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Call for Proposals NACTAR; (pre)clinical studies, Nederlandse Organisatie voor Wetenschappelijk Onderzoek

Applied and engineering sciences

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1 Introduction

The Dutch Ministry of Ministry of Health, Welfare and Sport (VWS) and NWO Domain for Applied and Engineering Sciences (NWO Domain AES) have jointly commissioned an ambitious research programme on the development of 'Novel Antibacterial Compounds and Therapies Antagonizing Resistance' (NACTAR). The main goal of the NACTAR programme is to facilitate research and development of new antimicrobial molecules and alternatives to antibiotics, which should become available for a fair and affordable price.
Elaborate background information on the NACTAR programme, as well as information on the research projects already funded by the programme, can be found on the website of the NACTAR research programme. Links to additional relevant websites can be found below in this document.

This document details the conditions governing proposals submitted to NWO Domain AES for the funding of **(pre)clinical studies** under the NACTAR programme. NWO Domain AES will handle the application process and assessment procedure. The NWO Grant rules 2017 version 2019 and the Guidelines Users' Committee NWO domain TTW 2017 will apply unless Programme-specific conditions, as specified in this call for proposals, are applicable.

Before submitting your application electronically via ISAAC, NWO Domain AES recommends that you visit its website (www.nwo.nl/ttw) to verify that you have the latest version of this document, and that you read the **guidelines** carefully. Moreover, please familiarize yourself with **ISAAC** (www.isaac.nwo.nl) before you start the submission of your proposal.

Partners in the NACTAR Programme

VWS issues this call for (pre)clinical studies within the NACTAR programme together with NWO Domain AES. This Programme connects to the National Antibiotic Development Platform (NADP). The NADP was established by the Netherlands Centre for One Health (NCOH), the Dutch antimicrobial research initiative CARES, the Center for Sustainable AntiMicrobials (CeSAM) and (previously) ImmunoValley with support of VWS.

Scope of the NACTAR Programme

Antimicrobial resistance (AMR) is one of the major threats to human health in the 21st century. In many countries, infections caused by multi-drug resistant (MDR) bacteria are now a major cause of morbidity and mortality, and have markedly increased healthcare costs. The aim of the NACTAR programme is to discover, develop and exploit new resources for antibiotics and alternatives to antibiotics. This includes the use of microbial hosts and methodologies to synthesize new bioactive compounds and semi-synthetic variants, characterization of their antimicrobial activity and their efficacy in infectious disease animal models up to early stage clinical studies.

Examples of topics addressed within the NACTAR programme, as well as the NADP Research Agenda, include applications to exploit the potential of actinomycetes, filamentous fungi and other microbes known to produce clinically relevant antibacterial drugs; (bio)synthetic combinatorial approaches to increase structural diversity of existing and newly identified antibiotics; development of antibodies for the development of novel immunotherapies; development and testing of novel host-directed approaches to complement current treatments.

The preferred target organisms are those recently highlighted by the WHO as serious threats to human health, specifically the ESKAPE pathogens VRE, MRSA, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa and Escherichia coli, and in addition Streptococcus pneumoniae and Clostridium difficile. In addition, treatments that counteract biofilm formation, persistence and other antibacterial resistance mechanisms will also be considered.

For a detailed list of topics that are welcomed within the NACTAR Programme we refer to Appendix 3.1. Topics that are not considered within the NACTAR programme (out of scope) which are therefore not eligible for funding within this Call for proposals are listed in Appendix 3.2.

NACTAR Programme duration and programme committee

The NACTAR programme has a duration of 5 years and ends 1 January 2023. A Programme committee will be responsible for the overall direction and management of the programme and stimulates the collaboration between all granted projects under the NACTAR Programme, as well as the connection to ongoing applied research programmes and projects. NACTAR Programme days will be organised and all people involved in projects funded within the programme are expected to attend.

All members of the Programme committee are subject to confidentiality restrictions to protect any results of ideas laid down in the proposals and discussed during meetings. Programme committee meetings will be organised at least once a year unless the Programme committee decides differently based on particular needs.

Scope and Objectives of this NACTAR Call for (pre)clinical studies

This NACTAR call for (pre)clinical studies is funded by VWS, and the objective is to support studies that aim to bring newly developed antibiotic compounds, products and/or alternative treatments to the stage of (pre)clinical testing. It is expected that projects contribute to translation of previously developed compounds, therapies and/or treatments to the clinic, aimed at curing human infectious diseases caused by MDR bacteria, as defined above for the NACTAR Programme. To this end, activities may consist of (parts of) preclinical, phase 0, phase 1 or early stage phase 2 clinical study with clearly described (clinical) end-points (see Appendix 4). The intended approach must adhere to criteria from the European Medicines Authority (EMA) and/or the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH).

Appendix 4 indicates the type of studies that are not eligible for funding in this call for proposals, this include phase 2 Pre or Post (pivotal) market studies and phase 3 studies.

2 Specific requirements of this Call

Proposals should adhere to the programme guidelines as defined in this document. In summary:

- Proposals should address (one of the) NACTAR programme objectives and themes and fit into the NADP research agenda (see also Appendix 3).
- Utilization of project results should be in the perspective of development of new antibiotics and/or alternatives for antimicrobial use in **human** medicine.
- Proposals may consist of (parts of) preclinical, phase 0, phase 1 or early stage phase 2 clinical study (see Appendix 4).
- Clear (clinical) end-points and approach adhering to EMA / ICH criteria (as defined for instance in the ICH E8 document, see 'Links') must be described.

- Scientists employed by (Technical) Universities situated in the Kingdom of the Netherlands, as well as institutes eligible for funding by NWO, can submit a proposal (see 'Guidelines for Applicants').
- Relevant Intellectual Property (IP) for the proposed study is held by the knowledge institute applying for funding.
- Applicants adhere to NWO Domain AES IP-policy and NACTAR programme specific IP conditions (see below and Appendix 1).
- Maximum 1 relevant private partner (i.e. SME or Industry), with a track-record in antimicrobial development, may be involved in the proposed initiative. Co-funding of the proposed research by the private partner (in cash and/or in kind; ≤ 50% of the project budget) is permitted.
- Proposals should clearly describe how the consortium will be managed and how the application of results will be achieved.

Apart from the programme-specific guidelines defined in this document, the 'NWO Grant Rules 2017 version 2019' and 'Guidelines Users' Committee NWO domain TTW 2017'as published together with this call, apply.

Criteria for submission

Standard NWO guidelines apply with regard to who may submit an application in this programme (see 'Guideline for Applicants'). The application consists of two-phases: in Phase 1, pre-proposals will be evaluated, and applicants of positively evaluated pre-proposals will be invited to submit a full proposal (including required appendices) in Phase 2. Only (pre)proposals submitted via ISAAC, in English, will be considered (see 'Guidelines for Applicants').

Within this NACTAR call for preclinical studies, applicants may associate their name to one (1) proposal as main applicant and to one (1) proposal as co-applicant.

The funding that can be requested per proposal ranges from 200 k€ up to 1M euro (inclusive of Dutch VAT). The Assessment Committee will be instructed, when preparing its advice to the NWO Domain AES Board, to take into account the most efficient and effective distribution of the total available budget. To apply for (a significant part of) the total available budget, the applicant(s) should make a clear and strong case.

Please also note the Programme-specific requirements for co-funding and IP arrangements that must be adhered to. If applicable, co-funding provided by the user will be added to the total project budget. The budget may be spent on personnel (non-scientific personnel (e.g. research nurses), scientific personnel), consumables, 3rd party expert advice (e.g. from a clinical research organisation (CRO)), etc. Please see 'Guidelines for Applicants' for further details.

Criteria for co-funding

Co-funding of proposals submitted to this call is not required. However, in case a private partner (i.e. SME or Industry) decides to, or if applicants wish them to contribute to a proposal, please take into account that:
- Only 1 private partner per proposal is permitted;
- The total co-funding (in cash + in kind) must be 50% or less of the total project budget;
- Programme-specific IP conditions (see below) are in place;
- Guidelines exist with respect to allowed in kind co-funding contributions;
- After award of the project, the co-funding partner will be designated a user in the project;
- The user is requested to be actively involved in project meetings to stimulate application of the results.

If applicable, co-funding is calculated as the financial (in cash) and in-kind contributions of the user. In kind contributions are relevant capitalised personnel and/or material contributions from the user (see below). The level of co-funding (in cash and in kind) as well as the nature and relevance of co-funding (in kind) will be subject to assessment by the Assessment Committee.

Commitment of a user, as well as their contribution to the project (if applicable) should be confirmed in full proposal phase in a letter of support (see 'Notes on co-funding'). Relevant private partners aim to contribute to the goal of the programme, i.e. development of new antibacterial compounds and/or alternatives to antibiotics, as opposed to developing for instance 'enabling technologies'. The Assessment Committee is instructed to take this into consideration when evaluating the proposal.

Available budget

VWS has reserved 1 M€ of budget for preclinical and early stage clinical testing of promising novel

antibiotics and/or alternatives for antibiotics, that result from research within the scope of the NACTAR programme and the NADP Research Agenda. Both the available budget and the timelines agreed between VWS and NWO will allow for one (1) call for (pre)clinical proposals.

Project duration and budget

The funding that can be requested per project is minimum 200k€ up to maximum 1M euro (inclusive of Dutch VAT). The maximum project duration is 2 years. The projects must start within 6 months after award of the project. Duration of projects may not extend beyond the NACTAR Programme end date (see above).

Funding conditions and Intellectual property (IP) policy

This call is published by NWO Domain AES, therefore the 'NWO Grant Rules 2017 version 2019' and 'Guidelines Users' Committee NWO domain TTW 2017' as published together with this call are applicable to this programme, unless Programme-specific conditions as specified in this document apply. Management and administration of project (proposals) is done according to NWO Domain AES procedures.

As stated above, the NACTAR Programme focusses on development of new antimicrobial compounds and alternatives to antibiotics which should become **available and accessible** to the healthcare system for a **fair and affordable price**. VWS and NWO Domain AES are aware of growing public concerns with regard to the costs of healthcare in general, and of medicines and treatments in particular, especially if public funding was provided at any stage in its development. Therefore, VWS has initiated a national debate on socially responsible licensing (in Dutch: 'Maatschappelijk verantwoord licentiëren'), which has resulted in a list of 10 guiding principles with regards to socially responsible licensing ("guiding principles" available here in Dutch). Applicants must adhere to these guiding principles.

Therefore the guiding principles on socially responsible licensing, including the elements "availability" and "fair and affordable price" have to be part of any IP arrangements concerning new results generated in projects that are awarded under the NACTAR Programme. Please find a detailed explanation of the IP & publication guidelines further in the section 'Notes on Intellectual Property policy (IP policy) & Publication' and Appendix 1.

Background or sideground knowledge/IP generated outside the NACTAR Programme that is contributed to the project by the applicant is exempt from this demand, however, applicants and consortium partners are encouraged to take the above into consideration. For the avoidance of doubt, however, the guiding principles shall always apply to new results generated in projects awarded under the NACTAR Programme.

Resubmitting proposals

Proposals that were rejected in a previous STW, NWO or ZonMW evaluation procedure cannot be resubmitted in this call for proposals.

Submission of project idea for funding elsewhere

If identical or very similar proposals are or will be submitted to NWO, ZonMW or other funding bodies, this must be stated in the proposal. For the duration of the assessment procedure of this research programme call, the submission of identical or very similar proposals (this judgement of NWO Domain AES) to more than one NWO or ZonMW programmes is not permitted.

Deadlines and Time frame

Before submitting your application electronically via ISAAC, NWO Domain AES recommends that you visit its website (www.nwo.nl/ttw) to verify that you have the latest version of this document, and that you read the guidelines carefully.

NWO Domain AES adheres the NWO policy for deadlines. Your submission receives time and date of registration. Please be aware that submissions registrations of 14.01 CE(S)T on the day of deadline or later will not be considered. For this reason we recommend to familiarize oneself with ISAAC (www.isaac.nwo.nl) in advance of the deadline and before you start the submission of your proposal.

In the timeline below we have indicated deadlines for pre- and full proposals. Actions for applicants during the assessment procedure are marked with capital letters.

Time frame	
NWO information consults: depending on your need please fix an appointment with contactpersons (telephone or meeting)	November 5, 2019 November 25, 2019 December 17, 2019
Deadline pre-proposal (via ISAAC)	**January 14, 2020; 14:00h CE(S)T**
Assessment by Assessment Committee (AC)	End of January 2020
Advice AC to applicant	Early February, 2020
** **APPLICANT:** Deadline reaction period (via eMail)	Mid February, 2020
** Final decision of AC communicated to applicant	End of February, 2020
Deadline full proposals (via ISAAC)	**March 24, 2020; 14:00h CE(S)T**
APPLICANT: submission of revised version (via ISAAC)	Early April, 2020 (1 week)
Assessment by AC	April 2020
APPLICANT: Interviews (dates to be confirmed)	April 23 or 24, 2020
Advice AC to AES Board	May, 2020
Decision by AES Board	May, 2020
Ultimate project starting date (6 months after award)	December 1, 2020

*** These dates will apply when pre-selection on pre-proposals is executed as a result of substantial number of submissions relative to the available budget. You will be informed accordingly.*

3 Assessment procedure

An application can only be submitted via the online application system ISAAC (www.isaac.nwo.nl). Applications not submitted via ISAAC will not be taken into consideration. Please note that it is the responsibility of the applicant to ensure timely submission of his/her application to the correct Call for proposals. In case of doubt, please contact the contact persons at NWO Domain AES (see below).

The assessment procedure will be carried out under the coordination of the NWO Domain AES office and will consist of two phases, i.e. an obligatory pre-proposal phase followed by a full proposal phase. In each of the phases applications will be assessed in competition with the other applications submitted in this call for proposals by an independent Assessment Committee (see below).

Of note, the obligatory data management section in the application is not evaluated and hence not included in the decision about whether or not to award funding. However, NWO Domain AES and the Assessment Committee can issue advice with respect to the data management section.

3.1 Assessment criteria

The proposals are evaluated and scored according to the following three (3) criterions (please see below for information on assessment scale):

Criterion 1: Project approach & team (weighting factor1; cut off value: 2):
- quality of the proposal;
- composition of the project team;
- expertise, experience and motivation of the principal applicant and other persons or parties involved;
- clear description of approach (e.g. protocol) and phasing of the activities;
- justification of the requested budget, also in relation to the total requested budget.

Criterion 2: Relevance and innovative aspects (weighting factor 1; cut off value: 2):
- quality of the scientific state-of-the-art (functioning of the molecule or therapy is validated at the laboratory scale and/or by preclinical data (in the case of clinical study proposals));
- relevance of the proposed project to the NACTAR programme goals and NADP strategic research agenda;
- presence of innovative elements.

Criterion 3: Clinical and commercial potential (weighting factor 1; cut off value: 2):
- clinical need;
- IP / patent position and strategy;
- application possibilities (clinically applicable/GCP producible);
- in the case of phase I or early stage phase II proposals: realistic clinical end-points;
- in the case of phase I or early Phase II proposals: market and commercial perspectives.

3.2 Assessment of pre-proposals

NWO Domain AES confirms receipt of the pre-proposal submitted via ISAAC (see 'Guidelines for applicants'). Admission to the next stage of the procedure depends on how well the research topic as described in the pre-proposal fits into the scope and objectives of this Call. The Assessment Committee will assesses the pre-proposals based on **Criterion 2** (described above). The result of this assessment is communicated to the applicant as an 'advice' on whether or not to write a full proposal. As the final decision on whether or not to award the full proposal will be made by the same Assessment Committee, therefore applicants are strongly recommended to adhere to the advice they receive in this phase of the procedure.

In parallel to the assessment of pre-proposals by the Assessment Committee, NWO Domain AES verifies whether the pre-proposal adheres to the formal requirements of the research programme (see section 'Guidelines for applicants'). If relevant conditions are not (yet) fulfilled, the applicant(s) will receive notice with together with the outcome of the first Assessment Committee meeting. Applicants are required to incorporate the specified changes within the full proposal (see below).

Preselecting pre-proposals

NWO Domain AES is aware of the high workload that is intrinsic to proposal preparation and assessment procedures such as the one described in this document, both for applicants as well as for members of the Assessment Committee. In light of the available budget for this call and the effort that is required for preparation of a full proposal, the assessment procedure of this Call includes an optional preselection step on pre-proposals.

In particular, if at least four times more pre-proposals are submitted than can be funded from the available budget, NWO Domain AES retains the right to perform a preselection. You will be informed accordingly on this decision. In case of preselection, the Assessment Committee is asked to evaluate the pre-proposals based on '**Criterion 2**: Relevance and innovative aspects' **in relation to the requested budget**. The result of this assessment is communicated to the applicant as an 'invitation to write a full proposal' or a 'rejection'. In case of the latter, the main applicant is given a limited period (5 working days) to argue why they should be invited to submit a full proposal. The Assessment Committee will then evaluate any responses received from applicants, and provide feedback to those applicants within a similar time-frame (i.e. 5 working days).
Please note that the deadline for submission of full proposals will not change if the preselection procedure is executed unless otherwise advised.

3.3 Assessment of full proposals and eligibility for funding

Please note: Only proposals that have taken part in the pre-proposal phase, will be accepted at this stage.

NWO Domain AES confirms receipt of the full proposal submitted via ISAAC (see 'Guidelines for applicants'). NWO Domain AES will assess the admissibility of full proposals by checking whether they have met the required formal conditions as set out in the 'Guidelines for applicants'. If the required conditions are not fulfilled or the information requested is incomplete, the full proposal will not be considered. In that case, NWO Domain AES returns the full proposal to the main applicant within five to ten working days with a request for adjustments or additional information. The main applicant is given 5 workdays (1 week) – calculated from the date of NWO Domain AES's notification – to submit a revised version via ISAAC. If the information required is not provided, or is incomplete by the deadline, the full proposal is recorded as withdrawn.

Assessment Committee meeting and Interview

The main applicants of accepted full proposals will receive an invitation for **interview** as soon as the date is known. The interviews will take place during the second Assessment Committee meeting. Applicants will receive detailed information about the time and location of this meeting, as well as about the composition of the assessment committee in due course.

During the interview, the main applicant will be given the opportunity to explain their proposal orally by means of a short presentation to the Assessment Committee followed by a discussion. The main applicant can be accompanied by their co-applicant and/or a representative from the user (if applicable). If the main applicant is unable to present their proposal on the indicated date, the co-applicant may take their place or they may opt to be assessed based on written information provided to the committee before the assessment committee meeting.

Ranking and advice to AES Board

The Assessment Committee will assess each proposal based on the information presented in the full proposal, the interview and the applicant's response to questions from the Assessment Committee. Among other things, it will be assessed whether the minimum quality requirement has been met. To this end, each committee member assigns three ratings of equal weight – one for each of the quality criteria listed above the proposals. An **assessment scale** of 1 to 5 is used, in which: 1 = outstanding, 2 = good, 3 = satisfactory, 4 = moderate, 5 = unsatisfactory.

The **quality requirement** for this call under the NACTAR programme states that proposals are only eligible for funding if the average score is not higher than 2.0 for any of the three individual assessment criteria, and if the total sum of these criteria is not higher than 6.0.

The Assessment Committee will rank the proposals based on the total sum of the average score for the three assessment criteria and draw up a funding advice for the AES Domain Board, with due consideration for the quality requirement and taking into account the most efficient and effective distribution of the total available budget.

Assessment Committee

To guarantee the objectivity of the assessment as far as possible, NWO Domain AES assembles, in close collaboration with NADP, an independent multidisciplinary Assessment Committee which will be responsible for the overall assessment of the proposals submitted to this Call.

The Assessment Committee will be composed of approximately 5-9 members (depending on the total number of full proposals to be assessed), all independent national and/or international experts from the field of research relevant for this programme; universities, large research institutes, pharmaceutical industry, biotech SME companies, and other societal sectors (if relevant). By using this approach, every assessment can take into account the societal needs that science and technology can address in the context of this programme.

NWO Code for Dealing with Personal Interests

As described above, NWO Domain AES will ask active researchers from knowledge institutions and specialists from other knowledge-intensive organisations to participate in the assessment procedure. These persons are involved in current or new research themselves and are often part of large organisational associations and research networks. Consequently, the assessment of proposals and the decision-making process concerning the distribution of funding must not be affected by any bias or the appearance thereof.

NWO Domain AES therefore adheres to the NWO Code for Dealing with Personal Interests (hereafter referred to as the Code) to ensure that applicants receive a fair and transparent assessment. The Code describes the way of dealing with personal interests in the process of the preparation of, advising on and the decision-making about the distribution of resources. The Code also states the way in which decisions about dealing with personal interests in the process must be explained and recorded. This means that NWO is able to account for their actions at all times. Parties to which the Code applies are: referees, jury members, committee members, members of decision-making bodies and employees of NWO. The complete text of the NWO Code for Dealing with Personal Interests can be found at: https://www.nwo.nl/en/documents/nwo/legal/code-for-dealing-with-personal-interests.

Decision by the NWO Domain AES Board

The NWO Domain AES Board bases its decision on the prioritisation of the proposals. The priority ranking as established by the Assessment Committee is the primary starting point, however the available budget for the programme may result in deviation from the advice of the Assessment Committee. The AES Board does not assess the content of the proposals. In practice, unfortunately, the available budget will not be sufficient to fund every proposal of good quality.

4 After award

(see also the 'NWO Grant Rules 2017 version 2019' as published here)

After award of the application

The main applicant becomes the project leader. In the case of large projects, it is necessary to appoint separate sub-project leaders. If the proposal is successful, each research institute involved receives an

award letter with appendices. This sets out the legal and financial conditions of funding and should be signed individually for approval by each research institute.

Importantly, the grant decision only becomes valid after the following documents are completed, signed and received by NWO domain AES **within three (3) months** of the date of the Grant decision:

- a copy of the funding agreement, signed for agreement on behalf of the institution and also by the (co)project leader;
- the promised contribution(s) has/have been confirmed in writing by the user (NWO domain AES will take the initiative in this respect);
- the data management plan (an elaboration on the 'data management section' requested with the proposal) is received and approved by NWO domain AES.

The following document(s) need to be received by NWO domain AES **within six (6) months** of the date of the Grant decision:

- METC and/or CCMO approval of the intended clinical study (if applicable).

The project can start as soon as the above documents have been received and approved by NWO Domain AES, in which case the project leader will receive confirmation.

Start and starting date of the project

The credits allocated to the project do not become available until after the necessary documents have been signed and received by NWO Domain AES and all relevant award conditions have been fulfilled. If the latter is not yet the case, for example due to continuing negotiations about intellectual property, written permission to start the project can be requested from NWO Domain AES. Without such written permission, potential financial risks are borne by the applicant(s). The starting date of the project is the date on which an initial expenditure of allocated funds is undertaken. This is generally not the date of award. It usually relates to the appointment of the first staff member at the project's expense. The projects must start within **six (6) months** after award of the project. Duration of projects may not extend beyond the NACTAR Programme end date.

Programme committee

A Programme committee has been convened for the NACTAR Research programme, consisting of selected experts from the field that may or may not be involved in the research programme as (co-)project leader or user.

After granting of the research projects, the Programme committee is responsible for the overall directions and management of the programme. All members of the Programme committee are subject to confidentiality restrictions to protect any ideas laid down in the proposals. Programme committee meetings will be organised at least once a year unless the Programme committee decides differently based on particular needs.

NACTAR Programme meetings

During the course of the NACTAR programme, several programme meetings will be organised, during which parties involved in all projects that have been awarded, either in the first Call for research proposals (2017) or in the current Call for (pre)clinical proposals, are expected to participate. Naturally, all members of the Programme (scientists, users, Programme committee and/or other invited guests) are subject to confidentiality restrictions with regard to any results presented during the Programme meetings. Non-disclosure agreements (NDAs) will be arranged for any participant not yet included in the Programme.

Reporting and monitoring of progress

The project leader is responsible for steering the project towards achieving its milestones and deliverables during the timeframe as described in the awarded proposal. The project leader reports on the progress of the project twice a year, in writing, to the NWO Domain AES and NACTAR Programme committee, which will discuss the progress made. Progress reports always include a financial paragraph. As an exception – to be decided by NWO Domain AES – the reports may be provided in a different frequency. The NACTAR Programme committee will monitor progress and provide an advice to NWO Domain AES based on the information provided by the project leader.

Mid-term review

A mid-term review will be held approximately half way the intended duration of the project, and may

include a site-visit. The mid-term review is aimed at evaluating the progress of the project with the members of the NACTAR Programme Committee. NWO Domain AES will ask the Programme Committee to give their reasoned advice concerning the progress of the project, and may also consult the original members of the Assessment Committee.

Progress will be assessed against:
- feasibility of the project objectives;
- milestones and deliverables as described in the original project plan;
- necessity of the remaining funding for a successful completion of the project in accordance with the original project plan.

In the case of a negative advice, the project leader will be informed that a number of improvements to the project should be realised. The necessary mid-term review documentation will be provided in due course.

Open Access

All **scientific publications** resulting from research that is funded by grants derived from this call for proposals and approved by Programme Committee are to be immediately (at the time of publication) freely accessible worldwide (Open Access). There are several ways for researchers to publish Open Access. A detailed explanation regarding Open Access can be found on http://www.nwo.nl/openscience-en.

Data management

Responsible data management is part of good research. NWO wants research data that emerge from publicly funded research to become freely and sustainably available, as much as possible, for reuse by other researchers. Furthermore NWO wants to raise awareness among researchers about the importance of responsible data management. Proposals should therefore satisfy the data management protocol of NWO. This protocol consists of two steps:

Step 1: Data management section

The data management section is part of the proposal. Researchers should answer four questions about data management within their intended research project. Therefore before the research starts the researcher will be asked to think about how the data collected must be ordered and categorised so that it can be made freely available. Measures will often need to be taken during the production and analysis of the data to make their later storage and dissemination possible. Researchers can state which research data they consider to be relevant for storage and reuse (see Appendix 2).

Step 2: Data management plan

After a proposal has been awarded funding the researcher should elaborate the data management section into a data management plan. The plan should be submitted to NWO via ISAAC within a maximum of 4 months after the proposal has been awarded funding. NWO Domain AES will approve the plan as quickly as possible. Approval of the data management plan by NWO Domain AES is a condition for disbursement of the funding. The plan can be adjusted during the research.

Further information about the data management protocol of NWO can be found here.

Nagoya Protocol

The Nagoya Protocol became effective on 12 October 2014 and ensures an honest and reasonable distribution of benefits emerging from the use of genetic resources (Access and Benefit Sharing; ABS). Researchers who make use of genetic sources from the Netherlands or abroad for their research should familiarise themselves with the Nagoya Protocol (http://www.absfocalpoint.nl). NWO assumes that researchers will take all necessary actions with respect to the Nagoya Protocol.

Termination and termination date

The termination date of a project is the date on which the last temporary appointment is terminated and after which the final report on project results and outcome has been provided to the NWO Domain AES office. The project leader then receives two final forms from NWO Domain AES to round off the project in terms of both content and funding. Unallocated credits cease to be valid after the end of the project.

Discontinuation

NWO Domain AES may discontinue a project before the official termination date if the obligations 'NWO Grant Rules 2017 version 2019' are not or are no longer fulfilled, or if the scientific quality of the research and/or utilisation of the results of the research are inadequate.

5 Guidelines for Applicants

5.1 Drawing up and submitting the proposal via ISAAC.

A pre- and full proposal can only be submitted to NWO Domain AES via the online application system ISAAC. **Proposals not submitted via ISAAC will not be considered**. Applicants are required to use the obligatory pre- and full proposal format (as available from the programme website) when submitting their proposal. A principal applicant must submit his/her application via his/her own ISAAC account. If the principal applicant does not have an ISAAC account yet, then this should be created at least **one (1) week** before the application is submitted to ensure that any registration problems can be resolved on time. If the principal applicant already has an NWO-account, then he/she does not need to create a new account to submit an application.

Submitting an application consists of two steps:
- Entering several additional details online in ISAAC. **Make sure you allow enough time for this!**
- Submitting the application form
  - Download the relevant application form (pre-proposal or full proposal) from the electronic application system ISAAC or from NWO Domain AES's website (on the grant page for this programme).
  - Save the completed application form as a PDF file and upload it in ISAAC.

The information entered in the application in either the pre-proposal or full proposal stage should be complete and correct. Incomplete forms or forms that exceed the maximum permitted length may lead to your application not being considered.

Required formats

The pre-proposal (sections 2 – 5) should not exceed three (3) pages in A4 format, excluding title page and list of publications. Providing supplementary information within the proposal and/or via added appendices is not allowed. Use font Calibri 9,5 and programmed profiles. The application should be in English. In Section 4.2 of the pre-proposal application form, additional sub-chapters may be added.

The **full proposal** (sections 2 to 6, both included) should not exceed six (6) pages in A4 format (minimum Calibri 9.5), excluding list of references, abbreviations and required appendices. Additional supplementary information is not allowed. The application should be in English. In Section 4.1 of the application form, additional sub-chapters may be added.

Required appendices for full proposal phase

Appendices to the full proposal application form must be added separately and in PDF format (without security). Required attachments:
- Completed (English language) form 'Data management section'.
- Letter of support from co-funding private partner (if applicable)
- Written declaration 'tenure-track' position (principal) applicant (if applicable).

Appendices should be submitted separately in PDF format (without protection). The required appendices together with the application form (full proposal) is regarded as the full proposal. Appendices other than the required appendices will not be shared with the Assessment committee, and are therefore not considered in the assessment procedure.

Technical questions about the use of ISAAC

For technical questions about the use of ISAAC please contact the ISAAC helpdesk. Contact details can be found in section 'Contact Information'.

5.2 Who can apply?

Main and co-applicants

On approval of the project, the main applicant becomes the project leader and bears ultimate

responsibility for the realisation of the proposed project. All co-applicants must play an active role (associate supervisor and/or daily supervision of researchers appointed to the project) in the realisation of the project and may be designated as sub-project leaders in the event of several participating research institutes.

Who can act as main and co-applicants?

- Assistant, associate and full professors with a tenured position at:
  - Universities in the Kingdom of the Netherlands;
  - University medical centres;
  - NWO and KNAW -institutes;
  - the Netherlands Cancer Institute (NKI);
  - the Max Planck Institute for Psycholinguistics in Nijmegen;
  - Dubble beamline at the ESFR in Grenoble;
  - NCB Naturalis;
  - Advanced Research Centre for NanoLithography (ARCNL).
- Researchers with a tenure track appointment. NWO Domain AES defines a tenure track appointment as an appointment for experienced scientific researchers with prospects of permanent employment and a professorship in due course. The tenure track appointment must be confirmed in writing by an official letter from the university and funded from structural resources. NWO Domain AES will verify that the appointment meets these conditions and that it is guaranteed for the term of the project.

Main and co-applicants with a part-time appointment

- Main applicants and co-applicants employed on a part-time basis should in any case have access to sufficient university facilities and budget to carry out the project properly.
- Main applicants and co-applicants should carry out NWO Domain AES research while they are working for the research institute. If this is not the case, the other employer should sign a waiver so as to guarantee knowledge ownership by NWO and the research institute(s).

Who cannot apply?

Main applicants and co-applicants with one of the following positions are **not** eligible to apply:
- Personnel with a zero-hour appointment;
- Personnel with a temporary employment contract (e.g. postdocs, research fellows);
- Emeritus professors;
- Personnel of Universities of Applied Sciences (UAS, 'HBO' in Dutch);
- Personnel of institutes with an applied or technological objective, such as TNO, the Large Technological Institutes (GTIs) and the non-university part of the Wageningen University and Research Centre (WUR);
- Personnel of a research institute funded by a public-private targeted grant;
- Personnel of foreign research institutes;
- Personnel working for industry or private organisations.

5.3 What can be applied for?

Project-specific costs

NWO Domain AES funds project-specific costs of:
1. personnel temporarily appointed to the project at the research institute;
2. materials (consumables, small instruments and aids, and domestic travel expenses);
3. foreign travel.

The research institute is responsible for co-funding from direct government funding and hence for the necessary infrastructure and the supervision of project workers.

If an (co-)applicant cooperates with other institutes not eligible for NWO Domain AES funding, such as TNO or a foreign university, the non-eligible institutes are responsible for their own costs.

5.3.1 Notes on costs of personnel temporarily appointed to the project at the research institute

Temporary personnel positions can be requested for:
- postdoc (PD);

- other SP (scientific personnel, including additional researcher, holders of a master degree (MSc), medical graduates);
- NSP (non-scientific personnel, including technical assistant).

Notes on temporary personnel positions

Temporary personnel positions can be requested for up to the maximum project duration (i.e. two years). State the job group, the length of the appointment, the part-time percentage and the associated amount. For each position, NWO Domain AES uses a predetermined fixed maximum rate per year of appointment (see www.nwo.nl/ttw-aanvrager). In determining these rates, NWO Domain AES adopts the rates laid down in the most recent 'akkoord overlaten werkgeverschap NWO/VSNU', with no supplement for the risk of unemployment. Under this agreement, the personnel rates for the positions are determined annually after agreement on the long-range forecast for personnel rates. For proposals under this call please adhere to the tariffs for personnel July 1st, 2019.

For postdoc, scientific personnel and non-scientific personnel positions, NWO Domain AES does not accept liability under the Dutch Unemployment Insurance Act if the term of appointment is less than 12 months and/or the candidate has more than 1 year's relevant work experience in a previous, similar appointment.

The research institute appoints the personnel and bears the customary responsibilities of an employer.

Notes on permanent staff

The salary or allowance paid to the applicant/co-applicant and the salary or allowance paid to others person with a permanent appointment or other permanent association with the institute where the research is to take place are **not eligible** for reimbursement. Exceptions to this are the temporary appointment to a project of 1) a technical assistant (NSP) or 2) a scientist with an 'appointment on a project basis'. An NSP with an existing employment contract at the research institute can temporarily be appointed against the standard NSP rates at the expense of an AES project, if this NSP has a specific special expertise that is necessary for realising the research proposed. A scientist with an 'appointment on a project basis' at the research institute can temporarily be appointed against the standard scientific personnel (SP) rates at the expense of an AES project. The scientist concerned may not be registered as an applicant or co-applicant at AES/NWO. NWO Domain AES accepts no liability under the Dutch Unemployment Insurance Act in this case.

Notes on secondment

Temporary researchers are appointed to the research institute where the research is to be realised. Because NWO Domain AES imposes the condition that the majority of knowledge development must take place at the research institute, the secondment of university researchers to a company or other research institute is permitted only for a limited period, i.e. up to 50% of the extent of the appointment. This requires written permission from NWO Domain AES in advance. A secondment agreement shall be concluded.

Where the need arises, an applicant can submit a reasoned request to the AES office to grant leniency with regard to the 50% limit. Criteria for this are 1) there must be a need to use the infrastructure of the external party, 2) there must be a sufficient academic environment present at the external party for interaction with and supervision of the researcher and 3) the project leader and/or supervisor of the researcher must also be present at the external location concerned for some of their time.

5.3.2 Notes on costs of materials and domestic travel

NWO Domain AES funds consumables, small instruments and aids, and domestic travel expenses. The amounts entered in the budget are inclusive of Dutch VAT.

Notes on Material credit

Costs which ***CAN*** be charged to material credit:
- Materials which no longer have an economic value after use. This concerns consumables, small instruments and aids;
- Specified compound items. Fixed instalments or rates in particular (e.g. bench fees and fees for standard analyses) must be substantiated. Within the rates accepted by NWO Domain AES, only the consumables costs can be charged to NWO Domain AES;
- Costs of domestic travel;

- Costs of project-specific courses for NWO Domain AES researchers which are necessary for the conduct of the research;
- Posters for disseminating knowledge at conferences and symposia;
- Costs for the use of cleanrooms insofar as these fall under the cleanroom regulation (see www.nwo.nl/ttw-aanvrager);
- Costs for research activities executed by dedicated specialists employed at research institutions not eligible for NWO funding can be limitedly reimbursed. **Please contact the AES office**.

Costs which ***CANNOT*** be charged to material credit:
- 'Miscellaneous' or 'unforeseen' items, unspecified bench fees;.
- Patent costs. Where appropriate, NWO Domain AES will consider the extent to which it will bear such costs;
- Costs of all types of publications or costs of purchasing books and/or journals;
- Costs of printing a thesis. A separate reimbursement scheme exists for this (see www.nwo.nl/ttw);
- Costs of general courses which form part of researchers' generic education (e.g. English, presentation skills, literature searching, laboratory animal science, use of isotopes);
- Costs of desktop computer, laptops, notebooks or similar for administrative purposes (text and data processing) and costs for computer use;
- Generic software. NWO Domain AES assumes that generic software is available via campus licences,
- Costs associated with the use of computing facilities at SURFsara. If necessary, these costs can be requested from the Netherlands eScience Center (NLeSC) in Amsterdam;
- Costs of using existing infrastructure (depreciation charges), salary costs of permanent personnel, accommodation costs, overheads and administrative and technical support, where these are part of the research institute's customary package of facilities;
- Costs (excluding material costs and cleanroom regulation) of university facilities (e.g. glasshouse space, laboratory animal facilities, specialist research facilities).

5.4 Notes on User, co-funding and letters of support

See also 'Specific requirements of the programme'.

User

Co-funding of proposals submitted to this call is not required. However, in case a private partner (company (SME or Industry)) decides to, or if applicants wish them to contribute to a proposal, after award of the project, the co-funding partner will be designated a user in the project. The user is requested to be actively involved in project meetings to stimulate application of the results. Only one (1) private partner is allowed to participate in a proposal, regardless of whether they provide co-funding.

Co-funding

If applicable, co-funding is calculated as the financial (in cash) and in-kind contributions of the user. In kind contributions are relevant capitalised personnel and/or material contributions from the user (see below). The level of co-funding (in cash and in kind) as well as the nature and relevance of co-funding (in kind) will be subject to assessment by the Assessment Committee.

Commitment of a user, as well as their contribution to the project (if applicable) should be confirmed in a letter of support (see below). Relevant private partners aim to contribute to the goal of the programme, i.e. development of new antibacterial compounds and/or alternatives to antibiotics, as opposed to developing for instance 'enabling technologies'. The Assessment Committee is instructed to take this into consideration when evaluating the proposal.

Definitions

- Total project costs: necessary financial resources plus in-kind contributions;
- Financial contribution: Financial contributions are used to cover part of the project costs and so, together with the contribution from NWO Domain AES, constitute the necessary financial resources;
- In kind contributions: In-kind contributions means capitalised personnel and/or material contributions from user;
- NWO Domain AES contribution is defined as total project costs minus financial contribution from user.

5.4.1 Notes on Criteria relating to co-funding

- NWO Domain AES uses the financial co-funding to cover part of the project costs. After a project is approved, NWO Domain AES sends an invoice to the user who has pledged a financial contribution. Once the funds have been received, they are allocated to the project;
- NWO Domain AES accepts personnel input and material contributions as co-funding on the condition that these are capitalised and that they form an integral part of the project. This should be made clear in the description and planning/phasing of the research;
- NWO Domain AES is the main funder of the projects. Project applications where the co-funding from the user exceeds the amount to be borne by NWO Domain AES will not be considered;
- NWO Domain AES assumes that the provider of co-funding has an interest as user and therefore as applier of the project results outside science. The co-funder therefore is always asked to actively participate in (mid-term) project reporting and (Programme) meetings;
- Government agencies can play various roles in AES projects, namely: (1) as a research partner (without entitlement to AES funding), (2) as a subcontractor of a specific assignment (at market rate) or (3) as a user. Government agencies may act as user under the same conditions as private user;
- The co-funding to be provided by the user must be confirmed in a letter of support (see below).

See for programme specific requirements the sections 'Letters of support' and the 'Notes on Intellectual Property & Publication arrangements' later in this document.

Notes on Criteria relating to in-kind co-funding

Part of the project activities may be conducted by third parties. A condition is that the expertise provided in the form of man-hours is not already available at the research institute(s) and is used specifically for the AES project. For personnel support by third parties, NWO Domain AES applies fixed rates in order to capitalise the number of man-hours used (up to 1400 direct hours/year/fte) for a senior or junior researcher. For the current rates, see www.nwo.nl/ttw.

- For pledges of material resources, charge the cost price. Commercial rates are not accepted. For pledges of equipment, take previous depreciation and intensity of use into account;
- Pledges in the form of supplies of services are possible only if the service can be itemised as an identifiable **new** endeavour. The service should not already be available at the research institute(s) realising the research. Applicants may wish to claim services already supplied (such as a database, software or plant lines) as in-kind co-funding. Acceptance is not automatic in such cases. Contact NWO Domain AES about this. Further consultations will take place to decide whether a specific value can be determined for this supply of services.

NOT permissible as the co-funding

NWO Domain AES guards against the improper mixing of funding sources: co-funding can never come from direct or indirect (NWO, KNAW) government funding. As a result, co-funding can also never come from the research institute of the (co-) applicant(s) or from institutes which are themselves eligible to apply to NWO Domain AES.

- Discounts on (commercial) rates for materials, equipment and/or services, for example;
- Costs relating to overheads, supervision, consultancy and/or participation in the user committee;
- Costs of services that are conditional. No conditions may be imposed on the provision of co-funding. Nor may the provision of co-funding be contingent upon reaching a certain stage in the research plan (e.g. go/no-go moment);
- Costs which are not paid by NWO Domain AES (e.g. costs relating to the exploitation of the research results, service costs equipment);
- Costs of equipment if one of the (main) aims of the proposal is to improve this equipment or to create added value for it.

5.4.2 Letters of support

A letter of support is obligatory if co-funding is provided by the user. NWO Domain AES advises applicants to ensure that the user pays particular attention to endorsing the importance of the use of project results for their operations. The letter of support should satisfy the following requirements:

A. General requirements

- Letters of support must be printed on the letter paper of the co-funder;
- Letters of support must be recent (i.e. preferably not older than 6 months);
- Letters of support are addressed to the project leader;
- Letters of support must be written in English;

- The address on the letter is complete and correct;
- Letters of support must be signed by an authorised signatory;
- The cash contribution stated in the letter is exclusive of Dutch VAT and paid to NWO Domain AES plus Dutch VAT (21%).

B. Specific requirements

- Brief description of the company and the core business (type of company, size, which service, products);
- A statement that the company is interested in and will commit itself to the project;
- An explanation as to why the company is interested in the project results. How does this project fit in their strategy?
- A brief explanation as to why this particular research group and proposal are receiving support;
- What the company will contribute in concrete terms (incl. capitalisation) and why this fits in the proposal/planning;
- Further specification of the in-kind support, both hours (number and/or tariff applied) and materials (numbers; cost price; tariff; percentage that can be attributed to the project, etc.);
- A clear statement that the company provides the contribution described without additional conditions.

C. Declaration and signing by the User

In the final paragraph of the support letter should include the following statements from the company and the representative signs for this:
- The company states that it has read the proposal;
- The company states that it will actively participate in the project team;
- The company states that it agrees to the 'NWO Grant Rules 2017 version 2019', the 'Guidelines Users' Committee NWO domain TTW 2017' and Programme-specific IP arrangements, in particular the guiding principles on socially responsible licensing.

If so desired the company can satisfy the requirements by submitting together with the letter of support a checked off and signed list of the conditions stated under A, B and C.

Letters of support are unconditional and do not contain any opt-out clauses!

The amounts stated in the letters of support must correspond with the amounts stated in the budget presented in the application. A copy or scan of the letter will suffice for the submission of a proposal. NWO Domain AES will not approach persons or organisations who have signed letters of support to act as referees (see also NWO Code for Dealing with Personal Interests).

After the proposal has been awarded funding NWO Domain AES will request a confirmation of the co-funding ("confirmation obligation third parties") and in relevant cases will record any further arrangements in an agreement.

5.5 Notes on Intellectual Property policy (IP policy) & Publication arrangements

NWO Domain AES facilitates the transfer of knowledge between the technical sciences and users. In this process it is important that a responsible approach is taken with regard to research results in general, and patentable inventions and discoveries in particular. NWO Domain AES's aim is firstly to exploit and publish the results of research as widely as possible, whilst retaining the possibility to establish IP rights and to subsequently transfer these rights to user(s) or grant a licence to user(s) for these and, secondly, to stimulate collaboration between researchers and various external companies.

NWO Domain AES adheres to a set of rules concerning Intellectual Property (IP) that support NWO Domain AES's mission. NWO Domain AES's policy is in line with the IP policy adopted by the Dutch Council Research Science [*Nederlandse Organisatie voor Wetenschappelijk Onderzoek*, NWO] and with the '*Rules of Play for public-private collaboration*' as presented to the Lower House of the Dutch Parliament on 25 June 2013. A detailed description of these rules can be found in Appendix 1.

Arrangements with regards to newly developed IP resulting from the projects funded under this Call for proposals all need to adhere to the standard NWO Domain AES Intellectual Property policy (also known as 'Option 1'). For the avoidance of doubt: 'Option 2', i.e. the option sometimes provided by NWO Domain AES to applicants and their partners to make their own IP arrangements, is **not** available for proposals submitted in this Call for proposals.

Programme-specific IP&P conditions: Available and accessible / fair and affordable price

As described above in the chapter 'Specific requirements of this Call', programme-specific conditions with regard to IP developed in projects that are funded under this Call for proposal apply. Any IP arrangements concerning new results generated in projects that are awarded under the NACTAR Programme are required to adhere to the guiding principles on socially responsible licensing, including the elements "availability" and "fair and affordable price". Please find a detailed explanation of the NWO Domain AES IP & P guidelines further in Appendix 1.

Background or sideground knowledge/IP generated outside the NACTAR Programme that is contributed to the project by the applicant is exempt from this demand, however, applicants and consortium partners are encouraged to take the above into consideration. For the avoidance of doubt, however, the guiding principles shall always apply to new results generated in projects awarded under the NACTAR Programme.

5.6 Notes relating to the application forms

Please contact the NWO Domain AES office should you have questions concerning the formats. The proposal, both in pre-proposal and in full proposal stage, should be written in English. Please note that a pre-proposal does not require all the sections mentioned below. Section numbers of pre-proposal form are indicated with "(= section xx in…)" where applicable and different from full proposal form.

1. Contact details

1.1. Main applicant

The name and address of the main applicant in English. State the additional information, including English name of the organisation/division of the organisation, percentage of full-time appointment and confirmation of permanent employment.

1.2. Co-applicant(s)

State the name and address of the co-applicants, in English. Also state the additional information, including % of full-time appointment and confirmation of permanent employment.

1.3. Partner (if applicable; = section 3 in pre-proposal)

State the contact details (name of private partner/company and person to contact, address, telephone number, e-mail address) as well as the type of organisation (e.g. Industry, SME) and the core business of the private partner wishing to participate in (and/or contribute to) the proposed project.

2. Summary

The summary should be clear to the members of the Assessment Committee who may not be a specialist in the field of your proposed project. It is therefore vital that this section is worded clearly and concisely, so as to be convincing to committee members. In addition, the summary may be used by NWO Domain AES for publication purposes; applicants should be aware of this in their wording of this section.

2.1. Title

State the title of the project and an abbreviated title, if any.

2.2: Abstract

Add a general summary for NWO Domain AES's website (max. 50 words; be aware of risks with respect to intellectual property). Use this summary online in ISAAC.

2.3. Key words

State the specific keywords for the research and specialist area, including popular scientific terms.

3. Composition of the team

State the composition of the team which will realise the project and the distribution of tasks and

responsibilities. The Assessment Committee must be able to infer from the contents of this section that the people involved in the project bring relevant expertise in order to achieve the project's goals:

- If more than one research institute is participating in a project, indicate the intended sub-project leaders in addition to the project leader.
- If more than one research institute and/or research group is involved in the project then also indicate which of the co-applicants per research institute and/or research group is the research leader and who is responsible for supervising the researchers.
- In the case of a part-time appointment of a (co-)applicant which is less than 0.4 fte, the proposal should indicate which of the permanent staff is responsible for the day-to-day supervision of the project workers.
- The project leader is responsible in all cases for coordination and communication between the participating institutes/research groups/ researchers.
- In the case a private partner (user) is involved: describe why their participation in the project is relevant with regard to achieving the projects' results.

4. Description of the proposed project

This section should contain sufficient information to enable the Assessment Committee to assess the quality of the proposal. Make sure the assessment criteria are addressed fully in the respective sections.

4.1. Background and (pre)clinical approach

Describe the underlying scientific basis and the content of the project, included the (pre)clinical phase of the study. Indicate the methods and techniques to be used to tackle the problem, the knowledge already available, the state of the art including innovative and unique approaches, what has still to be developed and the instruments or models to be used to that end. It is not sufficient to state only the scientific question. Sub-headings may be introduced to facilitate reading.

4.2 Relevance of the project and contribution to NACTAR Programme goals

Describe how the project is relevant to achieving the NACTAR Programme and NADP research agenda goals as described in this Call for proposals.

4.3. Commercial potential and envisaged application of the results

Describe the commercial potential of the projects' results as well as their envisaged application. If applicable, describe here the background of the commitment of the private partner as well as the IP strategy.

4.4. Existing infrastructure

Specify the research institute(s)/department(s)/ research group(s) where the research will physically take place. This information is used to determine whether the research can be realised at the research institute(s) mentioned. The available infrastructure includes furnished laboratory space and necessary equipment.

4.5. Time plan and division of tasks (= section 5.1 in pre-proposal[1])

Describe the proposed project planning over the years. Indicate the phasing and give a clear description of the step-by-step plan (subsidiary aims and/or ultimate aims) and the intended results. Describe how you will manage your project towards reaching the project goals and obtaining the intended results. If different lines of the project are dependent on each other, indicate this. A schematic representation of the research planning (e.g. including deliverables and/or milestones) is compulsory. The overall duration of the project plan may not exceed two (2) years.

4.6. Request for support elsewhere

State whether funding has been requested elsewhere for this proposal or parts thereof. If so, indicate the grant provider(s) in question and the status of that application or those applications at the time of submission to NWO Domain AES.

[1] *Note on pre-proposal: an outline suffices at this stage.*

5. Intellectual property

State all information relevant to the proposal in relation to NWO Domain AES's IP policy, and the programme-specific IP guidelines as described in this Call for proposals (e.g. Appendix 1). Providing the requested information is compulsory.

5.1. Patents (IP position) and contracts

1) Give a summary of patents held and/or patent applications made by intended parties to the project in the field of the proposal. Indicate whether the patents and/or patent applications are in the name of the research institute(s) involved or in the name of third parties. If the research institutes involved have relevant patents, indicate whether agreements have been reached in this respect with third parties. A reference to paragraph 9.3 may be included.
2) Indicate whether there are any patents and/or patent applications which obstruct the utilisation of the intended project results. If such an obstacle exists, explain whether there is still sufficient likelihood of protecting the intended project results by means of a patent.
3) If the patenting of research results is not expedient, explain why not.
4) State whether there are any existing contracts (including material transfer agreements, licences, cooperation agreements) with third parties in relation to the subject of the research, and whether or not these may obstruct the utilisation of the projects' results.

5.2. IP strategy

Describe here how the IP that is available to the project team will be used, and how any newly developed IP will be protected.

6. Financial planning

Justify the need for both the personnel credits requested and the necessary materials and investments in equipment. This section should contain sufficient information to enable an expert reviewer to form an opinion on the requested budget.

6.1. Personnel positions

State the necessary temporary personnel positions. Temporary personnel positions can be requested for: postdoc (PD), other SP (scientific personnel, including additional researcher, holders of a masters degree, medical graduates), NSP (non-scientific personnel, including technical assistant). Please use personel tariffs date July 1st, 2019.

6.2. Consumables

In accordance with the standards that apply within your research institute, specify the costs of consumables, small instruments and aids, and domestic travel expenses. The amounts entered in the budget are inclusive of Dutch VAT.

6.3. Contribution from user (if applicable)

State the financial, personnel and/or material co-funding made available by the user for the purposes of the project, if applicable. Make sure the contribution adheres to the AES criteria as described in this Call text, and is confirmed in a letter of support.

6.4. Cost Breakdown (= section 5.2 in pre-proposal[2])

Complete the cost breakdown, stating any financial contribution(s) and/or capitalised contribution(s) from the user (if applicable).

- Total project costs is sum of sections 6.1, 6.2 and 6.3
- Make sure that the capitalised contributions in the budget (6.3) and the letter of support agree.
- The main applicant's research institute concludes a funding agreement with NWO.

7. Declaration and signing by the applicant (= section 6 in pre-proposal)

After completing the sections of the application form please read the declarations carefully. Check the

[2] *Note on pre-proposal: an outline suffices at this stage. A table is included for your convenience.*

boxes for acceptance and declaration. Make sure the main applicant signs the application form before uploading to ISAAC (as PDF).

8. Abbreviations and acronyms

It is important that Assessment Committee members are able to read the proposal easily. Abbreviations and acronyms should therefore be explained at least once. This can be done in the text itself or in a separate list. Keep the use of abbreviations in summaries to a minimum.

9. References (= section 7 in pre-proposal)

9.1. Selection of key publications research group

State the key publications of the research group(s) in relation to the proposal. Also state any relevant published patents.

9.2. List of publications cited

State the publications cited (preferably without *et al*). Identify those in which members of the research group(s) submitting the application are involved, by the use of a bold font.

9.3. Patents

State the relevant patents in relation to the proposed project. State number, title, patent holder etc.

Finally

In the event of uncertainties or costs to be claimed which are not mentioned in this document, NWO Domain AES recommends that you contact the AES office before submitting the application.

6 Contact information

NWO Domain Applied and Engineering Sciences

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Technical questions about the online application system ISAAC

For technical questions about the use of ISAAC please contact the ISAAC helpdesk. Please read the manual (tab 'Help') first before consulting the helpdesk. The ISAAC helpdesk can be contacted from Monday to Friday between 10:00 and 17:00 hours CE(S)T on +31 (0)20-3467179. You can also submit your question by e-mail to **isaac.helpdesk@nwo.nl**. You will then receive an answer within two working days.

Links

- Ministry of Health, Welfare and Sport
  https://www.government.nl/ministries/ministry-of-health-welfare-and-sport
- Netherlands Organisation for Scientific Research (NWO):
  http://www.nwo.nl/
- NWO Domain AES
  https://www.nwo.nl/over-nwo/organisatie/nwo-onderdelen/ttw
- NWO Domain Science
  http://www.nwo.nl/en/about-nwo/organisation/nwo-Domains/enw
- NWO Grant Rules 2017, version 2019
  https://www.nwo.nl/en/documents/nwo/legal/nwo-grant-rules-1-may-2017
- NWO Guidelines Users' Committee 2017
  https://www.nwo.nl/en/documents/nwo/innovational-research-incentives-scheme---brochure-guidelines-users%E2%80%99-committee-nwo-domain-ttw-2017
- Topsector Chemistry: Knowledge & Innovation Agenda (in Dutch):
  http://topsectorchemie.nl/kia
- Topsector Chemistry: Roadmap Chemistry of Life (in Dutch):
  http://www.topsectorchemie.nl/chemistry-of-life
- Netherlands Antibiotic Development Platform (NADP):
  http://nadp.nl/
- Netherlands Centre for One Health (NCOH):
  http://ncoh.nl/
- Netherlands Organisation for Health Research and Development (ZonMW) research programme on antimicrobial resistance:
  https://www.zonmw.nl/en/research-and-results/one-health/programmas/programme-detail/priority-medicines-antimicrobial-resistance/
- Innovative Medicines Initiative overview of ongoing projects:
  http://www.imi.europa.eu/content/ongoing-projects
- EU Joint Programming Initiative on Antibiotic Resistance (JPI AMR):
  http://www.jpiamr.eu/
- World Health Organisation publication on important antimicrobial target organisms:
  http://www.who.int/mediacentre/news/releases/2017/bacteria-antibiotics-needed/en/
- EMA Guidelines on early stage clinical trials:
  https://www.ema.europa.eu/en/strategies-identify-mitigate-risks-first-human-early-clinical-trials-investigational-medicinal
- EMA/ICH Note for Guidance on General Considerations for Clinical Trials (CPMP/ICH/291/95):
  https://www.ema.europa.eu/en/documents/scientific-guideline/ich-e-8-general-considerations-clinical-trials-step-5_en.pdf
- Socially responsible licencing (Dutch: Maatschappelijk Verantwoord Licentieren)
  https://www.nfu.nl/actueel/nfu-stelt-principes-op-voor-maatschappelijk-verantwoord-licentieren
- ISAAC:
  https://www.isaac.nwo.nl; *An ISAAC manual can be found in ISAAC (tab 'Help')*
- ISAAC helpdesk:
  isaac.helpdesk@nwo.nl
- NWO Code for Dealing with Personal Interests:
  https://www.nwo.nl/en/documents/nwo/legal/code-for-dealing-with-personal-interests
- NWO Data Management Policy
  https://www.nwo.nl/en/policies/open+science/data+management
- Information on NWO Domain AES standards, e.g. salary, personnel cost as co-funding etc.:
  http://www.ttw.nwo.nl/en/content/applicant
- Nagoya Protocol:
  https://www.cbd.int

APPENDIX 1: IP ARRANGEMENTS

See also 'Notes on IP' above, for more background information on the IP and Publication guidelines that are applicable to projects funded under this Call for proposals.

A1.1 Programme-specific Intellectual Property & Publication conditions

Specifically for this programme the IP arrangements should adhere to the guiding principles on **socially responsible licensing**, and reflect that the to be developed products will become **available and accessible** for the healthcare system for a **fair and affordable** price. The arrangements should at least contain provisions that ensure that these criteria will have effect in subsequent agreements related to the research and/or the commercialisation of results deriving thereof. Next to this all prices, percentages and distribution of IP-rights related to the commercialisation of (future) products, need to be underpinned. NWO Domain AES and the Ministry of Health will jointly assess and approve the arrangements.

Background or sideground knowledge/IP generated outside the NACTAR Programme that is contributed to the project by the applicant is exempt from this demand, however, applicants and consortium partners are encouraged to take the guiding principles on **socially responsible licensing** into consideration. For the avoidance of doubt, however, the guiding principles shall always apply to new results generated in projects awarded under the NACTAR Programme.

A1.2 NWO Domain AES makes Intellectual Property & Publication arrangements

NWO Domain AES takes the lead in the negotiations on the subject of new IP&P arrangements. Once a project has been approved, any user that contributes to the project receives a letter from NWO Domain AES informing them that the project has been awarded to the knowledge institution. In addition, NWO Domain AES asks the user to sign the letter to (re)confirm its participation in and contribution to the project, and to confirm that they adhere to the Programme's and NWO Domain AES's IP policy.

The main principles of NWO Domain AES's IP policy are as follows:

Ownership of the results of research

The results of research carried out by the research institute(s) in the context of a AES project are owned jointly by the participating institute(s) and by NWO.

- Ownership of the results of research that are generated exclusively by user(s) in the context of a AES project is vested in the user(s) in question. The user(s) will allow NWO Domain AES and the research institute 'freedom to operate'.
- The results of research that are generated jointly by the research institute(s) and the user(s) in the context of a AES project are owned jointly by the participating institute(s) and by NWO. If the co-inventing user has itself provided more than 10% of the project funding in the form of personnel, that user will be granted a non-exclusive, royalty-free and non-transferable licence for the use of the invention, patent or patent application.
- Existing IP rights continue to be vested in the holder(s) of such right who contribute these rights to the project. Insofar as it is possible under the law, and insofar as it is not detrimental to the reasonable commercial interests of the right holder, this/these right holder(s) will facilitate, at their own discretion and in all reasonableness, a freedom to operate.
- 'Freedom to operate' means that the holder of the intellectual property right grants licences to others within the project:
    - insofar as legally possible;
    - insofar as necessary for the project (without charge);
    - insofar as necessary for the exploitation of the results of the research and possible concomitant results (at a fair market price);
    - insofar as such freedom to operate is not detrimental to the reasonable commercial interests of the right holder.

Protection of research results, confidentiality and publications

NWO Domain AES attaches considerable importance to the protection of knowledge in the process of knowledge transfer. Users admitted to the user committee, undertake to maintain confidentiality with regard to the research results. However, parties can agree – either prior to or during the lifecycle of the project – that protection of the knowledge generated by the project can be suspended if that would be beneficial to the commercial exploitation of the expertise and intellectual property generated by the project.

Research results that are not susceptible to IP protection, and not subject to a written know-how licence, can be used freely by all parties. The researcher is obliged to report any invention to NWO Domain AES immediately. Draft publications are submitted to the user committee by NWO Domain AES; the committee is asked whether, in their opinion, the publication contains a patentable invention and/or whether there are utilisation opportunities. If knowledge protection measures need to be taken, such as the submission of a patent application, NWO Domain AES may decide to suspend the publication for up to 9 months.

Commercial usage rights to results that accrue in part or in whole to NWO Domain AES and the research institute(s)

- Contribution 0–10%
  A user who contributes less than 10 percent to the costs of the research project by way of in-kind or in-cash resources will be the first party to receive information about the results of the research. Companies are at liberty to use the results generated by the research for internal, non-commercial purposes.
- Contribution between 10% and 30%: Right of option
  A user who contributes more than 10 percent to the costs of the research project by way of in-kind or in-cash resources is also entitled to a right of option on a licence to, or the transfer of the results of the research when full or joint rights are held by NWO and the research institute(s). If a user exercises this option, the transfer of an exclusive or non-exclusive licence will be effected against payment of a fair market price (see below). If multiple users are eligible for an option, an agreement will be made as to the scope of their usage. If this is not possible, the contributing users will be granted a joint option on a semi-exclusive licence.
- Contribution between 30% and 50%: Right of option on a commercial NERF right
  A user who contributes more than 30 percent to the costs of the research project by way of in-kind or in-cash resources will also have the same rights as a user who contributes more than 10 percent. If the user exercises his right of option, that user is entitled to a non-exclusive, royalty-free (NERF) and non-transferable commercial right of use.
  If required, NWO Domain AES or the research institute(s) will oversee the administration of the patent application process for the first 30 months following the patent application. Before the end of that period, NWO Domain AES, the research institute and the user in question will make arrangements about the further handling of the patent application.
  If one or more users within the project are eligible for an option, an agreement will be made as to the scope of the option on an exclusive licence. If this is not possible, the contributing users will be granted a joint option on a semi-exclusive licence.
  The total value of co-funding of any AES project may not exceed 50 percent.
- The percentage is calculated by comparing the entire contribution made by the private party (in-kind plus in-cash) against the contribution from NWO Domain AES plus all other in-kind and in-cash contributions.

Combining contributions from companies

Companies have the opportunity to combine their contributions within a single AES project so as to achieve a more favourable cumulative percentage. The companies are then, as a group, eligible for the abovementioned rights (right of option and/or non-exclusive commercial right of use). To be eligible for such aggregation, it is a condition that the companies in question notify NWO Domain AES of this in writing. This letter must also appoint an official secretary/a representative who will be responsible for negotiating with NWO Domain AES on behalf of the parties concerned as to how the option will be exercised. The letter must be signed by all companies involved. It should, preferably, be submitted to NWO Domain AES together with the proposal or, if not, within six (6) months of the approval of the project.

Patent costs

The following provisions apply if the user deems it desirable that a patent application be submitted:
- The patent application is submitted in the name of NWO and the research institute(s) where the invention or discovery takes place.
- The user bears the costs of the patent. The patent costs are not offset in the calculation of a fair market price.
- If there are multiple licensees, the patent costs will be shared among them.

Licensing

The right to use or apply research results is acquired through a licence, transfer agreement or know

how agreement. In all cases, a licence agreement or transfer agreement will contain provisions concerning:

- exclusivity or non-exclusivity;
- royalty-free research and education licence for NWO and the research institute(s) concerned;
- determination of a fair market price (with the exception of a NERF licence when contributions exceed 30%);
- anti-freezer clause or best endeavours obligation concerning application or commercialisation
- reporting obligations;
- indemnification against liability on the part of NWO and the knowledge institute(s);
- market price + discount arrangements.
  The market price will be determined by negotiation between the parties; a record will be kept of these negotiations. In determining the fee to be paid, use can be made of the 'market-based approach' (i.e. market comparison), the 'income-based approach' (i.e. what income is expected), and the 'cost-based approach' (i.e. what has it cost to achieve the research results). The services of an impartial expert can also be called upon, or a combination of the above methods can be chosen. The user will be entitled to a discount on the fair market price fee which is related to the level of the contribution provided towards the costs of the research project.
- Income received from transfer or licensing will be disbursed to the research institutes for further research.

Provisions ensuring compliance with the guiding principles on **socially responsible licensing** use or exploitation of results. Should any obstacles to the implementation of NWO Domain AES's IP policy emerge, NWO Domain AES will impose additional conditions. If it emerges during the course of the project that the project leader has failed to notify NWO Domain AES about such relevant information, NWO Domain AES may suspend the project until the obstacles concerned have been removed. NWO Domain AES may request access to contracts and/or patents in this respect. Contracts must not be in conflict with NWO Domain AES's IP policy. If it emerges that NWO Domain AES cannot have free access to the results of the AES research, NWO Domain AES may decide not to award or to discontinue the project.

APPENDIX 2: SPECIMEN FORM 'DATA MANAGEMENT'

A2.1 Notes on Data management section

NWO wants to contribute to the development of good data management by asking researchers to make all relevant data sustainably available for reuse. Therefore in the data management section, researchers will be asked before their research starts to think about how the data collected should be ordered and categorised such that it can be made freely available. Researchers will often need to take measures to this effect during the production and analysis of the data.
NWO understands 'data' to include collected, unprocessed data as well as analysed, generated data. This includes all conceivable forms of digital and non-digital data (such as samples, completed questionnaires, sound recordings, etc.).

NWO only requires the storage of data that are relevant for reuse. NWO assumes that within disciplines there are widely held opinions about which data are relevant for storage and reuse. Research results should be stored in such a way that they can be retrieved and reused in the long term, also by researchers in disciplines and organisations other than those in which the research took place. The operating principle is that all stored data are, in principle, freely accessible and that access is only limited if aspects such as privacy, public security, ethical limitations, property rights and commercial interests require that.

The costs of data management are eligible for funding and should be included in the project budget. Important factors that determine the costs are:
- the type of data;
- the capacity needed for storage and backup;
- the amount of manual work needed to allocate metadata and the compilation of other documentation such as codebooks and the queries used in the statistical package;
- the extent to which the data needs to be protected;
- the hiring in of external data management expertise or other expertise.

With the data management section NWO mainly wants to raise awareness about the importance of responsible data management. The section is therefore not included in a committee's decision about whether a proposal should be awarded funding or not. NWO Domain AES does, however, submit this section to the Assessment committee for advice. After a proposal has been awarded funding the researcher should elaborate the section into a data management plan. For this, applicants can make use of the advice they have received.

A2.2 Questions Data management section

1. Will data be collected or generated that are suitable for reuse?
   Yes: Then answer questions 2 to 4
   No: Then explain why the research will not result in reusable data or in data that cannot be stored or data that for other reasons are not relevant for reuse
2. Where will the data be stored during the research?
3. After the project has been completed, how will the data be stored for the long-term and made available for the use by third parties? To whom will the data be accessible?
4. Which facilities (ICT, (secure) archive, refrigerators or legal expertise) do you expect will be needed for the storage of data during the research and after the research? Are these available?[3]

[3] *ICT facilities for data storage are considered to be resources such as data storage capacity, bandwidth for data transport and calculating power for data processing.*

APPENDIX 3: SCOPE OF THE NACTAR PROGRAMME

A3.1 Topics which are welcomed within this call for proposals

1. Development of novel antibacterial lead compounds

- Novel antibiotic (sub-)classes
- Novel antibiotics of known classes of natural products, e.g. polyketides (PKS), non-ribosomal peptides
- (NRPS), β-lactams, ribosomally synthesized post-translationally modified peptides (RiPPs)
- Screening of underexplored natural resources; harnessing biodiversity
- Genomics-based approaches including heterologous gene expression
- Synthetic antibiotics, bioinspired compounds, structure-based design
- Novel molecules that specifically target resistance mechanisms (such as clavulanic acid that inhibits β-lactamases)
- Synergistic action between two compounds that enhance activity and reduce toxicity and rate of resistance development
- Novel molecules (or concepts) that target biofilm formation and eradication
- Generation of lead compounds for preclinical testing (including studies on pharmacokinetics and pharmacodynamics (PK/PD), toxicity etc; go beyond 'hit'-identification
- Novel chemical classes (from natural sources or via semi-synthesis)
- Activation of cryptic biosynthetic gene clusters for antibiotics.
- Derivatives of existing (biologically active) molecules which require more than incremental improvement (novelty)
- Structure-based design
- Mode of action studies complementary to drug development

2. New Antibacterial Therapies

- Novel concepts or innovative combinations
- Immunotherapy
- Studies on derivatives of existing approaches which require more than incremental improvement (novelty)
- Alternatives to antibiotics (e.g. phage therapy) and new interventions
- Generation of new leads for preclinical testing (including studies on pharmacokinetics and pharmacodynamics (PK/PD), toxicity etc; go beyond 'hit'-identification
- Target development, provided that specific known targets are addressed
- Anti-biofilm therapies
- Host-directed therapies
- Design therapy includes prevention/ counteracting antibiotic resistance
- Screening of novel natural resources; harnessing biodiversity
- Mode of action studies complementary to drug development
- Unconventional approaches not mentioned but with strong potential to lead to solutions to treat infectious diseases

A3.2 Topics which are not considered within this call for proposals

- Proposals with the **sole** aim of:
  - development or improvement of vaccines
  - development or improvement of diagnostic tools
  - development or improvement of enabling technologies
  - development of phage therapy in general (as opposed to: developing a specific phage therapy directed at a specific (type of) infection)
  - fundamental research on vital biological processes in bacteria which may in time identify potential drug targets (e.g. cell division, membrane transporters, protein biosynthesis etc.)
  - identification of potential drug targets without lead compound development, e.g. by library screening for potential drug targets
  - (fundamental) research on 'mode of action' of a potential therapy or drug molecule
- Proposals focusing on:
  - antibiotic resistance (AMR) in the sense of monitoring and/or regulation
  - surveillance of antibiotic use
  - organisms other than bacteria (i.e. fungi, parasites, viruses, insects, crops/plants, pests)
  - development of biocides and disinfectants
  - development of conventional immunomodulatory compounds
  - crop protection
  - veterinary use alone

- ‘alternative therapies’ as in non-conventional ‘alternative medicine’, molecules/compounds derived from protected/endangered sources, homeopathy, herbal medicine, complex often undefined mixtures of natural products etc.

When in doubt if your proposal would fit in the scope of the Programme, we urge you to contact the NWO Domain AES Programme office well ahead of the deadline for submission.

Applicants who have an interest in these topics are invited to apply for a grant in the NWO Domain AES Open Technology Programme.

APPENDIX 4: ELIGIBILITY OF (PRE)CLINICAL PHASES

This call for proposals aims to bring newly developed antibiotic compounds, products and/or alternative treatments to the stage of (pre)clinical testing and activities may consist of (parts of) preclinical, phase 0, phase 1 or early stage phase 2 clinical study with clearly described (clinical) end-points.

The intended approach must adhere to criteria from the European Medicines Authority (EMA) and/or the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH).

Early non-clinical studies should provide sufficient information to support selection of the initial human dose and safe duration of exposure, and to provide information about physiological and toxicological effects of a new drug.

Study **endpoints** are the response variables that are chosen to assess drug effects that are related to pharmacokinetic parameters, pharmacodynamic measures, efficacy and safety. A primary endpoint(s) should reflect clinically relevant effects and is typically selected based on the principal objective of the study. Secondary endpoints assess other drug effects that may or may not be related to the primary endpoint. Endpoints and the plan for their analysis should be prospectively specified in the protocol.

To further clarify the type f studies that are in or out of scope for this call we provide the following guiding overview

A4.1 Eligible for funding

- Ph 0, Human pharmacology (micro dosing) – assess pharmacogenetics
- Ph I, Human pharmacology – first in human, safety and tolerance
- Ph II, Study with Phase I component – safety, efficacy, maximum tolerated doses
- Ph II, efficacy and safety
- Ph II, Early feasibility / pilot
- Ph II, Traditional feasibility

A4.2 Not eligible for funding

- Ph II, Pre- and Post market (pivotal) studies
- Ph III, Comparison new treatment to available best / existing standard treatment

For more information on these topics, please refer to the standards as published by EMA and ICH.