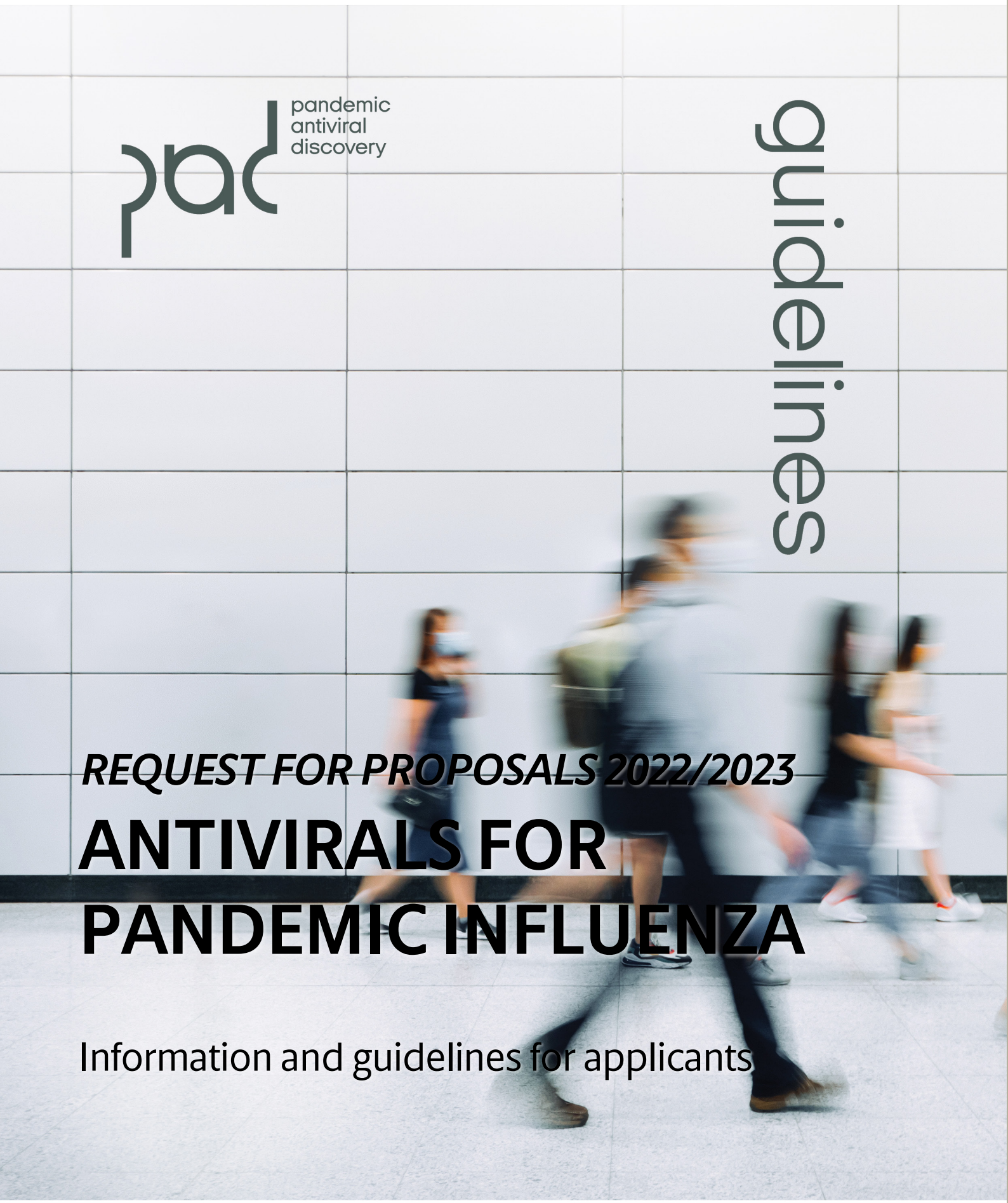
pandemic
antiviral
discovery

guidelines



REQUEST FOR PROPOSALS 2022/2023

ANTIVIRALS FOR PANDEMIC INFLUENZA

Information and guidelines for applicants

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About PAD – Pandemic Antiviral Discovery

PAD – Pandemic Antiviral Discovery – is a global philanthropic initiative launched by: Bill & Melinda Gates Foundation and Open Philanthropy in the US, and the Novo Nordisk Foundation (NNF) in Denmark. The aspiration for PAD is to help researchers worldwide identify and develop phase 2-ready antiviral drug candidates targeting pandemic threat viruses, including coronaviruses, paramyxoviruses, and orthomyxoviruses. This will greatly improve the chances that effective antivirals can be developed and deployed much faster next time the world faces a pandemic threat.

Important information:

The PAD - Request for Proposals (RfP) process will be managed using NNF's Application and Grant Management System, *NORMA*.
https://norma.novonordiskfonden.dk/
The visuals and content of the system is designed for applications submitted to NNF, as is the RfP template for this call. The PAD founding partners Bill & Melinda Gates Foundation, Open Philanthropy and NNF will have access to all the proposals submitted to this RfP.

RfP form opens:
6 October 2022

RfP deadline for submission:
22 November 2022 at 2 pm Central European Time

Contact info
For technical questions regarding the application system NORMA:
norma-support@novo.dk
For questions regarding the scope and content of the RfP that is not sufficiently addressed in these guidelines:
FGO@novo.dk

PAD – ANTIVIRALS FOR PANDEMIC INFLUENZA - REQUEST FOR PROPOSALS 2022/2023

These guidelines are intended to assist you in the process of submitting a Phase 1 proposal 'concept note' addressing this PAD request for proposals (RfP). It is important that you carefully read these guidelines, as they contain the complete call text and instructions regarding the 'concept note' and additional information to include in the proposal.

- Section 1 describes the overall frame and conditions of the RfP and specifies the overall criteria.
- Section 2 provides the technical guidance for how to access and navigate in the application and grant management system NORMA.
- Section 3 aids with essential information to include and best practice of how to apply for this specific RfP using the specific forms and fields available in *NORMA*.

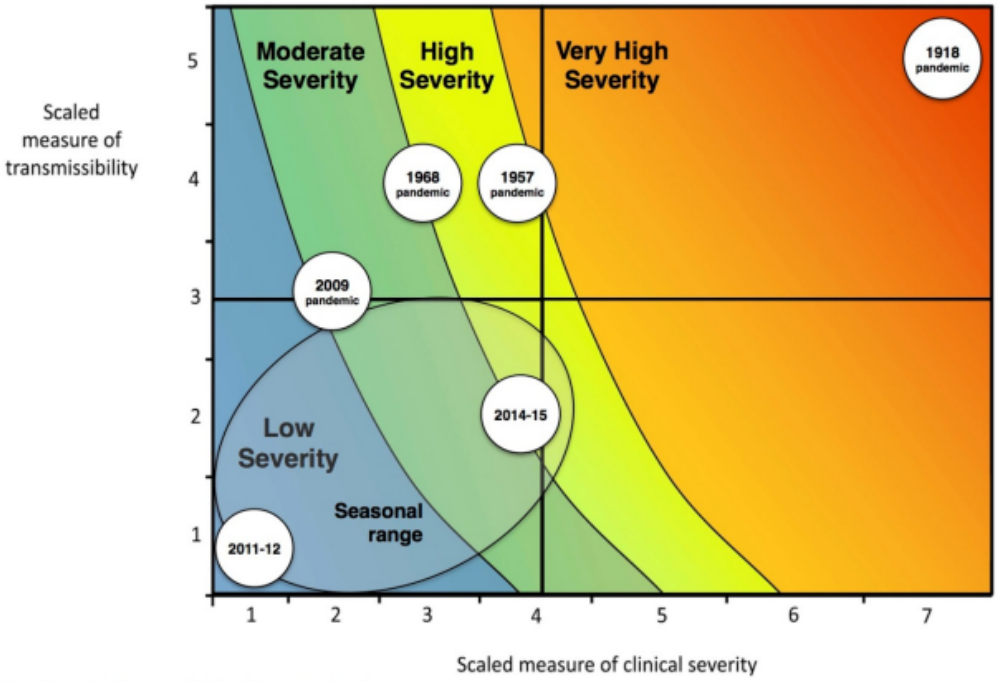
PAD will treat all applicant and proposal information confidentially. Read more about how NNF processes personal data in the 'privacy notice' on the Novo Nordisk Foundation website.

1.1 AMBITION & FOCUS

1.1.1 Background

Pandemic influenza is a global outbreak of a new influenza virus resulting from major antigenic shifts in the virus with the ability to efficiently spread from person to person. Pandemic influenza strains arise through zoonotic transmission of a new influenza virus strain with unique antigenic properties and ability to spread by aerosol transmission. Because the new virus strain has unique antigenic properties, there is very little pre-existing immunity in the population to restrict virus replication and spread. Pandemic influenza remains a substantial threat to public health. There have been six major influenza epidemics with the 1918 flu pandemic being the most severe and leading to the deaths of 50–100 million people worldwide. Pandemic influenza can be characterized by the level of clinical severity and transmissibility of the circulation strains.

Figure: Mapping of pandemic influenza: transmissibility and clinical severity.
Adapted from Reed et al. 2013; doi: 10.3201/eid1901.120124



Therapeutic strategies: Seasonal influenza can be managed through yearly vaccinations, however, vaccines are only 30% to 60% effective depending on the vaccine and circulating virus strains[1]. There are several antiviral therapeutics to treat seasonal influenza. Typically, treatment of patients within 48h of symptom onset results in improved clinical outcomes and may reduce transmission[2]. While these drugs could be used for pandemic influenza, drug resistance is a major concern. The amantadine class of antivirals are no longer prescribed due to widespread resistance and resistance to neuraminidase and endonuclease inhibitors has been observed in circulating influenza virus strains[3].

Antiviral drugs currently marketed for treatment of seasonal influenza virus

Target	Indication / Dosing	Representative drugs	Status	Challenges
M2	S, BID 5-days	Amantidine	Market	Widespread resistance, BID dosing
Neuraminidase	S, PEP, BID 5-days	Tamiflu	Market	Resistance, BID dosing
Endonuclease	S, PEP, single dose	Xofluza	Market	Resistance
RdRp	S, BID 5 days	Lagevrio	Market (Japan)	Low efficacy, safety concerns, BID dosing

S = seasonal, PEP = post-exposure prophylactic, BID – twice per day

Given the challenges with generated effective influenza vaccines and the potential for drug resistance to reduce effectiveness of currently available antiviral drugs, new therapeutic strategies are warranted.

[1] CDC, 2022
[2] For a review: Hayden et al., 2022; DOI: 10.1093/cid/ciab625
[3] Gorvokova et al., 2022; doi: 10.1016/j.antiviral.2022.105281

PAD Initiative focus: The aspiration of PAD is to catalyze the discovery and early development of Phase II-ready antiviral medicines in preparation for future outbreaks of infectious diseases with pandemic potential. PAD funding can support preclinical activities and phase I clinical trials, but not later stage clinical trials. With equitable access as a core principle of the initiative, the founding partners are committed to ensuring that discoveries and innovations supported by PAD are accessible for people in low- and middle-income countries. By focusing on small molecules for oral delivery, these efforts can help ensure the world is prepared to quickly develop and deploy effective, accessible antiviral drugs next time the world faces a pandemic threat.

1.1.2 RfP Purpose and areas of support

This RfP will support research designed to develop **novel small-molecule antivirals targeting pandemic influenza**. There is a need for cheap and safe antiviral compounds that target viral/host proteins and pathways necessary for replication and pathogenesis that are clearly differentiated from currently marketed drugs for seasonal influenza. Attributes that define differentiation include improved clinical efficacy over standard of care, shorter duration of therapy, reduced dosing frequency, improved safety, lower cost of goods, higher barrier to resistance and/or novel targets/mechanism of action.

Proposals should be consistent with at least one of these 4 areas:

1. Direct acting antivirals with data demonstrating clear differentiation from currently marketed influenza antiviral products
2. Host targeted therapies with data demonstrating clear benefit over currently marketed influenza virus therapeutics
3. Compounds that target multiple pathways or mechanisms to reduce the likelihood of resistance emergence
4. Compounds demonstrating activity against drug resistant influenza variants

Special consideration will be given to therapeutic modalities that are suitable for deployment in low resource settings.

Projects that fall outside the 4 defined areas and **projects on vaccines, antibody and nanobody therapy, diagnostics, clinical trials (Phase II, III, IV), formulation development, and epidemiology are excluded from the RFP** and will not be considered for funding.

1.2 ELIGIBILITY

If the eligibility criteria listed below are not adhered to in the submitted proposal, it will receive an administrative rejection

- PAD seeks to actively engage researchers from all over the world as part of the drug discovery process, but applicants must be established investigators with their own line of research and must be employed for the duration of the project at the administrating institution registered in the proposal.
- The administrating institution/organization must be able to accept and manage the potential grant. Projects can be anchored at any type of research organization, including academia, not-for profit and commercial organizations.
- The scope of the project must be within the scientific scope of this RfP and support the PAD aspirations.

- An applicant (i.e., the principal investigator (PI) responsible for the project and submitting the proposal) may submit only one proposal to this specific RfP. Different PI's can be anchored at the same institution/organization. Co-applicants can be a part of more than one proposal to this RfP, and an applicant on one proposal can be a co-applicant or collaborator on other proposals.

The proposal must contain all information requested in these guidelines and be submitted via NORMA. Applications submitted by post or e-mail, without a hosting letter, or without an attached budget will not be considered and will receive an administrative rejection.

1.3 FUNDING

A total of up to USD 25 million is expected to be allocated to proposals submitted to this RfP, but this amount is not fixed and may be updated depending on the quantity and quality of the proposals. The number of proposals supported will depend on the quality and expected budget. Exploratory projects should not exceed a budget of approximately USD 2 million and later-stage validation projects should not exceed a budget of approximately USD 10 million.

It is expected that the projects applied for will be between 1 and 3 years in duration. Under exceptional circumstances a longer project period can be negotiated with the PAD partners later in the application process.

1.4 LANGUAGE

The proposal and any additional uploads must be written in English.

1.5 APPLICATION AND EVALUATION PROCESS

The proposal must be completed and submitted using NNF's[4] online application and grant management system, NORMA, which can be accessed from:
https://norma.novonordiskfonden.dk
Further information on how to access and navigate in NORMA can be found in Section 2.

The application and evaluation process consists of different phases. These guidelines cover the first phase of the application process. The entire process from the Phase 1 proposal 'concept note' to potential grant is outlined below.

External peer reviewers may be involved at all stages of the evaluation process.

The first phase starts by submitting a proposal to this RfP. Deadline for submitting proposals for the first phase of the RfP is: **22 November 2022 at 2 pm Central European Time**. Proposals and material submitted will be evaluated by scientific program officers from Bill and Melinda Gates Foundation, Open Philanthropy and Novo Nordisk Foundation. Based on this evaluation, the outcome can be either an invitation to submit a full proposal to one of the three foundations or a rejection letter informing the applicants that their proposal will not be considered for funding.

[4] The PAD founding partners Bill & Melinda Gates Foundation, Open Philanthropy and NNF will have access to all the proposals submitted to this RfP If you would like more information about how the PAD Partners store and process your data please contact info@padinitiative.com.

Notification of outcome of the first phase is expected **by the end of May 2023**. Applicants will be notified by e-mail. The notification e-mail will be sent from noreply@norma.novonordiskfonden.dk to the e-mail address entered on NORMA registration.

IMPORTANT: No feedback will be provided in case a proposal submitted to the RfP is not invited to submit a full proposal.

Upon invitation to submit a full proposal to one of the three foundations, applicants will work directly with that specific foundation to develop the full application, and the processes may differ depending on the foundation. A full proposal will meet the specifications of the granting organization and may include background, preliminary data, specific aims, clear go/no go decision gates, milestones, timeline of deliverables, and a full budget with justification of line items. Applicants should be prepared to develop the full proposals in May-June 2023. Specific timeframes and deadlines will vary depending on the Foundation. Being invited to submit a full proposal is not a guarantee that a grant will ultimately be awarded.

Grants originating from this RfP are expected to be awarded by December 2023.

1.6 ASSESSMENT CRITERIA

The projects will be assessed based on quality of the science, novelty, state-of-the-art, and feasibility. Projects will also be assessed on justified fit with the scope and ambition of this RfP, the fit within the overall PAD portfolio, and how the proposed novel influenza antivirals can bolster pandemic preparedness and antiviral resistance liability, globally. The applicant and proposed team/collaborators will be assessed on their experience, record, and ability to deliver on the proposed project.

The PAD funding partners will distribute the selected funding opportunities from this RfP among themselves. Closeness of project to the respective foundations' 'core', geography, available budget etc. can influence which PAD funding partner will ultimately fund a given project.

2 THE APPLICATION AND GRANT MANAGEMENT SYSTEM – NORMA

Section 2 provides the technical guidance for how to access and navigate in the application and grant management system NORMA. All the fields in the application system must be completed in accordance with these guidelines.

2.1 USER REGISTRATION

NORMA can be accessed through the PAD website https://padinitiative.com or directly at: https://norma.novonordiskfonden.dk

Before you begin, please read the instructions on the login page.

If you do not have a user profile in NORMA, you can register by clicking REGISTER from the login-page. Here you can also retrieve forgotten passwords by clicking the FORGOT PASSWORD-link. The main applicant should only have one user profile. Please use your work e-mail address for registration. After registration, you will receive an e-mail with your username and a temporary password, which you can then use to log in to NORMA. After logging in for the first time you will be asked to provide a password of your own choosing.

A registered user who submits a proposal is legally responsible for the truthfulness of the content of the proposal.

If you experience technical problems, please contact NORMA Support: norma-support@novo.dk.

An applicant cannot change the e-mail address provided at registration. Please contact NORMA Support if you need to change your e-mail address.

2.2 CREATING AN APPLICATION

Initiate an application by finding the call you wish to apply for in the OPEN CALLS-section on the Applicant Portal in NORMA i.e., **PAD – Antivirals for Pandemic Influenza – Request for Proposals 2022/2023 and** click APPLY NOW next to the call.

Proposals can be edited up until the deadline. A draft proposal can be saved by clicking SAVE DRAFT and may be cancelled at any time up until the deadline by clicking CANCEL APPLICATION. A proposal is not submitted to NNF until an applicant has clicked SUBMIT and has received confirmation that the proposal has been successfully submitted.

You can review the proposal at any time by reopening from within NORMA. Opening the proposal will also allow you to download the proposal in its entirety as a PDF. Make sure the PDF is readable and formatted appropriately before submitting your proposal.

2.3 TEXT AND ILLUSTRATIONS

For all proposals, the individual fields must be completed in accordance with these guidelines and the instructions supplied in NORMA. Fields marked with a red star (*) are obligatory to fill in.

To prevent loss of data, it is essential to press SAVE DRAFT before you leave NORMA or navigate in the system.

TEXT FIELDS

Text from Microsoft Word or comparable word processors can be copied and pasted into most text fields of the proposal. It is, however, important to check that formatting, special characters, and symbols have not been converted or lost in the text fields after copying and pasting. If the formatting looks wrong in NORMA or in the PDF, try changing all text to Normal using the FORMAT dropdown. It is the responsibility of the applicant to ensure that the pdf looks correct before submitting.

The available options for formatting text are at the top of the text fields. Some shorter text fields do not have the option to use rich text formatting

ILLUSTRATIONS

Illustrations such as figures, charts, tables, images, etc. related to the project description can be uploaded under PHASE 1 PROPOSAL. A maximum of four illustrations are allowed. The illustrations will be placed on a separate page in the proposal PDF but can be referenced throughout the project proposal as needed. For readability, please name the files numerically by the order in which they are referenced.

The following file formats for illustrations are accepted in the system: JPG, JPEG, PNG and BMP. The maximum accepted size for each illustration is 1050*1650 pixels.

2.4 SUBMITTING THE APPLICATION

The proposal in its entirety must be submitted electronically via the application system by clicking SUBMIT. It is not possible to submit a proposal or any part of it by standard mail or e-mail. Any material submitted outside the application system will not be included in the evaluation and will not be returned.

Please remember to check that the PDF version of the proposal is legible and contains all data and uploads before submitting.

All applicants must read and accept NNF's Standards for Good Research Practice before submitting the proposal. Further, the applicant must declare that the information provided in the proposal is true and accurate.

A proposal cannot be submitted unless all the required fields have been completed. Proposals can be cancelled at any time before submission. If you need to withdraw a proposal after the deadline, please get in touch with PAD via e-mail, using the contact information on page 3.

A list of any incorrect or incomplete entries will be autogenerated when you click SUBMIT. Amending incorrect or incomplete entries can be time-consuming, so we recommend submitting proposals well before the deadline.

3 REQUEST FOR PROPOSALS CONTENT

This section provides guidelines on the content required in the sections of the online application form for this call.

3.1 APPLICANT

The APPLICANT-tab contains information about the main applicant of the specific RfP. If collaborators besides the main applicant are involved in the project these collaborators should be listed under supplementary information and their contributions to the project should briefly be described in the 'proposal' section (see specific information in section 3.3). Information about the applicant is collected through individual tasks in the APPLICANT DETAILS-section including personal details, institutional details, applicant experience, publications, etc.

CV can be a maximum of 4,000 characters (including spaces, line breaks and special characters). Please provide your brief CV including:

- A hyperlink to your professional webpage (if possible, from the website of the administrating institution)
- Education
- Employment history
- Academic applicants should also summarise recent/active research funding

Publication list can be a maximum of 8,000 characters (including spaces, line breaks and special characters).
Please provide the complete reference information for your most important publications (up to 10) relating to the proposal submitted to this call. Applicants are strongly encouraged to provide a full list of publications in ORCID or include a hyperlink to an updated profile with a full publication list for the applicant on either Google Scholar, Web of Science, or Scopus.

Summary of own research: Please describe main scientific achievements, and how it has led to the proposed project. Elaborate on why and how you will dedicate your time to this project.

Supplementary Information can be a maximum 2,000 characters (including spaces, line breaks and special characters): In this field, please list and describe the roles of the collaborators, if any, (including sub grantees, sub- contractors or collaboration partners, but excluding employees) that will be involved in the project (you are encouraged to include a hyper-link to their professional webpage). At this stage of the application process, it is not required that commitment letters are submitted from collaborators, but it is expected that any named collaborators are committed to participating in the project.

Please DO NOT upload CV and publication list under the upload tab under SUPPORTING DOCUMENTS under the APPLICANT DETAILS, but instead follow the directions in Section 3.3 regarding required uploads.

3.2 INSTITUTION

Please provide information about the institution/organization where the grant will be administrated. This institution must be where the applicant is employed during the grant period and importantly the institution which will be responsible for budgeting, accounting and staff supported by the grant and ultimately will be responsible for a potential grant. A preliminary hosting letter is required (uploaded as a PDF). The institution must be able to receive and administer grants.

Registering a new administrating institution in NORMA can take up two working days. The proposal can be edited but cannot be submitted before this information is registered. We therefore recommend that you register an administrating institution in good time.

3.3 PHASE 1 PROPOSAL

Describe the project using the following fields on the PHASE 1 PROPOSAL tab:

EXPECTED GRANT PERIOD
Please enter the project start date as 1 December 2023 and the expected project end date, so it fits with the expected project duration (1-3 years).

By entering project start and project end dates, the system will calculate the total project duration. If the project end date is one day into a new year, the system will automatically add an additional project year. This may make you unable to submit your application. As an example, if the requested grant period is 2 years, the start and end dates should be 1 December 2023 to 30 November 2025.

These dates are not binding and can be changed if invited to submit a full proposal but are mandatory fields in NORMA. The grants originating from this RfP are expected to be awarded by the end of 2023, and the start and end dates for the project will be agreed upon, when developing the full proposal.

PROJECT TITLE (maximum 150 characters, including spaces)
Please provide a short title for the project.

TOTAL REQUESTED BUDGET
As stated below under 'uploads' a high-level budget must be uploaded using the Excel template provided in NORMA (a link can be found in the instructions for the Phase 1 Proposal tab in NORMA). The estimated requested grant total in USD from the budget template must be entered in this field.

How to best use the budget template: A short 'guide' is provided in the first 'tab' in the excel template. The budget should be estimated in your local currency, and then the budget template includes a column with your estimates, which you will have to convert into USD. Please specify the applied currency exchange rate. The total amount requested in USD must match the amount entered in the 'Total requested budget' field. Include all expected direct costs in the budget, but

do not include indirect costs/overhead, as the amount of indirect costs allowed varies depending on the foundation potentially funding the proposal. The high-level budget submitted in this first round is not binding and can be changed/negotiated if invited to submit a full proposal.

PAD does not allow double funding of projects. I.e., if full or partial funding for the project has been or is obtained by other mechanisms, these specific budget posts cannot also be funded by PAD. If such funding (full or partial) is secured post-submission, PAD should be contacted as soon as possible (FGO@novo.dk).

BRIEF PROJECT DESCRIPTION (maximum 2000 characters, including spaces)
Please provide a brief stand-alone summary of the project describing the scientific goals, significance, originality, and potential impact of the research program on the development of novel antivirals targeting pandemic influenza.

PROJECT DESCRIPTION (maximum 10,000 characters including spaces)
Please describe your proposed research project. Include:

- The research questions and objectives/goals of the research project
- The most relevant scientific background in brief
- An outline of the research to be conducted (with an estimated timeline). Include in the outline:
    - The general experimental approaches
    - The main research methods, tools and technologies to be utilized and developed
    - A brief description of the research group and, if relevant, how named collaborators will contribute to the project.
    - The expected experimental outcomes and significance
- Include supporting data as figures/illustrations (uploads)

Abbreviations should be defined at first use.

ILLUSTRATION UPLOADS
A maximum of four illustrations (figures/charts/images/tables/etc.) of up to 50 MB each can be uploaded here. Accepted formats are .jpg, .png, .gif, .bmp.

The illustrations will be integrated in the proposal PDF.

LITERATURE REFERENCES
Please provide the reference information for the literature cited in the project description (maximum 4000 characters, including spaces).

LAY PROJECT DESCRIPTION
Please provide a brief summary for non-experts in lay language. If the application is awarded a grant, the text may be used for publication (maximum 1000 characters, including spaces).

UPLOADS

Please include only the following uploads in this RfP:

- A high-level budget with project expenses estimates using the budget template provided in NORMA (a link can be found in the instructions for the Phase 1 Proposal tab in NORMA).
- A hosting letter from the administrating institution/organization confirming that, if granted:
    - The administrating institution/organization will host the project
    - The administrating institution/organization is able to manage the grant and commits to budgeting, controlling, accounting and auditing of the total grant
    - The applicant is an established investigator with their own line of research and will be employed for the duration of the project at the administrating institution
    - The hosting letter must specify the name of the main applicant and project title, be on official letterhead of the administrating institution/organization and be signed by the management of the administrating institution/organization. If the main applicant is Head of Department or otherwise part of the management, the hosting letter must be signed by someone from the management level above the main applicant.

All uploads must be in PDF format. NORMA automatically places these uploads at the end of the proposal. Please respect the page limitation and the upload requirements stated in the call. Uploads in excess of these limits will not be considered for evaluation.

October 2022

PAD – Pandemic Antiviral Dicovery

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