



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

OCT 21 2002

Michael F. Jacobson
Executive Director
Center for Science in the Public Interest
1275 Connecticut Ave, N.W.
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Washington, DC 20009

Re: Docket No. 98P-0504/CP1

Dear Dr. Jacobson:

This letter responds to the citizen petition submitted by the Center for Science in the Public Interest (CSPI), dated June 29, 1998. In that petition, CSPI requested that the Food and Drug Administration (FDA) establish a performance standard that would require the reduction of *Vibrio vulnificus* to nondetectable levels in raw molluscan shellfish which are (i) intended for raw consumption and (ii) harvested from waters to which deaths or illnesses from *Vibrio vulnificus*-contaminated shellfish have been traced.

In the petition, CSPI justified its request for this performance standard with the following arguments:

1. Shellfish contaminated with *Vibrio vulnificus* pose a serious public health problem (petition at 5-7);
2. Deaths and illnesses from *Vibrio vulnificus* have been traced to shellfish from the warm Gulf and Atlantic coast waters (id. at 7-10);
3. Current harvesting practices allow high levels of *Vibrio vulnificus* to develop in the shellfish (id. at 10-12);
4. Previous regulatory efforts have not significantly reduced deaths and illnesses from *Vibrio vulnificus* (id. at 12-15);
5. The technology exists to reduce levels of *Vibrio vulnificus* to nondetectable levels through post-harvest treatment (id. at 15-17).

FDA published a notice in the Federal Register (64 FR 3300, January 21, 1999) announcing CSPI's request that FDA establish a performance standard for *Vibrio vulnificus* in raw molluscan shellfish. The notice invited public comment in eight specific areas bearing on the nature of a standard, the status of pathogen reduction technologies, and the costs and benefits of complying with a regulatory standard for

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Vibrio vulnificus. FDA received over 475 letters, each containing one or more comments, in response to the notice. Most opposed the petitioned performance standard.

After reviewing the citizen petition and the comments filed in response to FDA's notice of the petition, FDA has concluded that the best course of action at the present time is to work with the Interstate Shellfish Sanitation Conference (ISSC), which adopted a control strategy for *Vibrio vulnificus* in July 2001. Therefore, for the reasons discussed below, FDA will decline to adopt a performance standard for *Vibrio vulnificus* in raw molluscan shellfish at the present time and will work with and support the ISSC in the implementation of the ISSC's control strategy for *Vibrio vulnificus* in raw or undercooked oysters.

I. The Interstate Shellfish Sanitation Conference (ISSC)

Formed in 1982 to foster and promote shellfish sanitation through the cooperation of state and federal agencies and the shellfish industry, the ISSC is comprised primarily of state shellfish control agencies, FDA, and representatives of the shellfish industry. To achieve its purpose, the ISSC adopts uniform shellfish safety procedures for implementation by member states; if FDA concurs with the ISSC's changes, they are incorporated into the National Shellfish Sanitation Program's (NSSP) catalogue of safety procedures, referred to as the model ordinance. All of the states that harvest shellfish for commercial distribution participate in the ISSC, as do a number of states that "receive" such shellfish. Additionally, four countries – Canada, Chile, South Korea, and New Zealand – have memoranda of understanding with FDA in which they agree to abide by NSSP shellfish safety policies for exports to the United States. FDA oversees ISSC member states' and foreign countries' shellfish safety programs by (1) conducting evaluations to ensure that they comply with NSSP policy and applicable federal regulations, and (2) providing technical assistance, such as helping to conduct water quality studies or helping with implementation of new shellfish safety policies.

A crucial aspect of the ISSC program is surveillance of the shellfish growing waters for contaminants that would warrant closure of the waters until abatement of the contamination. Because the thousands of miles of growing waters are state resources, the states have traditionally assumed responsibility for the day-to-day operation of the ISSC shellfish safety program, while FDA has assumed the role of overseeing the state programs to ensure compliance with the requirements of the program. Although FDA has not vested the states or the ISSC with the power to act on its behalf, FDA has historically worked cooperatively with the ISSC and the member states on shellfish safety policies.

Since its establishment, the ISSC has proven effective in preventing the reoccurrence of illnesses associated with sewage-borne bacterial pathogens, primarily because it has the states' cooperation in the opening, closing, and patrol of shellfish harvesting waters [FDA, "National Shellfish Sanitation Program, Guide for the Control of Molluscan Shellfish, 1997 Revision, page 143]. The epidemiology of typhoid fever in the twentieth century in the United States illustrates the important role the NSSP plays in reducing the incidence of major diseases. During the early part of the 1900s, i.e., prior to the inauguration of the NSSP, major outbreaks of molluscan shellfish-borne typhoid fever were not uncommon (Pennington, BC, Steward WB, Pollard WM,

Marvel P, De Silver JF. Report on typhoid fever at Atlantic City to the Atlantic City Academy of Medicine. *The Philadelphia Medical Journal*, November, 1902; pages 634-35)(Lumsden LL, Hasseltine HE, Leake JP, Veldee MV. A typhoid fever epidemic caused by oyster-borne infection. *Pub Health Rep* 1925; Supp. No. 50; pages 1-102)(Ramsey GH, McGinnes GF, Neal PR. An outbreak of typhoid fever and gastroenteritis attributed to the consumption of raw oysters. *Pub Health Rep* 1928;43:2395-2405). For example, the largest molluscan-borne outbreak of typhoid fever in the United States, linked to raw oysters in this instance, occurred in 1924-1925 (Lumsden LL, Hasseltine HE, Leake JP, Veldee MV. A typhoid fever epidemic caused by oyster-borne infection. *Pub Health Rep* 1925; Supp. No. 50; pages 1-102). Outbreaks were reported in Chicago, New York City, and Washington, D.C., with 10 other cities reporting a markedly increased prevalence of the infection. Nationwide, more than 1,500 cases and 150 deaths occurred above normal expectancy for the period, and nearly 80 percent of cases reported eating raw oysters in the 30 day period before becoming ill. The implicated oysters were harvested from approved New York waters; however, they were subsequently stored in waters that may have been contaminated with human sewage. As the twentieth century progressed, i.e., after the inauguration of the NSSP, typhoid fever in general, and outbreaks of molluscan shellfish-borne infection in particular, became less frequent. For example, in general, fewer than 500 cases of typhoid fever are reported nationally each year in the United States and many of these cases acquired the infection abroad (Ryan CA, Hargrett-Bean NT, Blake PA. *Salmonella typhi* infections in the United States, 1975-1984: increasing role of foreign travel. *Rev Infect Dis* 1989;2:1-8). This dramatic decrease in what was once a major shellfish-borne infection suggests that the cooperative effort enacted in the United States to enhance the sanitation of molluscan shellfish had a salutary effect on the epidemiology of typhoid fever.

In this regard, the ISSC provides a significant public health benefit for a relatively small investment of federal resources. By working with the ISSC, FDA is able to achieve improvements in shellfish safety, while at the same time conserving its limited resources for use in areas that lack this level of state-industry cooperation.

II. *Vibrio vulnificus*

Since the mid-1990s, there have averaged approximately 30 annual reported cases of septicemia, about half causing death, from raw oysters containing *Vibrio vulnificus* bacteria [FDA, Southeast Region, report, "*Vibrio vulnificus* Cases" 4/22/02)]. Although these bacteria can be found in the waters of many regions during warm months, illnesses have been linked almost exclusively to raw oysters from the Gulf of Mexico [FDA, Southeast Region, report, "*Vibrio vulnificus* Cases" 4/22/02)]. Septicemia from *Vibrio vulnificus* occurs most often in individuals whose immune systems have become compromised through one or more identified medical conditions, particularly liver disease and diabetes [FDA, Southeast Region, report, "*Vibrio vulnificus* Cases" 4/22/02)]. FDA estimates that there are between 12 and 30 million such medically compromised individuals in the United States [Klontz, Karl C., memorandum, "Estimated number of persons at increased risk for *Vibrio vulnificus* septicemia, Nov. 21, 1997.]. FDA agrees with CSPI that *Vibrio vulnificus* represents an important public health issue that needs to

be addressed. The consequences of septicemia from this organism can be severe, even for those who survive (e.g. loss of limb, long convalescence).

As noted in your petition, FDA has sought information on the nature of the public health issues associated with the presence of *Vibrio vulnificus* in raw Gulf oysters since the threat first became clear in the late 1980s, and has been working on developing controls to reduce the risk to susceptible individuals. To gain a better understanding of the underlying science, public health risks, and possible measures that could be applied to control the hazard, FDA co-sponsored two national workshops on *Vibrio vulnificus* in 1988 and 1994. These workshops revealed serious gaps in scientific knowledge. For instance, the range of infectious doses has not been established for *Vibrio vulnificus*; and it has not yet been determined whether there are particular strains of *Vibrio vulnificus* that are responsible for infection or whether the susceptibility to infection of at risk individuals changes over time. We also do not yet know what portion of the level of *Vibrio vulnificus* necessary to cause illness is present at the time of harvest and what portion is attained during post-harvest outgrowth of the bacteria in the oyster.

III. Previous control efforts

The early control strategies undertaken by FDA and the ISSC to minimize the risk from *Vibrio vulnificus* in oysters include consumer education, product labeling, and post-harvest refrigeration controls. In 1991, the ISSC adopted a consumer information statement about the risk of consuming raw shellfish, for use by the states, and several states independently adopted mandatory point-of-purchase consumer advisories directed toward at risk individuals.

In 1994, FDA requested that the ISSC consider requiring that all raw oysters harvested from the Gulf of Mexico between April and October be diverted to the "cooked trade" so that such oysters could not be sold for raw consumption [Interstate Shellfish Sanitation Conference Issue 94-257, 1994]. After considerable controversy and debate, the ISSC chose not to adopt such a policy.

In 1995, FDA worked with the ISSC to develop a two-year Interim Control Plan that placed limits on the time that oysters could remain without refrigeration or ice after harvest [FDA, "National Shellfish Sanitation Program Guide for the Control of Molluscan Shellfish, Model Ordinance, Chap. VIII@.03, 1997 Revision]. The idea was to use post-harvest cooling to minimize the rate of bacterial growth in the oysters and to determine whether this strategy notably reduced illnesses from *Vibrio vulnificus*. In effect, this was an experiment agreed to by the states in the Gulf region at some burden to a number of harvesters [Anderson, Donald W. et al, "Cost of Restrictions on Gulf Oyster Harvesting for Control of *Vibrio vulnificus*-Caused Disease," Research Triangle Institute, 1996, pp 4-19 and 4-20.]. The controls that were implemented did not result in any measurable reduction in the number of *Vibrio vulnificus* illnesses [FDA, Southeast Region, report, "*Vibrio vulnificus* Cases" 4/22/02)].

The promise of new post-harvest pathogen control technologies, such as a mild pasteurization process, appears to have been one impetus for the CSPI petition. [petition at 15-17] As the petition notes, recently developed post-harvest technologies promise to make available controls that will destroy *Vibrio vulnificus* while retaining the organoleptic properties of the raw oysters that are desirable to the consumer [Muth, Mary K., et al, "Economic Impact of Requiring Post-Harvest Treatment of Oysters," Research Triangle Institute, March, 2000, Chapter 3]. As previously indicated, the absence of effective process controls to reduce the bacteria had severely limited the available options to reduce illnesses from *Vibrio vulnificus* in raw oysters. Since 1998, however, mild pasteurization has been utilized on a commercial basis and other methods have been developed. One method, hydrostatic pressure, can provide economies to the industry because it also "shucks" the oyster in the process [id.]. Another method, "individual quick freezing" (IQF), can provide extended shelf life in addition to reducing *Vibrio vulnificus* [id.]. The availability of practical control technologies such as these was a factor in the ISSC's decision in 1999 to establish a Vibrio Management Committee to consider all possible control opportunities in a risk management scenario [Moore, Ken, Interstate Shellfish Sanitation Conference, letter, 11/15/99].

IV. Current ISSC Control Strategy for *Vibrio vulnificus*

The Vibrio Management Committee, of which FDA is a member, proposed and the ISSC voted in 2001 to require member states to develop and implement *Vibrio vulnificus* management plans if they have had two or more confirmed shellfish-borne *Vibrio vulnificus* illnesses since 1995 traced to commercially harvested raw or undercooked oysters that originated from their waters. The states linked to two or more illnesses (i.e., "source states") are Texas, Louisiana, Mississippi, and Florida. Each of these four states must have *Vibrio vulnificus* management plans that define the administrative procedures and resources that are necessary for the state to accomplish its portion of the collective illness reduction program [Interstate Shellfish Sanitation Conference 2001 Biannual Meeting Norfolk, VA, July 21-27, 2001 ("Summary of Actions") 2001, p. 74]. These state plans must be designed to collectively reduce the rate of *Vibrio vulnificus* illnesses reported by a group of states that consistently have reported such illnesses (i.e., California, Florida, Louisiana, and Texas). The plans apply to commercially harvested raw or undercooked oysters. The goal is to reduce the average rate of illness per year in these four "reporting states" by 40 percent for years 2005 and 2006 (average), and by 60 percent for years 2007 and 2008 (average) from the average illness rate for the years 1995-1999. In other words, the goal is to reduce the average rate of illness per year from 0.306 illnesses per million population to 0.184 illnesses per million population during 2005 and 2006 and to 0.122 illnesses per million population during 2007 and 2008. This translates to a reduction from approximately 22 illnesses per year to approximately 14 illnesses per year during 2005 and 2006 and to approximately 10 illnesses per year during 2007 and 2008 in the four reporting states [id. at 74].

If the 60 percent illness reduction goal is not collectively achieved by the end of 2008, the source states will be required to ensure that their oysters are not marketed for raw

consumption during the key illness associated months without first being subjected to a post-harvest treatment designed to reduce *Vibrio vulnificus* to nondetectable levels. This could be accomplished in a number of ways, including: implementing seasonal closure of waters for all oysters intended for the raw market; implementing seasonal post-harvest treatment of all oysters intended for the raw market; or implementing seasonal labeling of all oysters to require shucking [*id.* at 75].

Additionally, the source state management plans must include steps designed to encourage the industry to voluntarily construct sufficient capacity to post-harvest treat 25 percent of all oysters intended for the raw market during the months of May through September, by December 31, 2004 and 50 percent by December 31, 2006 [*id.* at 75]. If the 40 percent illness reduction goal is not achieved collectively by December 31, 2006, then source states must mandate a post harvest treatment capacity of 50 percent of all oysters intended for the raw market during the months of May through September [*id.* at 75].

FDA believes that the prospect of closing states' shellfish growing waters or requiring shellfish to be shucked instead of sold for raw consumption if the illness reduction goals are not met by the beginning of 2008 will provide a significant incentive for states to promote, and industry to voluntarily adopt, post-harvest treatment technology well before the deadline. Moreover, while the ISSC's *Vibrio vulnificus* risk management strategy establishes an illness reduction goal of 60 percent, FDA believes that market forces will likely cause that goal to be substantially exceeded. This is because: 1) once a processor has invested the capital necessary to purchase post-harvest treatment equipment to treat during the key illness associated months, there will be little additional incremental expense to produce the treated product during other months that are associated with lower numbers of *Vibrio vulnificus* illness, thus providing incentive for the processor to offer it, and consumers to demand it, year round; 2) at least one of the post-harvest treatment technologies offers labor savings and, potentially, overall cost savings, again providing incentive for individual processors to offer it and consumers to demand it year round; and, 3) FDA anticipates that as consumers and buyers become accustomed to the product, they will appreciate its public health benefits and become familiar with its sensory qualities and, as a result, demand it year round. Consequently, in the agency's view, post-harvest treatment will be an essential component of the strategy. The combined forces of the prospect of mandatory diversion of product away from the raw trade, federal and state post-harvest treatment incentives, and consumers and buyers seeking added assurance of safety will accelerate post-harvest treatment implementation.

Education also is a component of the ISSC plan. Source states must include in their *Vibrio vulnificus* management plans how they will implement their portion of the ISSC Consumer Education Program, which targets individuals who consume raw oysters and whose health conditions place them at increased risk for *Vibrio vulnificus* infection. The education component has the advantage that it is already ongoing and can be implemented by states with their existing statutory authorities. Other controls that could be phased in may require new regulations or laws and states will need some time to make

these mandatory. However, it must be emphasized that active attempts to bring about other control measures, such as voluntary post-harvest treatment are all progressing simultaneously with the educational initiative. For example, FDA is working with the ISSC to: 1) validate post-harvest treatment technologies; and, 2) conduct taste tests of post-harvest treated products in comparison to traditional products. These are necessary steps in the development of buyer demand for, and investor acceptance of, post-harvest treated product. Additional accomplishments by the ISSC, FDA and the states in furtherance of the *Vibrio vulnificus* illness reduction goals are provided in the Addendum to this letter.

Finally, as a member of the Vibrio Management Committee, FDA will be actively participating in the ISSC's efforts to implement this control plan. FDA also will be evaluating the states over the course of the plan's implementation schedule to ensure that they are complying with its provisions, e.g., the development and implementation of *Vibrio vulnificus* management plans. Furthermore, FDA continues to conduct research on post-harvest treatment technologies to facilitate their adoption by the industry.

V. Advantages to ISSC Control Strategy

FDA believes that participation in the ISSC program is the optimal course of action at the present time. There are several advantages to this approach as compared to the CSPI proposed course of action. First, FDA's reliance on the partnerships established through the ISSC has a number of important benefits. ISSC members have participated fully in the development of the control measures contained in the ISSC plan. They have judged that it is a workable plan in each of their local environments, as well as workable in a collective sense. They have invested their word and commitment to making the ISSC strategy a success. These are commitments by the states and industry formulated under a long-standing regulatory partnership. Past experience indicates that these commitments will be honored.

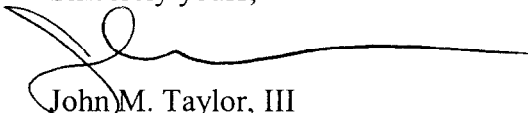
Second, the time frame for implementation of the ISSC plan is consistent with the time that it could take FDA to adopt a *Vibrio vulnificus* standard by rulemaking. The rulemaking process can be a lengthy one, and FDA is never assured that a regulation, if proposed, will survive public comment and become final. Public comments received by FDA to the Notice published in the Federal Register indicate substantial support for the ISSC plan and significant opposition from many quarters to a regulatory standard for raw shellfish, or to an approach that circumvents the ISSC. Moreover, if FDA attempted to establish a performance standard for *Vibrio vulnificus*, it likely would see no improvements in this area until the regulation actually became effective, whereas under the ISSC plan, states and industry have already begun working toward a solution to the *Vibrio vulnificus* problem.

Third, working through the ISSC is currently the most efficient use of FDA's resources. States have existing programs in place to open and close shellfish harvest waters, to patrol the closed waters, and to conduct frequent inspections of shellfish processing

plants. The ISSC's federal-state cooperative approach allows FDA to leverage the considerable state resources that are already devoted exclusively to shellfish management and safety. This leveraging enables FDA to apply more of its limited public health resources to other matters, many of which may be more effectively regulated by the federal government than by state governments.

Therefore, for all of the above reasons, i.e., because FDA is working with the ISSC and the states to fashion an appropriate remedy, because that process is already underway, and because FDA has reason to believe it will be successful, we are advising you, in accordance with 21 CFR 10.30(e)(3), that FDA is denying your petition.

Sincerely yours,



John M. Taylor, III
Senior Associate Commissioner
for Regulatory Affairs

Enclosure: (1)
Addendum (2 pages)

ADDENDUM

The ISSC established a Vibrio Management Committee (VMC) of Federal and state regulators and industry representatives from all regions of the country to oversee its efforts to achieve the illness reduction goal. This committee met on July 17-18, 2002, to review progress during the first year of its efforts under the 2001 strategy and to set work plans for the future. Among the accomplishments to date are:

1. Post-harvest treatment (PHT) capacity has increased substantially, such that presently the industry is capable of annually treating approximately 96,000,000 pounds of product harvested in the four source states. This represents 23.5% of product harvested by those states. Approximately 51,000,000 pounds of this capacity (53%) is in facilities with processes approved for production of products bearing a *V. vulnificus* reduction label (i.e. reduce *V. vulnificus* to less than 3 MPN/gram). The remainder of the capacity is in facilities with such approval pending or anticipated, or for which such approval is not likely to be sought (i.e., treatment that significantly reduces the level of *V. vulnificus*, but not to the level of non-detectable). As noted, the goal contained in the 2001 strategy is to achieve 25% capacity by 2004 and 50% by 2006. PHT capacity is derived from: one facility that uses the low temperature pasteurization process; three facilities that use the ultra high-pressure process; five facilities that use the individual quick freezing (IQF) process; and one facility that uses a rack freezing process. All of these processes have been approved for production of product bearing a *V. vulnificus* reduction label at one or more facilities. At the request of the ISSC, the Gulf Oyster Industry Council will refine these estimates of PHT capacity within the next several months. The ISSC has also developed a procedure whereby the four source states will annually provide definitive figures on PHT capacity in time for assessment of compliance with the 2004 capacity goal.
2. All four source states associated with *V. vulnificus* illness have, with the assistance of ISSC staff and FDA, developed draft *V. vulnificus* management plans, as required by the 2001 strategy. Among other things, these plans identify state efforts to promote voluntary implementation of PHT, education of at-risk consumers, and preparation for the eventuality of mandating PHT or harvest restrictions if the illness reduction goals are not met. Further refinements of these plans are expected.
3. Research has been funded by the ISSC and is ongoing on the effectiveness of onboard or dockside refrigeration at reducing *V. vulnificus* levels in oysters, a technique that showed promise in earlier research and which is practiced by a small percentage of the oyster harvesting fleet.
4. Research is ongoing by FDA to further study the effects of ultra high pressure processing in the reduction of reducing *V. vulnificus* levels in oysters.

5. The ISSC and FDA have begun to formulate a study, to be funded by the ISSC, to validate the effectiveness of a variety of IQF freezing processes, to reduce the burden on processors that intend to invest in this post-harvest treatment technique.
6. The ISSC has begun to formulate a study on consumer acceptance and shelf-life of PHT oysters to assist processors in marketing these products to prospective buyers.
7. The ISSC has adopted an interim protocol for the validation of PHT processes, to make these studies uniform from state to state, minimizing the burden on processors that intend to ship PHT product to multiple states, and ensuring that *V. vulnificus* reduction claims on these products are well-founded. As of August 15, 2002, FDA has consulted with the states in validation of three PHT processes, representing four processing facilities.
8. The ISSC and FDA have developed *V. vulnificus* educational materials for at-risk consumers (English and Spanish), health care providers, and the media. All of these materials encourage at-risk consumers to avoid the consumption of raw oysters or to substitute PHT oysters for traditional, untreated oysters. In the past six months, the ISSC has distributed well in excess of: 50,000 copies of the consumer brochure; 25,000 copies of the health care provider fact sheet; 200 packets of detailed information, including a one-hour video tape, for clinicians; and 50 media kits, including video segments, for Gulf Coast TV stations. In addition, the ISSC has partnered with a number of national, regional, and local health and veterans associations, such as the American Liver Foundation, to amplify their *V. vulnificus* education efforts. The Gulf and South Atlantic Fisheries Foundation is seeking substantial congressional funding to enable it to engage in an expanded educational program similar to the one administered to date by the ISSC.
9. FDA has provided \$100,000 to the State of California for the education of the at-risk Hispanic population on the risks of consuming raw oysters. The agency is in the process of assisting the state in the development of the education campaign.