serious enough to cause seizure of their products. FDA's district offices recommended products of four other manufacturers be seized. FDA had not made a decision on these recommendations as of March 25, 1993. Inspections at two other manufacturing facilities found that good manufacturing practices were not followed and one product was misbranded. As a result, the manufacturers voluntarily discontinued marketing their products.

An FDA official claimed that FDA is unable to inspect more manufacturers in part because of limited resources. But an equally important reason for its inability to inspect more facilities would seem to be that it does not have a complete inventory of manufacturers because it has not reviewed EPA's list of 1,200 hospital disinfectants to determine what number of them are intended for use with medical devices.

Conclusions

FDA's current regulation of sterilants and disinfectants has not provided adequate assurance that these products are safe and effective in killing harmful microorganisms. In view of the importance of these products, we believe that FDA should give more attention to assuring their safety and efficacy.

Because manufacturers have not generally complied with registration and premarket-authorization requirements, FDA should make a more concerted effort to identify manufacturers and seek compliance with the requirements. In this regard, FDA should contact and direct all manufacturers who should but have not submitted premarket

notifications, to do so. Manufacturers are responsible for demonstrating the safety and efficacy of their products. In the absence of a premarket notification, FDA has a responsibility to prohibit the sale of a product.

FDA's proposed efforts to request information from known manufacturers are a positive step in strengthening its regulation of hospital sterilants and disinfectants. However, FDA needs to develop a strategy for assuring that (1) information submitted by manufacturers is reviewed in a timely manner and (2) manufacturers comply with law and FDA regulations. Regarding the latter, FDA could obtain periodically EPA information on hospital sterilants and disinfectants and use the information to monitor and enforce compliance with laws and regulations pertaining to these products.

To make efficient use of its limited resources, FDA should coordinate its testing of products with EPA so that the same product is not tested separately by FDA for each agency. FDA and EPA have been negotiating a memorandum of understanding regarding the regulation of hospital sterilants and disinfectants. FDA and EPA officials declined to discuss the specifics of the proposed memorandum as it was still being negotiated. As a minimum, we believe that the memorandum should cover testing of products to avoid unnecessary duplication.

Recommendations to the Commissioner of the Food and Drug Administration

We recommend that the Commissioner of FDA (1) develop a plan to identify all manufacturers of sterilants and disinfectants to ensure that they comply with the law, (2) devise a strategy to ensure that in the future sterilants and disinfectants are not marketed without FDA's prior authorization, and (3) in coordination with EPA develop procedures that would satisfy the requirements of both FDA and EPA for testing hospital sterilants and disinfectants to avoid unnecessary duplication of product testing.

Scope and Methodology

To evaluate the Food and Drug Administration's effectiveness in regulating hospital sterilants and disinfectants, we reviewed applicable laws and regulations and FDA's policies and procedures for implementing them. We reviewed FDA's data bases to determine whether the manufacturers of these products were complying with regulatory requirements by (1) registering their products with FDA and (2) obtaining authorization from FDA before marketing these products. Registration enables FDA to identify the manufacturers and the products. Requiring premarket notifications for products provides FDA the opportunity to review data that are intended to support the products' safety and efficacy.

In addition, we reviewed FDA's plans for conducting independent laboratory tests for safety and efficacy on these products and for conducting facility inspections to assure compliance with manufacturing standards. To obtain an understanding of the rationale for these plans, we discussed the plans with FDA officials who have regulatory responsibility for products that kill harmful microorganisms.

To determine the circumstances and rationale for removing Sporicidin products from the market, we reviewed FDA and EPA policies and plans for testing the safety and efficacy for hospital sterilants and disinfectants and interviewed cognizant FDA, EPA, and FTC officials. Also, we reviewed pertinent documentation from the regulatory agencies to establish the chronology of events that precipitated seizure of Sporicidin products. We interviewed Sporicidin International officials to obtain their perspective of the actions taken against the company.

Because the regulatory actions against the company were based largely on (1) the results of FDA's laboratory tests of the Sporicidin cold sterilant and (2) the failure of Sporicidin International to obtain authorization from FDA to market the product, we discussed the laboratory testing with cognizant FDA laboratory officials, and reviewed FDA policy and procedures for approving sterilants before marketing. Also, because FDA is required to periodically inspect facilities that manufactured the products, we reviewed FDA's inspection procedures and the results of facility inspections. We obtained information on actions that FDA had taken or was in the process of taking against other manufacturers of similar products.

We provided draft copies of our report to the regulatory agencies for comment and incorporated their comments as appropriate in the report. We also provided Sporicidin International an opportunity to review segments of the draft report that related to its products. The company

subsequently provided written comments to us (see app. IV) which we responded to beginning on page 17.

We conducted our review between May 1992 and March 1993 in accordance with generally accepted government auditing standards.

Comments From Sporicidin International

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March 5, 1993

Mr. Albert B. Jojokian
Assistant Director
NGB/Health Financing & Policy
U.S. General Accounting Office
441 G Street, N.W.
Washington, D.C. 20548

Re: **SPORICIDIN'S COMMENTS ON THE GAO "DRAFT" REPORT ON FDA, EPA AND FTC TREATMENT OF SPORICIDIN**

Dear Mr. Jojokian:

The GAO report fails to address key issues, ignores significant documentary evidence, and over-simplifies complex regulatory and scientific issues. In the spirit of fairness that every American expects from a *government agency, we respectfully request the GAO to revisit the voluminous information and data which* Sporicidin and the House Government Operations Committee gave to the GAO investigators during the past 2 years. None of the material was referenced in the report. The issuance of the report should be delayed until this material is evaluated and included. We cannot understand how the GAO can produce a fair, unbiased report without evaluating and commenting on the available evidence. Many of the key documents *are attached to this letter for your convenience. (The superscript numbers indicate the tab numbers for the* documents described.)

BRIEF HISTORY

1. *On 12/13/91, the EPA and FDA seized Sporicidin.* EPA *and FDA press releases*[1] *on the* same day said the Centers for Disease Control informed EPA and FDA that CDC has no report of any illness resulting from the use of Sporicidin products in the products' 14 year history. At the time, annual medical and hospital sales were $10 million.
2. FDA enforcement personnel recently informed the GAO and Congressman Dingell's staff that FDA has no evidence of any illness or infection due to failure of Sporicidin products to work as claimed.
3. On 12/12/91, one day before the seizure, EPA stated in a notarized letter that ..."the products [i.e., Sporicidin Cold Sterilizing Solution, or "SCSS"] may be sold and marketed in the United States of America for the uses indicated on the label".[2]
4. *On 2/12/93, 14 months after being forced to suspend operations, all Sporicidin disinfectant* products were issued FDA 510(k) marketing authorizations with no changes in the ingredients or in the EPA-registered germicidal claims.[3] But, the Government's actions have cost Sporicidin over $5,000,000 (to date) and the loss of its market share, internationally.

The GAO report makes no mention of this background.

INFECTION CONTROL

THERE IS NO VALID SCIENTIFIC TEST BASIS FOR THE CHARGES AGAINST SPORICIDIN

1. In the 12/6/90 Federal Register, EPA listed 10 reasons why the AOAC Sporicidal Test is *unreliable, inconsistent and non-reproducible.*[4] The EPA and FDA know this test is faulty. Yet, EPA and FDA regulatory actions are based on this test.
2. EPA is funding $490,000 in research to find a reliable test.
3. GAO does not address the faulty AOAC Sporicidal Test and the much-criticized FDA lab's testing, nor the related scientific issues which are critical to an unbiased report.[5,6,7]
4. According to FDA staff, "If you're lucky, you pass the test on the day FDA tests your product."
5. The FDA lab that performed the test for EPA did not follow Good Laboratory Practices (GLP) and Quality Assurance/Quality Control (QA/QC).[8,9,10,11]
6. EPA fines industry and laboratories that submit non-GLP data to EPA under FIFRA, yet EPA's prosecution of Sporicidin is based on non-GLP data.[12]
7. A U.S. District Court Judge (*Metrex* vs. *EPA*) has found "not valid" essentially identical "test results" (same test, same lab, same lab technicians, same time frame, same types of inconsistent data and failure to follow GLP and QA). The Judge found EPA's reliance on the FDA lab's performance of the test to be legally arbitrary and capricious. The Judge enjoined EPA from publicly disclosing the "test results".[13]
8. GAO refers to several irrelevant, refuted, or fictitious tests.
9. GAO apparently had no scientific expertise on its evaluation team, and did not bring in any expert consultant.

The GAO report is silent on the un-reliability of the AOAC Sporicidal Test and the FDA laboratory's non-GLP, non-QA/QC testing.

THE AGENCIES' REGULATORY METHODS CONFLICT

1. EPA, FDA and CDC have different and conflicting definitions for hospital germicides. This is a major cause of confusion for industry in attempting to conform to government regulations, and for users.[14]
2. FDA requires Sporicidin to conduct specific testing for 510(k) marketing clearance for Sporicidin Cold Sterilizing Solution (SCSS), but EPA refuses to allow shipment of samples to laboratories for the FDA testing and has proposed a $30,000 fine on Sporicidin for sending samples to laboratories.
3. Each agency requires different tests, and has its own standards and its own philosophies.

The GAO report is silent on the different agencies' conflicting definitions, and on the restrictions EPA has placed on testing.

THE AGENCIES ARE ENGAGING IN ARBITRARY, SELECTIVE ENFORCEMENT

1. FDA forced all Sporicidin products off the market on 12/13/91 because of lack of 510(k) premarketing authorization. The products have been available since 1976, registered with

EPA under FIFRA. No other hospital disinfectant was taken off the market even though their products did not have 510(k)s.

2. Sporicidin responded to FDA's 510(k) information requests from October 1990 onward. FDA planned to terminate all Sporicidin's 510(k) applications in 1991, without proper cause.[15]
3. On 10/23/92 FDA wrote: "[...] the chemical germicides manufactured by Metrex Research Corporation and Johnson & Johnson [...] have not been cleared through the premarket notification process [510(k)] and thus are not legally marketed in the United States."[16]
4. On 12/2/92 FDA wrote: "I can assure you that [FDA] is not concentrating on any single individual or firm and is enforcing all of its laws as equitable [sic] as possible".[17]
5. EPA and FDA are also aware that J&J's former research director for the Cidex products has given sworn testimony in the *Metrex* case in Colorado federal court that in hundreds of tests Cidex and Metrex products failed the required AOAC Sporicidal test 20-25% of the time.[18]
6. In spite of the above, neither FDA nor EPA has taken action against the Cidex (J&J) product line.

The GAO report makes no mention of these arbitrary actions.

FDA IGNORES THE ADMINISTRATIVE PROCEDURE ACT (APA)

1. FDA has not followed Administrative Procedure Act requirements for public notice and comment on regulations for germicide 510(k)s.[19]
2. FDA issued an unofficial "Guidance" document for germicide 510(k)s in January 1992, more than one month after FDA had seized Sporicidin products for lack of a 510(k).
3. The Chemical Specialties Manufacturers Association has publicly criticized FDA's regulatory process and the "Guidance" document.

The GAO report is silent on FDA's violations of the Administrative Procedure Act, and on industry's legal and scientific arguments against FDA's regulation of liquid germicides.

FTC

1. GAO accepted the FTC's conclusion that Sporicidin claimed sterilization or high-level disinfection for SCSS diluted 1:16 and that the claim was false and deceptive. This is an erroneous conclusion by FTC and GAO because Sporicidin never made that sterilization claim, and Sporicidin has four letters from CDC saying it is a high-level disinfectant.[20]
2. GAO ignores a comprehensive critique by Dr. Frank Engley of numerous articles cited by FTC. Dr. Engley, a prominent, world-renowned microbiologist, concluded "...the articles are not reliable and competent scientific evidence of Sporicidin's efficacy".[21]
3. GAO ignores the part of the Sporicidin-FTC settlement that says the settlement does not constitute an admission of violations of law as alleged in the FTC's Complaint.

The GAO report failed to independently assess the facts of the FTC allegations.

THE GAO REPORT MAKES AN ISSUE ABOUT ALLEGED LACK OF GOOD MANUFACTURING PRACTICES (GMP)

1. GMP is not an issue in the FDA's Complaint.
2. EPA inspected the manufacturing facilities under FIFRA during the 14-year history of Sporicidin. Now, we have dual regulation by both EPA and FDA.
3. Sporicidin and its contract manufacturers took corrective steps in response to the FDA inspections.

GOVERNMENT EMPLOYEES ARE PARTICIPATING IN COMPANY-FUNDED TRAVEL AND ACTIVITIES THAT ARE OBVIOUS CONFLICTS OF INTEREST

1. FDA and CDC employees have traveled extensively in the U.S. and abroad to China, Russia, etc., as evidenced by travel records obtained under FOIA, with costs paid by Johnson & Johnson, our major competitor. Even if the travel is technically legal under FDA and CDC agency rules, this presents the clear appearance of conflicts of interest.
2. These same individuals who traveled for the major competitor are directly involved in the current enforcement actions against Sporicidin.

The GAO report ignores these serious conflicts of interests.

CONCLUSION

GAO has taken statements and documents provided by FDA, EPA, and FTC at face value. On the other hand, statements and documents provided by Sporicidin and the U.S. House of Representatives Government Operations Committee were completely ignored in the GAO report. The report reflects no independent, objective, investigation of the facts, and no critical analysis of the policy and legal positions asserted by the three agencies. The report is highly biased and misleading regarding the propriety of the agencies' actions.

As The Washington Post reported, the Sporicidin case cries for a full-fledged investigation to untangle questions of ethics, conflicts of interest, sloppy laboratory testing, selective enforcement, interagency feuding, and bureaucratic arrogance that permeate this case.

We hereby request:

1. That these comments be included in their entirety in the final GAO report .
2. That Sporicidin be granted an "exit meeting" before the final GAO report is released.

Sincerely,

Robert I. Schattner, D.D.S.
President

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