Office of Orphan Products Development (OOPD)
Clinical Trial Grants for the Orphan Products Grants Program

Application Instructions and Helpful Hints

Application Due Date:

Please see the **Request for Application** (RFA) for details of the next submission deadline.

Helpful Hints:

- Applicants should first review the following prior to submission:
  - RFA
  - RFA Grant Opportunity Package via Grants.gov
  - "Rare Diseases" Common Issues in Drug Development Guidance for Industry"
- Applicants are encouraged to apply early to allow adequate time to make any corrections to errors found in the application during the submission process by the due date.
- Applicants should be aware that on-time submission means that an application must be submitted error free (of both Grants.gov and eRA Commons errors) by 11:59 PM Eastern Time on the application due date. **Late applications will not be accepted for this funding opportunity announcement (FOA).**
- All applications must be submitted electronically through Grants.gov.
- **The final version of the protocol submitted to OOPD in the grant application must be submitted to the applicable FDA IND/IDE review division before the grant application deadline. See RFA for more details.**

Pre-Application Registrations:

Helpful Hint: ***Registration can take 6 weeks or more,*** *so applicants are encouraged to begin the pre-application/registration process well before the grant submission date.*

Prior to electronically submitting a grant application, the following steps are required:

Step 1: Register with the System for Award Management (SAM) - Applicants must complete and maintain an active registration, which requires renewal at least annually. The renewal process may require as much time as the initial registration. SAM registration includes the assignment of a Commercial and Government Entity (CAGE) Code for domestic organizations which have not already been assigned a CAGE Code.

- NATO Commercial and Government Entity (NCAGE) Code – Foreign organizations must obtain an NCAGE code (in lieu of a CAGE code) in order to register in SAM.
- Unique Entity Identifier (UEI) - A UEI is issued as part of the SAM.gov registration process. The same UEI must be used for all registrations, as well as on the grant application.

Step 2: Register with and obtain Username & Password on Grants.gov

Further detail for Steps 1 and 2 above can be found at:
https://grants.gov/applicants/grant-applications/how-to-apply-for-grants

Step 3: Register with eRA Commons

- Once the unique organization identifier is established, organizations can register with eRA Commons in tandem with completing their full SAM and Grants.gov registrations; all registrations must be in place by time of submission. eRA Commons requires organizations to identify at least one Signing Official (SO) and at least one Program Director/Principal Investigator (PD/PI) account in order to submit an application.

General Application Instructions:

Application materials will open via Grants.gov approximately 60 days prior to the application receipt date. At that time (and after the pre-application process has been completed), applicants can download a copy of the application package on Grants.gov, complete it offline, and then upload and submit their application by following the instructions in the How to Apply for Grants link on the website.

Note: Not all of the information in the Application Guide will apply to the Orphan Products Clinical Trials Grant application. Applicants are strongly encouraged to use the ''Applicant FAQs'' posted on Grants.gov under the announcement number when preparing their submission.

Tips for Completing Form SF424 (R&R)

This is not a full instruction guide and **does not cover all sections** of the SF424 (R&R) forms. Please refer to the applicable SF424 (R&R) Application Guide posted by NIH for detailed instructions on completing the SF424 (R&R) forms.

The following are FDA/OOPD specific items that you may need to complete the application.

Please note that the page limitations for the application are the same as the page limits on the Application Guide. Specifically, the Research Strategy section page limit is 12 pages.

A resubmission application must include an Introduction Section of the Research Strategy (1 page maximum) addressing the most recent objective review critique (Summary Statement).

Applications may not be accepted for review and may be returned for the following reasons:

- The applicant organization is ineligible.
- The application is received after the specified receipt date.
- The application is incomplete.
- The application is not responsive to the Request for Applications (RFA).
- The material presented in the application is insufficient to permit an adequate review.

A. SF424 (R&R) "APPLICATION FOR FEDERAL ASSISTANCE" (Page 1):

Type of Submission:
"Pre-application" is not used in FDA's grant application process.

Date Received by State/State Application Identifier:
Leave these fields blank.

Federal Identifier/Agency Routing Identifier:
If the "Type of Application" is "New" leave the Federal Identifier field blank. If you are submitting a "Changed/Corrected" application, please enter the Grants.gov tracking number previously assigned.

Agency Routing Identifier:
Leave this section blank as it is not used by FDA.

Type of Application:
For this RFA, "New," "Resubmission," "Renewal," and Revision" applications will be accepted. Check only one application type.

Name of Federal Agency:
Enter "Food and Drug Administration" in this block.

Descriptive Title of Applicant's Project:
In the title block, be sure to include **ALL** of the following information in the order provided: (1) the phase of the study; (2) the generic name of the product(s) (i.e. drugs, biologics, medical devices, and medical foods) to be studied; (3) the name of the disease(s)/condition(s) to be studied; (4) the **IND/IDE number**; and (5) **the date the protocol you are requesting funding for was submitted to the IND/IDE.**

Helpful Hint: *Please note that the title field is limited to 200 characters, including the spaces between words and punctuation to avoid errors. Use abbreviations as needed to ensure the descriptive title information does not become truncated. An appropriate descriptive title example is "**Ph 2a** Study of **Drug** for **Disease (**IND **123,456 -mm/dd/yyyy)**"*

- *Applications must use the generic name of the proposed product(s).*
- *The final version of the clinical protocol that is included in the grant application must be submitted to the applicable FDA Review Division **IND or IDE a minimum of 30 days before the grant application deadline.** The **number of the assigned IND/IDE** and the **date of submission** of this final clinical protocol to the IND/IDE should be included on the SF424 Form (R&R) of the grant application after the title of the grant in the "Descriptive Title of Applicant's Project" field.*
- *Use abbreviations as needed to ensure the descriptive title information is not truncated.*

Proposed Project (Start and Ending Date):
Start Date: This should be the date that the clinical trial is proposed to begin, not

necessarily the date funding is expected.

Ending Date: This should be the date that the clinical trial is proposed to end.

B. SF424 (R&R) "APPLICATION FOR FEDERAL ASSISTANCE" (Page 2):

"Estimated Project Funding" section describes two types of funds:

Total Federal Funds Requested:
Enter total (direct and indirect) federal funds requested from OOPD for the entire project period for a maximum of 4 years.

Total Non-Federal Funds Requested:
Enter total amounts that will be used for this study that are not from federal sources. Please include sources and more detailed information on allocations in the budget justification sections.

C. SF424 "RESEARCH & RELATED Other Project Information":

Human Subjects:
All OOPD clinical trials grants involve human subject participation in a clinical trial and thus, are not exempt from federal regulations regarding human subject protection. Always check "no" to the question "is the project exempt from Federal regulations?"

Vertebrate Animals:
"No" should be checked to "are vertebrate animals used."

Project Summary/Abstract (Project Description):
The Project Summary must contain a concise, self-contained summary of the proposed clinical study suitable for dissemination to the public. It should be informative to a technical audience and understandable to lay readers. The Project Summary is meant to serve as a succinct, accurate description of the proposed work when separated from the application.

In writing your summary or abstract, please state the broad, long-term objectives and specific aims, making reference to the health relatedness of the project (e.g., how this helps address significant unmet medical needs for patients with rare diseases). Clearly state project objectives, including such items as a brief background and rationale, hypotheses and expected results, specific aims, unique features, and study design and methods for achieving the stated goals. Avoid describing past accomplishments and use of first person. Do not include proprietary or confidential information or trade secrets, as summary or abstract may be used for purposes other than grant review.

Helpful Hint: *Be concise and complete.* ***There is a one-page limit for this section*** *(no longer than 30 lines of text). This page limit is based on a single-spaced text with 0.5-inch page margins in 11 point font or larger. An abstract exceeding the allowable length may be flagged as an error upon submission. This would require a*

corrective action before the application can be accepted.

Project Narrative (Public Health Relevance Statement):
In two or three sentences, describe the relevance of the project to public health using succinct, plain language that can be understood by a lay audience.

Facilities and Other Resources:
Describe the resources available at each performance site. Describe how the scientific environment and existing resources in which the research will be done contributes to the probability of success (e.g., institutional support, physical resources, intellectual rapport, and database platforms). Describe any special facilities used for working with biohazards or other potentially dangerous substances. Information about select agents must be described in the Research Plan (Select Agent Research). "Select agents" means those biological agents or toxins that have the potential to pose a severe threat to public health and safety, animal or plant health, or animal or plant product.

Clinical resources associated with the study performance site(s) need to be described in detail. A discussion of the resources available to the applicant to show adequate enrollment can be achieved within the proposed timeframe of the study should be included, such as the number of patients presenting to the clinic yearly with the disease or condition that meet the proposed entry criteria of the study along with a discussion of any competing clinical trials or other potential barriers that may limit enrollment. If there are multiple performance sites, describe the resources available at each site.

Helpful Hint: *Failure to provide justification that adequate enrollment can be attained within the proposed study timeframe is a frequent weakness of grant applications.*

Other Attachments: Foreign Component:
Please provide justification if the proposed study requires the use of unusual talent, resources, populations, or environmental conditions in other countries that are not readily available in the United States (U.S.), or if the study requires the use of these to augment existing US resources. Indicate how the proposed project is relevant to the mission and objectives of FDA and has the potential for significantly advancing sciences in the U.S.

"Senior/Key Person Profile (Expanded) Form":
Provide a Biographical Sketch (biosketch) for each senior/key person involved with the study. Key personnel include all principal investigators, co-investigators, and performance site investigators responsible for the design and conduct of the study.

Helpful Hint: *Failure to include a detailed biosketch that supports the role of each senior/key person is a frequent weakness of grant applications.* *See Biosketch Format Pages, Instructions and Samples for more information.*

Budget:

FDA's Orphan Products Clinical Trial Grants Program uses the Research & Related (R&R) Budget Component. Application budgets are limited to $650,000 per year in total costs (direct and indirect costs) for up to a maximum of 4 years of support.

Innovative and Efficient Trial Approaches: Applicants may request additional funding over the above listed maximum for innovative and efficient trial approaches. The additional funding request shall not exceed an additional $250,000 total costs per year (to a maximum total award cost of $900,000 per year) for up to 4 years. Justification for the additional funding request must be reflected in the budget request and will be reviewed annually by the program. **Applications requesting additional funding for innovative and efficient trial approaches must submit a clear description and justification as an appendix (limited to 3 pages).**

Applicants must provide a detailed budget for each requested year and attach a budget justification. Reviewers will consider whether the budget and the requested period of support are fully justified and reasonable in relation to the proposed research.

Budget justification should:

- Clearly explain the rationale for all costs requested in the proposed project.
- Include a rationale if the budget has more than a standard escalation from the initial to the future year(s) of support.
- Explain any exclusions applied to the Facilities and Administrative (F&A) base calculation.
- Provide a rationale if any of the requested costs are higher than usual and customary.
- Be appropriate for the length of the study and not be padded to meet the maximal limitations of the RFA.
- Correlate with all costs specified in the detailed budget.
- State if the overall costs for the proposed study exceeds the limitations of this funding mechanism, and if so, explain how the additional costs to complete the proposed study will be covered (e.g., other grants, corporate funding).
- State if other grants have been or will be applied for and describe contingency plans should those funds not be obtained.

The PHS 398 Modular Budget program does not apply to the Orphan Products Clinical Trials Grants Program and should not be used.

Helpful Hint: *Failure to include a well justified budget (R&R Budget Component Item K)is a frequent weakness of OOPD grant applications.*

Budgets for Multiple Institutions - R&R Subaward Budget Attachment(s) Form:

When multiple institutions are involved, one institution must be designated as the primary institution; funding for the other institution(s) must be requested via a subcontract to be administered by the primary institution. Individual budgets for

all institutions that will be subcontracts should be attached separately to the R&R Subaward Budget Attachment(s) Form. A separate budget justification should also be submitted for each subaward.

D. SF424 "PHS 398 Research Plan":

The goal of FDA's Orphan Products Clinical Trial Grants Program is to support clinical trials of products evaluating efficacy and/or safety in support of a new indication or change in labeling to address unmet needs in rare diseases or conditions. Through the funding of collaborative, efficient, and/or innovative clinical trials, FDA expects to increase the number of approved treatments for rare diseases and exert a broad and positive impact on rare disease drug development.

Application Type:
For this RFA all applications will be "New," "Resubmission," "Renewal," or Revision."

Research Plan Attachments:
The Research Plan should include sufficient information for evaluation of the project independent of other documents such as previous applications. Be specific and informative and avoid redundancies.

Each of the items below should be saved and attached as a single file. Begin each text section of the Research Plan with a section header: Introduction, Specific Aims, Research Strategy, etc.

Helpful Hint: *Please follow the page limitations for each section. Agency validations will include checks for page limits, which may result in errors. However, while these computer validations help minimize incomplete and/or noncompliant applications, they do not replace the validations conducted by FDA staff. Failure to comply with the requirements at any point may delay the review process.*

Introduction:
A resubmission application must include an Introduction Section of the Research Strategy (1 additional page maximum) addressing the most recent objective review critique (Summary Statement). A resubmission application must also be complete and stand-alone from previous versions. Resubmissions are intended for those applications that were previously submitted to OOPD, reviewed and received a score on the application and do not require an IND protocol amendment prior to application resubmission.

Specific Aims:
This section is limited to 1 page. Generally, this section begins with a brief narrative describing the overall goals and objectives of the project and the hypothesis to be tested. The section should concisely state how the proposed study will exert a sustained, powerful influence on the research field(s) involved and provide essential data needed to support a new indication or a change in labeling and be followed by a list of the Specific Aims.

Research Strategy:

The Research Strategy Section is limited to 12 pages. FDA does not follow the order/headings that are included in the NIH's 424 R&R Application Guide.

The following sections should be included under the Research Strategy section of the application (see RFA for additional details on each scoring criteria):

1. **Rationale:**
   The soundness of rationale in relation to the current understanding of the rare disease(s) and the likelihood the proposal will facilitate a clinical trial in support of a new indication(s) for use or change in labeling of a product(s) to address unmet needs in a rare disease(s).

2. **Study Design:**
   The quality and appropriateness of the study design, research methodology, and data analyses to accomplish the specific aims of the proposed study and its potential to make an impact for rare diseases.

3. **Inclusion of Patient Input:**
   The inclusion of patient and caregiver perspectives in the planning and design of the clinical study to improve protocol design and medical product development.

4. **Investigator, Infrastructure, and Financial Resources:**
   The probability of success of the proposed project given the environment in which the work will be done.

5. **Ability to Advance the Current Field:**
   The ability of the project to shift current research or clinical practice paradigms towards future product development and to exert a significant influence on product development.

Rare Disease Prevalence:

The **Rationale Section** of the Research Strategy should also include a subsection with the heading "Rare Disease Prevalence." This subsection should include documentation to support that the estimated prevalence of the orphan disease or condition in the United States is less than 200,000 (or in the case of an acute disease (i.e., less than 1 year duration), the annual incidence of the disease must be less than 200,000 per year; or in the case of a vaccine or diagnostic, information to support that the product will be administered to fewer than 200,000 people in the United States per year). (Please Note: Applications may be considered for the use of a product in an orphan subset of a non-rare disease or condition when the applicant can explain based on a characteristic or feature of the product (e.g., mechanism of action, toxicity profile, prior clinical experience) why the product will be limited to use in the subset of question. **An orphan subset is not based on an unmet need, or how a sponsor may wish to study or indicate a product. The explanation for the orphan subset must make it clear to OOPD that the product would not be appropriate in the disease or condition outside of the subset,** including pediatric subpopulations). For studies proposing assessing multiple rare diseases, supportive prevalence data for each rare disease is required.

Additional information may be required upon request, for example, regarding population estimate and rationale. This additional information may be required, in part, to assure that human clinical trials of drugs are eligible to receive funding under the OOPD Grants Program.

Helpful Hint: *Orphan drug designation is encouraged (although not required), especially if it is questionable whether the population served by the proposed use would qualify for orphan drug status.*

Support of Product Development:

The **Rationale Section** of the Research Strategy should also include a subsection with the heading "Support of Product Development." This subsection should include an explanation of how the proposed study will either help support product approval or provide essential data needed for product development. If the proposal is for multiple products or multiple rare diseases, a plan as to how the applicant intends to proceed with product development (potentially in collaboration with multiple sponsors) should be provided in the grant application.

Study Monitoring Plan:

The **Study Design Section** of the Research Strategy should include a subsection with the specific heading "Study Monitoring Plan." This subsection should include a proposed plan for monitoring. 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 (IMM). Monitoring activities should be appropriate to the study, study phase, population, research environment, and degree of risk involved. Guidance is available at: https://www.fda.gov/media/116754/download. This section will detail the parties responsible for monitoring, what will be monitored, and the frequency (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. Guidance on these topics is available at:
http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM127073.pdf

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, including evaluating the informed consent documents as well as the plan to monitor the integrity of the data collected and protocol compliance. Any comments and concerns will be included in an administrative note in the summary statement. OOPD staff will ensure that all concerns are resolved before a grant award is made.

Other Research Plan Section:

Vertebrate Animals:
Not applicable for OOPD's clinical trial grants.

Select Agent Research:
Typically not applicable for OOPD's clinical trial grants.

Multiple PD/PI Leadership Plan:
For applications designating multiple PDs/PIs, a new section of the research plan, entitled Multiple PD/PI Leadership Plan [item 7 of the PHS 398 Research Plan] must be included. For example, please describe: (1) the rationale for choosing a multiple PD/PI approach; (2) leadership team governance and organizational structure; (3) communication plans; (4) process for making decisions on scientific direction; (5) procedures for resolving conflicts; and (6) roles and responsibilities for PDs/PIs and other collaborators.

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

Consortium/Contractual Arrangements:
Explain the programmatic, fiscal, and administrative arrangements to be made between the applicant organization and the consortium organization(s) as outlined in the How to Apply – Application Guide.

Letters of support:
Letters of support should be included for the following areas:
1) Study Sites: The leader(s) of the existing clinical research institutions that will conduct the study should describe their site support, including relevant resources and study infrastructure and an estimate of the number of patients with the target rare disease(s) who would be eligible for the study;
2) Product Availability: There must be evidence that the product(s) to be studied is available to the applicant in the form and quantity needed for the clinical trial proposed. A current letter(s) from the supplier as an appendix will be acceptable. If negotiations regarding the supply of the study product(s) 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(s) will be necessary before an award is made; and
3) Patient Engagement: There must be evidence that patient input has been obtained in a meaningful way. A current letter(s) from patient(s)/caregiver(s)/patient organizations describing early and ongoing engagement in trial design should be provided.

Resource Sharing Plan:
Individuals are required to comply with the instructions for the Resource Sharing Plans as provided in the SF424 (R&R) Application Guide, with the following modification:

- All applications, regardless of the amount of direct costs requested for any one year, should address a Data Sharing Plan.

Appendix:
The Appendix is used to allow the applicant to include certain required and supportive documents. A maximum of 10 appendices are allowed. Please do not use the appendix

to circumvent page limits. Follow all instructions for the appendix as described in the SF424 (R&R) Application Guide with the following additional instructions:

The appendices should include the following, as appropriate for the proposed study:

1. **Protocol:** The full final protocol (IND/IDE submitted protocol) must be provided in an appendix section. This same final protocol needs to have been submitted to the IND/IDE 30 days prior to applying for a grant application.

2. **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 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.

3. **Innovative and Efficient Trial Approaches:** Applications requesting additional funding (up to $250,000 total costs per year) for innovative and efficient trial approaches must submit a clear description and justification as to how the requirements as outlined below are met **(limited to 3 pages)**:
    - Innovative trial designs such as seamless and adaptive trial designs, which compress the phases of a trial into one continuous trial, as well as basket, umbrella and platform trials, which allow for testing of multiple drugs and/or multiple diseases using a common infrastructure.
    - Innovative methods using data simulations and modeling toward the study of safety and efficacy of a product.

    OOPD encourages applicants to refer to: "Interacting with the FDA on Complex Innovative Trial Designs" and "Adaptive Design Clinical Trials for Drugs and Biologics" for guidance on complex innovative designs and the use of data simulations and modeling for clinical trials intended to support the effectiveness and safety of drugs and biologics.

    Applications not meeting these requirements may be requested to reduce their budget.

4. **Summary Statement:** Resubmissions must provide the previous OOPD Summary Statement in an appendix section and should include a point-by-point rebuttal to those critiques.

An application that does not observe the required page limitations may be delayed or rejected in the review process. Applicants must follow the specific instructions on Appendix materials as described in the SF424 (R&R) Application Guide.

Helpful Hint: *Missing study protocols and informed consent/assent documents are a frequent weakness noted by panel reviewers of OOPD's grant applications. The study protocol must have been submitted to the IND/IDE Review Division. When submitting your protocol to the IND/IDE Review division (at least 30 days prior to the grant receipt date,) please indicate in the cover letter your intent of applying for an FDA Office of Orphan Products Development Clinical Trials grant and how the*

study will be used for future marketing approval and product development. To qualify for programmatic/scientific review, the study protocol proposed in the grant application must be deemed as safe to proceed under an active IND or IDE (i.e., not on clinical hold and not exempt).

Items that should not be included in the appendix:

- Photographs or color images of gels, micrographs, etc. These images must be included in the Research Strategy PDF. However, images embedded in publications are allowed.
- Publications that are publicly accessible. For such publications, the URL or PMC submission identification numbers along with the full reference should be included as appropriate in the Bibliography and References cited section, the Progress Report Publication List section, and/or the Biographical Sketch section.

All attachments must in PDF format and not be password protected. There is a limit of 10 appendices. If the pages in any attachment are greater than 11 x 11 inches or less than 8.5 x 8.5 inches, please adjust with software that can change the page size from actual to an 8.5 x 11 inch size. See the applicable SF424 (R&R) Application Guide for page limitations and appendix guidance in detail.

Applicants are encouraged to be as concise as possible while including the information needed for expert scientific review of their proposal; however, the appendices should not be used to circumvent page limitations, such as the specified page limit for the Research Strategy.

Helpful Hint: *Appendices should be given a name that is meaningful to reviewers rather than relying on sequential order. Appendix material may not appear in the assembled application in the order attached. Thus, it is important to use filenames for attachments that are descriptive of the content. A summary sheet listing all items included as appendices is encouraged but not required. When including a summary sheet, it should be included in the first appendix attachment. Applications that do not follow the appendix requirements may be delayed in the review process. Extensive appendices are noted by panel reviewers of OOPD grant applications as being extremely difficult to review in their entirety.*

Protection for Human Subjects:

This section describes compliance with protection of the rights and welfare of the participants in a research project.

All institutions engaged in human subject research financially supported by HHS must file an assurance of protection for human subjects with the Office of Human Research Protections (OHRP) (45 CFR part 46). See OHRP for guidance on human subject protection issues. Federal regulations (45 CFR part 46) require that applications and proposals involving human subjects must be evaluated with reference to the risks to the subjects, the adequacy of protection against these risks, the potential benefits of the

research to the subjects and others, and the importance of the knowledge gained or to be gained.

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.

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 an 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 21 CFR part 56). Applicants are encouraged to review the regulations, guidance, and information sheets on human subject protection and good clinical practice available at FDA's site on Clinical Trials and Human Subject Protection.

Helpful Hint: *Failure to submit at least a draft a consent/assent form is a frequent weakness noted by panel reviewers of OOPD grant applications.*

While IRB approval is not needed at time of submission of a grant application, IRB approval from the IRB of record must be on file with the FDA grants management office before an award to fund the study will be made. If IRB approval has been attained, please specify such in this section and include a copy of the approval letter.

Inclusion of Women, Minorities, and Individuals Across the Lifespan:

When the proposed project involves human subjects and/or FDA-defined clinical research, the committee will evaluate the proposed plans for the inclusion (or exclusion) of individuals on the basis of sex/gender, race, and ethnicity, as well as the inclusion (or exclusion) of all ages (including children and older adults) to determine if it is justified in terms of the scientific goals and research strategy proposed. For additional information on review of the Inclusion section, please refer to the Guidelines for the Review of Inclusion in Clinical Research.

E. Other Information:

Please be aware that the following documentation must be received by the FDA before an award is made:

- **Federal Wide Assurance**
  Federal Wide Assurance (FWA or assurance) obtained from Office for Human Research Protections (OHRP) 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. 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.
- **IRB of Record**
  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. An awardee institution must have its own IRB of record. 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 the OHRP.
- **IND/IDE**
  The purpose of this RFA is to fund clinical trials of products evaluating efficacy and/or safety in support of a new indication or change in labeling to address unmet needs in rare diseases or conditions. The study protocol proposed in the grant application (including studies of already approved products evaluating new orphan indications) is subject to 21 CFR 312.2b and 21 CFR 812.2 due to the use of it to support a new indication or change in labeling, with the exception noted below. 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 or exempt. The proposed clinical protocol (the same protocol that is included in the grant application) should be submitted to the applicable FDA IND/IDE review division a minimum of 30 days before the grant application deadline to allow for review within the division and a decision by the review division on status of that IND.

  Only medical foods that do not need pre-market approval and 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 grant application from the FDA Center for Devices and Radiologic Health indicating the device is an NSR device.**

Useful links:

- **FDA Office of Orphan Products Development**
- **FDA Orphan Products Grants Program**
- **Clinical Trials RFA**
- **Grants.gov**
- **Grants Forms Library**
- **Grants.gov Applicant FAQs**
- **Grants.gov Submitting Your Application**
- **Grants 101**

- **How to Apply – Application Guide**
- **eRA Commons Registration Process**
- **eRA Help**
- **Dun and Bradstreet DUNS Number**
- **System for Award Management (SAM)**
- **Credential Provider Registration**
- **Office of Human Subjects Protections (Federalwide Assurance)**
- **Office of Research Integrity**
- **PHS Administrative Action Bulletin Board**
- **HHS Financial Management (Indirect Cost Negotiations)**
- **Salary Cap Summary (FY 1990 – Present)**

Additional Resources for Applicants:

- **Rare Diseases: Common Issues in Drug Development**
- **Interacting with the FDA on Complex Innovative Trial Designs for Drugs and Biological Products**
- **Adaptive Clinical Trial Designs for Drugs and Biologics**
- **Use of Electronic Health Records Data in Clinical Investigations**
- **Submitting Documents Using Real-World Data and Real-World Evidence to FDA for Drugs and Biologics**
- **Real-World Data: Assessing Electronic Health Records and Medical Claims Data to Support Regulatory Decision-Making for Drug and Biological Products**
- **Good Clinical Practice: Integrated Addendum to ICH E6(R1)**