

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

DAB

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Food Safety Research: Availability of Cooperative Agreements; Request for Applications

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of research funds for fiscal year (FY) 2001 to support research in the following areas: Analytical detection of bovine spongiform encephalopathy and other transmissible spongiform encephalopathies (BSE/TSE) in FDA-regulated products, consumer refrigeration storage length practices for unopened and opened packages of ready-to-eat foods, microbial contamination of agricultural water, and transfer coefficients to describe the potential for *Listeria* cross-contamination in the retail environment. Approximately \$700,000 will be available in FY 2001. FDA anticipates making up to four awards of \$100,000 to \$200,000 (direct plus indirect costs) per award per year. Support of these agreements may be up to 3 years. Budgets for all years requested may not exceed \$200,000 (direct plus indirect costs). Any application received that exceeds this amount will not be considered responsive and will be returned to the applicant without being reviewed. The number of agreements funded will depend on the quality of the applications received and the availability of Federal funds to support the projects. After the first year, additional years of noncompetitive support are predicated upon performance and the availability of Federal funds.

DATES: Submit applications by [*insert date 45 days after date of publication in the Federal Register*].

ADDRESSES: Completed applications should be submitted to: Maura C. Stephanos, Grants Management Specialist, Grants Management Staff (HFA-520), Division of Contracts and

Procurement Management, Food and Drug Administration, 5600 Fishers Lane, rm. 2129, Rockville, MD 20857, 301-827-7183, FAX 301-827-7106, e-mail: mstepha1@oc.fda.gov. (Applications hand-carried or commercially delivered should be addressed to rm. 2129, 5630 Fishers Lane, Rockville, MD 20857).

Application forms are available either from Maura C. Stephanos (address above) or via the Internet at <http://grants.nih.gov/grants/funding/phs398/phs398.html>. NOTE: Do not send applications to the Center for Scientific Research (CSR), National Institutes of Health (NIH).

FOR FURTHER INFORMATION CONTACT:

Regarding the administrative and financial management aspects of this notice: Maura C. Stephanos (address above).

Regarding the programmatic aspects of this notice: John W. Newland, Microbial Research Coordinator, Office of Science (HFS-32), Center for Food Safety and Applied Nutrition, Food and Drug Administration, 200 C St. SW., Washington, DC 20204, 202-260-0536, e-mail: john.newland@cfsan.fda.gov.

SUPPLEMENTARY INFORMATION: FDA will support the research studies covered by this notice under section 301 of the Public Health Service Act (42 U.S.C. 241). FDA's research program is described in the Catalog of Federal Domestic Assistance, No. 93.103.

The Public Health Service (PHS) strongly encourages all award recipients to provide a smoke-free workplace and to discourage the use of all tobacco products. This is consistent with the PHS mission to protect and advance the physical and mental health of the American people.

FDA is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2010," a national effort to reduce morbidity and mortality and to improve quality of life. Applicants may obtain a hard copy of the "Healthy People 2010" objectives, vols. I and II, conference edition (B0074) for \$22 per set, by writing to the Office of Disease Prevention and Health Promotion (ODPHP) Communication Support Center (Center), P.O. Box 37366, Washington, DC 20013-7366. Each of the 28 chapters of "Healthy People 2010" is priced at \$2

per copy. Telephone orders can be placed at the Center on 301-468-5690. The Center also sells the complete conference edition in CD-ROM format (B0071) for \$5. This publication is available as well on the Internet at <http://health.gov/healthypeople>. Internet viewers should proceed to "Publications."

I. Background

FDA is committed to reducing the incidence of foodborne illness to the greatest extent feasible. Research in food safety seeks to reduce the incidence of foodborne illness by improving our ability to detect and enumerate pathogens in the food supply and to find new and improved ways to control them. The Center for Food Safety and Applied Nutrition (CFSAN) supports multiyear cooperative agreements intended to help achieve the goal of reducing the incidence of foodborne illness. President Clinton's food safety initiative (FSI) inaugurated this extramural program that supports a novel collaborative research effort between CFSAN and academic scientists, and leveraged expertise not found within FDA, to complement and accelerate ongoing research. Collaborations such as these provide information critical to food safety guidance and policymaking, and stimulate fruitful interactions between FDA scientists and those within the greater research community.

In continuation of this effort CFSAN/FSI will provide FY 2001 funds to be used for research to help ensure the agency has the following capacities: To detect the presence of human pathogens that may become present in FDA regulated products; to more fully understand how consumer practices in the handling of ready-to-eat food products may affect their microbiological safety; to obtain a more precise understanding of the potential for cross contamination by *Listeria monocytogenes* between foods and food contact surfaces; and to understand mechanisms of microbial contamination of agricultural water that subsequently result in the occurrence of pathogens on raw produce.

II. Research Goals and Objectives

Proposed projects designed to fulfill the specific objectives of any one of the following requested projects will be considered for funding. Applications may address only one project and its objectives per application. However, applicants may submit more than one application for more than one project. The projects and their objectives are as follows.

A. Project 1: Analytical Detection of Bovine Spongiform Encephalopathy and Other Transmissible Spongiform Encephalopathies (BSE/TSE) in Products Regulated by CFSAN

The objective of this project is the development of a practical analytical technique for the detection of the BSE/TSE infective agent in products regulated by CFSAN (i.e., foods, including infant formula, dietary supplements, and cosmetics). Diagnostic tests to detect the BSE/TSE infective agent in a variety of FDA regulated products are currently unavailable. FDA's high priority products include milk and dairy products, food grade gelatin, dietary supplements, and foods containing beef at less than 3 percent. This research will provide detection methodology critical to support food surveillance programs designed to keep BSE and other TSEs out of U.S. foods, cosmetics, and dietary supplements.

B. Project 2: Consumer Refrigeration Storage Length Practices for Unopened and Opened Packages of Ready-to-Eat Foods

The objective of this project is to understand more fully how consumer practices in the handling of ready-to-eat food products may affect the microbiological safety of these foods. Values that were used in the Department of Health and Human Services (DHHS)/U.S. Department of Agriculture (USDA) draft *Listeria monocytogenes* risk assessment to estimate time of storage in the home before consumption were largely based on expert opinion. The agency seeks to improve the estimates of risk associated with consumer storage practices through survey data on the storage of ready-to-eat foods (as specified in the draft risk assessment, see <http://www.foodsafety.gov>) in

home refrigerators. Proposed investigations should focus on the duration of refrigerated storage of unopened and opened food packages of ready-to-eat foods.

C. Project 3: Microbial Contamination of Agricultural Water

The objective of this project is to understand mechanisms of microbial contamination of agricultural water that subsequently result in the occurrence of pathogens on raw produce. In produce-related outbreak investigations and produce pathogen surveys agricultural water quality has been repeatedly identified as a potential source of microbial pathogen contamination. Farm investigations have found examples where water used for agriculture purposes was contaminated by raw human or animal waste. There are no guidelines for microbiological criteria for water used in agriculture. Research must specifically focus on characterizing the role of agricultural water on pathogen (and possibly fecal indicator) occurrence, survival, propagation, and attachment to raw produce. The effects of farm production practices, such as spray and furrow irrigation and pesticide applications, on microbial pathogen occurrence, survival, propagation, and attachment should also be addressed. Applications should include the following pathogens of concern, *Salmonella*, *Shigella*, *Escherichia coli* O157:H7, and *Cyclospora*.

D. Project 4: Transfer Coefficients to Describe the Potential for Listeria Cross-Contamination in the Retail Environment

The objective of this project is to quantify the potential for *Listeria* cross-contamination in the retail environment. The presence of *Listeria* in ready-to-eat foods is well established. Specific information is lacking, however, about the mechanism(s) and frequency of cross-contamination within the retail and food service environment, especially in food preparation and dispensing areas. Information is needed about the potential for transfer from microbially contaminated food to soiled and unsoiled surfaces, from microbially contaminated surfaces (soiled and unsoiled) to food, and the potential involvement of surface biofilms on cross-contamination potential. Specifically, this

transfer potential should be quantified and expressed as transfer coefficients that apply to *Listeria* cross contamination that occurs within the retail environment.

III. Human Subject Protection and Informed Consent

A. Protection of Human Research Subjects

Some activities carried out by a recipient under this announcement may be governed by DHHS regulations for the protection of human research subjects (45 CFR part 46), as well as by the FDA Risk in Human Subjects Committee (RIHSC) (21 CFR parts 50 and 56). These regulations require recipients to establish procedures for the protection of subjects involved in any research activities. Prior to funding and upon request of the Office for Human Research Protection (OHRP) (formerly the Office for Protection from Research Risks (OPRR), prospective recipients must have on file with OHRP an assurance to comply with 45 CFR part 46. This assurance to comply is called an assurance document. It includes the designated institutional review board (IRB) for review and approval of procedures for carrying out any research activities occurring in conjunction with this award. If an applicable assurance document for the applicant is not already on file with OHRP, a formal request for the required assurance will be issued by OHRP at an appropriate point in the review process, prior to award, and examples of required materials will be supplied at that time. No applicant or performance site without an approved and applicable assurance on file with OHRP may spend funds on human subject activities or accrue subjects. No performance site, even with an OHRP-approved and applicable assurance, may proceed without approval by OHRP of an applicable assurance for the recipients. Applicants may wish to visit the OHRP website at <http://ohrp.osophs.dhhs.gov> to obtain preliminary guidance on human subject issues. Applicants wishing to contact OHRP should provide their institutional affiliation, geographic location, and all available request for applications (RFA) citation information.

Applicants are advised that the section on human subjects in the application kit entitled "Section C. Specific Instructions—Forms, Item 4, Human Subjects," on pages 7 and 8 of the

application kit, should be carefully reviewed for the certification of IRB approval requirements. Documentation of IRB approval for every participating center is required to be on file with the grants management officer, FDA. The goal should be to include enough information on the protection of human subjects in a sufficiently clear fashion so reviewers will have adequate material to make a complete review. Those approved applicants who do not have a current multiple project assurance with OHRP will be required to obtain a single project assurance from OHRP prior to award.

B. Informed Consent

Consent and/or assent forms, and any additional information to be given to a subject, should accompany the application. Information that is given to the subject or the subject's representative must be in language that the subject or his or her representative can understand. No informed consent, whether oral or written, may include any language through which the subject or the subject's representative is made to waive any of the subject's legal rights, or by which the subject or representative releases or appears to release the investigator, the sponsor, or the institution or its agent from liability.

If a study involves both adults and children, separate consent forms should be provided for the adults and the parents or guardians of the children.

C. Elements of Informed Consent

The regulations on informed consent are set forth in 45 CFR 46.116 and 21 CFR 50.25. The basic elements of informed consent are as follows:

1. Basic Elements of Informed Consent

In seeking informed consent, the following information shall be provided to each subject:

- A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental.

- A description of any reasonably foreseeable risks or discomforts to the subject.
- A description of any benefits to the subject or to others which may reasonably be expected from the research.
- A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject.
- A statement that describes the extent, if any, to which confidentiality of records identifying the subject will be maintained, and that notes the possibility that FDA may inspect the records.
- For research involving more than minimal risk, an explanation as to whether any compensation and any medical treatments are available if injury occurs and, if so, what they consist of or where further information may be obtained.
- An explanation of whom to contact for answers to pertinent questions about the research and research subject's rights, and whom to contact in the event of research-related injury to the subject.
- A statement that participation is voluntary, that refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and that the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

2. Additional Elements of Informed Consent

When appropriate, one or more of the following elements of information shall also be provided to each subject.

- A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable.
- Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent.
- Any costs to the subject that may result from participation in the research.

- The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject.
- A statement that significant new findings developed during the course of the research that may relate to the subject's willingness to continue participation will be provided to the subject.
- The approximate number of subjects involved in the study.
- The informed consent requirements are not intended to preempt any applicable Federal, State, or local laws which require additional information to be disclosed for informed consent to be legally effective.
- Nothing in the notice is intended to limit the authority of a physician to provide emergency medical care to the extent that a physician is permitted to do so under applicable Federal, State, or local law.

IV. Mechanism of Support

A. Award Instrument

Support for this program will be in the form of cooperative agreements. These cooperative agreements will be subject to all policies and requirements that govern the research grant programs of PHS, including the provisions of 42 CFR part 52 and 45 CFR parts 74 and 92. The regulations issued under Executive Order 12372 do not apply to this program. The NIH modular grant program does not apply to this FDA program.

B. Eligibility

These cooperative agreements are available to any public or private nonprofit entity (including State and local units of government) and any for-profit entity. For-profit entities must commit to excluding fees or profit in their request for support to receive awards. Organizations described in section 501(c)(4) of the Internal Revenue Code of 1968 that engage in lobbying are not eligible to receive awards.

C. Length of Support

The length of support will be for up to 3 years. Funding beyond the first year will be noncompetitive and will depend on:

1. Satisfactory performance during the preceding year, and
2. Availability of Federal FY funds.

V. Reporting Requirements

Annual financial status reports (FSR) (SF-269) are required. An original FSR and two copies shall be submitted to FDA's grants management officer (address same as given above for grants management specialist) within 90 days of the budget expiration date of the cooperative agreement. Failure to file the FSR on time may be grounds for suspension or termination of the agreement. Program progress reports will be required quarterly and will be due 30 days following each quarter of the applicable budget period except that the fourth quarterly report which will serve as the annual report and will be due 90 days after the budget expiration date. For continuing agreements, an annual program progress report is also required. Submission of the noncompeting continuation application (PHS 2590) will be considered as the annual program progress report. The recipient will be advised of the suggested format for the program progress report at the time an award is made. In addition, the principal investigator will be required to present the progress of the study at an annual FDA extramural research review workshop in Washington, DC. Travel costs for this requirement should be specifically requested by the applicant as part of their application. A final FSR, program progress report and invention statement, must be submitted within 90 days after the expiration of the project period, as noted on the notice of grant award.

Program monitoring of recipients will be conducted on an ongoing basis and written reports will be reviewed and evaluated at least quarterly by the project officer and the project advisory group. Project monitoring may also be in the form of telephone conversations between the project officer/grants management specialist and the principal investigator and/or a site visit with appropriate officials of the recipient organization. A record of these monitoring activities will be

duly recorded in an official file specific for each cooperative agreement and may be available to the recipient of the cooperative agreement upon request.

VI. Delineation of Substantive Involvement

Inherent in the cooperative agreement award is substantive involvement by the awarding agency. Accordingly, FDA will have a substantive involvement in the programmatic activities of all the projects funded under this RFA. Substantive involvement includes but is not limited to the following:

1. FDA will provide guidance and direction with regard to the scientific approach and methodology that may be used by the investigator.
2. FDA will participate with the recipient in determining and executing any: (a) Methodological approaches to be used, (b) procedures and techniques to be performed, (c) sampling plans proposed, (d) interpretation of results, and (e) microorganisms and commodities to be used.
3. FDA will collaborate with the recipient and have final approval on the experimental protocols. This collaboration may include protocol design, data analysis, interpretation of findings, coauthorship of publications and the development and filing of patents.

VII. Review Procedure and Criteria

A. Review Method

All applications submitted in response to this RFA will first be reviewed by grants management and program staff for responsiveness. Applications will be considered not responsive if they are not in compliance with sections VII.B and VIII of this document. If applications are found to be not responsive to this announcement they will be returned to the applicant without further consideration.

Responsive applications will be reviewed and evaluated for scientific and technical merit by an ad hoc panel of experts in the subject field of the specific application.

Responsive applications will also be subject to a second level of review by a National Advisory Council for concurrence with the recommendations made by the first level reviewers. Final funding decisions will be made by the Commissioner of Food and Drugs or his/her designee.

B. Review Criteria

Applicants must clearly state in their application for which of the requested projects they are applying. Applications will be reviewed, and ranked. There is no assurance that awards will be made in all projects. Funding will start with the highest ranked application, and additional awards will be made based on the next highest ranking application, etc., until all available funds have been exhausted. All applications will be evaluated by program and grants management staff for responsiveness. Applicants are strongly encouraged to contact FDA to resolve any questions regarding criteria prior to the submission of their application. All questions of a technical or scientific nature should be directed to the CFSAN program staff, and all questions of an administrative or financial nature should be directed to the grants management staff. (See the **FOR FURTHER INFORMATION CONTACT** section at the beginning of this document for addresses.)

All applications will be reviewed and scored on the following criteria:

1. Soundness of the scientific rationale for the proposed study and appropriateness of the study design and its ability to address all of the objectives of the RFA;
2. Availability and adequacy of laboratory facilities, equipment, and support services, e.g., biostatistics computational support, databases, etc.;
3. Research experience, training, and competence of the principal investigator and support staff, and;
4. Whether the proposed study is within the budget guidelines and proposed costs have been adequately justified and fully documented.

VIII. Submission Requirements

The original and two copies of the completed grant application form PHS 398 (Rev. 4/98) or the original and two copies of PHS 5161-1 (Rev. 7/00) for State and local governments, with copies of the appendices for each of the copies, should be delivered to Maura C. Stephanos (address above). State and local governments may choose to use the PHS 398 application form in lieu of PHS 5161-1. The application receipt date is [*insert date 45 days after date of publication in the Federal Register*]. No supplemental or addendum material will be accepted after the receipt date. The outside of the mailing package and item 2 of the application face page should be labeled: "Response to RFA-FDA-CFSAN-01-3, Project 1, 2, 3 or 4."

IX. Method of Application

A. Submission Instructions

Applications will be accepted during normal business hours, 8 a.m. to 4:30 p.m., Monday through Friday, on or before the established receipt date. Applications will be considered received on time if sent or mailed on or before the receipt date as evidenced by a legible U.S. Postal Service dated postmark or a legible date receipt from a commercial carrier, unless they arrive too late for orderly processing. Private metered postmarks shall not be acceptable as proof of timely mailing. Applications not received on time will not be considered for review and will be returned to the applicant. (Applicants should note that the U.S. Postal Service does not uniformly provide dated postmarks. Before relying on this method, applicants should check with their local post office.) Do not send applications to CSR, NIH. Any application that is sent to NIH, that is then forwarded to FDA and not received in time for orderly processing will be deemed not responsive and returned to the applicant. Applications must be submitted via mail or hand delivery as stated above. FDA is unable to receive applications electronically. Applicants are advised that FDA does not adhere to the page limitations or the type size and line spacing requirements imposed by NIH on its applications.

B. Format for Application

Submission of the application must be on grant application form PHS 398 (Rev. 4/98) or PHS 5161-1 (Rev. 7/00). All "General Instructions" and "Specific Instructions" in the application kit should be followed with the exception of the receipt dates and the mailing label address.

The face page of the application should reflect the request for applications number, RFA-FDA-CFSAN-01-3, Project 1, 2, 3, or 4. Data included in the application, if restricted with the legend specified below, may be entitled to confidential treatment as trade secret or confidential commercial information within the meaning of the Freedom of Information Act (5 U.S.C. 552(b)(4)) and FDA's implementing regulations (21 CFR 20.61).

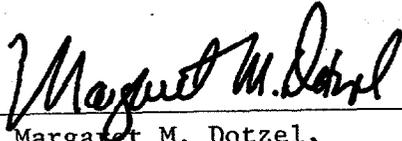
Information collection requirements requested on Form PHS 398 and the instructions have been submitted by PHS to the Office of Management and Budget (OMB) and were approved and assigned OMB control number 0925-0001. The requirements requested on Form PHS 5161-1 were approved and assigned OMB control number 0348-0043.

C. Legend

Unless disclosure is required by the Freedom of Information Act as amended (5 U.S.C. 552) as determined by the freedom of information officials of DHHS or by a court, data contained in the portions of this application that have been specifically identified by page number, paragraph, etc., by the applicant as containing restricted information shall not be used or disclosed except for evaluation purposes.

Dated: 5/15/01
May 15, 2001.

oc0186



Margaret M. Dotzel,
Associate Commissioner for Policy.

CERTIFIED TO BE A TRUE
COPY OF THE ORIGINAL



[FR Doc. 01-????? Filed ??-??-01; 8:45 am]

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