sought. (These access procedures are in accordance with the Department regulation 45 CFR 5b.5(a)(2).)

CONTESTING RECORD PROCEDURES:

Contact the system manager named above, and reasonably identify the record and specify the information to be contested. State the corrective action sought and the reasons for the correction with supporting justification. (These procedures are in accordance with Department regulation 45 CFR 5b.7.)

RECORD SOURCE CATEGORIES:

Information is reported by private long term care insurance companies selling policies that have been certified by a state insurance commissioner as Partnership qualified in a state that had obtained a Medicaid state plan amendment approved after of May 14, 1993.

SYSTEMS EXEMPTED FROM CERTAIN PROVISIONS OF THE ACT:

None.

[FR Doc. E8–28345 Filed 12–17–08; 8:45 am]

BILLING CODE 4154–05–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2008–N–0613]

Clinical Studies of Safety and Effectiveness of Orphan Products

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration's (FDA) Office of Orphan Product Development (OPD) is providing notice of a funding opportunity announcement for Federal assistance. The goal of the OPD grant program is to support the clinical development of products for use in rare diseases or conditions where no current therapy exists or where the proposed product will be superior to the existing therapy. FDA provides grants for clinical studies on safety and/or effectiveness that will either result in, or substantially contribute to, market approval of these products.

DATES: See section IV.E of the **SUPPLEMENTARY INFORMATION** section for application submission dates.

FOR FURTHER INFORMATION CONTACT:

Scientific/Research Contact: Katherine Needleman, Office of Orphan Products Development, Food and Drug Administration (HF–35), rm. 6A–55, 5600 Fishers Lane, Rockville, MD 20857, 301–827–3666, e-mail: *katherine.needleman@fda.hhs.gov*.

Financial/Grants Management Contact: Vieda Hubbard, Office of Acquisitions & Grant Services, 5630 Fishers Lane (HFA–500), rm. 2104, Rockville, MD 20857, 301–827–7177, e-mail: *vieda.hubbard@fda.hhs.gov*.

SUPPLEMENTARY INFORMATION:

I. Funding Opportunity Description

Research Project Grants (R01)
Request for Application (RFA) Number: RFA–FD–09–001
Catalog of Federal Domestic Assistance Number(s): 93.103

A. Research Objectives

1. Background

OPD was created to identify and promote the development of orphan products. Orphan products are drugs, biologics, medical devices, and foods for medical purposes that are indicated for a rare disease or condition (that is, one with prevalence, not incidence, of fewer than 200,000 people in the United States). Diagnostics and vaccines will qualify for orphan status only if the U.S. population to whom they will be administered is fewer than 200,000 people per year.

2. Research Objectives

The goal of FDA's OPD grant program is to support the clinical development of products for use in rare diseases or conditions where no current therapy exists or where the proposed product will be superior to the existing therapy. FDA provides grants for clinical studies on safety and/or effectiveness that will either result in, or substantially contribute to, market approval of these products. Applicants must include, in the application's ''Background and Significance'' section, documentation to support the estimated prevalence of the orphan disease or condition (or in the case of a vaccine or diagnostic, information to support the estimates of how many people will be administered the diagnostic or vaccine annually) and an explanation of how the proposed study will either help gain product approval or provide essential data needed for product development.

See section VII.A of this document for policies related to this announcement.

II. Award Information

A. Mechanism of Support

Support will be in the form of a research project (R01) grant. The R01 grant is an award made to support a discrete, specified, circumscribed project to be performed by the named investigator(s) in an area representing the investigator's specific interest and competencies, based on the mission of FDA. The Project Director/Principal Investigator (PD/PI) will be solely responsible for planning, directing, and executing the proposed project.

All awards will be subject to all policies and requirements that govern the research grant programs of the Public Health Service (PHS) as incorporated in the Department of Health and Human Services (HHS) Grants Policy Statement, dated January 1, 2007 (*http://www.hhs.gov/grantsnet/adminis/gpd/index.htm*), 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 National Institutes of Health (NIH) modular grant program does not apply to this FDA grant program. All grant awards are subject to applicable requirements for clinical investigations imposed by sections 505, 512, and 515 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355, 360b, and 360e), section 351 of the PHS Act, regulations issued under any of these sections, and other applicable HHS statutes and regulations regarding human subject protection.

Except for applications for studies of medical foods that do not need premarket approval, FDA will only award grants to support premarket clinical studies to determine safety and effectiveness for approval under section 505 or 515 of the Federal Food, Drug, and Cosmetic Act or safety, purity, and potency for licensing under section 351 of the PHS Act. FDA will support the clinical studies covered by this notice under the authority of section 301 of the PHS Act (42 U.S.C. 241). FDA's research program is described in the Catalog of Federal Domestic Assistance (CFDA) No. 93.103.

B. Funds Available

1. Award Amount

Of the estimated FY 2010 funding ($14.1 million), approximately $10 million will fund noncompeting continuation awards, and approximately $4.1 million will fund 10 to 12 new awards, subject to availability of funds. It is anticipated that funding for the number of noncompeting continuation awards and new awards in FY 2011 will be similar to FY 2010. Grants will be awarded up to $200,000 or up to $400,000 in total (direct plus indirect) costs per year for up to 4 years. Please note that the dollar limitation will apply to total costs, not direct costs, as in

previous years. A fourth year of funding is available only for phase 2 or 3 clinical studies. Applications for the smaller grants ($200,000) may be for phase 1, 2, or 3 studies. Study proposals for the larger grants ($400,000) must be for studies continuing in phase 2 or 3 of investigation. Budgets for each year of requested support may not exceed the $200,000 or $400,000 total cost limit, whichever is applicable.

Phase 1 studies, including the initial introduction of an investigational new drug (IND) or device into humans, are usually conducted in healthy volunteer subjects, and are designed to determine the metabolic and pharmacological actions of the product in humans, and the side effects, including those associated with increasing drug doses. In some phase 1 studies that include subjects with the rare disorder, it may also be possible to gain early evidence on effectiveness.

Phase 2 studies include early controlled clinical studies conducted to: (1) Evaluate the effectiveness of the product for a particular indication in patients with the disease or condition and (2) determine the common short-term side effects and risks associated with it.

Phase 3 studies gather more information about effectiveness and safety that is necessary to evaluate the overall risk-benefit ratio of the product and to provide an acceptable basis for product labeling.

2. Length of Support

The length of support will depend on the nature of the study. For those studies with an expected duration of more than 1 year, a second, third, or fourth year of noncompetitive continuation of support will depend on the following factors: (1) Performance during the preceding year, (2) compliance with regulatory requirements of IND/investigational device exemption (IDE), and (3) availability of Federal funds.

3. Funding Plan

In addition to the requirement for an active IND/IDE discussed in section V.C of this document, documentation of assurances with the Office of Human Research Protection (OHRP) (see section IV.F.1 of this document) must be on file with the FDA grants management office before an award is made. Any institution receiving Federal funds must have an institutional review board (IRB) of record even if that institution is overseeing research conducted at other performance sites. To avoid funding studies that may not receive or may experience a delay in receiving IRB approval, documentation of IRB approval and Federal Wide Assurance (FWA or assurance) for the IRB of record for all performance sites must be on file with the FDA grants management office before an award to fund the study will be made. In addition, if a grant is awarded, grantees will be informed of any additional documentation that should be submitted to FDA's IRB.

Because the nature and scope of the proposed research will vary from application to application, it is anticipated that the size and duration of each award will also vary. Although the financial plans of FDA provide support for this program, awards under this funding opportunity are contingent upon the availability of funds.

FDA grants policies as described in the HHS Grants Policy Statement: (*http://www.hhs.gov/grantsnet/adminis/gpd/index.htm*) will apply to the applications submitted and awards made in response to this FOA.

III. Eligibility Information

A. Eligible Applicants

1. Eligible Institutions

The grants are available to any foreign or domestic, public or private, for-profit or nonprofit entity (including State and local units of government). Federal agencies that are not part of HHS may apply. Agencies that are part of HHS may not apply. For-profit entities must commit to excluding fees or profit in their request for support to receive grant awards. Organizations that engage in lobbying activities, as described in section 501(c)(4) of the Internal Revenue Code of 1968, are not eligible to receive grant awards.

2. Eligible Individuals

Any individual(s) with the skills, knowledge, and resources necessary to carry out the proposed research as the PD/PI is invited to work with his/her organization to develop an application for support. Individuals from under-represented racial and ethnic groups as well as individuals with disabilities are always encouraged to apply for FDA support.

More than one PD/PI (i.e., multiple PDs/PIs) may be designated on the application for projects that require a ''team science'' approach and therefore clearly do not fit the single-PD/PI model. Additional information on the implementation plans and policies and procedures to formally allow more than one PD/PI on individual research projects is available at *http://grants.nih.gov/grants/multi_pi*.[1] All PDs/PIs must be registered in the NIH electronic Research Administration (eRA) Commons (hereafter called eRA Commons or the Commons) prior to the submission of the application. (See *http://era.nih.gov/ElectronicReceipt/preparing.htm* for instructions.)

When multiple PDs/PIs are proposed, FDA requires one PD/PI to be designated as the ''Contact'' PI. The ''Contact'' PI will be responsible for: (1) All communication between the PDs/PIs and FDA, (2) assembling the application materials outlined in section IV of this document, and (3) coordinating progress reports for the project. The contact PD/PI must meet all eligibility requirements for PD/PI status in the same way as other PDs/PIs, but has no other special roles or responsibilities within the project team beyond those mentioned in the previous sentence.

The decision of whether to apply for a single PD/PI or multiple PD/PI grant is the responsibility of the investigators and applicant organizations and should be determined by the scientific goals of the project. Applications for multiple PD/PI grants will require additional information, as outlined in the instructions in section IV of this document, and the FDA review criteria for approach, investigator, and environment has been modified to accommodate applications involving either a single PD/PI or multiple PDs/PIs as indicated in section IV of this document. A weak or inappropriate PD/PI can have a negative effect on the review. Multiple PDs/PIs on a project share the authority and responsibility for leading and directing the project, intellectually and logistically. Each PD/PI is responsible and accountable to the grantee organization, or, as appropriate, to a collaborating organization, for the proper conduct of the project or program, including the submission of all required reports. For further information on multiple PDs/PIs, please see *http://grants.nih.gov/grants/multi_pi*.

B. Cost Sharing or Matching

This grant program does not require the applicant to match or share in the project costs if an award is made.

C. Other Special Eligibility Criteria

Applicants may submit more than one application, provided each application is scientifically distinct.

[1] FDA has verified the Web site addresses throughout this document, but FDA is not responsible for any subsequent changes to the Web sites after this document publishes in the **Federal Register**.

IV. Application and Submission Information

To comply with the President's Management Agenda, HHS is participating, as a partner, in the new governmentwide grants.gov application site. Applicants should apply electronically by visiting the Web site www.grants.gov and following instructions under ''Apply for Grants.''Users of grants.gov will be able to download a copy of the application package, complete it offline, and then upload and submit the application via the grants.gov Web site. We strongly encourage using the ''Tips'' posted on www.grants.gov under the announcement number when preparing your submission. This process is similar to the R01 Grant Application process currently used at NIH. You can visit the following Web site for helpful background on preparing to apply, preparing an application, and submitting an application to Grants.gov: *http://era.nih.gov/ElectronicReceipt/*. In order to apply electronically, the applicant must have a Data Universal Number System (DUNS) number, and register in the Central Contractor Registration (CCR) database, in eRA Commons (*http://era.nih.gov/ElectronicReceipt/preparing.htm*), and in grants.gov (further explained in the following section IV.A of this document).

A. Registration Information

To download a SF424 (R&R) Application Package and SF424 (R&R) Application Guide for completing the SF424 (R&R) forms for this FOA, link to *http://www.grants.gov/Apply/* (hereafter called Grants.gov/Apply) and follow the directions provided on that Web site.

A one-time registration is required for institutions/organizations at both:

- Grants.gov (*http://www.grants.gov/GetStarted*) and
- eRA Commons (*http://era.nih.gov/ElectronicReceipt/preparing.htm*).

A registration process with Grants.gov and eRA Commons is necessary before submission and applicants are highly encouraged to start the process at least 4 weeks prior to the grant submission date. PDs/PIs should work with their institutions/organizations to make sure they are registered in the eRA Commons.

Several additional separate actions are required before an applicant institution/organization can submit an electronic application, as follows:

(1) Organizational/Institutional Registration at: *http://www.grants.gov/applicants/get_registered.jsp.*

- Your organization will need to obtain a DUNS number (*https://eupdate.dnb.com/requestoptions/government/ccrreg/*) and register with the CCR (*http://www.ccr.gov/*) as part of the Grants.gov registration process.
- The DUNS number is a 9-digit identification number that uniquely identifies business entities.
- The CCR database is a governmentwide warehouse of commercial and financial information for all organizations conducting business with the Federal Government.
- If your organization does not have a Taxpayer Identification Number (TIN) or Employer Identification Number (EIN), allow for extra time. A valid TIN or EIN is necessary for CCR registration.
- The CCR also validates the EIN against Internal Revenue Service records—a step that will take an additional 1 to 2 business days.
- Tips for foreign organization registration are available at: *http://era.nih.gov/ElectronicReceipt/preparing.htm#4*.
- Direct questions regarding Grants.gov registration can be directed to the

Grants.gov Customer Support Center: (*http://www.grants.gov/help/help.jsp*), 1–800–518–4726, Monday through Friday, 7 a.m. to 9 p.m., e.s.t., e-mail: *support@grants.gov*.

(2) Organizational/Institutional Registration on the eRA Commons (*https://commons.era.nih.gov/commons/registration/registrationInstructions.jsp*)

- To find out if an organization is already Commons-registered, see the ''List of Grantee Organizations Registered in eRA Commons''(*http://era.nih.gov/userreports/ipf_com_org_list.cfm*).
- Direct questions regarding the Commons registration can be directed to: eRA Commons Help Desk, 301–402–7469 or 866–504–9552 (toll free), TTY: 301–451–5939, Monday through Friday, 7 a.m. to 8 p.m., e.s.t., e-mail: *commons@od.nih.gov*.

(3) PD/PI Registration on the eRA Commons Web site at: *http://era.nih.gov/docs/COM_UGV2630.pdf*.

- The individual(s) designated as PDs/PIs on the application must also be registered in the eRA Commons. In the case of multiple PDs/PIs, all PDs/PIs must be registered in the eRA Commons prior to the submission of the application.
- Each PD/PI must hold a PD/PI account in the Commons. Applicants should not share a Commons account for both an Authorized Organization Representative/Signing Official (AOR/SO) role and a PD/PI role; however, if they have both a PD/PI role and an Internet Assisted Review (IAR) role, both roles should exist under one Commons account. When multiple PDs/PIs are proposed, all PDs/PIs at the applicant organization must be affiliated with that organization. PDs/PIs located at another institution need not be affiliated with the applicant organization, but must be affiliated with their own organization to be able to access the Commons.
- This registration/affiliation must be done by the AOR/SO or their designee who is already registered in the Commons.
- Both the PD/PI(s) and AOR/SO need separate accounts in the eRA Commons since both are authorized to view the application image.Note that if a PD/PI is already registered in the eRA Commons, another registration to apply for an FDA opportunity is not necessary.

Note that if a PD/PI is also an NIH peer reviewer with an Individual DUNS and CCR registration, that particular DUNS number and CCR registration are for the individual reviewer only. These are different than any DUNS number and CCR registration used by an applicant organization. Individual DUNS and CCR registration should be used only for the purposes of personal reimbursement and should not be used on any grant applications submitted to the Federal Government.

Several of the steps of the registration process could take 4 weeks or more. Therefore, applicants should immediately check with their business official to determine whether their organization/institution is already registered in both Grants.gov and the Commons (*https://commons.era.nih.gov/commons/*). The FDA will accept electronic applications only from organizations that have completed all necessary registrations.

If you experience technical difficulties with your online submission, you should contact the grants.gov Customer Response Center: (*http://www.grants.gov/contactus/contactus.jsp*. If the Customer Response Center is unable to resolve your problem, please contact Marc Pitts, Grants Management Specialist, Division of Acquisition Support and Grants (DASG), Office of Acquisition & Grant Services (OAGS), Food and Drug Administration, 301–827–7162, e-mail: *marc.pitts@fda.hhs.gov*.

B. Request Application Information

In FYs 2010 and 2011, all applications must be submitted electronically through Grants.gov. Applicants must download the SF424 (R&R) application forms and the SF424 (R&R) Application Guide for this FOA through Grants.gov/Apply.

Note: Only the forms package directly attached to a specific FOA can be used. You will not be able to use any other SF424 (R&R) forms (e.g., sample forms, forms from another FOA), although some of the ''Attachment'' files may be useable for more than one FOA.

For further assistance, contact Marc Pitts at 301–827–7162. Telecommunications for the hearing impaired: 301–480–0434.

C. Content and Form of Application Submission

Prepare all applications using the SF424 (R&R) application forms along with the SF424 (R&R) Application Guide for this FOA through *http://www.grants.gov/applicants/apply_for_grants.jsp*.

Note: The following link provides additional information to the Adobe transition submission process: (*http://era.nih.gov/ElectronicReceipt/files/adobe_transition.pdf*).

The SF424 (R&R) Application Guide is critical to submitting a complete and accurate application to FDA. Some fields within the SF424 (R&R) application components, although not marked as mandatory, are required by FDA (e.g., the ''Credential'' log-in field of the ''Research & Related Senior/Key Person Profile'' component must contain the PD/PI's assigned eRA Commons User ID). Agency-specific instructions for such fields are clearly identified in the Application Guide. For additional information, see ''Frequently Asked Questions—Application Guide, Electronic Submission of Grant Applications'' (*http://era.nih.gov/ElectronicReceipt/faq_prepare_app.htm#1*).

Prepare all applications using the SF424 (R&R) application forms along with the SF424 (R&R) Application Guide for this FOA through Grants.gov/Apply at: *http://www.grants.gov/applicants/apply_for_grants.jsp*.

Note that the move to electronic applications has brought a change in terminology. The new Grants.gov terminology is as follows:

New = New

Resubmission = A Revised or Amended application

Renewal = Competing Continuation

Continuation = Noncompeting Progress Report

Revision = Competing Supplement

The SF424 (R&R) application has several components. Some components are required, others are optional. The forms package associated with this FOA in Grants.gov/APPLY includes all applicable components, required and optional. A completed application in response to this FOA includes the data in the following components:

Required Components

SF424 (R&R) (Cover component)

Research & Related Project/Performance Site Locations

Research & Related Other Project Information

Research & Related Senior/Key Person

PHS398 Cover Page Supplement

PHS398 Research Plan

PHS398 Checklist

PHS398 Research & Related Budget

Research & Related Subaward Budget Attachment(s) Form

Optional Components

PHS398 Cover Letter File

Foreign Organizations—(Non-domestic (non-U.S.) Entity)

Applications from foreign organizations must:

- Request budgets in U.S. dollars.
- Prepare detailed budgets for all applications (that is, complete the Research & Related Budget component of the SF424).
- Not seek charge back of customs and import fees.
- Make every effort to comply with the format specifications, which are based upon a standard U.S. paper size of 8.5'' x 11'' within each portable document format (PDF).
- Comply with Federal/FDA policies on human subjects, animals, and biohazards.
- Comply with Federal/FDA biosafety and biosecurity regulations. See section VI.B of this document, ''Administrative and National Policy Requirements.''
- Indicate in the 398 Research Plan how the proposed project has specific relevance to FDA's mission and objectives and has the potential for significantly advancing sciences in the United States.

Proposed research should provide special opportunities for furthering research programs through the use of unusual talent, resources, populations, or environmental conditions in other countries that are not readily available in the United States or that augment existing U.S. resources.

D. Special Instructions

1. Applicants Who Are Submitting a Renewal or Revision

Applicants submitting a renewal or resubmission are required to enter the previous grant number into the Federal Identifier field in the SF424 (R&R) Cover Component form (box #8). Renewal and resubmission applications that do not include this number will receive an error message. Applicants should log on to the eRA Commons to obtain the previous grant number. If the number is not available in Commons, contact Marc Pitts at 301–827–7162 at FDA to get the previous grant number in order to submit the application. Visit *http://era.nih.gov/ElectronicReceipt/resubmission_FAQ.htm* for additional information. If an application for the same study was submitted in response to a previous RFA but has not yet been funded, an application in response to this notice will be considered a request to withdraw the previous application. The applicant for a resubmitted application should address the issues presented in the summary statement from the previous review and include a copy of the summary statement itself as part of the resubmitted application. An application that has received two prior disapprovals is not eligible for resubmission.

2. Applications With Multiple PDs/PIs

When multiple PDs/PIs are proposed, FDA requires one PD/PI to be designated as the ''Contact'' PI. The ''Contact PI will be responsible for: (1) All communication between the PDs/PIs and FDA, (2) assembling the application materials outlined below, and (3) coordinating progress reports for the project. The contact PD/PI must meet all eligibility requirements for PD/PI status in the same way as other PDs/PIs, but has no other special roles or responsibilities within the project team beyond those mentioned in the previous sentence.

Information for the Contact PD/PI should be entered in item 15 of the SF424 (R&R) Cover component. All other PDs/PIs should be listed in the Research & Related Senior/Key Person component and assigned the project role of ''PD/PI.'' Please remember that all PDs/PIs must be registered in the eRA Commons prior to application submission. The Commons ID of each PD/PI must be included in the ''Credential'' field of the Research & Related Senior/Key Person component. Failure to include this data field will cause the application to be rejected.

All projects proposing multiple PDs/PIs will be required to include a new section describing the leadership of the project.

Multiple PD/PI Leadership Plan: For applications designating multiple PDs/PIs, a new section of the research plan entitled ''Multiple PD/PI Leadership Plan'' (section 14 of the PHS398 Research Plan component), must be included. A rationale for choosing a multiple PD/PI approach should be described. The governance and organizational structure of the research project should be described, and should include communication plans, process

for making decisions on scientific direction, and procedures for resolving conflicts. The roles and administrative, technical, and scientific responsibilities for the project or program should be delineated for the PDs/PIs, including responsibilities for human subjects or animal studies as appropriate.

If budget allocation is planned, the distribution of resources to specific components of the project or the individual PDs/PIs should be delineated in the Leadership Plan. In the event of an award, the requested allocations may be reflected in a footnote on the Notice of Award (NoA).

3. Applications Involving a Single Institution

When all PDs/PIs are within a single institution, follow the instructions contained in the SF424 (R&R) Application Guide: (*http://grants.nih.gov/grants/funding/424/index.htm*).

4. Applications Involving Multiple Institutions

When multiple institutions are involved, one institution must be designated as the prime institution and funding for the other institution(s) must be requested via a subcontract to be administered by the prime institution. When submitting a detailed budget, the prime institution should submit its budget using the Research & Related Budget component. All other institutions should have their individual budgets attached separately to the Research &Related Subaward Budget Attachment(s) Form. See section 4.8 of the SF424 (R&R) Application Guide for further instruction regarding the use of the subaward budget form.

Information concerning the consortium/subcontract budget is provided in the budget justification. Separate budgets for each consortium/subcontract grantee are required.

E. Submission Dates and Times

1. Submission, Review, and Anticipated Start Dates

Opening Date: January 4, 2009, for FY 2010 and January 3, 2010, for FY 2011 (Earliest date an application may be submitted to Grants.gov)
Application Due Date(s): February 4, 2009, in FY 2010 and February 3, 2010, in FY 2011
Peer Review Date(s): May/June 2009 and 2010 and November/December 2009 and 2010
Council Review Date(s): September 2009 and September 2010
Earliest Anticipated Start Date(s): November 2009 and November 2010

Please note that there is only one receipt date for FY 2010 and one receipt date for FY 2011 for new and resubmitted applications.Resubmissions and applications that were submitted previously but were deemed non-responsive to the RFA due to technical or IND issues will be allowed to resubmit on October 15, 2009, and October 15, 2010. Resubmissions will also be accepted in the February receipt dates in both FYs.

Note: On time submission requires that applications be successfully submitted to Grants.gov no later than 5 p.m. local time (of the applicant institution/organization). Applications must be received by the close of business on February 4, 2009. Late applications may be accepted under extreme circumstances beyond the control of the applicant. Applications not received on time will not be considered for review and will generally be returned to the applicant.

The protocol in the grant application should be submitted to the IND/IDE no later than January 5, 2009, for FY 2010 and no later than January 4, 2010, for FY 2011. The current version of the protocol that is included in the grant application and is intended to be used if the study is funded is the protocol that must be submitted to the IND/IDE before the application is reviewed. The date that corresponds with the IND/IDE submission/amendment date that corresponds to the protocol in the grant application should be reported in the title of the grant with the IND/IDE number.

a. *Letter of intent.* A letter of intent is not required for the funding opportunity.

2. Submitting an Application Electronically to FDA

To submit an application in response to this FOA, applicants should access this FOA via *http://www.grants.gov/Apply* and follow steps 1 through 4. Note: Applications must only be submitted electronically.

3. Application Processing

Applications may be submitted on or after the opening date and must be successfully received by Grants.gov no later than 5 p.m. local time (of the applicant institution/organization) on the application submission/receipt date(s). (See section IV.D.1. of this document.) If an application is not submitted by the receipt date(s) and time, the application may be delayed in the review process or not reviewed.

Once an application package has been successfully submitted through Grants.gov, any errors have been addressed, and the assembled application has been created in the eRA Commons, the PD/PI and the AOR/SO have 2 business days to view the application image to determine if any further action is necessary.

- If everything is acceptable, no further action is necessary. The application will automatically move forward for processing after 2 business days, excluding Federal holidays.
- Prior to the submission deadline, the AOR/SO can ''Reject'' the assembled application and submit a changed/corrected application within the 2-day viewing window. This option should be used if it is determined that some part of the application was lost or did not transfer correctly during the submission process, the AOR/SO will have the option to ''Reject'' the application and submit a Changed/Corrected application. In these cases, please contact the eRA Help Desk to ensure that the issues are addressed and corrected. Once rejected, applicants should follow the instructions for correcting errors in section 2.12 of the SF424 (R&R) Application Guide (*http://grants.nih.gov/grants/funding/424/index.htm#*), including the requirement for cover letters on late applications. The ''Reject'' feature should also be used if you determine that warnings are applicable to your application and need to be addressed now. Remember, warnings do not stop further application processing. If an application submission results in warnings (but no errors), it will automatically move forward after 2 weekdays if no action is taken. Some warnings may need to be addressed later in the process. If the 2-day window falls after the submission deadline, the AOR/SO will have the option to ''Reject'' the application if, due to an eRA Commons or Grants.gov system issue, the application does not correctly reflect the submitted application package (e.g., some part of the application was lost or didn't transfer correctly during the submission process). The AOR/SO should first contact the eRA Commons Helpdesk (*http://ithelpdesk.nih.gov/eRA/*) to confirm the system error, document the issue, and determine the best course of action. FDA will not penalize the applicant for an eRA Commons or Grants.gov system issue.
- If the AOR/SO chooses to ''Reject'' the image after the submission deadline for a reason other than an eRA Commons or Grants.gov system failure, a changed/corrected application still can be submitted but it will be subject to the NIH/FDA late policy (*http://grants.nih.gov/grants/guide/notice-files/NOT-OD-05-030.html*) guidelines and may not be accepted. The reason for this

delay should be explained in the cover letter attachment. Late applications may be accepted under extreme circumstances beyond the control of the applicant. In the absence of such extreme circumstances beyond the applicant's control, applications not received on time will not be considered for review and will generally be returned to the applicant.

- Both the AOR/SO and PD/PI will receive e-mail notifications when the application is rejected or the application automatically moves forward in the process after 2 days.
- In unusual circumstances, the following can occur: Additional information may be considered, on a case-by-case basis, for inclusion in the ad hoc expert panel review, however, FDA cannot assure inclusion of any information after the receipt date other than evidence of final IRB approval, FWA or assurance, and certification of adequate supply of study product.

Upon receipt, applications will be evaluated for completeness. Incomplete applications will not be reviewed.

There will be an acknowledgement of receipt of applications from Grants.gov and the Commons. The submitting AOR receives the Grants.gov acknowledgments. The AOR and the PI receive Commons acknowledgments. Information related to the assignment of an application to a Scientific Review Group is also in the Commons.

Note: Because e-mail can be unreliable, it is the responsibility of the applicant to check periodically on their application status in the Commons.

FDA will not accept any application in response to this FOA that is essentially the same as one currently pending initial merit review unless the applicant withdraws the pending application. FDA will not accept any application that is essentially the same as one already reviewed. However, FDA will accept a resubmission application, but such application must include an introduction (3 pages maximum) addressing the critique from the previous review.

F. Intergovernmental Review

This initiative is not subject to Intergovernmental Review under the terms of Executive Order 12372.

G. Funding Restrictions

All FDA awards are subject to the terms and conditions, cost principles, and other considerations described in the HHS Grants Policy Statement *http://www.hhs.gov/grantsnet/adminis/gpd/index.htm*.

1. Protection of Human Research Subjects

All institutions engaged in human subject research financially supported by HHS must file an assurance of protection for human subjects with the OHRP (45 CFR part 46). Applicants are advised to visit the OHRP Web site at *http://www.hhs.gov/ohrp* for guidance on human subject protection issues. Also refer to section VII of this document.

The requirement to file an assurance applies to both ''awardee'' and collaborating ''performance site'' institutions. Awardee institutions are automatically considered to be ''engaged'' in human subject research whenever they receive a direct HHS award to support such research, even where all activities involving human subjects are carried out by a subcontractor or collaborator. In such cases, the awardee institution bears the responsibility for protecting human subjects under the award. Please see the following link for more on Engagement of Institutions in Research *http://www.hhs.gov/ohrp/humansubjects/assurance/engage.htm*.

The awardee institution is also responsible for, among other things, ensuring that all collaborating performance site institutions engaged in the research hold an approved assurance prior to their initiation of the research. No awardee or performance site institution may spend funds on human subject research or enroll subjects without the approved and applicable assurance(s) on file with OHRP. An awardee institution must, therefore, have its own IRB of record and assurance. The IRB of record may be an IRB already being used by one of the ''performance sites,'' but it must specifically be registered as the IRB of record with OHRP.

For further information, applicants should review the section on human subjects in the application instructions as posted on the Grants.gov application Web site. The clinical protocol should comply with ICHE6 ''Good Clinical Practice Consolidated Guidance'' which sets an international ethical and scientific quality standard for designing, conducting, recording, and reporting trials that involve the participation of human subjects. All human subject research regulated by FDA is also subject to FDA's regulations regarding the protection of human subjects (21 CFR parts 50 and 56). Applicants are encouraged to review the regulations, guidance, and information sheets on human subject protection and good clinical practice available on the Internet at *http://www.fda.gov/oc/gcp/*.

2. Key Personnel and Human Subject Protection Education

The awardee institution is responsible for ensuring that all key personnel receive appropriate training in their human subject protection responsibilities. Key personnel include all PIs, co-investigators, and performance site investigators responsible for the design and conduct of the study. HHS, FDA, and OPD do not prescribe or endorse any specific education programs. Many institutions have already developed educational programs on the protection of research subjects and have made participation in such programs a requirement for their investigators. Other sources of appropriate instruction might include the online tutorials offered by the Office of Human Subjects Research, NIH at *http://ohsr.od.nih.gov/* and by OHRP at *http://www.hhs.gov/ohrp/education/*.

Within 30 days of the award, the PI should provide a letter to FDA's grants management office that includes the names of the key personnel, the title of the human subjects protection education program completed for each key personnel, and a one-sentence description of the program. This letter should be signed by the PI and cosigned by an institution official and sent to the Grants Management Specialist whose name appears on the official Notice of Grant Award (NGA).

H. Other Submission Requirements

1. Informed Consent

Consent forms, assent forms, and any other information given to a subject are part of the grant application and must be provided, even if in a draft form. The consent forms should be attached in an appendix section. The applicant is referred to HHS and FDA regulations at 45 CFR 46.116 and 21 CFR 50.25 for details regarding the required elements of informed consent.

2. PD/PI Credential (e.g., Agency Login)

FDA requires the PD/PI(s) to fill in his/her Commons User ID in the ''PROFILE—Project Director/Principal Investigator'' section, ''Credential'' log-in field of the ''Research & Related Senior/Key Person Profile'' component.

3. Organizational DUNS

The applicant organization must include its DUNS number in its Organization Profile in the eRA Commons. This DUNS number must match the DUNS number provided at CCR registration with Grants.gov. For additional information, see ''Frequently

Asked Questions—Application Guide, Electronic Submission of Grant Applications'' at: *http://era.nih.gov/ElectronicReceipt/faq_prepare_app.htm#1*.

4. PHS398 Research Plan Component Sections

Page limitations of the PHS398 Research Plan component must be followed as outlined in the SF424 (R&R) Application Guide. Although each section of the Research Plan component needs to be uploaded separately as a PDF attachment, applicants are encouraged to construct the Research Plan component as a single document, separating sections into distinct PDF attachments just before uploading the files. This approach will enable applicants to better monitor formatting requirements such as page limits. All attachments must be provided to FDA in PDF format, filenames must be included with no spaces or special characters, and a .pdf extension must be used.

All application instructions outlined in the SF424 (R&R) Application Guide must be followed. Note: The link below provides additional information regarding the Adobe transition submission process: (*http://era.nih.gov/ElectronicReceipt/files/adobe_transition.pdf*).

5. Appendix Materials

Applicants must follow the specific instructions on Appendix materials as described in the SF424 (R&R) Application Guide. (See *http://grants.nih.gov/grants/funding/424/index.htm*.)

Do not use the appendix to circumvent the page limitations of the Research Plan component. An application that does not observe the required page limitations may be delayed in the review process.

6. Resource Sharing Plan(s)

Not Applicable

7. Foreign Applications(Non-domestic (non-U.S.) Entity)

Indicate how the proposed project has specific relevance to the mission and objectives of FDA and has the potential for significantly advancing sciences in the United States.

V. Application Review Information

A. General Information

FDA grants management and program staff will review all applications sent in response to this notice. To be responsive, an application must be submitted in accordance with the requirements of this notice.

Applications found to be non-responsive will be returned to the applicant without further consideration.

Applicants are strongly encouraged to contact FDA to resolve any questions about criteria before submitting their application. Please direct all questions of a technical or scientific nature to the OPD program staff and all questions of an administrative or financial nature to the grants management staff (see **FOR FURTHER INFORMATION CONTACT**).

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. Consultation with the proper FDA review division may also occur during this phase of the review to determine whether the proposed study will provide acceptable data that could contribute to product approval. Responsive applications will be subject to a second review by the National Cancer Institute, National Cancer Advisory Board (NCAB) for concurrence with the recommendations made by the first-level reviewers, and funding decisions will be made by the Commissioner of Food and Drugs or his designee.

A score will be assigned to each application based on the scientific/technical review criteria. The review panel may advise the program staff about the appropriateness of the proposal to the goals of the OPD grant program.

Applications submitted in response to this FOA will compete for available funds with all other recommended applications submitted in response to this FOA. The following will be considered in making funding decisions:

- Scientific merit of the proposed project as determined by peer review,
- Availability of funds, and
- Relevance of the proposed project to program priorities.

The goal of FDA's OPD grant program is to support the clinical development of products for use in rare diseases or conditions where no current therapy exists or where the product will improve the existing therapy. In their written critiques, reviewers will be asked to comment on each of the following criteria in order to judge the likelihood that the proposed research will have a substantial impact on the pursuit of these goals. Each of these criteria will be addressed and considered in assigning the overall score, and weighted as appropriate for each application. Note that an application does not need to be strong in all categories to be judged likely to have major scientific impact and thus deserve a meritorious priority score.

Investigators: Assessing the competence of the principal investigator(s) and key personnel to conduct the proposed research.This includes their academic qualifications, research experiences, productivity, and any special attributes.

Resources and Environment: Evaluating any special attributes or deficiencies relevant to the conduct of the proposed studies.

Budget: Evaluating whether all items of the requested budget are appropriate and justified.

Human Subjects and Monitoring: Evaluating possible physical, psychological, or social injury patients might experience as subjects in the proposed research. Discussing whether the rights and welfare of the individuals will be adequately protected. Assessing the safety-monitoring plan including the reporting of adverse events. Evaluating the informed consent documents as well as the plan to monitor the integrity of the data collected and the compliance with the protocol.

B. Scientific/Technical Review Criteria

The ad hoc expert panel will review the application based on the following scientific and technical merit criteria:

(1) The soundness of the rationale for the proposed study;

(2) The quality and appropriateness of the study design, including the design of the monitoring plans;

(3) The statistical justification for the number of patients chosen for the study, based on the proposed outcome measures, and the appropriateness of the statistical procedures for analysis of the results;

(4) The adequacy of the evidence that the proposed number of eligible subjects can be recruited in the requested timeframe;

(5) The qualifications of the investigator and support staff, and the resources available to them;

(6) The adequacy of the justification for the request for financial support;

(7) The adequacy of plans for complying with regulations for protection of human subjects and monitoring; and

(8) The ability of the applicant to complete the proposed study within its budget and within time limits stated in this RFA.

C. Program Review Criteria

(1) Applications must propose clinical trials intended to provide safety and/or efficacy data.

(2) There must be an explanation in the ''Background and Significance''

section of how the proposed study will either contribute to product approval or provide essential data needed for product development.

(3) The ''Background and Significance'' section of the application must contain information documenting the prevalence, not incidence, of the population to be served by the product is fewer than 200,000 individuals in the United States. The applicant should include a detailed explanation supplemented by authoritative references in support of the prevalence figure. Diagnostic tests and vaccines will qualify only if the population to whom they will be administered is fewer than 200,000 individuals in the United States per year.

(4) The study protocol proposed in the grant application must be under an active IND or IDE (not on clinical hold) to qualify the application for scientific and technical review. Additional IND/IDE information is described as follows:

The proposed clinical protocol should be submitted to the applicable FDA IND/IDE review division a minimum of 30 days before the grant application deadline. The number assigned to the IND/IDE that includes the proposed study should appear on the face page of the application with the title of the project. The date the subject protocol was submitted to FDA for the IND/IDE review should also be provided. Protocols that would otherwise be eligible for an exemption from the IND regulations must be conducted under an active IND to be eligible for funding under this FDA grant program. If the sponsor of the IND/IDE is other than the principal investigator listed on the application, a letter from the sponsor permitting access to the IND/IDE must be submitted in both the IND/IDE and in the grant application. The name(s) of the principal investigator(s) named in the application and in the study protocol must be submitted to the IND/IDE. Studies of already approved products, evaluating new orphan indications, are also subject to these IND/IDE requirements.

Only medical foods that do not need premarket approval and medical devices that are classified as non-significant risk (NSR) are free from these IND/IDE requirements. Applicants studying an NSR device should provide a letter in the application from FDA's Center for Devices and Radiological Health indicating the device is an NSR device.

(5) The requested budget must be within the limits, either $200,000 in total costs per year for up to 3 years for any phase study, or $400,000 in total costs per year for up to 4 years for phase 2 or 3 studies. Any application received that requests support over the maximum amount allowable for that particular study will be considered non-responsive.

(6) In an appendix to the application, there must be evidence that the product to be studied is available to the applicant in the form and quantity needed for the clinical trial proposed.A current letter from the supplier as an appendix will be acceptable. If negotiations regarding the supply of the study product are underway but have not been finalized at the time of application, please provide a letter indicating such in the application. Verification of adequate supply of study product will be necessary before an award is made.

(7) The protocol should be submitted in the application. The protocol may be included as an appendix. Page limits, font size, and margins should comply with the Application Guide, Electronic Submission of Grant Applications (*http://era.nih.gov/ElectronicReceipt/faq_prepare_app.htm#1*).

D. Additional Review Criteria

In addition to the previously mentioned criteria, the following items will continue to be considered in the determination of scientific merit and the priority score:

Resubmission Applications (formerly ''revised/amended'' applications): The adequacy of the responses to comments from the previous scientific review group will be assessed including the appropriateness of the improvements in the resubmission application.

Protection of Human Subjects from Research Risk: The involvement of human subjects and protections from research risk relating to their participation in the proposed research will be assessed. See the ''Human Subjects Sections'' of the PHS398 Research Plan component of the SF424 (R&R).

Inclusion of Women, Minorities and Children in Research: The adequacy of plans to include subjects from both genders, all racial and ethnic groups (and subgroups), and children as appropriate for the scientific goals of the research will be assessed. Plans for the recruitment and retention of subjects will also be evaluated. See the ''Human Subjects Sections'' of the PHS398 Research Plan component of the SF424 (R&R).

Care and Use of Vertebrate Animals in Research: The adequacy of the plans for care and use of vertebrate animals to be used in the project will be assessed. See the ''Other Research Plan Sections'' of the PHS398 Research Plan component of the SF424 (R&R).

Biohazards: If materials or procedures are proposed that are potentially hazardous to research personnel and/or the environment, determine if the proposed protection is adequate.

E. Additional Review Considerations

Budget and Period of Support: The reasonableness of the proposed budget and the appropriateness of the requested period of support in relation to the proposed research may be assessed by the reviewers. The priority score should not be affected by the evaluation of the budget.

Applications from Foreign Organizations: Whether the project presents special opportunities for furthering research programs through the use of unusual talent, resources, populations, or environmental conditions in other countries that are not readily available in the United States or that augment existing U.S. resources will be assessed.

F. Sharing Research Data

Sharing research data is not applicable.

G. Sharing Research Resources

Sharing research resources is not applicable.

H. Anticipated Announcement and Award Dates

Earliest anticipated start/award date(s): November 1, 2009, and November 1, 2010.

VI. Award Administration Information

A. Award Notices

After the review of the application is completed, the PD/PI will be able to access his or her summary statement (written critique) via the eRA Commons.

If the application is under consideration for funding, FDA may request information from the applicant prior to making the award. For details, applicants may refer to the HHS Grants Policy Statement: (*http://www.hhs.gov/grantsnet/adminis/gpd/index.htm*).

A formal notification in the form of a NoA will be provided to the applicant organization. The NoA signed by the grants management officer is the authorizing document. Once all administrative and programmatic issues have been resolved, the NoA will be generated via e-mail notification from the awarding component to the grantee business official.

Selection of an application for award is not an authorization to begin performance. Any costs incurred before receipt of the NoA are at the recipient's risk. These costs may be reimbursed only to the extent considered allowable

pre-award costs. See section IV.G, ''Funding Restrictions.''

B. Administrative and National Policy Requirements

All FDA grant and cooperative agreement awards include the HHS Grants Policy Statement as part of the NoA. For these terms of award, see the HHS Grants Policy Statement at: *http://www.hhs.gov/grantsnet/adminis/gpd/index.htm*.

C. Reporting

1. Monitoring Activities

a. *OPD monitoring of clinical trials language*. These guidelines are intended to provide information for principal investigators who are conducting clinical trials. The procedures outlined herein are in addition to (and not in lieu of) IRB, OHRP, and other FDA requirements.

It is an OPD policy that data and safety monitoring of a clinical trial is to be commensurate with the risks posed to study participants and with the size and complexity of the study. In addition, the OPD requires that a Grantee and any third party engaged in supporting the clinical research be responsible for oversight of data and safety monitoring, ensuring that monitoring systems are in place, that the quality of the monitoring activity is appropriate, and that the OPD Project Officer is informed of recommendations emanating from monitoring activities.

b. *FDA requirements for monitoring*. The OPD requires that each clinical trial it supports, regardless of phase, has data and safety monitoring procedures in place to safeguard the well-being of study participants and to ensure scientific integrity. Monitoring must be performed on a regular basis throughout the subject accrual, treatment, and followup periods.

The specific approach to monitoring will depend on features of the clinical trial to be conducted e.g., several levels of monitoring: Data and Safety Monitoring Board (DSMB), Study Monitoring Committee (SMC) and Independent Medical Monitor.

Monitoring activities should be appropriate to the study, study phase, population, research environment, and degree of risk involved.

In small, single-site studies, safety monitoring is often performed by the independent medical monitor or a safety monitoring committee in conjunction with the study statistician. All phase 3 studies and any high risk phase 1 or 2 clinical trial will also require a DSMB. It may be desirable to utilize a DSMB for:

- Trials involving highly experimental therapies or specialized review procedures external to the OPD (e.g., gene therapy or xenotransplantation);
- Trials involving substantial risk to study participants (e.g., studies with irreversible outcomes); or
- Trials involving particularly vulnerable study participants (e.g., children or persons with impaired ability to consent).

c. *Study monitoring plan*. The OPD requires that the protocol document include a section describing the proposed plan for interim data monitoring. This section will detail who is to be responsible for interim monitoring (i.e., a DSMB, an SMC, or the study investigator), what data will be monitored (i.e., performance and safety data only vs. efficacy data as well), the timing of the first data review (e.g., ''the first interim look will occur when the initial 20 participants have completed the 6-month followup visit''), and the frequency of interim reviews (which will depend on such factors as the study design, interventions and anticipated recruitment rate). The plan will specify ''stopping guidelines'' and other criteria for the monitors to follow in their review of the interim data.

A preliminary monitoring plan must be submitted as part of the Research Plan portion of the grant application for a clinical trial. The plan will be examined as part of the peer review process, and any comments and concerns will be included in an administrative note in the summary statement. OPD staff will ensure that all concerns are resolved before the grant award is made.

2. Oversight Activities

The program project officer will monitor grantees periodically. The monitoring may be in the form of telephone conversations, e-mails, or written correspondence between the project officer/grants management officer or specialist and the principal investigator. Information including, but not limited to, information regarding study progress, enrollment, problems, adverse events, changes in protocol, and study monitoring activities will be requested. Periodic site visits with officials of the grantee organization may also occur. The results of these monitoring activities will be recorded in the official grant file and will be available to the grantee upon request consistent with applicable disclosure statutes and with FDA disclosure regulations. Also, the grantee organization must comply with all special terms and conditions of the grant, including those which state that future funding of the study will depend on recommendations from the OPD project officer. The scope of the recommendations will confirm the following: (1) There has been acceptable progress toward enrollment, based on specific circumstances of the study; (2) there is an adequate supply of the product/device; and (3) there is continued compliance with all applicable FDA and HHS regulatory requirements for the trial.

In addition to the requirement for an active IND/IDE discussed in section V.C of this document, documentation of assurances with the OHRP (see section IV.F.1 of this document) must be on file with FDA's grants management office before an award is made. Any institution receiving Federal funds must have an IRB of record even if that institution is overseeing research conducted at other performance sites. To avoid funding studies that may not receive or may experience a delay in receiving IRB approval, documentation of IRB approval and (FWA or assurance) for the IRB of record for all performance sites must be on file with the FDA grants management office before an award to fund the study will be made. In addition, if a grant is awarded, grantees will be informed of any additional documentation that should be submitted to FDA's IRB.

3. Reporting Requirement

The grantee must file a final program progress report, financial status report, and invention statement within 90 days after the end date of the project period as noted on the notice of grant award.

When multiple years are involved, awardees will be required to submit the Non-Competing Grant Progress Report (PHS 2590) annually and financial statements as required in the HHS Grants Policy Statement, dated October 1, 2006, (*http://www.hhs.gov/grantsnet/adminis/gpd/*). Also, all new and continuing grants must comply with all regulatory requirements necessary to keep the status of their IND/IDE ''active'' and ''in effect,'' that is, not on ''clinical hold.'' Failure to meet regulatory requirements will be grounds for suspension or termination of the grant.

Awardees will be required to submit the Non-Competing Continuation Grant Progress Report (PHS 2590) (*http://grants.nih.gov/grants/funding/2590/2590.htm*) annually and financial statements as required in the HHS Grants Policy Statement *http://www.hhs.gov/grantsnet/adminis/gpd/index.htm*.

A listing and a justification for any study changes that occurred in the past year must be included in the Non-Competing Continuation Grant Progress Report (PHS 2590).

A final progress report, invention statement, and Financial Status Report are required when an award is relinquished when a recipient changes institutions or when an award is terminated.

VII. Other Information

A. Required Federal Citations

1. Clinical Trials Data Bank

The Food and Drug Administration Amendments Act of 2007 (FDAAA) contains provisions that expand the current database known as ClinicalTrials.gov to include additional requirements for individuals and entities, including grantees, who are involved in conducting clinical trials that involve products regulated by FDA or that are funded by HHS, including FDA. These additional requirements include mandatory registration of certain types of clinical trials, as well as reporting of results for certain trials for inclusion in the ClinicalTrials.gov database. ClinicalTrials.gov, which was created after the Food and Drug Administration Modernization Act of 1997, provides patients, family members, healthcare providers, researchers, and members of the public easy access to information on clinical trials for a wide range of diseases and conditions. The U.S. National Library of Medicine has developed this site in collaboration with NIH and FDA. ClinicalTrials.gov is available to the public through the Internet at *http://clinicaltrials.gov*.

ClinicalTrials.gov contains information about certain clinical trials, both federally and privately funded, of drugs (including biological products) and medical devices. The types of trials that are required to be registered, and for which results must be reported, are known as ''applicable clinical trials.'' FDAAA defines the types of clinical trials that are ''applicable clinical trials'' and, therefore, are subject to the registration and results reporting requirements. The registry listing for each trial includes information such as descriptive information about the trial, patient eligibility criteria, recruitment status, location information on the clinical trial sites, and points of contact for those wanting to enroll in the trial. The database also contains information on the results of clinical trials. More detailed information on the definition of ''applicable clinical trial'' and the registry and results reporting requirements can be found at *http://grants.nih.gov/grants/guide/notice-files/NOT-OD-08-014.html* and *http://prsinfo.clinicaltrials.gov/fdaaa.html*.

FDAAA also added new requirements concerning clinical trials supported by grants from HHS, including FDA. Under these provisions, any grant or progress report forms required under a grant from any part of HHS, including FDA, must include a certification that the person responsible for entering information into ClinicalTrials.gov (the ''responsible party'') has submitted all required information to the database. There are also provisions regarding when agencies within HHS, including FDA, are required to verify compliance with the database requirements before releasing funding to grantees.OPD program staff will be providing additional information on these requirements, including the appropriate means by which to certify that a grantee has complied with the database requirements.

2. Data and Safety Monitoring Plan

Data and safety monitoring may be required for certain types of clinical trials. See section VI.C.1.c for more details and other FDA monitoring requirements. The establishment of DSMBs is required for multi-site clinical trials involving interventions that entail potential risk to the participants, and generally for phase 3 clinical trials. Although phase 1 and phase 2 clinical trials may also use DSMBs, smaller clinical trials may not require this oversight format, and alternative monitoring plans may be appropriate.

3. Access to Research Data Through the Freedom of Information Act (FOIA)

FOIA, (5 U.S.C. 552), provides individuals with a right to access certain records in the possession of the Federal government, subject to certain exemptions. The government may withhold information under the exemptions and exclusions contained in the FOIA. The exact language of the exemptions can be found in the FOIA. Additional guidance on the exemptions and how they apply to certain documents can be found in the HHS regulations implementing the FOIA (45 CFR part 5) and FDA regulations implementing the FOIA(21 CFR part 20). (Also see the HHS Web site: (*http://www.hhs.gov/foia/*).

Data included in the application may be considered trade secret or confidential commercial information within the meaning of relevant statutes and implementing regulations. FDA will protect trade secret or confidential commercial information to the extent allowed under applicable law.

4. Use of Animals in Research

Recipients of PHS support for activities involving live vertebrate animals must comply with PHS Policy on Humane Care and Use of Laboratory Animals (*http://grants.nih.gov/grants/olaw/references/PHSPolicyLabAnimals.pdf*) as mandated by the Health Research Extension Act of 1985 (*http://grants.nih.gov/grants/olaw/references/hrea1985.htm*), and the U.S. Department of Agriculture Animal Welfare Regulations (*http://www.nal.usda.gov/awic/legislat/usdaleg1.htm*) as applicable.

5. Inclusion of Women And Minorities in Clinical Research

Applicants for PHS clinical research grants are encouraged to include minorities and women in study populations so research findings can be of benefit to all people at risk of the disease or condition under study. It is recommended that applicants place special emphasis on including minorities and women in studies of diseases, disorders, and conditions that disproportionately affect them. This policy applies to research subjects of all ages. If women or minorities are excluded or poorly represented in clinical research, the applicant should provide a clear and compelling rationale that shows inclusion is inappropriate.

6. Inclusion of Children as Participants in Clinical Research

FDA regulations at 21 CFR part 50, subpart D, contain additional requirements that must be met by IRBs reviewing clinical investigations regulated by FDA and involving children as subjects. FDA is part of HHS; accordingly, the research project grants under this program are supported by HHS, and HHS regulations at 45 CFR part 46, subpart D also apply to research involving children as subjects.

7. Standards for Privacy of Individually Identifiable Health Information

HHS issued final modification to the ''Standards for Privacy of Individually Identifiable Health Information,'' the ''Privacy Rule,'' on August 14, 2002. The Privacy Rule is a federal regulation under the Health Insurance Portability and Accountability Act of 1996 that governs the protection of individually identifiable health information, and is administered and enforced by the HHS Office for Civil Rights (OCR).

Decisions about applicability and implementation of the Privacy Rule reside with the researcher and his/her institution. The OCR Web site *http://www.hhs.gov/ocr/* provides information on the Privacy Rule.

8. Healthy People 2010

PHS is committed to achieving the health promotion and disease prevention objectives of ''Healthy People 2010,'' a PHS-led national activity for setting priority areas. This FOA is related to one or more of the priority areas. Potential applicants may obtain a copy of ''Healthy People 2010'' at *http://www.health.gov/healthypeople*.

9. Smoke-Free Workplace

PHS strongly encourages all grant recipients to provide a smoke-free workplace and discourage the use of all tobacco products. In addition, Public Law 103–227, the Pro-Children Act of 1994, prohibits smoking in certain facilities (or in some cases, any portion of a facility) in which regular or routine education, library, day care, health care, or early childhood development services are provided to children. This is consistent with the PHS mission to protect and advance the physical and mental health of the American people.

10. Authority and Regulation

This program is not subject to the intergovernmental review requirements of Executive Order 12372. FDA's research program is described in the Catalog of Federal Domestic Assistance (CFDA), No. 93.103 *http://www.cfda.gov/*.

FDA will support the clinical studies covered by this notice under the authority of section 301 of the PHS Act as amended (42 U.S.C. 241) and under applicable regulations at 42 CFR part 52 and 45 CFR parts 74 and 92. All grant awards are subject to applicable requirements for clinical investigations imposed by sections 505, 512, and 515 of the Federal Food, Drug, and Cosmetic Act or safety, purity, and potency for licensing under section 351 of the PHS Act, including regulations issued under any of these sections.

All human subject research regulated by FDA is also subject to FDA's regulations regarding the protection of human subjects (21 CFR parts 50 and 56). Applicants are encouraged to review the regulations, guidance, and information sheets on human subject protection and Good Clinical Practice available on the Internet at *http://www.fda.gov/oc/gcp/*.

The applicant is referred to HHS regulations at 45 CFR 46.116 and 21 CFR 50.25 for details regarding the required elements of informed consent.

All awards will be subject to all policies and requirements that govern the research grant programs of the PHS as incorporated in the HHS Grants Policy Statement, dated January 1, 2007, (*http://www.hhs.gov/grantsnet/adminis/gpd/index.htm*).

11. Human Subjects Protection

Federal regulations (45 CFR part 46) require that applications and proposals involving human subjects must be evaluated with reference to: (1) The risks to the subjects, (2) the adequacy of protection against these risks, (3) the potential benefits of the research to the subjects and others, and (4) the importance of the knowledge gained or to be gained (*http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm*).

12. Human Embryonic Stem Cell Research and Cloning

Section 498 of the PHS Act places certain restrictions on human fetal research.In addition, under currently applicable executive orders, HHS funds may not be used to support human embryo research under any extramural award instrument. HHS funds may not be used for the creation of a human embryo for research purposes or for research in which a human embryo is destroyed, discarded, or knowingly subjected to risk of injury or death greater than that allowed for research on fetuses *in utero* under 45 CFR 46.204 and 46.207 and subsection 498(b) of the PHS Act (42 U.S.C. 289g(b)). The term ''human embryo'' includes any organism not protected as a human subject under 45 CFR part 46, as of the date of enactment of the governing appropriations act, that is derived by fertilization, parthenogenesis, cloning, or any other means from one or more human gametes or human diploid cells.

In addition, HHS is prohibited, by a March 4, 1997, Presidential memorandum, from using Federal funds for cloning human beings. In implementing this program, FDA will comply with all applicable statutes, regulations, presidential memoranda and Executive orders.

Criteria for Federal funding of research on hESCs can be found at: *http://www.hhs.gov/faq/research/stemcell/r-0006.html* and *http://stemcells.nih.gov/research/registry/eligibilityCriteria.asp*.

Dated: December 9, 2008.

Jeffrey Shuren,

Associate Commissioner for Policy and Planning.

[FR Doc. E8–30061 Filed 12–17–08; 8:45 am]

BILLING CODE 4160–01–S

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Center for Scientific Review; Notice of Closed Meeting

Pursuant to section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2), notice is hereby given of the following meeting.

The meeting will be closed to the public in accordance with the provisions set forth in sections 552b(c)(4) and 552b(c)(6), Title 5 U.S.C., as amended. The grant applications and the discussions could disclose confidential trade secrets or commercial property such as patentable material, and personal information concerning individuals associated with the grant applications, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy.

Name of Committee: Center for Scientific Review Special Emphasis Panel; Member Conflict: Behavior and Health.

Date: December 19, 2008.

Time: 10 a.m. to 12 p.m.

Agenda: To review and evaluate grant applications.

Place: National Institutes of Health, 6701 Rockledge Drive, Bethesda, MD 20892 (Telephone Conference Call).

Contact Person: Gayle M. Boyd, PhD, Scientific Review Officer, Center for Scientific Review, National Institutes of Health, 6701 Rockledge Drive, Room 3141, MSC 7808, Bethesda, MD 20892, 301–451–9956, *gboyd@mail.nih.gov*.

This notice is being published less than 15 days prior to the meeting due to the timing limitations imposed by the review and funding cycle.

(Catalogue of Federal Domestic Assistance Program Nos. 93.306, Comparative Medicine; 93.333, Clinical Research, 93.306, 93.333, 93.337, 93.393–93.396, 93.837–93.844, 93.846–93.878, 93.892, 93.893, National Institutes of Health, HHS)

Dated: December 9, 2008.

Jennifer Spaeth,

Director, Office of Federal Advisory Committee Policy.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Center for Scientific Review; Notice of Closed Meetings

Pursuant to section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2), notice