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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 99N-1075]

Risk Assessment on the Potential Public Health Impact of *Vibrio Parahaemolyticus* in Molluscan Shellfish; Request for Scientific Data and Information.

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice; request for scientific data and information.

SUMMARY: The Food and Drug Administration (FDA) is announcing a call for scientific data and information relevant to the agency's planned risk assessment on the potential public health impact of pathogenic *Vibrio parahaemolyticus* infections resulting from the consumption of raw molluscan shellfish. The risk assessment will assist FDA by providing a scientific framework for developing food safety policies relating to raw molluscan shellfish contaminated with pathogenic *V. parahaemolyticus*. FDA plans to hold public meetings to present the process of the risk assessment, to present information collected, and to allow interested parties additional opportunities to present data to facilitate this effort.

DATES: Submit scientific data and information by (*insert date 60 days after date of publication in the Federal Register*).

ADDRESSES: Submit scientific data and information to the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Marianna D. Miliotis, Center for Food Safety and Applied Nutrition (HFS-327), Food and Drug Administration, 200 C St., SW., rm. 3472, Washington, DC 20204, 202-205-4824, FAX 202-205-4939, or e-mail 'mmilioti@bangate.fda.gov.'

SUPPLEMENTARY INFORMATION:

I. Background

A. *Vibrio parahaemolyticus*

V. parahaemolyticus is a gram-negative, halophilic bacterium that occurs naturally in estuarine environments and, therefore, can be present in many fishery products, including molluscan shellfish (Ref. 1). The organism can cause acute gastroenteritis in consumers (Refs. 2, 3, and 4), and in some individuals can also cause septicemia (Ref. 5) and even death (Ref. 6), though such cases have been reported only rarely. Worldwide, this organism is one of the leading causes of foodborne illnesses (Ref. 7). In the United States, the outbreaks caused by this organism usually have been associated with cooked crabs (Ref. 8), and illnesses transmitted by raw molluscan shellfish generally have been limited to sporadic cases (Ref. 9). However, in 1997 *V. parahaemolyticus* from molluscan shellfish caused a large outbreak of illness involving a total of **209** individuals in the Pacific Northwest region, from California to British Columbia (Ref. 10). Many of these cases implicated oysters from specific growing areas, and the magnitude of this outbreak was considerably larger than any previously caused by shellfish in the United States. In 1998, outbreaks caused by molluscan shellfish-borne *V. parahaemolyticus* occurred again, this time in three different coastal regions of the United States. Overall, more than 500 individuals from the Gulf Coast (Ref. 11), the Northeast (Ref. 12), and the Pacific Northwest (Ref. 13) reportedly became ill after consuming raw molluscan shellfish, and many of these cases were culture confirmed as attributable to *V. parahaemolyticus*.

V. parahaemolyticus has been widely studied for years, and many of the factors influencing its pathogenicity and natural occurrence have been reported. For example, the organism is mesophilic, halophilic, grows optimally in alkaline pH, and causes illnesses and outbreaks principally during warmer weather months (Refs. 2, 5, and 14). However, those environmental factors and production practices that influence the incidence and prevalence of the organism and which would enable reliable estimates of risks associated with the consumption of seafood, especially molluscan shellfish, remain unknown.

Investigations of both the 1997 and the June 1998 outbreaks demonstrated both epidemiological and direct relationships between illness and raw oyster consumption (Refs. 10 and 11). Moreover, accounts from some patients indicated that illness may result from the consumption of a single infected oyster, which suggests the possibility of a highly virulent strain, or a low infectious dose. A single serotype of *V. parahaemolyticus*, that being 03:K6, was identified as predominant in the June 1998 outbreak (Ref. 11). In September 1998, the same serotype of *V. parahaemolyticus* again was identified in a U.S. outbreak caused by raw oysters, this time in the Northeast region (Ref. 12). Prior to 1998, with the exception of one isolated case in 1972 (Ref. 15), serotype 03:K6 had been associated only with outbreaks in Asian countries (Japan, Bangladesh, Laos, and Taiwan) (Ref. 16). Notably, this serotype has repeatedly been associated with outbreaks, whereas most other serotypes are primarily associated with sporadic cases. For example, in Japan there were 43 *V. parahaemolyticus* outbreaks involving 1,131 patients during the summer of 1998. Thirty of the outbreaks (70 percent) were due to serotype 03:K6 (Ref. 16). Based on all information available, the Centers for Disease Control and Prevention (CDC) have described the 03:K6 serotype as “an outbreak strain” of *V. parahaemolyticus*, and FDA concurs with this current assessment. Other serotypes of the organism, such as O4:K8 currently seen predominantly in Japan (Ref. 17), may also merit special concern. FDA therefore believes that the U.S. outbreaks of illness in 1997 and 1998 have identified certain serotypes of *V. parahaemolyticus* as important emerging pathogens linked to the consumption of raw molluscan shellfish, particularly oysters.

However, since not all *V. parahaemolyticus* strains are enteropathogenic as determined by their ability to produce a thermostable direct hemolysin (TDH) (Ref. 18), FDA is concerned that determining the total concentration of this species in shellfish is unlikely to be useful for evaluating the risk of illness posed by *V. parahaemolyticus*. Other strain characteristics, such as invasion of the enterocytes (Ref. 19) and production of an enterotoxin (Ref. 20) may also be important

to pathogenicity and thus useful in identification of pathogenic *V. parahaemolyticus*, other than the production of TDH.

B. Current Efforts

FDA and the States share responsibility for the safety of molluscan shellfish for human consumption through the National Shellfish Sanitation Program (NSSP), a long-standing Federal/State cooperative program recognized by FDA for the sanitary control of molluscan shellfish produced and sold for human consumption. To promote safety, the NSSP has developed and maintained recommended shellfish sanitation control practices for adoption by member States. These control practices or guidelines are set out in the ‘ ‘NSSP Guide for the Control of Molluscan Shellfish’ ’ (Ref. 21) which also includes State growing area classification and dealer certification programs, and FDA evaluation of State shellfish control programs.

In 1984, FDA entered into a Memorandum of Understanding (MOU) with the Interstate Shellfish Sanitation Conference (ISSC) recognizing the ISSC as the primary voluntary national organization of State shellfish regulatory officials that provides guidance and counsel on matters for the sanitary control of shellfish. The purpose of the ISSC is to provide a formal structure for State regulatory authorities to participate in establishing updated regulatory guidelines and procedures for uniform State application of the program. The ISSC has adopted formal procedures for State representatives to review shellfish sanitation issues and develop regulatory guidelines. Following FDA concurrence, these guidelines are published in revision of the NSSP guidelines mentioned above (Ref. 21).

Historically, most illness caused by consumption of molluscan shellfish can be traced back to pathogens resulting from sewage contaminated water, and the NSSP has focused on control measures to prevent illnesses caused by pathogens that may occur in fecal material (Ref. 22). *V. parahaemolyticus*, however, occurs naturally in estuarine environments. Thus, there is uncertainty about the effectiveness of current NSSP measures to control *V. parahaemolyticus* in molluscan shellfish.

In addition, FDA has previously indicated that *V. parahaemolyticus* in raw molluscan shellfish should not exceed a level of 10,000 cells per gram. This limit was based on data and reports from human volunteer studies (Refs. 2, 3, 14 and 23) conducted more than 25 years ago, and on investigations of U.S. outbreaks caused predominantly by cross contamination of cooked crabs (Ref. 8), which supported an estimation of minimum infectious dose of about 10^5 cells. However, the overall levels of *V. parahaemolyticus* found in oysters from harvest sites implicated during the 1997 and 1998 U.S. outbreaks suggest that the number of pathogenic cells required to cause illness is probably far less than previously believed, and it may be as low as 100 and 1,000 cells. FDA now believes the 10,000 cells per gram level may be inadequate to protect the public health and did not rely on this level during the recent outbreaks. Instead, during the recent U.S. outbreaks, closing shellfish waters to harvesting was based on the occurrence of human illness. Reopening was based primarily on two factors: (1) Change in a season and/or conditions, particularly temperature, to those which historically have not been associated with illness, and (2) absence of the particular strains of *V. parahaemolyticus* associated with the outbreak. However, it is not certain that these measures are the most appropriate or effective.

II. Questions to be Considered by the Risk Assessment

FDA is requesting scientific data and information that will allow it to respond to the following questions:

1. What is the frequency of occurrence of pathogenic strains of *V. parahaemolyticus* in the shellfish waters? What parameters (e.g., water temperature, salinity, turbidity, and nutrient profiles) can be used as indicators of the presence of the organism in growing waters?

2. What is the frequency of occurrence of pathogenic strains of *V. parahaemolyticus* in molluscan shellfish, and what are the numbers of viable pathogenic organisms at time of consumption? How are levels present in the bivalves at the time of consumption related to the initial levels in the growing waters?

3. What is known about the dose-response relationship from outbreak, epidemiological, animal and other studies? What are the differences in dose-response relations among different strains and serotypes of *V. parahaemolyticus*, and among the different human susceptible subpopulations?

4. What is the role of postharvest handling that may be influencing the numbers of *V. parahaemolyticus* in oysters? What reductions in risks can be achieved by intervention strategies such as deputation or relaying?

5. What is the adequacy of current scientific knowledge, and where should future research be focused to reduce the uncertainty in the risk estimate?

111. Scope of the Risk Assessment

Risk assessment is separate from risk management and risk communication. Thus, FDA's risk assessment will determine the relationships between molluscan shellfish, *V. parahaemolyticus* and illnesses; it will not determine an acceptable level of pathogenic *V. parahaemolyticus*.

To accurately assess the exposure to pathogenic *V. parahaemolyticus*, the consumption of raw molluscan shellfish, especially oysters, will be considered. Exposure is a function of the *V. parahaemolyticus* prevalence in the shellfish and the consumption patterns of the population. The number of pathogenic *V. parahaemolyticus* in raw molluscan shellfish at consumption is the critical exposure information. Modeling will be used when *V. parahaemolyticus* data are collected during outbreaks, and at retail outlets to estimate actual exposure.

The risk assessment will produce estimates of illness for levels of pathogenic *V. parahaemolyticus* likely to be consumed by different subpopulations. All assumptions and uncertainties will be identified and documented.

FDA expects the risk assessment to provide the scientific underpinnings FDA needs to develop food safety policies that reduce the risk of disease resulting from ingestion of *V. parahaemolyticus* in molluscan shellfish, and other seafood consumed raw. Among other things, FDA anticipates that the data from the risk assessment will assist in determining the principal factors that should

be considered in developing criteria for closing of shellfish waters to harvest in order to prevent illness and reopening waters after outbreaks of *V. parahaemolyticus* are over.

IV. Request for Data and Information

FDA is requesting scientific data and information that will allow it to respond to the questions under section II of this document. The purpose of this request for data is to gather relevant information to facilitate a valid risk assessment of *V. parahaemolyticus* with the larger goal of providing a sound scientific basis for the food safety policies relating to raw molluscan shellfish contaminated with *V. parahaemolyticus*. FDA does not intend to utilize the submitted data and information to support future enforcement activity against seafood producers submitting the data. Accordingly, it is acceptable that data submitted in response to this notice be “blinded” in the sense that the data need not identify the particular seafood producer or processor that was the source of the samples underlying the results.

Two copies of the scientific data and information are to be submitted, except that individuals may submit one copy. Scientific data and information should be addressed to the Dockets Management Branch (address above) and be identified with the docket number found in brackets in the heading of this document. Received materials may be seen in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

V. References

The following references have been placed on display in the Dockets Management Branch (address above) and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday.

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Dated: 4/29/99
April 29, 1999



William K. Hubbard
Acting Deputy Commissioner for Policy

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