REQUEST FOR INITIAL PROPOSAL (RFIP) FOR AWARD OF A COOPERATIVE AGREEMENT

OVERVIEW INFORMATION

Funding Agency: U.S. Environmental Protection Agency

Laboratory: National Health and Environmental Effects Research Laboratory (NHEERL)

Division: Experimental Toxicology Division (ETD)

Funding Opportunity Title: Exploring Body Burdens of Polybrominated Diphenylethers (PBDEs) and Hexabromocyclododecane (HBCD)

Announcement Type: Initial Announcement

Funding Opportunity Number: EPA/ORD/NHEERL/ETD/04-001

Catalog of Federal Domestic Assistance (CFDA) Number:
66.511 ORD Consolidated Research

Action Dates: September 1, 2004
Final date to submit technical questions: October 1, 2004
Proposals due: November 1, 2004

Executive Summary: EPA desires to support research to expand current understanding of the impact of brominated flame retardants. A variety of brominated flame retardants are of particular concern. The polybrominated diphenylethers (PBDEs) are a class of chemicals widely used as flame retardants. A number of studies in the United States indicate that concentrations of PBDEs in human populations are quite high and seem to be increasing (1,2). Levels measured in breast milk of women in the U.S. are 10-100 times greater than in Europe (3). The flame retardant hexabromocyclododecane (HBCD) is also widely used, but there is significantly less information on its occurrence in humans and the environment. HBCD is used in polystyrene foams and as a backcoating in fabrics. Limited studies to date indicate the HBCD has a high potential to bioaccumulate, is likely very persistent, and seems to have similar neurotoxicological and thyroid disruption properties as some of the PBDEs. There is a need for further research to quantify the levels and body burdens of PBDEs and HBCD within the U.S. population, and to identify possible routes of exposure as well as to identify potential genetic differences that may affect body burdens.

The proposed project will extend previous work evaluating potential exposure to these

two classes of flame retardants and human body burdens. The proposed study will: characterize breast milk samples for PBDEs and HBCD; assess whether levels in dust correlate with body burdens of PBDEs and HBCD by testing house dust of women who have high body burdens of PBDEs and HBCD; explore whether body burdens of PBDEs are decreased in the subjects via lactation, and if so, at what rates; and explore the biological differences among the women that can explain the variability in body burdens. Therefore, the proposed study will correlate HBCD and PBDEs in the population by focusing on women with high and low concentrations of PBDE in breast milk by measuring PBDEs and HBCD in breast milk, urine, and house dust; sampling buccal cells for possible genetic analysis for connection to body burdens; and examining a possible relationship between body burdens and off-loading rates of PBDEs during lactation. The information from the study may be used to evaluate population differences and whether resources should be directed toward reducing exposures of breast-feeding women to certain flame retardant chemicals.

Anticipated Funding: Maximum of $200,000 - One award, which will not exceed $105,000 the first year, $55,000 the second year depending upon the availability of funds, and $40,000 the third year depending upon the availability of funds. **EPA will reject proposals that exceed these limits.** Future funding for the proposed project beyond the first year is not assured, but we want the proposals to include the year 2 and year 3 work in order to make it easier to fund that work should the money be available.

Eligible Applicants: States, territories and possessions, and Tribal nations of the United States, including the District of Columbia, public and private State universities and colleges, hospitals, laboratories, State and local government departments, other public or private nonprofit institutions, and in some cases, individuals who have demonstrated unusually high scientific ability. However, nonprofit organizations described in Section 501(c)(4) of the Internal Revenue Code that engage in lobbying activities as defined in Section 3 of the Lobbying Disclosure Act of 1995 are not eligible to apply.

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FULL TEXT OF ANNOUNCEMENT

I. Funding Opportunity Description

Title of Assistance Opportunity: Exploring Body Burdens of Polybrominated Diphenylethers (PBDEs) and Hexabromocyclododecane (HBCD)

Background: EPA desires to support research to expand current understanding of the impact of brominated flame retardants. A variety of brominated flame retardants are of particular concern. The polybrominated diphenylethers (PBDEs) are a class of chemicals widely used as flame retardants. A number of studies in the United States indicate that concentrations of PBDEs in human populations are quite high and seem to be increasing (1,2). Levels measured in breast milk of women in the U.S. are 10-100 times greater than in Europe (3). The flame retardant hexabromocyclododecane (HBCD) is also widely used, but there is significantly less information on its occurrence in humans and the environment. HBCD is used in polystyrene foams and as a backcoating in fabrics. Limited studies to date indicate the HBCD has a high potential to bioaccumulate, is likely very persistent, and seems to have similar neurotoxicological and thyroid disruption properties as some of the PBDEs. There is a need for further research to quantify the levels and body burdens of PBDEs and HBCD within the U.S. population, and to identify possible routes of exposure as well as to identify potential genetic differences that may affect body burdens.

The proposed project will extend previous work evaluating potential exposure to these two classes of flame retardants and human body burdens. The proposed study will: characterize breast milk samples for PBDEs and HBCD; assess whether levels in dust correlate with body burdens of PBDEs and HBCD by testing house dust of women who have high body burdens of PBDEs and HBCD; explore whether body burdens of PBDEs are decreased in the subjects via lactation, and if so, at what rates; and explore the biological differences among the women that can explain the variability in body burdens. Therefore, the proposed study will correlate HBCD and PBDEs in the population by focusing on women with high and low concentrations of PBDE in breast milk by measuring PBDEs and HBCD in breast milk, urine, and house dust; sampling buccal cells for possible genetic analysis for connection to body burdens; and examining a possible relationship between body burdens and off-loading rates of PBDEs during lactation. The information from the study may be used to evaluate population differences and whether resources should be directed toward reducing exposures of breast-feeding women to certain flame retardant chemicals.

There is rising concern about the brominated flame retardants (BFRs) due to the occurrence of several classes of BFRs in the environment and wildlife and people. Much of the work to date on BFRs has focused on the polybrominated diphenyl ethers (see 1,2,4). There is significantly less information about the toxicity and exposure to HBCD,

though it has similar properties to the PBDEs.

The PBDEs are chemical cousins of the polychlorinated biphenyls (PCBs) (1). Their toxicological and health properties have not been as well studied but, like PCBs, they are neurodevelopmental and reproductive toxicants, endocrine disruptors, and are likely carcinogens (1,4). PBDEs are major additives as flame retardants to polyurethane foam (15-30% by weight) used in furniture, and are also in the hard plastics (5-30% by weight) used in computer and television casings (1,5). They are not chemically-bound, and so are released from plastic and foam into the environment (6). They are found as widespread contaminants in wildlife and humans throughout the world (1,7). Levels have been increasing rapidly in wildlife and people over the last 20 years, and now approach or exceed the levels of PCBs in the U.S. but not in Europe. PBDE levels in San Francisco Bay region are among the highest in the world (8). The PBDE levels in sewage sludge, house dust, biota (fish, bird eggs, seals), and humans in the United States are 10 to100 times higher than European levels (3). In the U.S., the manufacturer has volunteered to phase out the penta- and octa- formulations by the end of 2003, and California banned the use of penta- and octa-BDE as of 2006.

HBCD is a non-aromatic, brominated cyclic alkane used primarily as an additive flame retardant in thermoplastic polymers with final applications in styrene (9). It has also been used, although to a lesser extent, in textile coatings, cable, latex binders, and unsaturated polyesters. Its total production is about 16,700 tons per year, making it the third most widely used brominated flame retardant after tetrabromobisphenol A (TBBPA) and the "deca" PBDE formulation. However, it is used more extensively in Europe than in the Americas, where it has been substituted for some of the non-foam applications for which PBDEs were formerly used. As is the case for the other major BFRs, HBCD is highly lipophilic with a log K_{ow} of 5.6 and has low water solubility (0.0034 mg/L) (10). Recent studies have shown that HBCD has a strong propensity to bioaccumulate, demonstrated by a bioconcentration factor of approximately 18,100 in fathead minnows, as well as fish-to-sediment ratios of up to 15 (11,12). In fact, HBCD is not only bioaccumulative, but is also persistent, with a half life of three days in air and 2-25 days in water (13). Limited toxicity testing has shown that HBCD is not acutely toxic, but may influence thyroid hormone levels. Recent studies by Eriksson and coworkers have demonstrated that early neonatal exposure of mice to HBCD can result in changes in spontaneous behavior, learning and memory defects, and a reduced number of nicotinic receptors (14). Co-exposure to PCBs, resulted in an apparent increase in the response observed with either commercial mixture alone. Several *in vitro* studies have supported the thesis that HBCD has the potential to cause neurobehavioral alterations.

Though analytical methods to detect HBCD are still being perfected, there is increasing evidence that HBCD is bioaccumulating in biota at rates equal to or greater than the PBDEs. Sampling in the Lake Ontario food web, Swiss lakes, Swedish shorebirds and English rivers have found levels of HBCD in sediment, eels, whitefish, trout, and

shorebird eggs. For the higher level predators, HBCD levels have been found to be near or greater than those of PBDEs, and are rising in some areas. The United Kingdom's Chemical Stakeholders Forum determined last March that HBCD is persistent, bioaccumulative, and toxic and "pose[s] a risk to the environment" (15). The EU is currently undertaking a risk assessment of the compound. There is little information regarding HBCD levels in humans.

The major sources and pathways of human exposures to PBDEs and HBCD are unknown (1,6,7). While PBDEs are persistent organic pollutants (POPs), it is unclear whether the general population is mainly exposed by ingestion via animal fats in the diet, as true of most other POPs**,** or whether other sources are important. PBDE body burdens vary more widely among American women than other similar POPs. Women at the high end of the general population have as much as 100 times the concentration of PBDEs than women in the U.S. at the low end (3). This variability is found in both composite and individual breast milk samples, and in samples from different areas of the country. Preliminary studies on PBDEs in food indicate other routes of exposure may be significant.

RESEARCH OBJECTIVES

This proposed study will address two major hypotheses to explain the unusually wide spread of PBDE body burdens: there is a wide range in background exposures; and, there are biological differences among the women that can explain the variability in body burderns. While PBDEs are POPs, it is unclear whether general population exposure is mainly via animal fats in the diet, as true of most other POPs, or whether other routes such as household dust may be important. Correlating house dust levels with body burdens can illuminate the relative contribution of inhalation versus other exposure pathways. If the genetic component is significant, it could indicate that average exposures are higher than previously believed. Finally, measuring the off-loading of PBDEs through lactation will help explain the relationship between past and ongoing exposures. The proposed project will help explain the variability, and potentially narrow he issue of where exposure occurs.

Exposure to PBDEs will be assessed in a group or cohort of women who have known concentrations (levels) of PBDEs in their donated breast milk samples and their dietary and lifestyle surveys have been completed. The women in this cohort must be from an area where high levels of PBDEs have been documented. The women in this cohort must be first time, breast-feeding mothers who have donated milk samples when their infants were 2 to 8 weeks old and these milk samples must have been analyzed and measured for levels of PBDEs. In addition, the dietary and lifestyle survey on these mothers (donors or participants) in this cohort must have been done and is known. This survey information will fully assess the exposures routes of these participants so that exposures via diet and house dust can be related to concentrations of PBDEs and HBCD in breast milk and body burdens.

From the homes of these particpants, house dust will be collected for measurement of PBDE levels. PBDE's are found in many products in the home: foam in furniture can contain up to 30% penta-BDE, and deca-BDE is prevalent in home electronics, small appliances, and back-coatings for furniture and textiles. PBDE levels in house dust samples collected in the U.S. are 50-fold higher than those in European samples. This corresponds to the 50-100-fold difference between U.S. and European body burdens. This study will be one of the first, and the most extensive, to examine the relationship between PBDE levels in house dust and body burdens in the U.S.

The proposed study will explore the critical issues related to body burden variability and will consist of three phases (PHASE ONE, PHASE TWO, and PHASE THREE). Future funding for year 2 and year 3 for the proposed project is not assured, but we want the proposals to include the work in year 2 (Phase Two) and year 3 (Phase Three) in order to make it easier to fund that work should the money be available. The three phases are the following:

PHASE ONE:

A. Exposure to PBDEs must be assessed in breast milk samples with known levels of PBDEs. These breast milk samples must have been collected from a group or cohort of women living in an area where high levels of PBDEs have been documented. In addition, survey information on dietary and lifestyle of each participant in the cohort must have been collected. The women in this cohort must be first time, breast-feeding mothers who donated milk samples when their infants were 2 to 8 weeks old.

The project manager shall uncover predictive indicators of high vs. moderate vs. low levels of PBDE in the samples of human milk from this cohort of women. The participants with high and low concentrations of PBDEs in their breast milk shall be identified for additional samplings. The additional samplings include:

1) collection of house dust samples and analysis for PBDEs, to assess possible routes of exposure and whether PBDE levels in dust correlate with the participant's body burdens (that is, determine the relationship between high body burdens of PBDEs and levels of PBDE in house dust, which is known to contain significant amounts of PBDEs); also duplicate samples of house dust shall be saved for future work and analyses with HBCD in PHASE TWO;

2) collection of urine and analysis for PBDEs to assess whether PBDE levels in urine correlate with body burdens (urine is necessary to understand whether PBDE body burdens are decreased in the participants via urinary excretion, if so, at what rates and is this related to a genetic difference) ; also duplicate samples of urine will be saved for future work and analyses with HBCD in PHASE TWO; and

3) collection of buccal cells to determine biological and genetic differences and polymorphisms by DNA analysis, these cells shalll be saved for future work and analyses in PHASE THREE.

B. In addition from this cohort of women, a subset of participants whose breast milk had high and moderate concentrations of PBDEs (body burdens) shall be identified for additional sampling of breast milk with samples to be collected every other month for 8 months along with urine samples. These breast milk and urine samples shall be analyzed for PBDEs. This part of the study will explore the possible relationship between body burdens and rates of off-loading (that is, whether PBDE body burdens are decreased in the participants via lactation, and if so, at what rates). For the classical POPs (e.g., PCBs, dioxin, organochlorine pesticides), breast milk levels (body burdens) decrease over the tenure of lactation because of the long half-lives of these POPs and the fact that off-loading is greater than the daily intake. If the levels do not decrease, it could suggest ongoing, high exposure.

PHASE TWO:

There is currently little or no information regarding body burdens of HBCD in the U.S. population. The levels of HBCD will be compared to levels of other flame retardants and POPs. This information will answer many important questions about whether HBCD is bioaccumulating in women and at what levels and whether it is bioaccumulating at lower, equal or higher rates than the PBDEs. By comparing HBCD levels to levels of other BFRs, it will provide information on whether humans accumulate HBCD in greater, equal, or lesser proportion to its use in commerce. If HBCD is found, then can the possible exposure routes be identified from the dietary and lifestyle exposure assessments?

Breast milk samples with measured levels of PBDEs in the above cohort of women who donated milk samples (PHASE ONE) will be analyzed for HBCD. The proposed project will expand the scope of the current data base of PBDEs by adding data on the levels of HBCD in human breast milk along with the correlations between PBDEs and HBCD. In addition, the house dust samples that were saved (from PHASE ONE) for PHASE TWO will be analyzed for HBCD to assess whether HBCD levels in dust correlate with the participant's body burdens, and making possible the correlations between body burdens of PBDEs and HBCD in relationship to the participant's house dust. Urine samples that were saved (from PHASE ONE) for PHASE TWO will be analyzed for HBCD to assess whether HBCD levels in urine correlate with body burdens.

PHASE THREE:

The buccal cells collected from the identified participants in PHASE ONE will be analyzed for DNA to evaluate possible biological and genetic differences that could explain the observed variability in PBDE levels. One of greatest interest at this point, based on some emerging results from studies in experimental animals, is that there may be polymorphisms in the MDR1 transporter gene which result in

haplotype differences in the population: i.e., some people rapidly excrete the PBDEs while others do not. Another possibility is that there is dfferential metabolism of the PBDEs by the cytochrome P450 (CYP) family of enzymes due to polymorphisms in these genes. The third is that there are polymorphisms in the UGT genes that are induced by the PBDEs and are responsible for the decrease in thyroid homeostasis that results from PBDE exposures. Genotyping could address all of these issues of genetic heterogeneity in the population that could provide a biological rationale for the observed differences in body burdens; and, identify the genetic basis of biological susceptability. For example, one would hypothesize that women with high levels of PBDEs have the low activity MDR transporter or have a high activity of CYPs. If this biological hypothesis is correct, it would suggest that exposure of the U.S. population is much higher overall than we have thought.

In conducting activities to achieve the purpose of this proposal, the recipient shall be responsible for the Recipient Activities listed in the below Funding Priorities/Focus section.

A. Recipient Activities

Funding Priorities/Focus: The purpose of this RFIP is to solicit proposals for a cooperative agreement to carry out research to expand current understanding of the impact of two classes of flame retardants on the occurrence in humans and the environment. Further research is needed to quantify the levels of PBDEs and HBCD within the U.S. population, and to identify the possible routes of exposure. Applicants responding to this RFIP shall address the reseach objectives and the three phases (Phase One, Phase Two, and Phase Three) of the study as stated above.

GPRA Goals, Objectives: The specific Government Performance Results Act (GPRA) Goals, Objectives and Sub-objectives that relate to this RFIP include:

GPRA GOAL: 4 - Healthy Communities and Ecosystems
4.5 - Science
4.5.2 - Research

Statutory Authority for Award of Assistance: This research is arthorized under the Toxic Substances Control Act (TSCA) of 1976, Section 10 (Research, Development, Collection, Dissemination, and Utilization of Data.).

II. Award Information

Amount and Range of Individual Award: Maximum of $200,000 - One award, which

will not exceed $105,000 the first year, $55,000 the second year depending upon the availability of funds, and $40,000 the third year depending upon the availability of funds. **EPA will reject proposals that exceed these limits.** Future funding for the proposed project beyond the first year is not assured, but we want the proposals to include the year 2 and year 3 work in order to make it easier to fund that work should the money be available.

Number of Awards: One

Funding: The EPA is expected to fund this award over a period of three years depending upon the availability of funds. Funding is not to exceed $105,000 the first year, $55,000 the second year depending upon the availability of funds, and $40,000 the third year depending upon the availability of funds. Future funding for the proposed project is not assured, but we want the proposals to include the year 2 and year 3 work in order to make it easier to fund that work shall the money be available.

Project Period: December 1, 2004 - November 30, 2007

Supplemental Applications: Applications for supplemental awards of existing EPA assistance agreements will not be eligible to compete for this assistance opportunity.

Type of Award: The Agency anticipates the award of a cooperative agreement.

Anticipated Federal Involvement: The recipient will make the final programmatic and scientific decisions. EPA and the Project Officer for this assistance agreement anticipate involvement in the implementation of the research as follows:

1. EPA is able to provide technical consultation in the design and conduct of the research including and consultation in analysis of research data and the interpretation and dissemination of research findings. However, the final decisions on these matters will be made by the recipient provided the design and conduct of the research is consistent with the scope of work EPA agreed to fund.

2. Provide consultation in the development of a research protocol for Institutional Review Board (IRB) review by all institutions participating in the research project. The EPA human subjects official will review and approve the protocol after review by all other participating institutions and on at least an annual basis until the project is completed.

3. Provide consultation in the development of a Quality Assurance Project Plan (QAPP). The EPA will review and approve the QAPP. In addition, the recipient will be subject to Technical Systems Reviews (TSRs) which will be conducted by EPA staff. The recipient shall be responsible for responding to TSR reports.

III. Eligibility Information

Eligible Applicants: Programs under CFDA 66.511 are available to each State, territory and possession, and Tribal nation of the United States, including the District of Columbia, for public and private State universities and colleges, hospitals, laboratories, State and local government departments, and other public or private nonprofit institutions, and in some cases, individuals who have demonstrated unusually high scientific ability. However, nonprofit organizations described in Section 501(c)(4) of the Internal Revenue Code that engage in lobbying activities as defined in Section 3 of the Lobbying Disclosure Act of 1995 are not eligible to apply.

Cost Sharing Requirements: None. However, the Agency will accept voluntary cost shares for eligible and allowable costs that address the RFIP focus of this cooperative agreement. No additional percentages will be added to an applicant's proposal that includes voluntary cost shares. Cost sharing will not have added weight to an applicant's proposal. Proposals with or without cost sharing will be evaluated equally.

Other Eligibility Criteria: Eligible nonprofit organizations include any organizations that meet the definition of nonprofit in OMB Circular A-122. However, nonprofit organizations described in Section 501(c)(4) of the Internal Revenue Code that engage in lobbying activities as defined in Section 3 of the Lobbying Disclosure Act of 1995 are not eligible to apply. Universities and educational institutions must be subject to OMB Circular A-21.

Groups of two or more eligible applicants may choose to form a coalition and submit a single application for this assistance agreement. Coalitions must identify which eligible organization will be the recipient of the assistance agreement, and which eligible organizations(s) will be subawardees of the recipient. Sub awards must be consistent with the definition of that term in 40 CFR 30.2(ff). The recipient must administer the assistance agreement, is accountable to EPA for proper expenditure of the funds, and will be the point of contact for the coalition. As provided in 40 CFR 30.2(gg), sub recipients are accountable to the recipient for proper use of EPA funding.

Coalitions may not include for profit organizations that will provide services or products to the successful applicant. For profit organizations are not eligible for sub awards. Any contracts for services or products funded with EPA financial assistance must be awarded under the competitive procurement procedures of 40 CFR Part 30. The regulations also contain limitations on consultant compensation. Applicants are not required to identify contractors or consultants in the proposal. Moreover, the fact a successful applicant has named a specific contractor or consultant in the proposal EPA approves does not relieve it of its obligations to comply with competitive procurement requirements or consultant compensation limitations.

Applications will be reviewed for threshold eligibility purposes during the Administrative Review and Relevance Review. Only applications that are found acceptable as a result of the administrative review and relevance review will be evaluated against the evaluation factors set forth in Section V. Initial proposals from eligible applicants deemed ineligible for award or that fail to meet either the administrative review or relevance review will be returned without further review. The Admininstrative Review and Relevance Review factors are as follows:

Administrative Review: All initial proposals will be subject to an administrative review to ensure that they conform with the requirements of this RFIP. EPA will reject any applications that fail to conform with the requirements of this RFIP.

Relevance Review: Initial proposals that are found administratively acceptable will be subjected to a review for relevancy to EPA's mission to support advancement of environmental science. Initial proposals will be rejected if they are found to lack relevance. Examples of proposals that lack relevance include situations where the:

1. Proposal is deficient technically with no chance for consideration.

2. Proposal fails to advance the objectives stated in the solicitation even if successfully performed.

3. Proposal essentially duplicates research already completed or underway.

4. Proposal fails to demonstrate a public purpose of support and stimulation; i.e., it implies the primary purpose is to provide direct support to the Federal government.

IV. Application and Submission Information

Address to Request Application Package: Janet J. Diliberto, United States Environmental Protection Agency (US EPA), National Health and Environmental Effects Research Laboratory (NHEERL), Experimental Toxicology Division, MD-B143-01, 109 T. W. Alexander Drive, Research Triangle Park, NC 27711 or diliberto.janet@epa.gov. Application information is also available from the EPA/ORD/NHEERL website at http://www.epa.gov/nheerl/about/researchopportunities.html under the heading Assistance Opportunities. This document, and any subsequent amendments, constitutes the entire Request for Initial Proposal.

Content and Form of Application Submission: At a minimum, the initial proposal shall consist of the following items:

1. A cover sheet that identifies the RFIP title and identification number, name and address of applicant, point of contact, telephone number, e-mail address for the applicant, applicant's DUNS number (see Section VIII), and the date of the submission.

2. Technical proposal that discusses the approach to accomplishing the goals (objectives and the three phases) stated under Funding Priorities/Focus, the capabilities (in terms of personnel and facilities) of the applicant to complete the research, the expected results from this research, how the research will advance and stimulate the public need and support the accomplishment of a public purpose and not principally the benefit or use of the Federal Government, and how the results will be made available to the public and government. The recipient will make the final programmatic and scientific decisions. In developing the technical proposal, the applicant must focus on the evaluation criteria set forth in Section V and structure the proposal to address each of the criteria in the order listed.

The page limitation of the technical proposal is 10 double-sided pages (20 pages total) with a minimum font size of 12. This page limitation will include all text, tables, figures, references, attachments, and appendices. In proposals that exceed the page limits, the extra pages will not be read. In addition, and not included in the page limit described above, a 2-page curriculum vitae must be included for the applicant and a 1-page curriculum vitae must be included for each of any other key personnel identified in the applicant's proposal.

3. A budget estimate for the project that is broken down into direct labor, fringe benefits, equipment, travel, other direct costs and overhead with summaries for each year and the total for the entire project. Indicate any proposed cost sharing (not required). The Agency will accept voluntary cost shares for eligible and allowable costs.

4. A Quality Management Plan that describes the applicant's quality system for its organization. The Plan must be prepared in accordance with the specifications provided in *EPA Requirements for Quality Management Plans (QA/R-2)* or address the same topics as required by QA/R-2. *QA/R-2* may be downloaded from the Internet at http://www.epa.gov/quality/qa_docs.html

Initial proposals should be submitted in the original with 3 copies and should be double-sided.

Submission Date, Time, and Location: To be considered timely, initial proposals must be received by **4:00 pm local time on Monday, November 1, 2004** from the U.S. Postal Service or other commercial delivery service. Proposals shall be submitted to Janet J. Diliberto, Project Officer, US Environmental Protection Agency, NHEERL/ETD, Mail Drop: B143-01, 109 T. W. Alexander Drive, Research Triangle Park, NC 27711. Initial proposals received after the deadline will not be considered and will be returned to the

submitter. Applicants that submit proposals by hand may request a receipt from the security guard at the main entrance of the U.S. EPA facility at 109 T. W. Alexander Drive, Research Triangle Park, NC.

Intergovernmental Review: This assistance opportunity is subject to Executive Order 12372, "Intergovernmental Review of Federal Programs." Applicants should contact their State's Single Point of Contact (SPOC) to find out how to comply with the State's process. The names and addresses of the SPOC's are listed in the Office of Management and Budget's home page at: http://www.whitehouse.gov/omb/grants/spoc.html.

Funding Restrictions: Funding of the award is not to exceed $105,000 the first year, $50,000 the second year, and $45,000 the third year depending upon the availability of funds. **EPA will reject proposals that exceed these limits.** Future funding for the proposed project beyond the first year is not assured, but we want the proposals to include the year 2 and year 3 work in order to make it easier to fund that work should the money be available.

Amendments: Amendments will be posted on this website and synopsized on fedgrants.gov and the due date for initial proposals will be extended if deemed appropriate.

Other Submission Requirements: None.

V. Application Review Information

Criteria: The criteria used to evaluate proposals include:

Administrative Review: As stated in Section III, all initial proposals will be subject to an administrative review to ensure that they conform with the requirements of this RFIP. EPA will reject any applications that fail to conform with the requirements of this RFIP.

Relevance Review: As stated in Section III, initial proposals that are found administratively acceptable will be subjected to a review for relevancy to EPA's mission to support advancement of environmental science. Initial proposals may be rejected if they are found to lack relevance. Examples of proposals that lack relevance include situations where the:

1. Proposal is deficient technically with no chance for consideration.

2. Proposal fails to advance the objectives stated in the solicitation even if successfully performed.

3. Proposal essentially duplicates research already completed or underway.

4. Proposal fails to demonstrate a public purpose of support and stimulation; i.e., it implies the primary purpose is to provide direct support to the Federal government.

Next Step in Review Process: Only initial proposals that meet the adminitrative review and relevance review will be subject to the technical review described below and be eligible for award. Initial proposals from eligible applicants that are deemed ineligible for award or that fail to meet either the administrative review or relevance review will be returned without further review.

Criteria For Technical Review: Initial proposals that are found administratively acceptable and relevant shall be reviewed for technical merit against the following criteria.

1. Technical approach for addressing the RFIP focus includes the use of a cohort of women living in a geographical area where high levels of PBDEs have been documented and previously reported. From these women, breast milk samples must have been collected and PBDEs levels must have been determined. In these women, a dietary and lifestyle information must has been collected. These women must be first time mothers (donors or participants) in their second to eighth week of lactation. All of these factors are important in linking human exposure to body burdens of PBDEs. This link is needed to meet the proposed project's research objectives of exploring the critical issues related to body burden variability of PBDEs and makes possible the exposure assessment of PBDEs in women. (40%)

2. Institutional capability for addressing the RFIP focus including laboratory space and equipment must be available for use under this assistance agreement near the same geographical region of the area where high levels of PBDEs have been documented and previously reported. (10%)

3. Qualifications of the applicant for addressing the RFIP focus include that the applicant must be familiar with the design and conduct of an epidemiology study as referred to in the research objectives and three phases of this assistance agreement. The applicant must be familiar with conduct of a human study, analytical chemisty, sampling and analyzing both human and environmental samples, and analyzing and reporting the data as related to this assistance agreement. The applicant must be associated with a geographical region where high levels of PBDEs have been documented and previously reported. (30%)

4. Past Performance. Demonstrated peer-reviewed publication record in projects of similar size and scope to this agreement. (10%)

5. Quality Management Plan. Current overall quality assurance plan for the applicant's organization. (10%)

Review and Selection Process:

Evaluation Process: The administrative and relevancy reviews will be conducted by EPA personnel who are not a part of the technical review panel. The review of the technical review criteria will be conducted by a technical review panel; the technical review panel shall consist of at least one internal EPA reviewer and at least two non-EPA reviewers who are able to demonstrate technical expertise in the areas related to the RFIP and DO NOT HAVE any conflicts of interest.

Source Selection: A preliminary selection of the applicant for award will be made based upon the ranking of the technical review panel and the other factors discussed above. The Decision Official is an Office of Research and Development (ORD) Manager who will preliminarily select which applicant should receive the award.

Full Application: The applicant selected for award will be requested to submit a full, detailed application in accordance with the guidance provided by EPA's Office of Grants and Debarment (http://www.epa.gov/ogd/).

Rejection Factors: Applications will be rejected because they fail to comply with the administrative requirements of the RFIP, they are found to lack relevancy, they are judged technically unacceptable, or they are not deemed suitable for award due to other factors (if identified). EPA reserves the right to reject all proposals or applications and make no awards.

Anticipated Announcement and Award Dates: The anticipated award date is December 1, 2004.

VI. Award Administration Information

Award Notices: Notice of award will be made in writing by an official in the EPA Grants Administration Division. Preliminary selection by the Decision Official in the Office of Research and Development does not guarantee an award will be made. Applicants are cautioned that only a grants officer can bind the Government to the expenditure of funds. No commitment on the part of EPA should be inferred from technical or budgetary discussions with an EPA Program Official. A Principal Investigator or organization that makes financial or personnel commitments in the absence of a grant or cooperative agreement signed by the EPA Grants Award Official does so at their own risk.

EPA will promptly notify in writing (postal or email) those applicants whose proposal has not been relected for award. An unsuccessful applicant may request a debriefing to better

understand the evaluated strengths and weaknesses of its proposal and the reason it was not selected for award.

Administrative and National Policy Requirements:

Regulations and OMB Coverage:

Grants and agreements with institutions of higher education, hospitals, and other non-profit organizations are subject to 40 CFR Parts 30 and 40 and OMB Circular A-122 for non-profits and A-21 for institutions of higher learning.

Grants and agreements with state, local, and tribal governments are subject to 40 CFR Parts 31 and 40 and OMB Circular A-87.

Disputes: Disputes will be resolved pursuant to the process described in 40 CFR 30.63 and Part 31, subpart F.

Programmatic Terms and Conditions: Terms and conditions will include a substantial EPA involvment provision and will be negotiated with the selected recipient covering the following requirements:

An acceptable quality assurance document, i.e., Quality Assurance Project Plan (QAPP), shall be due within 45 days of award.

Reporting:

Quarterly Progress Reports: The selected recipient will be required to submit quarterly progress reports (hard and electronic copies) summarizing technical progress, difficulties encountered, and planned activities for the next quarter. Each report shall include a summary of expenditures.

Final Report: The selected recipient will be required to submit a final report (hard and electronic copies) within 90 days of the completion of the period of performance.

VII. Agency Contact

The primary agency contact for this RFIP is Janet J. Diliberto at:

US Environmental Protection Agency
National Health and Environmental Effects Research Laboratory (NHEERL)
Experimental Toxicology Division
MD-B143-01
109 T. W. Alexander Drive

Research Triangle Park, NC 27711
Telephone: 919-541-7921
Fax: 919-541-9464
E-mail: diliberto.janet@epa.gov

If unable to reach Janet J. Diliberto, please contact Ms. Margaret Mann at:
Telephone: 919-541-4896
Fax: 919-541-2581
E-mail: mann.margaret@epa.gov

VIII. Other Information

Questions: Questions should be submitted in writing to Janet J. Diliberto. Do not attempt to seek information regarding this RFIP from any source other than those identified in Section VII as the information provided may be erroneous. Answers to significant clarifying questions will be posted on a web site. If there is a material change to the RFIP (i.e., an extension of the due date, increase or decrease in funding, change in criteria), then an amendment will be made to this RFIP.

Confidential Information: Clearly mark information considered to be confidential. EPA will make final confidentially decisions in accordance with Agency regulations at 40 CFR, Part 2, Subpart B. As noted above, initial proposals for research and demonstration projects will be provided to at least two non-EPA consultants for review. All reviewers will be required to sign confidentiality agreements certifying they will keep all deliberations confidential, and they will not copy any portions of any material provided by EPA for review, and they will return all material to EPA upon request. If you are unwilling to allow non-EPA consultants to review, please advise us of your decision in a cover letter to your proposal. The successful applicant must provide all data, methods, and models resulting from this agreement to EPA. The Agency will use and disseminate the information in accordance with EPA regulations at 40 CFR 30.36.

DUNS Number: Grant applicants are required to provide a Dun and Bradstreet (D&B) Data Universal Numbering System (DUNS) number when applying for Federal grants or cooperative agreements. OMB has determined that there is a need for improved statistical reporting of Federal grants and cooperative agreements. Use of the DUNS number government-wide will provide a means to identify entities receiving those awards and their business relationships. The identifier will be used for tracking purposes, and to validate address and point of contact information.

A DUNS number will be required whether an applicant is submitting a paper application or using the government-wide electronic portal (Grants.gov). The DUNS number will supplement other identifiers required by statute or regulation, such as tax identification numbers. Organizations can receive a DUNS number in one day, at no cost, by calling

the dedicated toll-free DUNS Number request line at 1–866–705– 5711. Individuals who would personally receive a grant or cooperative agreement award from the Federal government apart from any business or non-profit organization they may operate are exempt from this requirement. The website where an organization can obtain a DUNS number is: http://www.dnb.com. This takes 30 business days and there is no cost unless the organization requests expedited (1-day) processing, which includes a fee of $40.

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