



Alpha-1 Foundation
Letter of Intent
and Full Application
Instructions

2017-2018 In-Cycle Grants

VERSION 2
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Alpha-1 Foundation
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Coral Gables, FL 33134

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I. INTRODUCTION

MISSION

The Alpha-1 Foundation is committed to finding a cure for Alpha-1 Antitrypsin Deficiency and to improving the lives of individuals affected by Alpha-1 worldwide.

The specific aims of the Grants Award Program are to promote research that would eventually result in the improved health of individuals with AAT Deficiency. The Program supports basic science and clinical research, improved understanding of the pathogenesis of the clinical manifestations of AAT Deficiency, the development and testing of treatments for the disease, bioethics and social research, and the promotion of education of members of the medical community regarding AAT Deficiency.

To achieve these aims, the Foundation offers financial awards to support a wide range of meritorious research related to AAT Deficiency including basic laboratory investigations, epidemiology, clinical genetics, clinical trials, clinical management, ethical, legal, and social issues, and public education.

GOALS OF THE GRANTS AWARD PROGRAM

The Grants Award Program is the Alpha-1 Foundation's mechanism to fund a broad range of research that leads to improvements in the lives of people living with AAT Deficiency. The specific goals of the Program are 1) to promote basic science and clinical research related to the alpha-1 antitrypsin protein and AAT Deficiency; 2) to attract and train clinical researchers for the study of AAT Deficiency; 3) to support and encourage established scientists to work on clinical problems and ethical, legal, and social issues within the field of AAT research (with a preference given to new investigators); and ultimately, 4) to develop effective therapies for the clinical manifestations of AAT Deficiency.

The Alpha-1 Foundation will support a broad spectrum of research projects involving basic science, translational and clinical research, and ethical, legal, and social issues. The Foundation's research agenda can be found on the Foundation's website at www.alpha1.org.

Other topics may be reviewed for appropriateness of funding based on the investigator's Letter of Intent (LOI). Please see Section II of this document for more information about the LOI.

Applicants are encouraged to utilize the Alpha-1 Foundation research resources including:

- The Alpha-1 Research Registry, a database of diagnosed individuals and carriers available for participation in research studies and clinical trials, website: www.alpha1registry.org.
- The Alpha-1 DNA & Tissue Bank, a disease specific source of DNA and tissue available for use by qualified researchers, website: http://www.alphaone.ufl.edu/dna_tissue_bank1.html.
- The Alpha-1 National Targeted Detection Program, a program designed to understand the best methodology and targets for AAT testing.
- The Alpha-1 Coded Testing program, a confidential testing program for use by family members, symptomatic individuals or those not wanting genetic information in their medical record, website: http://www.alpha1registry.org/test_kit/home.html.
- The Lung Tissue Research Consortium, a resource program of the NHLBI that provides human lung tissues to qualified investigators for use in their research, enrolls donor subjects who are anticipating lung surgery, collects blood and extensive phenotypic data from the prospective donors, and then processes their surgical waste tissues for research use. See more at: <http://www.alpha1.org/Investigators/Resources/Lung-Tissue-Research-Consortium#sthash.GAI4DEg.dpuf>

OVERVIEW OF LOI & FULL APPLICATION REVIEW ADMINISTRATION PROCESS:

The procedure pertains to the following grant categories:

Grants: Bridge Grant
Pilot and Feasibility Grant
Postdoctoral Research Fellowship Grant
Research Grant

The process of receiving grant applications and awarding grants begins with announcements of the forthcoming grant opportunities. The Alpha-1 Foundation posts its announcements of upcoming funding opportunities on its website (www.alpha1.org), on proposalCENTRAL (<https://proposalCENTRAL.altum.com/Opportunities.asp?GMID=135>), and through other means relevant to the announced opportunities. These announcements are also emailed to those people who have made inquiries throughout the year. In addition, the announcements are emailed to those investigators who are part of the Foundation's research network.

The first document that is submitted by applicants is the LOI. The deadline for submitting an LOI is **September 22, 2017**, by 11:59PM ET. This document is a brief summary of the grant that the applicant intends to submit to the Foundation. The LOIs are reviewed by the Foundation's Grants Advisory Committee and discussed by conference call. If needed, input will be requested from ad hoc reviewers. The evaluation of the LOI is based on the following criteria: scientific merit, relevance to the Foundation's mission, innovation, potential impact and experience of the applicant. An overall score is assigned by each reviewer. If the proposed research involves training, the fellow's training program and the mentor's qualifications are also assessed. After having ranked the LOIs, the Grants Advisory Committee determines which applicants will be invited to submit a full application. The decision is communicated to all applicants irrespective of whether or not they are invited to submit a full application.

The deadline for submitting a full application is **February 16, 2018**, by 11:59PM ET. Applications undergo an initial administrative review to ensure completeness and accuracy, and additional documentation may be requested from the applicant. The proposals are then reviewed and scored by the Foundation's Grants Advisory Committee, and discussed in a face-to-face meeting for final ranking and recommendation for funding. If needed, input will be requested from ad hoc reviewers. The evaluation of the proposal is based on the following criteria: scientific merit, innovation and relevance to the Foundation's mission. If the proposed research involves training, the fellow's training program and the mentor's qualifications are also assessed. Reviewers are also asked to provide an overall score for the proposal. If needed, input will be requested from ad hoc reviewers. This meeting will be held in April 2016.

The Foundation's administrative review takes place in late April. Final funding decisions are made at this meeting based on the merit scores of the proposals, the Grants Advisory Committee recommendation regarding funding, and the dollar amount allocated by the Foundation for grant funding.

Once the funding decisions are made, each investigator who submitted a grant application receives a letter indicating whether the grant that he or she submitted will be funded. In addition, the investigator receives a summary statement reflecting reviewers' comments and critiques. **Note: Newly funded in-cycle Investigators are invited to attend the Alpha-1 Foundation's Awards Reception at the American Thoracic Society's (ATS) International Conference,**

which is tentatively scheduled for May 2018. The Foundation will use monies from the grant award to help pay for Investigator's travel to this reception.

Those grant applications that have been deemed to be funded will receive a Notice of Award packet that contains several regulatory documents. Once executed, the regulatory documents are returned to the Foundation. Subsequently, the first payment on the grant is issued. A grant may not begin until all regulatory documents including, but not limited to, the Notice of Award, Release of Information Form, Directory Form are executed and returned to the Alpha-1 Foundation. In projects involving human subjects that require IRB approval, the Principal Investigator must provide a copy of an IRB approval letter to the Foundation upon notification of approval of funding of the grant award and prior to the commencement of the proposed project. This policy applies to Institutional Animal Care and Use Committee Approvals as well.

The grant is administered according to the guidelines contained in this document, in addition to the Foundation's Terms and Conditions, which can be found on the Foundation's website at www.alpha1.org. Payments are issued on a quarterly basis. If the grant is a one-year award, a final progress report is due at the end of the grant's period of performance. If the grant is a two-year award, an annual and a final report are submitted to the Foundation. Each annual and final report is reviewed and approved by the Foundation's Scientific Director. Payments are withheld until the grant recipient ("Grantee") submits an appropriate and complete progress report to the Foundation. The Foundation may withhold the final payment if an abstract or paper has not been submitted by the Principal Investigator as part of the final progress report. The results of the progress reports are incorporated into the Scientific Director's annual report.

Scientific Meeting Sponsorship Grant and Travel Grant:

The process of receiving requests for funding for Scientific Meeting Sponsorships or Travel Grants begins with announcements of the forthcoming opportunities. The Foundation posts its announcements of these opportunities on its website. These announcements are also emailed to those people who have made inquiries throughout the year. In addition, the announcements are emailed to those investigators who participate in the Foundation's research network.

The document that is submitted by potential awardees is the LOI. This document is a brief summary of details associated with the meeting or

the purpose of the travel. Should the request for funding fall outside the grant review cycle, the Foundation will either provide rapid review or a Grants Advisory Committee member will be appointed to review the request. A merit score and recommendation for funding will be provided to the Alpha-1 Foundation within two (2) months of the receipt of a request, unless the request falls within the grant review cycle. If the request falls within the grant review period of time, the Scientific Meeting Sponsorship or Travel requests will be considered at the Foundation's regular Grants Advisory Committee meeting, held in **April 2018**.

In late April, the Foundation's administrative review takes place. The final funding decisions are made at this meeting based on the scores assigned to the Scientific Meeting Sponsorship or Travel requests and the funds available to fund Scientific Meeting Sponsorship or Travel Grants.

Once the funding decisions are made, each investigator who submitted a request will receive a letter indicating whether or not their request will be funded.

Those requests that have been approved for funding will receive a Notice of Award packet that contains several regulatory documents. Once executed, the regulatory documents are returned to the Foundation. Payment is issued as a reimbursement after the meeting has taken place.

Funded requests are administered according to the guidelines contained in this document. A report is due once the meeting or travel has been completed. The report is reviewed and approved by the Foundation's Scientific Director. Final Payment is withheld until the appropriate and complete report is submitted to the Foundation. The results of the report may be incorporated into Alpha-1 Foundation Development Reports, Scientific reports or publications.

TIMELINE FOR LETTERS OF INTENT AND FULL APPLICATIONS

The schedule for the submission of a LOI and a full application (Bridge, ELSI as a Pilot and Feasibility, Postdoctoral Research Fellowship or Research proposal, Pilot and Feasibility, Postdoctoral Research Fellowship and Research grant) is contained in the table below.

LOI applicants will be notified by **November 24, 2017** whether or not the Alpha-1 Foundation recommends that a full application be submitted.

2017–18 IN-CYCLE GRANTS TIMELINE	
Grant Announcement and Letter of Intent (LOI) application form available on proposalCENTRAL.	July 11, 2017
LOIs due to the Foundation. (Deadline to submit on proposalCENTRAL is 11:59PM ET)	September 22, 2017
LOIs released to reviewers via proposalCENTRAL.	October 10, 2017
LOI applicants invited to submit full application. Full application form available on proposalCENTRAL.	November 24, 2017
Full Applications due to the Foundation. (Deadline to submit on proposalCENTRAL is 11:59PM ET)	February 16, 2018
Full Applications released to reviewers via proposalCENTRAL.	February 23, 2018
Applicants notified of funding decision.	May 2, 2018
Funding begins.	July 1, 2018

Scientific Meeting Sponsorship and Travel grant applications must be received by the Alpha-1 Foundation at least 2 months prior to the anticipated meeting or travel. Please contact the Alpha-1 Foundation's Director of Research Administration, David Fernandez, at 305-567-9888 ext. 242 or at dfernandez@alpha1.org for further information regarding Scientific Meeting Sponsorship Grants and Travel Grants.

II. LETTER OF INTENT

GUIDELINES FOR PREPARING A LETTER OF INTENT

The submission of an LOI is required for each grant category. The Alpha-1 Foundation requires all applicants to submit their LOI online using proposalCENTRAL. Once you have created a profile and are logged in, the online application form is available here: <https://proposalCENTRAL.altum.com/Opportunities.asp?GMID=135>.

The Alpha-1 Foundation evaluates each LOI to determine the appropriateness and relevance of a proposed topic for funding. The LOI is treated as privileged material and is handled in a confidential manner. An applicant is not obligated to submit a grant application if an LOI is submitted. However, an applicant must submit an LOI in order to submit a grant application. A grant application that is submitted without a LOI will result in an automatic denial of funding and the application will be returned to the investigator.

Note: Applicants must first create a profile and be logged in to proposalCENTRAL in order to access the LOI application form.

Note: The LOI is not included in the review of a grant application.

Note: If an applicant plans to submit a revised grant application from a previous grant cycle, the LOI should state this intention and address the reviewers comments provided to the applicant. Please see the Revised Applications section of this document for more information on submitting a revised application.

Note: Applicants may submit only one (1) LOI per grant cycle.

Note: Any discussion or indication of interest prior to or after the submission of an LOI or grant application to the Alpha-1 Foundation should not be construed as a commitment of funding by the Alpha-1 Foundation.

Note: All documents submitted to the Alpha-1 Foundation must be translated to English if written in another language.

Requirements for a Letter of Intent:

The requirements pertain to the following grant categories:

- Grants:** Bridge Grant
Pilot and Feasibility Grant
Postdoctoral Research Fellowship Grant
Research Grant

Please see Section III of this document for descriptions of these various grant categories.

The Alpha-1 Foundation LOI Form Pages provided on proposalCENTRAL must be used to complete all LOIs except for Scientific Meeting Sponsorship Grant LOIs or Travel Grant LOIs.

The following information is required to submit a complete LOI application. Numbers correspond to the application sections found on the left side of the online application form on ProposalCENTRAL:

1. Title Page

- Please provide the project's title **(do not exceed 90 characters, including spaces)**, start and end dates **(dates must be in mm/dd/yyyy format)**, total amount

requested (**amount must be in \$USD**), and the grant category to which your LOI applies.

- **Note:** All applicants must indicate whether or not their LOI is a revised application from a previous grant submission using the yes/no dropdown menu. If your LOI is a revised application, provide the year in which the previous application was submitted.
- **Note:** Please make sure the total dollar amount requested and the dates of the proposed project coincide with the grant category to which your LOI applies.

2. Download Templates & Instructions

- This section contains links to download application instructions, Terms and Conditions governing Alpha-1 Foundation awards, the Biographical Sketch form, and any other documents that are pertinent to the LOI application process.

3. Enable Other Users to Access this Proposal

- This section allows you to give other users access to your LOI application. The completion of this section is optional.

4. Applicant Information

- This section is used to provide the contact information of the Principal Investigator, including his/her name, position title, mailing address, telephone number and applicant organization.

5. Institutional & Signing Official Information

- This section is used to provide the contact information of the Institutional & Signing Official. Please make sure to fill-out all of the information requested in this section.

6. Key Personnel Information

- This section should be used to provide information on any Key Personnel involved in the proposed project.
- **Note:** Postdoctoral Research Fellowship applicants must provide contact information for their Mentor.

7. Research Plan

- This section should be used to provide a description of the proposed research (**For each section of Research Plan, do not exceed 3,000 characters, including spaces**), including:
 - Scientific Question and Aims
 - Hypothesis and Significance
 - Brief Description of Approach
 - Description of Training Program (**if applicable, Postdoctoral Research Fellowship LOIs ONLY**)
 - References

8. Abstract & Keywords

- This section should be used to provide a lay abstract (**do not 3,000 characters, including spaces**) and list of keywords associated with the proposed project. Please make sure to select all terms (general and specific research areas) that are applicable to your LOI. This information will be used to assign the appropriate reviewers to your application.

9. Application Attachments

- This section should be used to attach any documents pertaining to your LOI application, including all Biographical Sketches, Diagrams/Figures, Introduction (**for revised applications ONLY**), etc.

10. Validate

- This section should be used in order to validate that all required information and file uploads have been provided before your application is submitted. Sections of the application in which the applicant is required to provide information are denoted by a red asterisk.

11. Submit

- This section should be used to submit your application.
- **Note:** You will not be able to submit your application if you have not provided all the required information. Any missing information will be listed on the screen after you click the submit button. If your submission is successful, a confirmation email will be sent to the email address in your proposalCENTRAL profile.
- **Note:** If you need to make changes to your application after it has been submitted, you may do so only after withdrawing the submission in proposalCENTRAL. Withdrawing your submitted application will NOT delete any of the information you provided in the application. ProposalCENTRAL will allow you to withdraw your application, make changes, and resubmit any time prior to the LOI application deadline. Once the deadline passes, you will not be allowed to modify and/or resubmit your application.

ELSI Relating to AAT Deficiency Grants: In addition to the core requirements noted above, the LOI must also state the grant category to which your LOI applies. For example, an applicant must indicate whether the LOI relates to the ELSI category for a Pilot and Feasibility Grant, the ELSI category for a Postdoctoral Research Fellowship Grant,

or the ELSI category for a Research Grant. Please indicate whether your LOI is ELSI related in the Abstract & Keywords section of the LOI.

Postdoctoral Research Fellowship Grants: In addition to the core requirements noted above, the LOI must also include an overall description of the postdoctoral fellow's training program (including course work), and identify the postdoctoral fellow's mentor and the role of the mentor. For example, an applicant should comment on the amount of time spent with a mentor on a weekly basis, how the interaction takes place, etc. Please provide this training program description using the space provided in the Research Plan section of the LOI.

Scientific Meeting Sponsorship Grants

Note: A full application is not necessary when requesting a Scientific Meeting Sponsorship Grant. The LOI should contain sufficient information for review.

Note: All applicants interested in applying for a Scientific Meeting Sponsorship Grant must first contact David Fernandez, Director of Research Administration, at dfernandez@alpha1.org before putting together and submitting their LOI application.

The LOI must comply with the following core requirements:

- The venue and dates of the meeting.
- The purpose of the meeting.
- The anticipated number of participants.
- The meeting's relevance to the Alpha-1 Foundation's mission statement.
- A budget that clearly documents and identifies the costs associated with the funds that may be provided by the Alpha-1 Foundation.
- If meeting materials are available (pre-program information, program book, list of accepted speakers, website link), they should be included in the request.
- Provide specific information describing how the Alpha-1 Foundation's sponsorship will be acknowledged (i.e. in the program book, in publications of the results of the meeting, etc).
- Provide a two (2) page abbreviated Biographical Sketch using the standard Alpha-1 Foundation format, including academic rank (if applicable), current position title, education, other research support and relevant peer reviewed publications.
 - The Biographical sketch must include other support from the past 3 years. This information should be as brief as

possible to include the title of the grant and the corresponding granting agency.

Travel Grants

Note: A full application is not necessary when requesting a Travel Grant to present at scientific meetings and conferences or to receive cross training. The LOI should contain sufficient information for review.

Note: All applicants interested in applying for a Travel Grant must first contact David Fernandez, Director of Research Administration, at dfernandez@alpha1.org before putting together and submitting their LOI application.

The LOI must comply with the following core requirements:

If an applicant is submitting a proposal for travel to a meeting in order to present data associated with AAT research then the following are content requirements of the LOI:

- The name and institution of the investigator who will be traveling.
- The location and name of the meeting.
- The purpose of the travel.
- A copy of the any material related to the purpose of the travel, including material that is to be presented must be included in the request.
- A budget that clearly documents and identifies the costs associated with the travel.
- Provide specific information describing how the Alpha-1 Foundation's sponsorship will be acknowledged.
- Provide a two (2) page abbreviated Biographical Sketch using the standard Alpha-1 Foundation format, including academic rank (if applicable), current position title, education, other research support and relevant peer reviewed publications.
 - The Biographical sketch must include other support from the past 3 years. This information should be as brief as possible to include the title of the grant and the corresponding granting agency.

If an applicant is submitting a proposal in order to travel to a recognized Alpha-1 laboratory under the direction of an established Alpha-1 researcher to receive cross training on research techniques, then the following are content requirements for the LOI:

To submit an application for travel for cross training please send a brief two to three page summary that includes:

- The name and institution of the investigator who will be traveling.
- The name and institutional affiliation of the host.
- The purpose of the travel (i.e., to train on diagnostic and therapeutic procedures, research related techniques, or to train on specialized equipment or software applicable to AAT-related research.)
- A letter of support from the host that indicates the visitor's role, time commitment and objectives for the proposed training as well as institutional commitment.
- Budget page that clearly documents and identifies the costs associated with the travel request.
- Provide a two (2) page abbreviated Biographical Sketch using the standard Alpha-1 Foundation format, including academic rank (if applicable), current position title, education, other research support and relevant peer reviewed publications.
 - The Biographical sketch must include other support from the past 3 years. This information should be as brief as possible to include the title of the grant and the corresponding granting agency.

Please see Section III of this document for descriptions of the Scientific Meeting and Travel Grant categories.

Revised Applications (all categories): An investigator is limited to submitting a maximum of 2 revised or amended versions of a grant application. Both revised grant applications must be submitted within two years of the original version of the application.

Before a revised grant application can be submitted, the Principal Investigator must first 1) have received the summary statement from the review of their previous grant application submission; and 2) submit an LOI that indicates it is a revised application and includes an introduction that addresses the reviewers comments provided in the previous grant application's summary statement.

The LOI must include an Introduction, not greater than 3 pages, that summarizes the additions, deletions and/or changes made to the revised application. This Introduction should be included as an attachment to the LOI application (using the Application Attachments section of the online LOI form). List each area of concern noted in the summary statement from the previous submitted application and provide a clear and detailed response to each concern. Clearly summarize the changes that have been made in the revised application.

Deadline to submit (all categories except for Scientific Meeting Sponsorship and Travel Grants):

Using the LOI form provided on the proposalCENTRAL website (<https://proposalCENTRAL.altum.com/default.asp?GMID=135>), applicants are to submit one (1) electronic version of the LOI. With the exception of Scientific Meeting Sponsorship Grants and Travel Grants, **the LOI must be submitted on proposalCENTRAL by Friday, September 22, 2017, 11:59pm ET.** For Scientific Meeting Sponsorship and Travel Grants, the electronic LOI must be received by the Alpha-1 Foundation **at least two (2) months prior** to the meeting or travel. If an LOI does not meet the content and format requirements as previously stipulated, the LOI will not be reviewed and it will be returned to the applicant. Additional appendices, insertions, or revisions to the application after the receipt date will not be accepted, unless specifically agreed to in writing by the Alpha-1 Foundation.

Where to submit (all categories except for Scientific Meeting Sponsorship and Travel Grants):

The Alpha-1 Foundation requires applicants to submit their applications online using proposalCENTRAL.

The online application form is available here:

<https://proposalCENTRAL.altum.com/default.asp?GMID=135>

Inquiries or technical issues regarding proposalCENTRAL and the online application process should be directed to customer support at:

Phone: 703-964-5840, Toll-free phone: 1-800-875-2562

Email: pcsupport@altum.com

Live customer support is only available from 8:30am – 5pm ET.

Where to Submit (Scientific Meeting Sponsorship and Travel Grants ONLY):

The Alpha-1 Foundation requires Scientific Meeting Sponsorship and Travel Grant applicants to submit their applications via email to David Fernandez, Director of Research Administration, at dfernandez@alpha1.org.

Note: All applicants interested in applying for a Scientific Meeting Sponsorship or Travel Grant must first contact David Fernandez, Director of Research Administration, at dfernandez@alpha1.org before putting together and submitting their LOI.

Period of Performance and Funding Level Information:

	Period of Performance	Funding Level*
Bridge Grant	Up to 1 year	Up to \$25,000/year
Pilot and Feasibility Grant	Up to 1 year	Up to \$75,000/year
Postdoctoral Research Fellowship Grant	Up to 2 years	Up to \$50,000/year
Research Grant	Up to 2 years	Up to \$100,000/year
Scientific Meeting Sponsorship Grant	N/A	Up to \$5,000
Travel Grant	N/A	Up to \$1,000

***The Alpha-1 Foundation requires that each applicant allocate \$1,000 of the total budget to pay for travel to the Alpha-1 Foundation’s Biennial Investigators’ Meeting for the first year of the proposal’s period of performance. In case the applicant cannot attend the Investigators’ Meeting, the \$1,000 budgetary line item is not refundable. The purpose of the Investigator’s meeting is to 1) Provide Alpha-1 Foundation supported Investigators with a forum to exchange research findings and interact with donors on an informal basis; 2) Foster innovative new research through free discussion at the meeting; 3) Cultivate new Investigators in AAT Deficiency research and retain them by promoting face-to-face interactions with established AAT Deficiency researchers, and 4) Allow the Foundation’s Medical and Scientific Advisory Committee (MASAC), Grants Advisory Committee (GAC), Board of Directors (BOD) members and donors to meet AAT Deficiency Investigators. Investigators will be asked to present their recent AAT-related research during this meeting. Following this meeting, the Investigators will attend a research update presentation and cocktail reception with the Foundation’s donors.**

Note: If you have any questions or require additional information, please contact David Fernandez, Director of Research Administration, at 305-567-9888 ext. 242, or via email at dfernandez@alpha1.org.

III. DESCRIPTIONS OF GRANT CATEGORIES

Bridge Grants

The objective of this grant is to provide support for excellent AAT-related research projects that have been submitted to and approved by the National Institutes of Health (NIH), but cannot be supported by the available NIH funds. Thus, this award complements the granting mechanism of the NIH for projects of potential interest to individuals served by the Alpha-1 Foundation. Funds provided by the Alpha-1 Foundation through this program are intended to lead to the development of sufficient preliminary data to make AAT-related applications highly competitive in the NIH review process. Information derived from Alpha-1 Foundation supported research studies is intended to lead to solicitation of additional, subsequent funds from other agencies such as the NIH.

Funding Level: Maximum of \$25,000 may be requested.

Period: Up to 1 year of support is available. Investigators are required to submit a final progress report for this grant category.

Funding: Full funding is contingent upon the timely receipt of a satisfactory and complete final progress report. Full funding is contingent upon the Foundation having sufficient working capital (as determined by the Foundation in its sole discretion). Applicants are not eligible to receive a second year of additional funding for a Bridge Grant, but are encouraged to apply to external funding sources (i.e., NIH) to continue research initiated as a Foundation grant.

ELSI Relating to Alpha-1 Antitrypsin Deficiency Grants

The objective of this grant is to provide funds to encourage the development of new information that contributes to the understanding of bioethical, legal, economic and/or social issues associated with AAT Deficiency. Proposals may come from a broad spectrum of disciplines, including humanities, social and natural sciences, and health professions. In particular, this grant mechanism seeks to support the development of novel approaches relating to informed consent, conflicts of interest, organ allocation, genetic testing and/or genetic

discrimination, but applications may address all of the following or other related areas:

- Surveying attitudes about genetic testing and screening; changing physician behavior and standards of care regarding testing; confidential testing; genetic counseling; public awareness and education about Alpha-1.
- Improving the quality of life of alpha-1 antitrypsin deficient patients and their families; chronic illness, terminal illness, advance CARE planning, and end of life issues; employment issues; family planning issues; investigations of the social or economic impacts of a diagnosis of AAT Deficiency including stigma post-diagnosis.
- The provision of an informed consent associated with AAT Deficiency testing, medical treatments, participation in research, or transplantation; other issues relating to participation in clinical trials or research studies.
- Issues relating to genetic discrimination including access to insurance coverage, social services, medical care, employment, and/or military service; the protection of confidentiality of patients and their families; legislation relating to genetic disease and alpha-1 antitrypsin deficient individuals.
- Equitable distribution of available medical therapies; availability and allocation of organs for transplantation associated with AAT Deficiency.
- Intellectual property rights; ownership of tissue, organs and DNA associated with research studies and clinical trials; patents relating to genetic research.

All proposals must be hypothesis-generating or hypothesis-testing, or generate new information on conceptual topics relevant to the Foundation's research mission. **Applicants may submit an ELSI proposal as a Pilot and Feasibility Grant, Postdoctoral Research Fellowship Grant or Research Grant. Please see the descriptions of each of these grant categories for information about the grant application requirements.** Projects submitted for Research Grant funding must provide sufficient preliminary data to justify the Foundation's support.

Funding Levels: An applicant may request support for a project with a period of performance of 1-2 years in length. ELSI projects may be

submitted under the following grant categories. Please see the specifics for each of these applications in each respective category.

- Pilot and Feasibility Grants: One (1) year award with a maximum budget of \$75,000
- Postdoctoral Research Fellowships: Two (2) year awards with a maximum budget of \$50,000/year
- Research Grants: Two (2) year awards with a maximum budget of \$100,000/year

Period: Up to 2 years of support is available, depending on the category in which the grant is submitted. Investigators are required to submit an annual and/or a final progress report for this grant, depending on the category in which the grant is submitted.

Funding: Full funding is contingent upon the timely receipt of a satisfactory and complete annual and final progress report. Full funding is contingent upon the Foundation having sufficient working capital (as determined by the Foundation in its sole discretion). Applicants are not eligible to receive a third year of additional funding for the ELSI Relating to AAT Deficiency Grant, but are encouraged to apply to external funding sources (i.e., NIH) to continue research initiated as a Foundation grant.

Pilot and Feasibility Grants

The objective of this grant is to provide funds to encourage the development and testing of new hypotheses and/or new methods in research areas relevant to AAT Deficiency. Proposed work must be hypothesis generating or hypothesis testing, reflecting innovative approaches to important questions in AAT research or development of novel methods, and providing sufficient preliminary data to justify the Foundation's support. Results from Pilot and Feasibility Grants should lead to the submission of applications for funding from other agencies (i.e. NIH). At the conclusion of the funding term, applicants are expected to apply for further funding by other mechanisms or from outside agencies. The award is not intended to support continuation of programs begun under other granting mechanisms.

Funding Level: Maximum of \$75,000 may be requested.

Period: Up to 1 year of support is available. Investigators are required to submit a final progress report for this grant category.

Funding: Full funding is contingent upon the timely receipt of a satisfactory and complete final progress report. Full funding is contingent upon the Foundation having sufficient working capital (as determined by the Foundation in its sole discretion). Applicants are not eligible to receive a second year of additional funding for a Pilot and Feasibility Grant, but are encouraged to apply to external funding sources (i.e., NIH) to continue research initiated as a Foundation grantee.

Deadlines:

Letter of Intent: September 22, 2017

Submission of Application: February 16, 2018

Postdoctoral Research Fellowship Grants

The objective of this grant is to provide support for postdoctoral research fellows who are starting their research careers and are working in the laboratories of established researchers or conducting research with the mentorship of established researchers. In addition, this grant category is intended to provide support for postdoctoral research fellows who intend to pursue a career in AAT research. Applications will be accepted from candidates holding an M.D., Ph.D. or equivalent degrees who are interested in conducting basic science, clinical research, or ethic, legal, social issues studies related to AAT Deficiency. Applicants must indicate a commitment to AAT-related research by focusing 50% of their time to AAT Deficiency research or clinical practice.

Funding Level: Maximum of \$50,000 per year may be requested.

Period: Up to 2 years of support is available. Investigators are required to submit an annual and a final progress report for this grant category.

Funding: Full funding is contingent upon the timely receipt of a satisfactory and complete annual and final progress report. Full funding is contingent upon the Foundation having sufficient working capital (as determined by the Foundation in its sole discretion). Applicants are not eligible to receive a third year of additional funding for a Postdoctoral Research Fellowship Grant, but are encouraged to apply to external funding sources (i.e., NIH) to continue research initiated as a Foundation grantee.

Deadlines:

Letter of Intent: September 22, 2017

Submission of Application: February 16, 2018

Important instructions for Postdoctoral Research Fellowship applications:

- The postdoctoral fellow must submit a Personal Statement of Interest containing the following criteria. This statement should be a maximum of two (2) pages and included as an attachment to the grant application. This statement must 1) Indicate or describe whether or not the postdoctoral fellow intends on pursuing a career in AAT research; 2) Describe his/her fellowship's training program (including course work) and the kind of interaction that takes place between the mentor and the postdoctoral fellow; 3) Describe how the fellow will integrate/utilize the research in his/her host laboratory for their scientific training; 4) Describe the research base of the mentor that will allow the fellow to achieve the goals that are outlined in their proposal; 5) Indicate the strengths the fellow will bring to work on AAT Deficiency, and how he/she will incorporate these strengths into this Postdoctoral Fellowship, and 6) Indicate the fellow's weaknesses in the field of AAT Deficiency research, and how these weaknesses will be addressed in this postdoctoral fellowship proposal.
- The mentor must submit a Biographical Sketch (≤5 pages) and a letter of support for the postdoctoral fellow and/or project (see next bullet point for specifics for this letter of support). This Biosketch should be included as an attachment to the grant application.
- The mentor must submit a letter of support containing the criteria below. This letter should be a maximum of two (2) pages and included as an attachment to the grant application. This letter should include 1) Mentor's name, position title and applicant organization; 2) Project title; 3) Key personnel, and 4) A description of his/her experience (e.g., number of trainees mentor has supervised) and the time commitment of investigators and/or collaborators who supervise the fellow.

Research Grants

The objective of this grant is to provide funds to encourage the development of new information that contributes to the understanding of the basic biology of alpha-1 antitrypsin expression, and the pathogenesis/management of AAT Deficiency. In addition, consideration will be given to those projects that provide insight into the development of information that may contribute to new therapies for AAT Deficiency. All proposals must be hypothesis generating or

hypothesis testing and provide sufficient preliminary data to justify the Alpha-1 Foundation's support.

Funding Level: Maximum of \$100,000 per year may be requested. The Principal Investigator should devote at least 10% effort to the Research Grant.

Period: Up to 2 years of support is available. Investigators are required to submit an annual and a final progress report for this grant category.

Funding: Full funding is contingent upon the timely receipt of a satisfactory and complete annual and final progress report. Full funding is contingent upon the Foundation having sufficient working capital (as determined by the Foundation in its sole discretion). Applicants are not eligible to receive a third year of additional funding for a Research Grant, but are encouraged to apply to external funding sources (i.e., NIH) to continue research initiated as a Foundation grantee.

Deadlines:

Letter of Intent: September 22, 2017

Submission of Application: February 16, 2018

Scientific Meeting Sponsorship Grants

The objective of this grant is to provide support for scientific meetings, workshops or conferences relevant to AAT Deficiency and the Alpha-1 Foundation's mission statement.

Funding Level: Scientific Meeting Sponsorship Grants are generally funded at a level of \$5,000. The funds are restricted for use during a specified period of time.

Period: Varies according to request. Investigators are required to submit a final progress report for this grant category.

Funding: Continued funding is not available for this type of grant.

Scientific Meeting Sponsorship Grant Application Format:

Standard Alpha-1 Foundation application forms are not used for this grant category. Applicants are requested to submit a summary (maximum of 6 pages including Biographical Sketch) to include the following information:

- 1) The venue and dates of the meeting.
- 2) The purpose of the meeting.

- 3) The anticipated number of participants.
- 4) The meeting's relevance to the Alpha-1 Foundation's mission statement.
- 5) A budget that clearly documents and identifies the costs associated with the funds that may be provided by the Alpha-1 Foundation.
- 6) If meeting materials are available (pre-program information, program book, list of accepted speakers, website link), they should be included in the request.
- 7) Provide specific information describing how the Alpha-1 Foundation's sponsorship will be acknowledged (i.e. in the program book, in publications of the results of the meeting, etc).
- 8) Provide a full Biographical Sketch (≤ 5 pages) using the standard Alpha-1 Foundation format.

Travel Grants

There are 2 types of Travel Grants:

1. The Alpha-1 Foundation provides funds to support travel to attend a scientific conference or meeting to present AAT related abstracts or posters at national and international meetings. Candidates must have an M.D., Ph.D. or equivalent degree, and at least one year of recent research experience related to AAT Deficiency. The award is intended primarily for travel support for an award recipient. If the grant is to be used for specialized training, a letter of support for the individual must be presented, and clearly indicate the visitor's role, time commitment and objectives for the proposed training as well as institutional commitment.
2. The Alpha-1 Foundation provides funds to support cross training at an established Alpha-1 laboratory by an established Alpha-1 investigator. Training may include training on diagnostic and therapeutic procedures, research related techniques, training on specialized equipment or software applicable to AAT-related research.

Funding Levels: Travel Grants are generally funded at a level of \$1,000. The funds are restricted for use during a specified period of time.

Period: Varies according to request. Investigators are required to submit a final progress report for this grant category.

Funding: Continued funding is not available for this type of grant.

Travel to Present Alpha-1 Research Grant Application Format:

Standard Alpha-1 Foundation application forms are not used for this grant category. The LOI is a substitute for the grant application. Please follow the LOI format instructions in Section II of this document. A standard application is not necessary for a Travel grant to present Alpha-1 research.

Travel to Receive Cross Training Grant Application Format:

Standard Alpha-1 Foundation application forms are not used for this grant category. Applicants are requested to submit a summary (maximum of 6 pages including Biographical Sketch) to include the following information:

- 1) The name and institution of the investigator who will be traveling.
- 2) Name and institutional affiliation of the host.
- 3) The purpose of the travel (i.e., to train on diagnostic and therapeutic procedures, research related techniques, or to train on specialized equipment or software applicable to AAT-related research.)
- 4) A letter of support from the host that indicates the visitor's role, time commitment and objectives for the proposed training as well as institutional commitment.
- 5) Budget page that clearly documents and identified the costs associated with the travel request.
- 6) Provide a full Biographical Sketch (≤5 pages) using the standard Alpha-1 Foundation format.

IV. GENERAL INSTRUCTIONS FOR SUBMITTING A FULL APPLICATION

Read all of the instructions thoroughly prior to preparing your full application.

These instructions pertain to applications for the following: Bridge Grants, ELSI Relating to AAT Deficiency Grants (available as a Pilot and Feasibility, Postdoctoral Research Fellowship, Research proposals), Pilot and Feasibility Grants, Postdoctoral Research Fellowship Grants, and Research Grants.

Note: All documents submitted to the Alpha-1 Foundation, including the research plan, data sharing plan, biographical sketches, letters of support, agreements, contracts, IRB approval letters, etc. must be translated to English if written in another language.

The Alpha-1 Foundation requires that all applicants submit their full applications online using proposalCENTRAL. **The full application**

forms are only accessible to LOI applicants who are invited by the Foundation to submit a full application. An applicant is not obligated to submit a full application if an LOI is submitted and invited for a full application. However, an applicant must submit an LOI in order to be eligible to submit a full application. **A full application that is submitted without a LOI, or submitted outside of proposalCENTRAL, will result in an automatic denial of funding and the application will be returned to the investigator.**

Deadline to Submit:

Using the online form provided on proposalCENTRAL, applicants are to submit one (1) electronic version of the full application. With the exception of Scientific Meeting Sponsorship Grants and Travel Grants, **the full application must be submitted on proposalCENTRAL by Friday, February 16, 2018, 11:59pm ET.** Scientific Meeting Sponsorship and Travel Grant applications must be received by the Alpha-1 Foundation **at least two (2) months prior** to the meeting or travel. Any application that is not complete in substance and format by the receipt date may result in an automatic denial of funding and will be returned to the applicant. Additional appendices, insertions, or revisions to the application after the receipt date will not be accepted unless specifically agreed to, in writing, by the Alpha-1 Foundation's Director of Research Administration.

Where to Submit:

The Alpha-1 Foundation requires applicants to submit their full applications online using proposalCENTRAL.

The online application form is available here:

<https://proposalCENTRAL.altum.com/default.asp?GMID=135>

Note: In order to access the full application form, applicants must be logged into the proposalCENTRAL profile used to submit their approved LOI. Once logged in, a link to the full application form will appear in the "manage proposals" tab.

Note: The research plan and data sharing plan must be uploaded using the "Application Attachments" section of the online application form.

Inquiries and Interactions:

All inquiries regarding the Alpha-1 Foundation's pre and post award grants' processes should be directed to:

David Fernandez, Director of Research Administration
Alpha-1 Foundation
3300 Ponce de Leon Blvd.
Coral Gables, FL 33134
Phone: 305-567-9888, extension 242
Fax: (305) 567-1317
Email: dfernandez@alpha1.org

All inquiries or technical issues regarding proposalCENTRAL and the online application process should be directed to customer support at:

Phone: 703-964-5840, Toll-free phone: 1-800-875-2562
Email: pcsupport@altum.com

Live customer support is only available from 8:30am – 5pm ET.

V. SPECIFIC INSTRUCTIONS FOR PREPARING A FULL APPLICATION

The following information is required to submit a complete full application. Numbers correspond to the application sections found on the left side of the online application form on proposalCENTRAL:

1. Title Page

- Please provide the project's title (**do not exceed 90 characters, including spaces**).

Note: Start and end dates and total amount requested will be automatically generated onto the title page after the budget form pages have been completed and saved.

Note: Alpha-1 Foundation grants generally begin July 1st. Applicants are responsible to note any potential overlap in funding for the proposed project, and to arrange for a delayed start date for their project to avoid an overlap with existing funding from another source. The Alpha-1 Foundation may not be able to honor any requests to start a grant before or after July 1st. As a result, no commitments or obligations should be made until the Foundation approves the actual start date of the grant and the Principal Investigator receives the approval in writing from the Alpha-1 Foundation.

Note: All applicants must indicate if their application is a revised application from a previous grant submission using the yes/no dropdown menu. If your application is a revised

application, provide the year in which the previous application was submitted.

2. Download Templates & Instructions

- This section contains links to download Application Instructions, Research Plan - Instructions and Format, Data Sharing Plan - Instructions and Format, Terms and Conditions governing Alpha-1 Foundation awards, the Biographical Sketch form, and any other documents that are pertinent to the full application process.

3. Enable Other Users to Access this Proposal

- This section allows you to give other users access to your full application. The completion of this section is optional.

4. Applicant Information

- This section is used to provide the contact information of the Principal Investigator, including his/her name, position title, mailing address, telephone number and applicant organization.
- **PI Institution:** Provide the name of the organization or institution that will be legally and financially responsible for the conduct of activities supported by the award.

5. Institutional & Signing Official Information

- This section is used to provide the contact information of the Institutional & Signing Official. Please make sure to fill-out all of the information requested in this section.

6. Key Personnel Information

- This section should be used to provide information on any Key Personnel involved in the proposed project. Key personnel are defined as individuals who substantively contribute to the scientific development or execution of the project, whether or not salaries are requested. Typically, these individuals have doctoral or other professional degrees, although individuals at the masters or baccalaureate level should be included if their involvement meets the definition of key personnel. Consultants should also be included if they meet the definition of Key Personnel.

- **Role:** Identify the role of each individual listed on the project. Describe and justify each individual's role in the project in the "Budget Summary & Justification" section of the application form. Provide a budgetary narrative for each personnel by position, role, and level of effort in the "Budget Period Detail" section of the application form. Consultants and any "to be appointed" positions must be identified and justified.
- **Name:** List the names of the applicant organization's personnel who will be involved in the project, regardless whether salary is requested. Include all collaborating investigators, individuals in training, and support staff.
- **Effort:** Provide the percent of effort for the applicant organization's personnel who will contribute to the project.
- **Note: A Biographical Sketch must be submitted for each person who is listed as key personnel, including consultants and mentors. A letter of support must be obtained from each key personnel listed on the application.** Letters of support and Biographical Sketches from key personnel, including consultants and mentors, must be uploaded using the "Application Attachments" section of the application form.

Note: All documents submitted as attachments to the application (research plan, data sharing plan, biographical sketches, letters of support, etc.) must be submitted as separate files. Please do not combine and upload all letters of support and/or biographical sketches into one .pdf or .doc file.

7. Abstract & Keywords

- This section should be used to provide a lay and scientific abstract (**for each abstract, do not exceed 3,000 characters, including spaces**) and list of keywords associated with the proposed project.
- **Lay Abstract:** Each grant application must include a succinct and complete lay summary of the project. The lay summary should be at a grade 8 level of understanding. Grant applications will not be reviewed unless a lay summary is provided at the time of the application submission.

- **Scientific Abstract:** State the application's broad, long-term objectives and specific aims, making reference to the relatedness of the project to Alpha-1 Antitrypsin Deficiency. Describe concisely the research design and methods for achieving these goals. Avoid summaries of past accomplishments and the use of the first person. This abstract is meant to serve as a succinct and accurate description of the proposed work when separated from the application. If the application is funded, this description, as is, will become public information. Therefore, do not include proprietary/confidential information.
- **Keywords List:** Please make sure to select all terms (general and specific research areas) that are applicable to your application. This information will be used to assign the appropriate reviewers to your application.

8. Budget Period Detail

- Enter the proposed Start and End Dates for each Budget Period and click "Save."

Personnel Costs:

- **Name.** Starting with the Principal Investigator, list the names of the applicant organization's personnel who will be involved in the project during the initial budget period, regardless whether salary is requested. Include all collaborating investigators, individuals in training, and support staff.
- **Role on Project.** Identify the role of each individual listed on the project. Describe and justify each individual's role in the grant in the "Budget Summary & Justification" section of the application. Provide a budgetary narrative for each personnel by position, role, and level of effort. Consultants and any "to be appointed" positions must be identified and justified.
- **Type of Appointment/Months.** Provide the number of months within the Initial Budget Period's for each applicant organization's personnel who will be working on the grant. Some personnel may be under contractual appointment with the applicant organization. In this case, provide the number of months reflected in the contractual appointment. The Alpha-1 Foundation's staff assumes that appointments at the applicant organization are full time for each personnel. If an

appointment is less than full time, e.g., 50 percent time, identify the individual with an asterisk (*) and provide a full explanation in the "Budget Summary & Justification" section of the application. An individual may have a split appointment, for example, for an academic period or summer period. For each appointment, identify and enter the number of months on separate lines.

- **Percent of Effort on Project.** Provide the percent of effort for the applicant organization's personnel who will contribute to the project.
- **Institutional Base Salary.** Provide each individual's institutional base salary. For the purposes of the grant application, the maximum institutional base salary is \$191,300.
- **Salary Requested.** Provide the dollar amounts for each applicant organization's personnel for which funds are requested. The salary requested is calculated by multiplying the individual's institutional base salary by the percent of effort on this project. Provide a justification for each personnel in the "Budget Summary & Justification" section of the application.
- **Fringe Requested.** Fringe benefits may be included in the direct salary costs.

Note: The Alpha-1 Foundation will only pay salary support for the actual time that each applicant organization's personnel spend on a grant. The amount of salary requested for any supported individual on a grant cannot exceed the percentage effort committed on the grant. The salary requested is calculated by multiplying the individual's institutional base salary by their percent of effort on this project. If a lesser amount is requested than is allowed (e.g., endowed position or institutional sources), provide a justification "Budget Summary & Justification" section of the application. In addition, it is prohibited for any personnel to indicate that more than 100% effort will be spent on the grant.

Note: Key personnel, including the Principal Investigator, should not request more than a 5% increase in salary funds received from an Alpha-1 Foundation grant. If more than 5%

is requested, adequate justification must be provided in the "Budget Summary & Justification" section of the application.

- **Special Instructions:** Joint University and Department of Veterans Affairs Appointments: Individuals with joint university and Department of Veterans Affairs appointments may request the university's share of their salary in proportion to the effort devoted to the research project. The individual's salary with the university determines the base for computing that request. Signature by the institutional official on the application certifies that: (1) the individual is applying as part of a joint appointment specified by a formal memorandum of understanding between the university and the Department of Veterans Affairs (VA); and (2) there is no possibility of dual compensation for the same work, or of an actual or apparent conflict of interest regarding such work.

Non-Personnel Costs:

- **Consultant:** An individual who provides professional advice or services for a fee, but typically not as an employee of the engaging party.
- **Consultant Costs:** Whether or not costs are involved, provide the names and organizational affiliations of all consultants, other than those involved in consortium/contractual arrangements, named in the grant application. Include information regarding consultant physicians who are involved with patient care or individuals who serve on external monitoring boards or advisory committees to the project. Describe the services to be performed in the "Budget Summary & Justification" section of the application. Include the number of days of anticipated consultation, the expected rate of compensation, travel, per diem, and other related costs. In addition, the application should include a Biographical Sketch for each consultant named in the application.
- **Equipment.** List each item of equipment separately and justify each purchase in the "Budget Summary & Justification" section of the application. **Major equipment may not be requested as part of a grant application, in accordance with Alpha-1 Foundation policies. Major equipment is defined as equipment that costs more than \$500.**

- **Supplies.** Itemize supplies in separate categories, such as glassware, chemicals, radioisotopes, etc. Categories in amounts less than \$1,000 do not have to be itemized. Any requests for supplies greater than \$1,000 must be adequately justified in the "Budget Summary & Justification" section of the application. If animals are to be purchased, applicants are required to state the species and the number to be used in the grant.
- **Travel.** Itemize travel requests and provide explanations in the "Budget Summary & Justification" section of the application. Discuss the purpose and destination of each trip and the number of individuals for whom funds are requested. The maximum amount of funds permitted for use for grant related travel is \$1,000 per year (**Does not include \$1,000 to travel to Alpha-1 Investigators' Meeting, described below**). If more than \$1,000 is requested per year, a detailed explanation should be provided in the "Budget Summary & Justification" section of the application. Grant related travel should involve travel to attend a meeting or conference in which data resulting from a Foundation supported grant is to be presented.

Note: Separate from the description above for travel to present Alpha-1 Foundation grant related data at conferences and meetings, **the Alpha-1 Foundation requires that each applicant allocate \$1,000 of the total budget to pay for travel to the Alpha-1 Foundation's Biennial Investigators' Meeting for the first year of the proposal's period of performance.** In case the applicant cannot attend the Investigators' Meeting, the \$1,000 budgetary line item is not refundable.

- **Patient Care Costs.** If inpatient and/or outpatient costs are requested, provide the names of any hospitals and/or clinics and the amounts requested for each in the "Budget Summary & Justification" section of the application. State whether each hospital or clinic has a currently effective DHHS-negotiated research patient care rate agreement and, if not, what basis is used for calculating costs. If an applicant does not have a DHHS-negotiated rate, the Alpha-1 Foundation awarding component can approve a provisional rate. Indicate, in detail, the basis for estimating costs in this category, including the number of patient days, estimated cost per day, and cost per

test or treatment. If both inpatient and outpatient costs are requested, provide information for each separately. If multiple sites are to be used, provide detailed information by site.

- **Include information regarding projected patient accrual for the project/budget periods and relate this information to the budget request for patient care costs. If patient accrual is anticipated to be lower at the start or during the course of the project, plan budget(s) accordingly.**
- **Provide specific information regarding anticipated sources of other support for patient care costs, e.g., third party recovery or pharmaceutical companies.**
- **Alterations and Renovations.** Costs for alterations and renovations are not an allowable expense on grants submitted to the Alpha-1 Foundation.
- **Other Expenses.** Itemize any other expenses by category and unit cost. These might include animal maintenance (unit care costs and number of care days), patient travel, donor fees, publication costs, computer charges, rentals and leases, equipment maintenance, service contracts, and tuition remission in lieu of salary. Provide an explanation and justification of the costs in the "Budget Summary & Justification" section of the application. **Publication expenses should be associated with the dissemination of grant results or data produced as a result of grantee's Alpha-1 Foundation sponsored grant. These publication expenses include the costs of producing publications, abstracts, manuscripts and/or presentations at scientific conferences or meetings based on or resulting from any study or research performed during the grant's period of performance. The recommended amount of money to request for publication expenses is \$500 per year in which funding is requested. If more than \$500 is requested per year, a detailed explanation and justification should be provided in the "Budget Summary & Justification" section of the application.**
- **Consortium/Contractual Costs.** List each participating consortium/contractual organization and the costs associated

with the consortium/contractual organization. Consortium arrangements may involve personnel costs, supplies, and other allowable costs, but may not include facilities and administrative (indirect) costs. Contractual costs for support services, such as the laboratory testing of biological materials, clinical services, or data processing, are occasionally sufficiently high to warrant a similar categorical breakdown of costs.

Note: The Alpha-1 Foundation does not pay for indirect costs, facilities and administrative costs or overhead costs. Fringe benefits, if applicable, must be included in the direct salary costs.

Note: All budgetary information supplied as part of the application must be in US dollars and reflect the currency exchange rate at the time of the grant application submission.

9. Budget Summary & Justification

- Provide a justification and explanation of the expenses listed for each period in the "Budget Period Detail" section of the application.

Note: Each expense item listed in the budget must be clearly justified in this section. List only the direct costs requested in this application.

Note: As part of the budget for the entire period of support, the Foundation requires that each applicant allocate \$1,000 of the total monies requested to pay for travel to attend the Alpha-1 Foundation's Investigators' Meeting in the first year of the proposal's period of performance. In case the applicant cannot attend the Investigator's meeting, the \$1,000 budgetary line item is not refundable.

10. Organization Assurances

- **Assurances/Certifications:** Each application to the Alpha-1 Foundation requires that the following assurances and certifications be accounted for by the official signing the application on behalf of the applicant organization.

Human Subjects

Research on Transplantation of Human Fetal Tissue

Women and Minority Inclusion Policy
Inclusion of Children Policy
Research Using Human Embryonic Stem Cells
Vertebrate Animals
Debarment and Suspension
Drug-Free Workplace
Lobbying
Non-Delinquency on Federal Debt
Research Misconduct
Civil Rights
Handicapped Individuals
Sex Discrimination
Age Discrimination
Recombinant DNA and Human Gene Transfer Research
Financial Conflict of Interest (except Phase I SBIR/STTR)
Certification of Research Institution Participation (STTR only)

Notice of Proprietary Information: When the application contains information that constitutes trade secrets; or information that is commercial or financial; or information that is confidential or privileged, the information must be identified by asterisks (*) in the Research Plan and Data Sharing Plan. The information is furnished to the Alpha-1 Foundation in confidence with the understanding that it shall be used or disclosed only for evaluation of this application; provided that, if a grant is awarded as a result of, or in connection with, the submission of this application, the Alpha-1 Foundation shall have the right to use or disclose the information to the extent authorized by law. This restriction does not limit the Alpha-1 Foundation's right to use the information if it is obtained without restriction from another source.

As part of the peer review process, the peer review group carefully considers protections from research risk. The peer review group will assess the adequacy of safeguards of the rights and welfare of research participants based on the information in the grant application. If you are uncertain whether or not your research proposal requires Institutional Review Board approval, please consult the National Institutes of Health (NIH) website and your Institutional Review Board. The Alpha-1 Foundation mirrors the NIH's policy on human subjects' research.

Should your proposal require the use of an IRB approval, the approval letter must be received by the Alpha-1 Foundation prior to the start of the grant. IRB approval is not required at the time of the grant application submission.

Human Subjects:

- **No Human Subjects:** Check "No" if activities involving human subjects are not planned at any time during the proposed project period. If the answer is "No", then the remaining parts of this section are not applicable to your grant application.
- **Human Subjects Involved:** Check "Yes" if activities involving human subjects are planned at any time during the proposed project period, either at the applicant organization, any other performance site or collaborating institution. "Yes" should be checked even if the research is exempt from the NIH's regulations for the protection of human subjects, or if the research will be conducted at an institution, or in a country, that does not require certification or review of human subject research. The Alpha-1 Foundation will only fund grants that provide assurance of protection for human subjects according to the standards set forth by the NIH.

Exemptions from Human Subjects Regulations: Check "Exempt" if the activities proposed are designated to be exempt from the regulations. Insert the exemption number corresponding to one of the six exemption categories described in the "Exemption Categories" section of this document.

Note: Inappropriate designations of the noninvolvement of human subjects or of exempt categories of research will be grounds for the Alpha-1 Foundation to reject the grant application without peer review. The Alpha-1 Foundation will make a final determination whether the proposed research is covered by the regulations or is in an exempt category, based on the information provided in the Research Plan. In doubtful cases, the Principal Investigator/Program Director should contact the Foundation's Director of Research Administration to discuss the specifics of your institution's policies and exemptions. Applicants may also consult the NIH's Office for Human Research Protections (OHRP) by accessing their website for guidance and further information.

Human Subjects Activities Not Exempt from Regulations: Check either "Approved" or "Pending" if the planned research activities involving human subjects are not exempt, and provide the approved or pending date of IRB approval.

Human Subjects Assurance Number: If the applicant organization has an approved Federal Wide Assurance (FWA), Multiple Project Assurance (MPA), Single Project Assurance (SPA) or Cooperative Project Assurance Number on file with the OHRP, this assurance number cannot be entered on this screen – it will appear only if properly entered in the institution profile (for the institution you selected in the institution section of the proposal). If no assurance number appears here, please contact your institution's grants and contacts office to have them add the assurance numbers to the institution profile. If you need assistance, please contact proposalCENTRAL customer support.

Check "Not applicable" if the applicant organization does not have an approved assurance on file with OHRP. Do not provide the human subjects assurance number of any collaborating institution. In this case, the applicant organization, by the signing off on the application, is declaring that it will comply with 45 CFR Part 46 and proceed to obtain a human subjects' assurance.

Note: If your proposed Research Plan requires IRB approval, the approval must be obtained and submitted to the Alpha-1 Foundation prior to starting the grant. A grant may not begin until all regulatory documents including, but not limited to, the Notice of Award, Release of Information Form, and Directory Form are executed and returned to the Alpha-1 Foundation. Also, a copy of the IRB or IACUC approval letter needs to be sent to the Foundation before the first payment is issued (if applicable). IRB approval is not required at the time of the grant application submission. If you are uncertain whether or not a proposal will ultimately require IRB approval, please consult the NIH's website and your Institutional Review Board. In addition, any modification to the proposal's Research Plan, required by the IRB or to address any human subjects concerns raised during the review, must be submitted and approved by the applicant organization's IRB before the grant award will be made. All IRB renewal approval letters must be

submitted to the Foundation. If a lapse in IRB approval has occurred, the Foundation will withhold any further payments until the renewal approval letter is submitted to the Foundation.

Note: If the application's IRB approval letter is written in any language other than in English, the Principal Investigator must supply the Foundation Director of Research Administration with an English translated version of the IRB approval letter.

Note: If a grant involves human subjects, each key personnel named in the grant application is required to have successfully obtained his or her NIH Human Subjects Research Certificate. The certificate can be obtained at the following website: "Protecting Human Research Participants" at <http://phrp.nihtraining.com/users/login.php>

Vertebrate Animals:

- **No Vertebrate Animals:** Check "No" if research activities involving vertebrate animals will not occur at any time during the proposed project period. If the answer is "No", then the remaining parts of this section are not applicable to your grant application.
- **Vertebrate Animals Involved:** Check "Yes" if activities involving vertebrate animals are planned at any time during the proposed project period, either at the applicant organization, any other performance site or collaborating institution. The Alpha-1 Foundation mirrors the NIH's policies on vertebrate animals' research. If you are uncertain whether or not a proposal requires Institutional Animal Care and Use Committee (IACUC) approval, please consult the NIH's website and your Institutional Review Board.

IACUC Certification: The Alpha-1 Foundation requires the submission of Institutional Animal Care and Use Committee (IACUC) approval when animal studies are involved. If your research activities require IACUC approval, check "Pending" in the space provided. If the IACUC review is unavoidably delayed beyond the submission of the application, enter "Pending" in the box requesting IACUC approval date. A follow-up certification of IACUC approval from an official signing for the applicant organization must then be sent to and received by the Director of Research Administration.

Note: If your proposed Research Plan requires Institutional Animal Care and Use Committee (IACUC) approval, the approval must be obtained and submitted to the Alpha-1 Foundation prior to starting the grant. IACUC approval is not required at the time of the grant application submission. If you are uncertain whether or not a proposal requires IACUC approval, please consult the NIH website and your IACUC. In addition, any modification to the proposal's Research Plan, required by the IACUC or to address any vertebrate animals concerns raised during the review, must be submitted and approved by the applicant organization's IACUC before the grant award will be made. All IACUC renewal approval letters must be submitted to the Foundation. If a lapse in IACUC approval has occurred, the Foundation will withhold any further payments until the renewal approval letter is submitted to the Foundation.

Animal Welfare Assurance: Provide the Assurance number of the applicant organization if the applicant organization has an approved Animal Welfare Assurance on file with the Office of Laboratory Animal Welfare (OLAW).

Note: This assurance number cannot be entered on this screen – it will appear only if properly entered in the institution profile (for the institution you selected in the institution section of the proposal). If no assurance number appears here, please contact your institution's grants and contacts office to have them add the assurance numbers to the institution profile. If you need assistance, please contact proposalCENTRAL customer support.

Special Populations:

- Investigators who conduct research involving fetuses, pregnant women, human in vitro fertilization, prisoners, or children must follow the provisions of the regulations in subparts B, C, and D of 45 CFR Part 46, respectively, which describe the additional protections required for these populations. Relevant information may be obtained at the OHRP website. Exemptions 1-6 listed in this document do not apply to research involving prisoners, fetuses, pregnant women, or human in vitro fertilization. Also, Exemption 2 below, for research involving survey or interview procedures or observation of public behavior, does not apply to research with children, except for research involving observations of

public behavior when the investigator(s) do not participate in the activities being observed.

- **Inclusion of Women and Minorities:** If you are conducting clinical research, use the "Inclusion of Women" and "Inclusion of Minorities" sections of the application form to address each of the items identified below with respect to your plans for the "Inclusion of Women" and/or the "Inclusion of Minorities" as they relate to the proposed research. Alpha-1 Foundation policy requires that women and members of minority groups and their subpopulations be included in all Alpha-1 Foundation supported biomedical and behavioral clinical research projects involving human subjects. The inclusion must be addressed in developing a research design appropriate to the scientific objectives of the study. Inclusion is required unless a clear and compelling rationale shows that inclusion is inappropriate with respect to the health of the subjects or that inclusion is inappropriate for the purpose of the study. Exclusion under other circumstances may be made based on a compelling rationale and justification. Cost is not an acceptable reason for exclusion except when the study would duplicate data from other sources. Women of childbearing potential should not be excluded routinely from participation in clinical research. This policy applies to research subjects of all ages.
- **Inclusion of Children:** The Alpha-1 Foundation policy requires that children (i.e., individuals under the age of 21) must be included in all human subjects' research, conducted or supported by the Alpha-1 Foundation unless there are clear and compelling reasons not to include them. Therefore, proposals for research involving human subjects must include a description of plans for including children. If children will be excluded from the research, the application or proposal must present an acceptable justification for the exclusion.

In the section entitled, "Inclusion of Children", the applicant should provide either a description of the plans to include children or if children will be excluded from the research. The grant application must provide an acceptable justification (see below) for the exclusion.

If children are included, the description of the plan should include a rationale for selecting or excluding a specific age range of children. When children are included, the plan also must include a description of the expertise of the investigative team for dealing with children at the ages included, of the appropriateness of the available facilities to accommodate the children, and the inclusion of a sufficient number of children to contribute to a meaningful analysis relative to the purpose of the study.

The Alpha-1 Foundation's Grants Advisory Committee will assess each application as being "acceptable" or "unacceptable" with regard to the age-appropriate inclusion or exclusion of children in the research project.

Justifications for Exclusion of Children

It is expected that children will be included in all research involving human subjects unless one or more of the following exclusionary circumstances can be fully justified:

1. The research topic to be studied is not relevant to children.
2. There are laws or regulations barring the inclusion of children in the research.
3. The knowledge being sought in the research is already available for children or will be obtained from another ongoing study, and an additional study will be redundant. Documentation of other studies justifying the exclusions should be provided.
4. A separate, age-specific study in children is warranted and preferable. Examples include:
 - a. The relative rarity of the condition in children, as compared to adults (in that extraordinary effort would be needed to include children, although in rare diseases or disorders where the applicant has made a particular effort to assemble an adult population, the same effort would be expected to assemble a similar child population with the rare condition); or

- b. The number of children is limited because the majority are already accessed by a nationwide pediatric disease research network; or
 - c. Issues of study design preclude direct applicability of hypotheses and/or interventions to both adults and children (including different cognitive, developmental, or disease stages or different age-related metabolic processes). While this situation may represent a justification for excluding children in some instances, consideration should be given to taking these differences into account in the study design and expanding the hypotheses tested, or the interventions, to allow children to be included rather than excluding them; or
5. Insufficient data are available in adults to judge potential risk in children (in which case one of the research objectives could be to obtain sufficient adult data to make this judgment). While children usually should not be the initial group to be involved in research studies, in some instances, the nature and seriousness of the illness may warrant their participation earlier based on careful risk and benefit analysis; or
 6. Study designs aimed at collecting additional data on pre-enrolled adult study subjects (e.g., longitudinal follow-up studies that did not include data on children); or
 7. Other special cases justified by the investigator and found acceptable to the review group and the Alpha-1 Foundation's Scientific Director.

Definition of a Child

For the purpose of implementing these guidelines, a child is defined as an individual under the age of 21 years.

The definition of child described above will pertain to these guidelines (notwithstanding the FDA definition of a child as an individual from infancy to 16 years of age, and varying definitions employed by some states). Generally,

state laws define what constitutes a "child," and such definitions dictate whether or not a person can legally consent to participate in a research study. However, state and country laws vary, and many do not address when a child can consent to participate in research. Federal regulations (45 CFR Part 46, subpart D, Sec.401-409) address DHHS protections for children who participate in research, and rely on State definitions of "child" for consent purposes. Consequently, the children included in this policy (persons under the age of 21) may differ in the age at which their own consent is required and sufficient to participate in research under state law. For example, some states consider a person age 18 to be an adult and therefore one who can provide consent without parental permission.

11. Application Attachments

- This section should be used to attach any documents pertaining to your application, **including the Research Plan, Data Sharing Plan**, all Biographical Sketches, Letters of Support, Diagrams/Figures, Description of training program and Personal Statement of Interest (**for Postdoctoral Research Fellowship applications ONLY**), Introduction (**for revised applications ONLY**), etc.
- **Biographical Sketch Format Page:** Provide the information requested on the Biographical Sketch Form Page, which can be downloaded in this section of the application. A Biographical Sketch must be provided for each key personnel, including mentors and consultants, named in the grant application.
 - Complete the educational block at the top of the format page. Additionally, provide the information described in A and B below.
 - A. Positions and Honors. List in chronological order previous positions, concluding with your present position. List any honors. Include present membership on any Federal Government public advisory committee and membership on any Alpha-1 Foundation Board, advisory committee, or working group.
 - B. Selected peer-reviewed publications or manuscripts in press (in chronological order).

Do not include manuscripts submitted or in preparation.

- Information provided on the Biographical Sketch Form will be used by the reviewers in the assessment of each individual's qualifications for a specific role in the proposed project, as well as to evaluate the overall qualifications of the research team.

New and revised applications may include the following materials as attachments:

- Surveys, questionnaires, data collection instruments, and clinical protocols.
- Diagrams/Figures.

Note: For Postdoctoral Research Fellowship and ELSI Postdoctoral Research Fellowship grant applications, the Personal Statement of Interest from the fellow, including the description of the training program, should be included as attachments.

Note: All Biographical Sketches provided may not exceed five pages.

Note: All documents submitted as attachments to the application (research plan, data sharing plan, biographical sketches, letters of support, etc.) must be submitted as separate files. For example, please do not combine and upload all letters of support and/or biographical sketches into one .pdf or .doc file.

12. Validate

- This section should be used in order to validate that all required information and file uploads have been provided before your application is submitted. Sections of the application in which the applicant is required to provide information are denoted by a red asterisk.

13. Submit

- This section should be used to submit your application.

Note: You will not be able to submit your application if you have not provided all the required information. Any missing information will be listed in this section after you click the submit button. If your submission is successful, a

confirmation email will be sent to the email address in your proposalCENTRAL profile.

Note: If you need to make changes to your application after it has been submitted, you may do so only after withdrawing the submission in proposalCENTRAL. Withdrawing your submitted application will NOT delete any of the information you provided in the application. ProposalCENTRAL will allow you to withdraw your application, make changes, and resubmit any time prior to the LOI application deadline. Once the deadline passes, you will not be allowed to modify and/or resubmit your application.

VI. Criteria for Funding, Notification & Conditions of Awards

Criteria for Funding

Topics deemed to be suitable for funding are determined by the Alpha-1 Foundation's Medical and Scientific Advisory Committee (MASAC) in collaboration with various Foundation working groups and other scientific committees and lay leaders. The Foundation's current research agenda can be found in the Research tab on the Foundation's website (www.alpha1.org).

The final funding decisions are made by the Alpha-1 Foundation based on the availability of funds and research priorities of the Foundation. The Foundation is a not for profit organization and grant funding is obtained as a result of the Foundation's fundraising efforts. Therefore, the Foundation's ability to fund grants is contingent upon the availability of funds.

Notification and Disbursement of Funding

Each applicant is notified, in writing, of the status of the grant application on behalf of the Alpha-1 Foundation's President and CEO. Each applicant organization is required to sign a Notice of Award that specifies the Foundation's terms and conditions of the award. The initial installment of award funds will be disbursed upon receipt of the executed regulatory documents.

Conditions of the Grant Award

In accordance with that mission, the Alpha-1 Foundation awards grants to certain researchers or research institutions based on the Foundation's criteria. In addition to the criteria contained in grant

applications, and the specific limitations applicable to each grant, as set forth in the Notice of Award, there are General Terms and Conditions that apply to all of the Foundation's grants. The Terms and Conditions document can be found on the Foundation's website (www.alpha1.org) and in the "Download Templates and Instructions" section of the application form on proposalCENTRAL. Compliance with such Terms and Conditions is also a condition of a grant award. Such Terms and Conditions are incorporated herein by reference and your acceptance of any award amount from the Alpha-1 Foundation constitutes your acknowledgement of receipt and agreement to comply with each and every of such Terms and Conditions.

The Foundation may, from time to time, revise and update the Terms. In the event there is a revision of the Terms, the Grantee and the Foundation must mutually agree to the revision in writing. The amended Terms will be submitted to the Grantee once both parties approve the revision.