EXPANDED ACCESS TALKING POINTS/FAQs

RFA-NS-26-001

Expanded Access Investigational New Drug (EA IND) Applications

Q: How many patients can be included in an intermediate size expanded access protocol?
A: Intermediate size expanded access supports more than one patient and can include hundreds of patients. There is a link to the FDA website defining intermediate size population in the beginning of the RFA text and here.

Q: How does FDA's review of expanded access requests intersect with NIH's grant approval process?
A: EA IND authorization is conducted through the FDA. Per the RFA, applicants to RFA-NS-26-001 must submit their EA IND application to the FDA by the time of application, and the EA IND must be allowed to proceed prior to award. NIH is not involved in the review or authorization of EA INDs.

Q: Can RFA-NS-26-001 support studies approved under Open Label Extensions?
A: No, studies under Open Label Extensions would not be eligible per the RFA. The proposed study must be conducted under an intermediate size EA IND.

Q: Can a third party submit and secure IND approval? Is a third party eligible to be the sponsor for the trial?
A: Per the ACT for ALS legislation and RFA, the sponsor of the Phase 3 ALS clinical trial IND should be an eligible drug sponsor. Drug sponsor eligibility is defined in the ACT for ALS legislation and RFA. There are no eligibility requirements for the EA IND sponsor.

Q: Is it possible for two or more PIs to apply for EA IND?
A: EA IND authorization is a function of the FDA. Please contact the FDA with specific questions about their expanded access IND application process. Guidance and contact information can be found at this webpage and this one.

Q: How will NIH ensure that the data from these studies will be shared broadly?
A: Expectations for data sharing are included in the request for application (RFA-NS-26-001) and the "Notice of Award" of all funded EA studies. This includes: 1) Submission of a complete de-identified dataset containing all variables collected in the intermediate size EA protocol for ALS, as well as a data

dictionary, to NINDS for data sharing within an agreed upon timeframe; 2) registration of the intermediate EA protocol for ALS with ClinicalTrials.gov, a database of federally and privately supported clinical research trials to test the effect of treatments and procedures for a wide range of diseases and conditions (also see: https://grants.nih.gov/policy/clinical-trials/reporting/index.htm); 3) publication of study results in compliance with the NIH Public Access Policy (see NOT-OD-25-047- and the Public Access website as well as the NIH Policy on the Dissemination of NIH-funded Clinical Trial Information, specifically, the primary study results will be submitted to ClinicalTrials.gov for public posting within one year of the primary completion date (date final subject was examined).

Small Business Eligibility

Q: How is small business concern eligibility determined?
A: A "small business concern" is defined by section 3(a) of the Small Business Act (15 U.S.C. 632(a)). The definition of a small business is complex, so we encourage you to reach out to discuss eligibility criteria. NINDS cannot determine eligibility, but we can help you work through the criteria. Ultimately, the drug sponsor is responsible for determining eligibility as a small business concern and will be required to certify eligibility prior to award.

Q: Please comment on the small business definition requirement for companies who are 50% or more owned by private equity, venture capital (VC) firms. Once a biotech company has gotten to a Phase 3 trial, it is likely that given the amount of capital needed to get that far they will be over 50% owned by such firms.
A: Small businesses can be eligible even if more than 50% is owned by venture capital firms or private equity. The conditions around eligibility for VC-funded small businesses are further outlined on the NIH Small business Education and Entrepreneurial Development (NIH SEED) website. The definition of a small business concern is outlined within the Small Business Act. https://www.gsa.gov/small-business

Q: Can the small business concern drug sponsor apply directly to RFA-NS-26-001?
A: No. RFA-NS-26-001 states that "Eligible applicants must be clinical trial sites that participate in a Phase 2/3 or Phase 3 efficacy clinical trial supported by a small business concern that is the FDA-designated sponsor of a drug or biological product which is the subject of an IND under section 505(i) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(i)) to prevent, diagnose, mitigate, treat, or cure ALS."

Q: Can the drug sponsor be a site investigator from an academic institution?
A: The FDA-designated sponsor on the phase 2/3 or phase 3 trial must be a small business. As stated in the RFA: "Eligible applicants must be clinical trial sites that participate in a phase 2/3 or phase 3 efficacy clinical trial (designed to provide pivotal data to support a marketing application) supported by a small business concern that is the FDA-designated sponsor of a drug or biological product which is the subject of an IND under section 505(i) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(i)) to prevent, diagnose, mitigate, treat, or cure ALS."

Q: Can a site investigator from an academic institution apply for an expanded access grant through this RFA?
A: Applicants must be clinical trial sites that participate in a Phase 2/3 or Phase 3 efficacy clinical trial in ALS (designed to provide pivotal data to support a marketing application) sponsored by a qualifying

small business concern. Thus, a site investigator at an academic institution participating in such a trial would be eligible to apply.

Q: Since small business drug sponsors cannot apply directly to the NIH Expanded Access Program (EAP), what potential roles can they play?
A: It is anticipated that the small business drug sponsor may be a partner in the project, such as a sub awardee or vendor.

Q: What are you doing to get applications in FY 2026?
A: A forecast alerting the community to this coming funding opportunity was released in August 2025. The RFA was released in May 2026 and was posted on grants.gov, several listservs, and social media accounts. We have also emailed prospective companies and ALS researchers. Additionally, we hosted an informational webinar in May. We continue to encourage potential applicants to contact NINDS program staff for individual consultations on applying. Their contact information is provided in the RFA.

Q: What companies/researchers are you contacting?
A: We are conducting outreach to similar networks as in previous years, including emails and announcements to:

- NIH Innovates channels on LinkedIn and X
- Over 200 people on the NIH ALS Listserv (NIH_ALS_INFORMATION@list.nih.gov), which includes academic & industry researchers, clinicians, advocates, and people affected by ALS.
- Northeast Amyotrophic Lateral Sclerosis Consortium® (NEALS) website and e-newsletter, includes 150 trial-ready sites
- ALL ALS Clinical Research Consortium
- Over 8,000 individuals on the NINDS Division of Translation Research listserv (NINDS-OTR@LIST.NIH.GOV), which includes small businesses, academics, and other interested parties
- 70 people on the NINDS Division of Clinical Research list
- Over 260 additional companies including those identified through ClinicalTrials.gov searches for ALS trials, and all companies that we have been made aware of through any other interaction.

Q: If a foreign company is conducting research in the US, is the center or network they are working with able to apply for the grant?
A: ACT for ALS language specifies that the qualifying Phase 3 clinical trial in ALS sponsor must be a U.S.-based small business. The drug sponsor itself must qualify under the Small Business Administration's definition of a small business, which includes being based in the U.S. in addition to other criteria. If the applicant is a U.S. Phase 3 clinical trial site sponsored by a foreign-based company, it is unlikely to qualify for this RFA. However, the definition of a small business is complex, so we encourage you to

reach out to discuss eligibility criteria. NINDS cannot determine eligibility, but we can help you work through the criteria.

Foreign components, as defined by NIH, are not allowed under this funding opportunity.

Q: Are STTR grants for technologies related to rehabilitations strategies to maximize quality of life included in this funding opportunity?
A: No, the applicant needs to be a Phase 2/3 or Phase 3 clinical trial site. However, projects focused on rehabilitation for ALS, are in scope for STTR funding opportunities that NINDS and other NIH ICs have participated in previously. Currently, a funding opportunity is forecasted (see grants.gov), but not yet open. Please reach out to learn more about these opportunities.

Q: Are devices eligible for this EA program?
A: No, devices are not eligible for this program. However, NINDS does have other funding opportunities to support clinical testing of devices in ALS and other neurological indications outside of this RFA. If this is your focus, please reach out for further information.

Clinical Trial Phase and Sites

Q: Why do applicants need to be a clinical trial sites for a Phase 2/3 or Phase 3 trial?
A: This eligibility criteria comes directly from ACT for ALS, which states that applicants must be a clinical trials site for a Phase 3 clinical trial for ALS sponsored by a U.S. based small business.

Q: How is NIH interpreting the "Phase 3 clinical trial" requirement? Are Phase 2/3 trials eligible? What about Phase 3 trials that have concluded but are awaiting regulatory consideration?
A: Phase 2/3 trials, ongoing Phase 3 trials, and concluded Phase 3 trials are eligible until a regulatory determination has been made regarding approval. This RFA allows for Phase 2/3 trials in recognition of the fact that clinical trials phases are not always distinct, particularly in rare disease clinical trials. In these cases, the Phase 2/3 trial is often intended to be the final study that FDA uses for approval.

As noted in the RFA, and consistent with the ACT for ALS, the investigational drug proposed under RFA-NS-26-001 must not be approved under a New Drug Application (NDA) or licensed under a Biologics License Application (BLA).

Q: Does the qualifying ALS Phase 3/efficacy clinical trial need to be ongoing at the time of application?
A: The IND for the ALS Phase 2/3 or Phase 3 efficacy clinical trial must be active at the time of award for applications selected for funding under RFA-NS-26-001. In cases where the Phase 2/3 or Phase 3 protocol is added to an existing IND, this protocol must be authorized by the FDA prior to an award being made for the expanded access grant. The grantee must provide documentation (i.e. email or letter) from FDA stating that the study may proceed prior to an award being made for the expanded access grant.

Q: Does the drug have to be in a Phase 3 trial (listed as "recruiting"), before the application deadline, in order to be eligible for this RFA?

A: For the Phase 3 clinical trial IND, that IND needs to be in place or awarded by the FDA by the time of the *award*. However, the Phase 3 trial does not need to be active or recruiting at the time of the *application*. For cases in which the Phase 3 trial is planned, not yet enrolling, or underway, progress in the planned Phase 2/3 or Phase 3 clinical will be monitored.

Q: Please clarify whether "in Phase 2/3 trial" is defined as having received a "May Proceed Letter " from FDA or the trial has already enrolled the first patient.
A: The IND / protocol of the eligible Phase 2/3 or Phase 3 ALS trial must be approved prior to award. As noted above, the trial does not need to enroll the first patient by the time of award. However, the Phase 2/3 or Phase 3 trial will be monitored for progress throughout the expanded access program.

Q: Does the expanded access IND need to be approved before submitting my application?
A: The intermediate size expanded access IND must be submitted to the FDA no later than the date of the submission of the application. FDA allocates 30 days to review and approve these protocols so the EA IND must be active by the time of award.

Q: If my Phase 3 trial has completed, am I still eligible?
A: If the regulatory determination has NOT been made regarding approval, it is eligible for this RFA. However, once the drug or biologic is approved by the FDA, it becomes ineligible. (In other words, the drug or biologic must not be approved under a New Drug Application or licensed under a Biologics License Application.)

Q: We have a large number of participating clinical sites in our study. Do we need site interest letters signed by all participating sites? Do signatures need to include the Business Official and Principal Investigator (PI)?
A: While interest letters are not required for all participating sites, they are recommended, particularly when recruitment may be a potential issue in the proposed study. While signatures from both the Business Official and PI are recommended, the PI signature alone is adequate.

Q: Are all Phase 2 clinical trials eligible, such as Phase 2A or 2B?
A: Investigational drugs in Phase 2a stage or Phase 2b stage clinical trials are not eligible under the RFA. Investigational drugs in a clinical trial staged as Phase 2/3 or Phase 3 are eligible.

Q: Will this grant program fund a Phase 1/2 clinical trial of a new chemical entity?
A: No. A Phase 1/2 clinical trial would not be eligible for funding under this RFA. To be eligible, applicants must be a trial site for a Phase 2/3, ongoing Phase 3, or completed Phase 3 trial awaiting regulatory determination regarding approval. Phase 1/2 trial sites are not eligible for this RFA.

Q: Would an investigational product that is in late phase development for another indication be eligible through this RFA?
A: The investigational product must be in an ALS Phase 2/3 trial, ongoing ALS Phase 3 trial, or awaiting regulatory determination after a completed ALS Phase 3 trial. An investigational product in late Phase development for another indication is eligible as long as the product is also being investigated in an ALS Phase 2/3 or Phase 3/efficacy clinical trial intended to support regulatory approval.

Q: Are other rare neurodegenerative diseases eligible for the EAP funds?
A: Only ALS studies are eligible for this RFA.

Q: Do all clinical trial sites need to be identified for the application?
A: The RFA does not require that all clinical sites be identified in the application. However, as stated in the Section 5 of RFA-NS-26-001, reviewers will evaluate "Approach" as part of the review process. This would include aspects of recruitment, retention, trial design, and proposed study populations which may be supported by providing detailed information on the clinical study within the application such as the proposed clinical sites.

Q: Does the PI of the Expanded Access Program need to be the lead PI of the ALS Phase 3 clinical trial?
A: The PI of the application for the Expanded Access study does not need to be the Phase 3 clinical trial lead PI; however, the application must be from a clinical trial site for the ALS Phase 3 clinical trial for that product.

Q: If a study is halted due to futility, but the IMP appears to be beneficial to a subgroup of participants, would this be considered?
A: Funding for the EA protocol may continue until the withdrawal or termination of the IND for the investigational agent by the sponsor or safety concerns (e.g., a decision by the FDA to put the EA protocol on hold due to information relevant to acceptability of the EA use).

Budget and Funding

Q: Will there be future funding and future RFAs to support this effort?
A: Future funding and future RFAs will be determined by Congressional appropriations for this program. As with all NIH-funded awards, funding of future years depends on availability of funds. ***NIH funds ALS-related research projects outside of the ACT for ALS. ALS researchers are encouraged to submit applications through the standard NIH grant process. Applications deemed meritorious through the peer-review process may be funded.***

Q: How much are you planning to spend on Expanded Access in FY 2026?
A: In FY 2026, $90 million was appropriated for ACT for ALS, of which 5 million is set aside for research outside of expanded access. Our first priority is to fund planned outyears of ongoing expanded access research grants already awarded in FY 2023 and FY 2024. As directed in the law and by Congress, our priority is to award as many new EA grants as possible with the remaining funds. The exact amount that we fund will be determined by how many applicants apply and their respective budgets, but we have tentatively projected $40 million in the Notice of Funding Opportunity (RFA-NS-26-001).

Q: Regarding grant applications awarded during FY 2026, would this funding be used for the TOTAL budgets (i.e. all years) for any newly awarded projects, or just Year 1 of the projects?
A: NINDS anticipates these funds will be allocated to the first-year budget periods of newly funded projects.

Q: What part of ACT for ALS indicates that the priority is the Expanded Access Program (EAP)?
A: Through the annual appropriations process, Congress directed NINDS to spend the funds that they appropriated for implementing ACT for ALS on expanded access first, then the HHS public-private partnership.

Q: What are the allowed and non-allowed budget items? Are there NINDS guidelines for what can be included in an EAP grant application budget (e.g., CRO, lab collection, etc.)?

A: Per RFA-NS-26-001 Section IV. Application and Submission Information, funds may be requested for:

- Payment to the manufacturer or sponsor for the direct costs of the investigational drug or biological product of the intermediate EA protocol for ALS, as authorized under section 312.8(d) of title 21, Code of Federal Regulations (or successor regulations)
- Direct costs incurred in providing such drug/biological product consistent with the research objectives of the grant
- Direct and indirect costs of participating clinical trial sites in conducting research with respect to such drug/biological product
- Personnel effort, support for study participant travel/meals, and other budget items within the overall budget cap to ensure that this goal of appropriate inclusion is met
- Costs associated with biospecimen collection and banking through BioSEND or other repository may be included, including collection kits & shipping (to sites & to repository). Applicants are encouraged to contact BioSEND directly to receive a detailed quote.
- Costs associated with the Data Management and Sharing Costs may be included in the budget:
    - Curating data
    - Developing supporting documentation
    - Formatting data according to accepted community standards, or for transmission to and storage at a selected repository for long-term preservation and access
    - De-identifying data
    - Preparing metadata to foster discoverability, interpretation, and reuse
    - Local data management considerations, such as unique and specialized information infrastructure necessary to provide local management and preservation (for example, before deposit into an established repository).
    - Preserving and sharing data through established repositories, such as data deposit fees.
    - If the Data Management & Sharing (DMS) plan proposes deposition to multiple repositories, costs associated with each proposed repository may be included.
- Additional information on allowable costs can be found at the NIH Grants Policy Statement

Q: Does the applicant need an EA IND "may proceed" response before submitting a grant application to NIH? Are there requirements for an EAP start date following grant award?

A: No, applicants do not need a "may proceed" response before submitting a grant application to NIH. However, the EA IND request must be submitted to the FDA *no later* than the same day the RFA application is submitted. As the FDA reviews all expanded access INDs within 30 days, it will be clear if the FDA accepts the proposed EA protocol review or has concerns by the time an award would be made.

Thus, the expanded access research program could start shortly after the time of award. Approval of the EA IND from FDA is required prior to an award being made.

Q: If my grant receives a meritorious score, would funding potentially be available for start-up activities before I receive the formal notice of award?

A: In specific circumstances, start up activities preceding initiation of the budget period may be allowable under RFA funding. Study PIs should contact the program officer to discuss further.

Study Design and Review

Q: Could you highlight some elements that will be important from the review perspective?
A: In addition to providing expanded access to these therapies, one of the main goals of these applications should be to address a research question relevant to ALS. The reviewers will focus on the research question and will use review criteria published in Section V of the RFA. Typically, the major drivers are the approach, rigor of the proposed experiments, and significance of the research question. There will also be evaluation of the impact and how the program will not detract from or interfere with any ongoing clinical trials.

Q: Given NINDS' focus on the need for biomarkers in the Strategic Plan, will NINDS ensure that every drug sponsor measures biomarkers?
A: Applicants are not required to include biomarkers in their proposals. Reviewers will review any research questions that are proposed. The RFA suggests that applicants could include biomarker collection and analysis, but collection of safety outcome information, survival, other significant medical events, patient experience data that is not specifically tied to efficacy, etc., are also acceptable. Outside of this RFA, NINDS offers a Translational Biomarker Program that is focused on improving the quality and efficiency of neurotherapeutic clinical research by supporting rigorous biomarker development and validation.

Q: Given that the goal of the bill was to provide EAP to as many people as possible, how does NINDS decide how many sites to approve so as to minimize administrative and IRB costs and to maximize treatment funding?
A: These studies are designed by investigators. Investigators propose the study sites, number of participants, and budget in their grant application to NIH. NIH reviews and funds grant applications using established grant review processes. If the grant application is deemed meritorious (i.e., scientifically rigorous and important) by the two-step peer review system and if there are sufficient funds, NIH funds the entire project as proposed by the applicants and does not make decisions at the level of individual study sites unless a concern is explicitly raised during peer review.

Q: Can you confirm that ACT for ALS EAP programs should focus on providing treatment through expanded access to participants who are not otherwise eligible to be part of a clinical trials?
A: The RFA states that applicants must address this issue. The ACT for ALS legislation requires that the EAP should not impede or interfere with ongoing clinical trials. The intent is to focus expanded access for individuals that are not otherwise eligible for investigational drugs. Thus, applicants are asked to explicitly address how their expanded access plans will not interfere with ongoing clinical trials.

Q: What role does NIH have in determining the number of participants in each EAP and does NIH determine eligibility criteria?
A: Applicants (not NIH) determine the number of participants each EAP will enroll. Similarly, applicants are responsible for proposing specific eligibility criteria for each EAP. As noted above, the legislation stipulates that the EAP must not interfere with other ongoing clinical trials.

Q: Do expanded access projects have milestones from time of award to site activation and patient enrollment?
A: Yes, expanded access grants are funded through a funding instrument called a cooperative agreement. In this type of award, at the outset, the study team & NIH Program staff work together to

create milestones intended to monitor how the study is progressing: these milestones may include key progress such as assembling study monitoring committees, site activation and patient enrollment targets. NIH retains the responsibility of continued active monitoring of the overall project to identify potential problems or barriers and to provide technical assistance. The grant recipient (PI and team) is responsible for managing day-to-day operations, including oversight of site-level activities, using their established policies & procedures.

NIH recognizes the importance of getting these expanded access studies up and running quickly. We actively work with each study team to overcome challenges they may encounter in standing up these programs. Study teams and NIH Program staff have become more efficient in anticipating and removing barriers in subsequent funding years.

Q: How will the ALS community be involved?
A: Per the RFA, applicants are strongly encouraged to establish relationships with patient advocacy groups and solicit their input on recruitment, the clinical meaningfulness of the question under study, the relevance of the proposed clinical outcomes, and approaches to minimizing the burden on study participants. Also, people with lived experience (PWLEs) of ALS (people living with ALS, caregivers, or people at risk for developing ALS) typically serve as part of study committees (e.g., the steering committee) for the expanded access trial.

Q: What are the necessary components of a complete grant application for both the drug sponsor and research institution?
A: Please see these annotated application forms for a list of application components: https://grants.nih.gov/grants/how-to-apply-application-guide/resources/annotated-form-sets.htm.

Q: What is a typical length of period of performance?
A: The period allowed is up to four (4) years, though no "typical" period length has been established given the newness of the program. The period of performance should be informed by the project plans, and applicants should consider time for recruitment, time necessary for the sites you are working with, the availability of the drug you are proposing, etc. All of these are factors that would determine a reasonable period of performance for your particular project within the limit of four years. Four years are not required.

Q: Section 2 of ACT for ALS, which authorizes the expanded access grant program, sunsets on September 30, 2026. What happens to grants that have been awarded before that date but have not yet completed the expanded access study?
A: Grants that have been awarded before September 30, 2026 will be allowed to continue contingent upon necessary authorities and appropriation of funds. However, NIH will not award new grants submitted after that date unless ACT for ALS is reauthorized.

Q: Will applications submitted to the November 2026 receipt date for RFA-26-001 be funded if ACT for ALS is not re-authorized?
A: ACT for ALS will sunset in September 2026. Applications submitted to the November 2026 receipt date for RFA 26-001 will only receive funding upon re-authorization of ACT for ALS and subsequent appropriations.

Q: How many patients will be treated across the active EAP funded studies (Pridopidine, RAPA501, CNM-Au8, and Ibudilast)? What is the total dollars committed, and where can I find more information about these studies?
A: Grant award information can be found by searching on NIH RePORTER (https://reporter.nih.gov/advanced-search). To get a comprehensive list of grants funded in FY2022, FY2023, FY2024, and FY2025, use the "Advanced Projects Search" tool and select "all FY" in the "Fiscal Year" field, and then scroll down to the "Opportunity Number" field and type in "RFA-NS-22-071; RFA-NS-23-012; RFA-NS-24-029; RFA-NS-25-024".

We have done that search for you, and the results can be found at the following link:
https://reporter.nih.gov/search/nAH3IbkgxkmIdyXrx47VoA/projects?shared=true
Of note, this link may eventually expire. If that happens, you may need to redo the search using the search parameters described above again.

Q: What other sources provide publicly available information about funded expanded access programs through ACT for ALS?
A: The Government Accountability Office (GAO) completed an evaluation which was published in 2026. The full report is available at the GAO website: https://www.gao.gov/products/gao-26-107691

Other

Q: How can I participate in an expanded access trial?
A: NIH is not involved in recruitment. The clinical sites or networks that receive grants through this research program are responsible for all aspects of recruiting study participants.

Q: Is an EA clinical trial required to post in ClinicalTrials.gov?
A: Yes. Like any other clinical trials, registration in ClinicalTrials.gov is required for these expanded access research programs. Also, awarded expanded access programs are asked to maintain an updated list of active participating clinical trial sites on ClinicalTrials.gov.

Q. Will there be EAPs for other neurological disorders?
A: At this time, there are no plans for other EA programs at NIH.

Q. Has a formal evaluation of the NIH ALS expanded access program been performed?
A: Yes. The ACT for ALS required an independent GAO report describing the impact of the EA program on research related to the prevention, diagnosis, and treatment of ALS. This report was released in February 2026. The independent report provided a comprehensive analysis of the EA program detailing the number of grants that were awarded, description of the research, the number of patients who received the investigational drug, and the status of FDA approval. The report can be found on the GAO website (https://www.gao.gov/products/gao-26-107691).

Q. Did the GAO report provide formal recommendations to NIH regarding the expanded access program?
A. No formal recommendations were provided to NIH.