Office of Orphan Products Development (OOPD) Clinical Trials Grants:

Application Instructions and Helpful Hints

Application Due Date:

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

A letter of intent will be due (not required) by a minimum of 30 days prior to the application submission.

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 is 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. Applicants should first review the Request for Application (RFA) that has been published in the NIH Guide prior to getting started.

The final version of the protocol submitted to OOPD in the grant application must be submitted to the applicable FDA IND/IDE review division a minimum of 30 days before the grant application deadline.

Pre-Application Registrations:

OOPD 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: Obtain a Dun and Bradstreet Universal Numbering System (DUNS) number

Step 2: Register with the System for Award Management (SAM) - A valid Taxpayer Identification Number (TIN) or Employer Identification Number (EIN) is necessary for SAM registration.

Step 3: Register with and obtain Username & Password on Grants.gov

> ***Steps 1 through 3 above, in detail, can be found at:***
> http://www.grants.gov/web/grants/applicants/organization-registration.html

Step 4: Register with eRA Commons

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 ''Tips'' 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 by this Agency.

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, unless you are submitting a "Changed/Corrected" application in which case you need to enter the grants.gov tracking number (########) previously assigned.

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

Type of Application:
For this RFA, "New" and "Resubmission" 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 name of the generic drug/device; (3) the name of the disease/condition to be studied; (4) the **IND/IDE number**; and (5) **the date the protocol you are requesting funding for was submitted to FDA review division.**

OOPD Hint: *Please note that the title field is limited to 200 characters, including the spaces between words and punctuation to avoid errors. An appropriate descriptive title example is "**Ph 2a** Study of **Drug** for **Disease** IND **123,456** (**mm/dd/yyyy**)."*

OOPD Hint: Applications must use the generic name of the proposed product(s).

OOPD Hint: *The final version of the clinical protocol that is included in the grant application must be submitted to the applicable FDA IND or IDE Review Division 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.*

OOPD Hint: *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:

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 of support.

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 are thus 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 other persons working in the same or related fields and, insofar as possible, understandable to a scientifically or technically literate lay reader. The Project Summary is meant to serve as a succinct and accurate description of the proposed work when separated from the application. State the application's broad, long-term objectives and specific aims, making reference to the health relatedness of the project (i.e., relevance to the mission of the Orphan Products Clinical Trials Grants). The objectives of the project should be clearly stated by 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. Make reference to the relevance of the project to the mission of the OOPD grants program. Avoid describing past accomplishments and use of first person. Do not include proprietary or confidential information or trade secrets, as this description may be used for purposes other than review.

OOPD Hint: *Be concise and succinct, but complete as* ***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 page with 0.5 inch margins in 11 point font or larger. An abstract which exceeds this allowable length may be flagged as an error by the Agency upon submission. This would require a corrective action before the application can be accepted.*

Project Narrative (Public Health Relevance Statement):
This section represents a second component of the Project Summary, which is Relevance. In two or three sentences, describe the relevance of the project to public health using succinct, plain language that can be understood by a general, lay audience. There is a one page limit for this section.

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).

Note: 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 that 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.

OOPD Hint: *Failure to provide justification that adequate enrollment can be attained within the proposed study timeframe is a frequent weakness of OOPD 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 (US), or if the study requires the use of these to augment existing US resources. 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.

"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.

OOPD Hint: *Failure to include a detailed biosketch that supports the role of each senior/key person in the proposed study is a frequent weakness of OOPD grant applications. A sample format of a biosketch can be found at* https://grants.nih.gov/node/826.

Budget:
The FDA OOPD Grant Programs uses the Research & Related (R&R) Budget Component. Application budgets are not limited, but need to reflect the actual needs of the proposed project.

An applicant planning to submit a grant application with $500,000 or more in direct costs for any year is required must provide a letter of request (separate from the Letter of Intent) to the Grants Program Director at least 4 weeks prior to the application deadline. Upon review, adequate requests will be issued a letter from the Scientific/Research Contact accepting the assignment of the application. This letter must be included as an appendix attachment in the final grant application. Applications submitted without this approval will not be reviewed. Final budget determinations will be made during the grant review.

Note: For the optional Innovative Demonstration Project Funding, the maximum amount requested shall not exceed $500,000 total costs per year. As with the overall application, it is expected that the time and scope of the project

is reflected in the budget request and will be reviewed annually by the program.

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.

The 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 (i.e. other grants, corporate funding, etc).
- State if other grants have been or will be applied for, and describe contingency plans should those funds not be obtained.

Note: The PHS 398 Modular Budget program does not apply to the OOPD Clinical Trials grants and should not be used.

OOPD 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 and 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 Research & Related Subaward Budget Attachment(s) Form. A separate budget justification should also be submitted for each subaward.

D. <u>SF424 "PHS 398 Research Plan":</u>

The goal of FDA's OOPD Clinical Trials Grants is to support fund well-controlled studies in support of a new indication or change in labeling of products to address unmet needs in rare diseases or conditions. Through the funding of efficient and innovative clinical studies evaluating safety and/or efficacy, FDA expects to increase the number of treatments for rare diseases with an unmet medical need and exert a broad and positive impact on rare disease drug development.

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

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.

Note: 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.

OOPD 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 otherwise 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.

Research Plan Section:
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 that 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 entirety of the Research Strategy Section is limited to **12 pages**. Please note, 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 scoring criteria for each):

1. Rationale
2. Study Design
3. Inclusion of Patient Input

4. Investigator(s)
5. Infrastructure and Financial Resources
6. Ability to Advance the Current Field

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 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). 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.

> ***OOPD 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 in collaboration with multiple sponsors should be provided in the grant application.

Study Monitoring Plan:
The **Study Design and Inclusion of Patient Input Section of the Research Strategy** should include a further subsection with the heading "Study Monitoring Plan." This subsection should include a 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 follow-up 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. Guidance on these topics is available at: http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM127073.pdf

Note: 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 grants.

Select Agent Research:
Typically not applicable for OOPD 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 [Section 10 of the Research Plan Component in the SF424 (R&R)], must be included. A rationale for choosing a multiple PD/PI approach should be described. The governance and organizational structure of the leadership team and 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 and other collaborators.

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).

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;
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.

OOPD Hint: *An inadequately justified or not well detailed statistical analysis is a frequent weakness noted by panel reviewers of OOPD grant applications.*

Appendix:
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 requirements:

The Appendices must include the following, as appropriate for the proposed study:

- **Protocol:** The full final protocol (IND/IDE submitted protocol) must be provided in an appendix section of the grant. This same final protocol needs to have been submitted to the IND/IDE 30 days prior to applying for a grant application.
- **Informed Consent:** Consent forms, assent forms, and any other information given to a subject must be provided. 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.
- **Summary Statement:** Resubmissions must provide the previous OOPD Summary Statement and may include a point by point rebuttal to those critiques.
- **Applicants requesting $500,000 or more in direct costs for any year** (independent of the optional Innovative Demonstration Project) must attach as an appendix, the prior approval letter from the FDA accepting the assignment of the application. Applications submitted without this approval will not be reviewed. Final budget determinations will be made during the grant review.
- **Innovative Demonstration Project (OPTIONAL):**
  Applicants submitting an optional **Innovative Demonstration Project** (5 pages maximum) must provide a description of how they will address the criteria of that project related to **one of the three goals described in the RFA**. **This section is a stand-alone section from the rest of the application and will be scored separately for potential additional funding.** Should this Innovative Demonstration Project not be funded, it should not affect the design and/or

feasibility of the main proposal submitted. This section must be attached as a stand alone appendix to the application. See RFA for scoring criteria and details.

- **Applications proposing an Innovative Demonstration Project** must submit a separate detailed budget and justification in addition to the main proposal and justification. **The Innovative Demonstration Project's budget and justification must be attached as a stand alone appendix**.

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 (See http://grants.nih.gov/grants/funding/424/index.htm)

OOPD Hint: It is a requirement to include as an appendix the same study protocol that has been submitted to the IND/IDE Review Division and the protocol that is intended to be used as the trial for the grant. Without this protocol, the application will be deemed non-responsive to the RFA and will not be reviewed. Informed consent/assent forms must also be included as an appendix.

The same protocol that is submitted to the grant and intended to be carried out under OOPD funding is required to have been submitted to an IND/IDE at least 30 days prior to submitting the grant application. Be sure to indicate in the IND cover letter to the review division 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. This will allow the review division to assess the IND. 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., **are no longer accepted as Appendix material**. 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.

Note: All attachments must in PDF format only and not be password protected. **There is a limit of 10 appendices total.** 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 at http://grants.nih.gov/grants/how-to-apply-application-guide.htm 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 <u>not</u> be used to circumvent page limitations, such as the specified page limit for the Research Strategy.

OOPD Hint: *It is recommended that all appendices 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, so it is important to use filenames for attachments that are descriptive of the content. A summary sheet listing all the items included as appendices is also 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. <u>Extensive appendices are noted by panel reviewers of OOPD grant applications as being extremely difficult to review in their entirety.</u>*

E. <u>PHS Human Subjects and Clinical Trials Information:</u>

When involving FDA-defined human subjects research, clinical research, and/or clinical trials follow all instructions for the PHS Human Subjects and Clinical Trials Information form in the SF424 (R&R) Application Guide. You must include at least one human subjects study record using the **Study Record: PHS Human Subjects and Clinical Trials Information** form.

<u>Protection for Human Subjects:</u>

The purpose of this section is to describe the involvement of human subjects to ensure the protection of the rights and welfare of the participants in a research project. The PHS Human Subjects and Clinical Trials Information form is used to collect information on human subjects research, clinical research, and/or clinical trials, including study population characteristics, protection and monitoring plans, and a protocol synopsis.

For research that involves human subjects but does not involve one of the six categories of research that are exempt under 45 CFR Part 46, the committee will evaluate the justification for involvement of human subjects and the proposed protections from research risk relating to their participation according to the following five review criteria: 1) risk to subjects, 2) adequacy of protection against risks, 3) potential benefits to the subjects and others, 4) importance of the knowledge to be gained, and 5) data and safety monitoring for clinical trials.

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). Applicants are advised to visit the OHRP Web site at http://www.hhs.gov/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 (http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html).

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 56). Applicants are encouraged to review the regulations, guidance, and information sheets on human subject protection and good clinical practice available at https://www.fda.gov/science-research/science-and-research-special-topics/clinical-trials-and-human-subject-protection.

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

Note: While IRB approval is not needed at time of submission of a grant application, IRB approval from the single 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 children 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.

F. 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 well-controlled studies in support of a new indication or change in labeling of products 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.

Useful links:
OOPD Web Page:
https://www.fda.gov/industry/developing-products-rare-diseases-conditions

RFA Link:
https://grants.nih.gov/grants/guide/rfa-files/RFA-FD-20-001.html

Grants 101:
http://www.grants.gov/web/grants/learn-grants/grants-101.html

eRA:
Creating User Accounts
http://grants.nih.gov/grants/ElectronicReceipt/files/Grantee_Registration_Process_for_Commons.pdf
https://commons.era.nih.gov/commons-help/174.htm

Federal Wide Assurance:
Office for Human Resource Protections
http://www.hhs.gov/ohrp/
http://ori.hhs.gov/reg-sub-part-a
http://ori.hhs.gov/phs-admin-action-bulletin-board

Dun and Bradstreet Universal Numbering System (DUNS) number:
http://fedgov.dnb.com/webform

System for Award Management (SAM): https://governmentcontractregistration.com/

Credential Provider registration:
https://apply07.grants.gov/apply/OrcRegister

HHS/Financial Management:
https://rates.psc.gov/

Orphan Research Grants Program Resource List:
Grants.Gov Submitting your Application
http://grants.nih.gov/grants/submitapplication.htm
NIH Forms and Applications http://grants.nih.gov/grants/forms.htm

Salary Cap Summary (FY 1990 to Present)
http://grants.nih.gov/grants/policy/salcap_summary.htm

Grants.gov Registration Instructions for Domestic and Foreign Organizations:
Grantee Registration Process in NIH eRA Commons: Detailed Steps
http://grants.nih.gov/grants/ElectronicReceipt/files/grantee_registration_process_for_commons.pdf

Additional Grants.gov Electronic Submission Process Resources: Grants.gov Applicant FAQs:
http://www.grants.gov/web/grants/applicants/applicant-faqs.html
How to Apply – Application Guide:
http://grants.nih.gov/grants/ElectronicReceipt/preparing.htm