



Ministerie van Infrastructuur en Milieu



Enabling new technology

Biotechnology and Safety

Call 2: New and Future Modern Biotechnology Techniques and Applications in relation to Environmental Safety

Guidelines for funding proposals for research under the
Biotechnology and Safety Programme, Call 2

Information & Match-making event : 15 September 2016

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Introduction

This brochure details the conditions governing proposals submitted to Technology Foundation STW¹ for the funding of scientific research under the 2nd Call in the Biotechnology and Safety Programme, which is commissioned by the Dutch Ministry for Infrastructure and the Environment.

Please note: Before submitting your application electronically via ISAAC, STW recommends that you visit its website (www.stw.nl) to check that you have the latest version of this brochure, and that you have read the guidelines carefully.

The Ministry of Infrastructure and the Environment is committed to improving quality of life, access and mobility in a clean, safe and sustainable environment. Three Directorates-General are concerned with developing policy in the areas of mobility, water management, aviation and maritime affairs, spatial planning and the environment. The Directorate-General for the Environment and International Affairs is working on a healthy and safe living environment. The STW research Programme 'Biotechnology and Safety' is commissioned by this latter Directorate-General.

Towards Modernisation of 'Biotechnology and Safety'

The research programme is part of the broader policy development programme 'Towards Modernisation of Biotechnology and Safety'. Key to this modernisation programme is the realisation that the current policy framework has to be adapted to the fast developments which are taking place in the field of modern biotechnology, in order to ensure safe and secure use of new and future biotechnology developments and applications. The 'Biotechnology and Safety' Research Programme is put into place to assure the generation of technical scientific knowledge needed for the envisaged modernisation.

The Dutch National Institute for Public Health and the Environment (RIVM) provides the Ministry of Infrastructure and the Environment with scientific, applied and risk assessment knowledge on biotechnology. Technology Foundation STW is responsible for managing and implementing the research programme.

About Technology Foundation STW

As a division for the Technical Sciences (TW), STW is part of the Netherlands Organisation for Scientific Research (NWO; see also www.nwo.nl). As such, STW provides indirect government funding.

STW's mission is to bring about knowledge transfer between technical sciences and users. STW does so:

- by bringing scientific researchers and potential users together;
- by funding excellent research in the technical and applied sciences.

¹ 'Stichting voor de Technische Wetenschappen' is the legally registered name of STW. This name is generally used only in official documents. In this document, the name 'Technology Foundation STW' or the abbreviation 'STW' will be used.

Utilisation

STW-funded research generates valuable knowledge. In addition to excellent science, STW aims to promote the application of knowledge. The term used by STW to refer to the set of activities aimed at maximising the possibility of research results being applied by third parties is 'utilisation'. In order to promote utilisation in addition to scientific quality, STW sets up a user committee for every project. STW expects applicants and users to actively collaborate towards promoting utilisation and towards STW's objective of transferring knowledge to users. Users, user committees and intellectual property play a crucial role in utilisation.

Users

Users of research are defined as natural persons or legal persons (at national or inter-national level) who are able to apply the results of the research. A distinction is sometimes drawn between direct users, usually companies, and end users. In that case, it is not sufficient to designate end users only. It is STW's explicit intention that potential technology users and end users outside the immediate circle and outside the research field of the researchers submitting the proposal should be involved in the project from beginning to end. Users should be able to apply the knowledge generated by the research in the medium to long term. (Potential) users should be indicated in the utilisation section of the research proposal.

Users in this Programme

This Programme is fully funded by the Dutch Ministry for Infrastructure and the Environment. Due to the specific goals of the Programme and the intended use of the project results, no financial or material contributions from private parties are allowed, with the exception of (access to) research data.

Objective of the Programme

This Programme on 'Biotechnology and Safety' stimulates the integration of risk research into current, near-future and future innovations in the field of modern biotechnology. Modern biotechnology is developing at an unparalleled pace, resulting in groundbreaking developments, such as CRISPR-Cas9, which have a wide array of new applications, ranging from personalised medicine to sustainable forms of energy and remediation. These developments have been described in several reports such as the 'Trend Analysis' from the Netherlands Commission on Genetic Modification (COGEM) and The Health Council of the Netherlands, and several reports on synthetic biology². These reports have identified new environmental safety issues that have to be dealt with when pursuing these developments. So to accompany developments in modern biotechnology, similar developments are needed in scientific knowledge on the environmental safety risks to secure safe use of biotechnology innovations.

Aim

As research on innovations does not automatically take into account the accompanying environmental risks, this Programme is aimed at building scientific knowledge with regard to safe modern biotechnology developments.

The Programme adheres to the Responsible Research and Innovation (RRI) approach, and particularly emphasises the starting point that innovations and research should anticipate and assess potential implications and societal expectations. This should result in a design that already takes potential adverse safety effects into account.

Inherently safe

The Ministry of Infrastructure and the Environment has included this starting point in its leading ambition: in 2050 all innovations should be 'inherently safe'. The concept of 'safe and secure by design' is seen as key in the attainment of this goal. This research programme must provide scientific knowledge that can be used to realise this ambition in the field of modern biotechnology, so these developments can be safely pursued.

Utilisation

This knowledge base must ultimately be useful to a wide range of stakeholders. The scientific community and the private sector should be able to apply the knowledge in order to incorporate safety in their innovations and product development processes; and risk assessors should be able to tackle future risk assessment problems. The government should be able to translate this knowledge into a modernised risk management system and accompanying regulations. Civil-society organisations and the interested public should be able to gain more insight into the relevant technological developments and their impact on society.

² See the 'Links' page at the end of this document.

New and future modern biotechnology techniques and applications in relation to environmental safety

In order to achieve the objectives stated above, two separate Calls for proposals have been published, each with different themes, and each adhering to a specific assessment procedure and deadline.

- Call 1 (published 30 April 2016, now closed): Current Genetic Modification Techniques and Applications in relation to Safety.
- Call 2 (published 30 June 2016): New and Future Modern Biotechnology Techniques and Applications in relation to Environmental Safety.

This document details the requirements for participating in Call 2: New and Future Modern Biotechnology Techniques and Applications in relation to Environmental Safety. Academic applicants are invited to submit proposals which are innovative in terms of creative research. Collaborations among scientists, such as interdisciplinary consortia (national or international), are highly recommended. The Programme aims to stimulate the use of current or planned research projects in the field of modern biotechnology. These research projects are to be extended with risk research as described in the calls.

The STW Board will decide on the funding of the full proposals.

Focus of this call for proposals

The proposed research projects should address one or more **new modern biotechnology developments** in relation to **cross-cutting safety issues**. Research should focus on knowledge of the effects of environmental risks and uncertainties when working on new or future modern biotechnology techniques and applications. More importantly, this knowledge should be aimed at how to minimise, assess and manage those risks to make sure biotechnology developments are safe. This means that the techniques and applications have no adverse effects on the environment³. In terms of providing a high level of environmental protection, three cross-cutting safety issues can be distinguished:

- creating inherent safety;
- developing new concepts and ways of assessing and/or managing risks;
- adapting the current risk assessment methods.

The proposed research programmes should address at least one of these cross-cutting safety issues, but preferably more than one. **Table 1** provides examples of specific safety issues related to new modern biotechnology developments and Appendix 1 lists information about the 6 groups of new modern biotechnological developments that have been identified.

Background

The following three **cross-cutting safety issues** have been distinguished for the proposed research:

Creating inherent safety

The following question is central when addressing this issue in your research: How do we design modern biotechnology applications that are inherently safe throughout the product lifecycle, i.e. from idea to design to development, production, use, waste and re-use? 'Inherently safe' refers to a

³ Environment is used comprehensively and includes environment, human health, animal welfare and food/feed.

condition of minimum hazard in normal or reasonably foreseeable use of a process or application. Safe-by-design will be elaborated in your proposal when addressing this issue.

Developing new concepts and ways of assessing and/or managing risks

Near-future and future modern biotechnological developments may provide such tremendous challenges for assessing and/or managing potential risks, that this calls for new conceptual frameworks to tackle these problems. Addressing this issue in your research project means providing insight into the specific risks of one or more new modern biotechnological developments. Your project should also develop a fresh approach or concept aimed at finding ways of assessing and/or managing the risks.

Adapting the current risk assessment methods

To assess the risks or uncertainties associated with activities involving genetically modified organisms (GMOs), European and Dutch legislation stipulates that an environmental risk assessment (ERA) be performed⁴. When carrying out an ERA, near-future modern biotechnology developments may present some challenging difficulties⁵. When addressing this safety issue in your research project, you should therefore consider the particular problems concerning the ERA that are encountered when doing research on one or more modern biotechnology developments. The key question when addressing this issue is as follows: How should potential new impacts be assessed when using current assessment methods?

Within **new and future modern biotechnology developments**, six areas have been identified:

- Advanced genome editing techniques (e.g. CRISPR/Cas9, TALEN, zinc-finger nucleases, meganucleases). Important safety aspects of these techniques include off-target effects and multiple changes introduced into the genome at the same time.
- Targeted regulation of gene expression. Gene expression can also be regulated without changing the DNA sequence, for example by using RNA interference or external factors to regulate gene expression (e.g. optogenetics, epigenetics). Safety-related aspects are for example unintended or transgenerational effects on gene expression, effects on non-target organisms and reversibility.
- Modularisation. This involves the use and design of modular genetic building blocks to design for example minimal cells, metabolic pathways or biosensors. Safety-related aspects include the effects of complex combinations of individual modular building blocks, how computer-aided design and self learning (AI) systems can be used to incorporate safety and how to validate and test the designed models.
- New forms of life. These range from protocells to cells made from artificial building blocks (e.g. XNA, non-canonical amino acids, synthetic ribosomes). Safety-related aspects include the level of containment of these non-natural systems in their specific environment (inside or outside the lab), the potential adaptation and interaction with the natural environment, and how to utilise new forms of life to improve safety (design safeguards).

⁴ Perseus (2016) *Taking stock of the environmental risk assessment of genetically modified plants and gene therapy*. This report is available as a download (PDF) from the STW website dedicated to this Programme

⁵ Committee on Gene Drive Research in Non-Human Organisms: *Recommendations for Responsible Conduct*; Board on Life Sciences; Division on Earth and Life Studies; National Academies of Sciences, Engineering, and Medicine. 2016. *Gene Drives on the Horizon: Advancing Science, Navigating Uncertainty, and Aligning Research with Public Values*. The National Academy Press. PDF Available at: <http://www.nap.edu/23405>

Westra, J., Vlugt, C.J.B. van der, Roesink C.H, Hogervorst, P.A.M., Glandorf, D.C.M. 2016. *Gene Drives: Policy Report*, RIVM. This report is available as a download (PDF) from the RIVM website (see 'Links' page in this document).

- **Converging technologies.** These are biotechnology developments which are integrated with other technologies e.g. nanotechnology, information technology or neurotechnology. Combining the use of modern biotechnology with that of other technologies may present new safety challenges, which may warrant adaptation or integration of existing risk assessment methods.
- **Safe and sustainable modern biotechnology.** By this we mean new applications of modern biotechnology specifically aimed at contributing to a sustainable and healthy society. Modern biotechnology can be applied to achieve sustainable solutions, e.g. new forms of energy, remediation, and water purification. Safety aspects resulting from these applications include the effects of the large-scale production of algae under non-contained or semi-contained conditions; applications to be used in non-contained ‘new’ settings such as in the home and in open water or remediation sites.

These six areas are described in further detail in Annex I.

		Cross-cutting safety issues		
Overview		Creating inherent safety	Finding new and alternative approaches to risk assessment and risk management	Adapting the current risk assessment method
New and future modern biotechnology developments	Advanced genome editing			
	Intentionally regulating gene expression			
	Modularisation	Proposals must address at least one of the cells in this matrix, but preferably several cells.		
	New forms of life (protocells, non-natural DNA & Amino acids)			
	Converging technologies			
	Safe and sustainable biotechnology			

Table 1: Overview of the cross-cutting safety issues and the new and future areas of development

Programme budget

The total Programme budget for this Call amounts to a maximum of € 6 million. The financial resources for the Programme are provided by the Dutch Ministry of Infrastructure and the Environment.

Specific requirements to the Programme

Project budget

The minimum subsidy contribution is 250.000,- euro per project (excl. VAT), and the maximum subsidy contribution is 750.000,- euro per project (excl. VAT).

As the Programme aims at generating new knowledge on all the biotechnology developments identified above as well as in particular the 3 cross-cutting safety issues, a fair distribution of projects across the cross-cutting safety issues will be pursued. Furthermore, all projects are encouraged to address more than one safety issue and/or biotechnology development. Projects which apply for a subsidy contribution higher than 500.000,- euro should address multiple cross-cutting safety issues and/or several of the described new biotechnology developments, or substantiate why they intend to spend the full amount on a single cross-cutting safety issue and/or single new biotechnology development.

Provided that proposals of sufficient quality (see 'Assessment Procedure', section 'Assessment by the Assessment Committee') are received, at least one project will be awarded for each of the cross-cutting safety issues as specified above. For each of the first two mentioned safety issues 'Creating inherent safety' and 'Finding new and alternative approaches to risk assessment and risk management' a maximum of four (4) projects may be awarded. For the third mentioned safety issue 'Adapting the current risk assessment method' a maximum of 2 (two) projects may be awarded.

In case no proposals of sufficient quality are submitted to a specific safety issue, no proposals will be awarded funding under that specific cross-cutting safety issue. In the case of remaining budget due to this lack of proposals of sufficient quality, or remaining after awarding the maximum number of projects for each safety issue mentioned above, the Assessment Committee may decide to advise the STW Board to award additional project proposals of sufficient quality for any one of the other cross-cutting safety issues. In this case, next to the quality of the proposals, also a fair distribution of budget over the safety issues and biotechnology developments will be taken into account in the advice of the Assessment Committee to the STW Board.

Multidisciplinarity

Scientists employed by Dutch universities or para-academic institutes eligible for STW-funding can submit a (pre-)proposal (also see section 'Who can apply'). Applicants are invited to form consortia of multiple academic institutes eligible for STW-funding in order to submit a joint research proposal. These consortia may include international academic (non-commercial) partners as co-applicants, and up to 40% of the requested budget may be allocated to the international partner(s). The STW office considers the main applicant to be the project leader and the contact person throughout the procedure. In case such an international consortium is awarded, the Dutch main applicant will become coordinator of the project and responsible for the distribution of funding to the international project partner(s).

Information & Match-making event

In order to provide information on this Programme and its research topics and to facilitate new and innovative collaboration in the context of the Programme, an 'Information & Match-making event' will be organised on Thursday 15 September 2016. Representatives from the Dutch Ministry for Infrastructure and the Environment, the Dutch National Institute for Public Health and the Environment (RIVM) and STW will be present to provide information on the Programme and the research topics. Prospective applicants will have the chance to present their wishes with regard to finding research partners as well as potential users for their project. Details on the 'Information & Match-making' event will be provided via the STW website.

Fit in the programme

Only those research proposals may be submitted that fit into the Call Topics as explained in the chapter "Objective of the Programme".

Involvement in multiple projects

Within this Call, a researcher may associate his/her name with only one research proposal as an applicant or co-applicant.

Duration of the programme

The Programme has a maximum duration of six years, individual projects will have maximum duration of 5 years.

Assessment procedure

The submission and evaluation process starts with a Call for full proposals. The STW Board will decide on the funding of the full proposals.

Please note: *it is the responsibility of the Applicant to ensure timely submission of his/her application to the correct Call in ISAAC. In case of doubt, please contact the contact persons at STW (see below).*

Deadline for submission of applications and processing period

!! The submission deadline for **full research proposals to Call 2** of the Biotechnology and Safety Programme is **Tuesday, 6 December 2016 at 14:00 hours CET** (Central European Time).

STW will assess whether the full research proposals adhere to the formal requirements of the Programme (see 'Formal requirements').

Formal requirements

STW confirms receipt of the research proposal. STW then verifies the formal requirements to determine whether the research proposal is eligible for consideration. If the relevant conditions (see section on 'Guidelines for applicants') are not fulfilled or the information requested is incomplete, the research proposal will not be considered. In that case, STW may return the research proposal to the main applicant with a request for adjustments or additional information which has to be delivered within 5 working days. If the information required is not provided, or is incomplete, by the given deadline, the research proposal is recorded as withdrawn and will not be taken further in the assessment procedure.

Assessment of relevance

The assessment of the Fit into the Objectives of the Programme is one of three criteria (see 'Annex 2: Evaluation items' and 'Annex 3: Evaluation scales') contributing to the final ranking of the proposals following the review by external experts. The fit into the Objective of the Programme is determined both by the external referees and by the Assessment Committee. Proposals where the fit into the Programme Objective is either not substantiated or insufficiently so will receive a lower score in the evaluation procedure, and thereby will significantly lower their chance of receiving funding.

Preselection

If at least four times more proposals are submitted than can be funded within the Call, STW retains the right to perform a preselection. In this case, 'Fit into the Programme Objective' will be the criterium as determined by the Assessment Committee.

Assessment by referees

STW submits full research proposals that adhere to the formal requirements to a number of (inter)national experts in the relevant specialist area (peer review). These referees are drawn from the scientific world and large research institutes. Referees remain anonymous. They will, individually without any interaction with fellow referees or applicants, each review one (1) proposal on the basis of

criteria for scientific quality, utilisation potential and fit into the Programme, as stated in the paragraph 'Items for evaluation'. The questions submitted to referees are available as Annex 2 in this document. STW recommends that applicants anticipate these questions in the research proposal. To ensure a balanced review, STW aims to have the research proposal assessed by three to five referees.

STW gives applicants the opportunity to provide suggestions for referees. For this, when submitting via ISAAC, please add a list of the names and contact information for a maximum of five independent referees **with relevant expertise**.

STW does not use a non-referee list, which allows certain referees to be excluded in advance. However, the applicant(s) may ask STW to exclude up to two people or organisations from acting as referees. STW will grant this request only if the provision of information from the research proposal to that referee might obstruct the utilisation.

STW combines the individual referees' comments, anonymised and if necessary paraphrased, into a 'basis for a protocol'.

Applicants' rebuttal

STW will invite the main applicant to respond to the referees' comments in the 'basis for a protocol' through the online application system ISAAC. The applicant will have five (5) working days to respond to the referees' comments, therefore it is advised to make note of the period in which the referees' comments may be expected (see the Programme timeline). The main applicant responds to each question or comment individually. The combined referees' comments including the responses from the applicant(s) form the protocol used by the Assessment committee members in arriving at their assessment.

Assessment by the Assessment committee

The Assessment committee, consisting of 5-7 independent experts from relevant areas in the field (i.e. science, risk assessment and government), will rank the full proposals. The committee members will give grades on a scale from 1 to 9 (see scale definition below) for three ratings of equal weight to each proposal, one for scientific quality, one for utilisation (prospects), and one for fit in the Programme. Thereafter a preliminary ranking is made. The committee will then define the final ranking based on the average grades given by the committee members individually, and (if necessary) other strategic arguments. The committee finalises a ranking of the proposals including an argumentation in case it wishes to deviate from the ranking obtained by averaged scores.

Score:

- 1 Excellent
- 2 Between excellent and very good
- 3 Very Good
- 4 Between very good and good
- 5 Good
- 6 Between good and moderate
- 7 Moderate
- 8 Between moderate and very moderate
- 9 Very moderate

Proposals can only be considered for funding if both the scientific quality criterion and the utilisation quality criterion together score no more than 7.0 and the individual criterions score no more than 4.0 Annex 3 contains a further explanation of the meaning of the quality scores.

The STW Board bases its decision on the prioritisation of the research proposals. The order established by the Assessment committee rankings is the primary starting point. A secondary consideration may be the available budget and any additional policy considerations. The STW Board does not assess the scientific content of the research proposals. In practice, unfortunately, the available budget may not be sufficient to fund every proposal of good quality. The STW Board may attach additional conditions to an award. These conditions may relate to matters such as intellectual property, participation by (potential) users, major investments and/or special infrastructure facilities.

NWO Code of Conduct on Conflicts of Interest

STW asks active researchers from research institutes and specialists from other knowledge-intensive organisations to participate in assessment procedures. These people are themselves involved in ongoing or new research and often belong to large organisational associations and research networks. Therefore, any conflict of interests, or anything that remotely resembles this, must be avoided in the assessment of research proposals.

To ensure a fair assessment and transparency for applicants, STW uses a code of conduct on conflicts of interest that is in line with the NWO Code of Conduct on Conflicts of Interest. This code identifies possible forms of conflicts of interest and indicates the steps to be taken to avoid conflicts of interest. Parties subject to the code of conduct are: referees, committee members, committee members, members of decision-making bodies and STW officers.

The full text of the code of conduct on conflicts of interest used by STW is available at:
<http://www.nwo.nl/en/documents/nwo/legal/nwo-code-of-conduct-on-conflicts-of-interest> .

After award

After awarding

The main applicant becomes the project leader. In the case of large projects and consortia containing international partners it is necessary to appoint separate sub-project leaders. The main applicant will be responsible for managing the project and the distribution of funds to the international partners. 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. The credits for materials, travel and investments are initially allocated for up to two years. The personnel credit per post is initially allocated for up to three years. STW reserves any remaining funds for the continuation after two years.

Start and starting date of the project

The credits allocated do not become available until after the necessary documents have been signed and received by STW and all relevant award conditions have been fulfilled. If the latter is not yet the case, written permission to start the project can be requested from STW. 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. Projects awarded in this Call are expected to have started no later than **1 October 2017**.

User committees

STW ensures that the knowledge generated by the research is practically and effectively transferred to users by consulting with the project leader of each research project to set up a user committee on the basis of the users proposed in the project plan.

User committee meetings are attended by the applicants/co-applicants, project/subproject leaders, the researchers temporarily appointed to the project and the representatives of potential users. The project leader acts as chairman and STW runs the secretariat. A minimum of three users should sit on the user committee (see below, section 'Users'). Applicants are asked to involve relevant stakeholders as users in their projects.

During the course of a research project, STW may change the composition of the user committee if there are grounds for doing so; such changes will always be made with the approval of the project leader. In doing so, STW will make due allowance for the advice of the sitting users. The guiding principle will be to ensure that the composition of the user committee maximises the likelihood of the results being applied and that the interchange of ideas, including confidential information, remains possible.

The committee can advise the project leader on the direction the research should take in order to promote the application of the results. The project leader always holds ultimate responsibility for the realisation of the research in accordance with the approved project plan.

The members of the user committee are formally invited by STW to sit on the user committee. Those participating in the user committee commit themselves to the conditions included in the 'General Conditions'.

Programme Committee

After awarding the research projects, a Programme committee (PC) will be installed by the Ministry of Infrastructure and the Environment. The PC is responsible for the overall directions and management of the programme. PC meetings will be organised twice a year unless the PC decides differently based on needs. All members of the PC will sign a NDA to protect any ideas laid down in the project proposals. STW shall appoint a programme manager to the PC who shall not have voting rights but will assist regarding for example the administration of the PC and the organisation of meetings.

Reporting

The project leader reports on the progress of the project twice a year, in writing, and the user committee then meets to discuss the progress made. As an exception – to be decided by STW – the user committee may meet less frequently.

In addition to the user committee meetings, there will be Program Meetings both at the mid-term and at the end of the Programme. The members of the Programme Committee will be invited to participate at these meetings, and play a role in evaluating progress of the Programme as a whole.

Utilisation of the research results is always on the meeting agenda. It covers collaboration with (potential) users and the dissemination of the generated knowledge. All results of the project are confidential until STW has given permission for publication.

A publication is the disclosure of results by any means, such as a text (including publications, abstracts, announcements on a website), illustration or an image or sound carrier, with the exception of disclosure resulting from a patent or patent application.

Continuation

In the case of projects with a term of three years or more, the user committee advises STW on the continuation of the project based on progress made. On that basis, STW decides on the allocation of the credits reserved at the time of award.

Extension

An extension after the end of a project is possible only in very limited cases, and only possible if the extension does not extend beyond the final date of the Programme. The prospects in terms of utilisation are crucial in this respect. From the utilisation perspective, funds remaining on the project can be used to extend one staff position (1 fte) for a period of up to three months.

Termination and termination date

The termination date of a project is the date on which the last temporary appointment is terminated. The project leader then receives two final forms from STW to round off the project in terms of both content and funding. Unallocated credits cease to be valid after the end of the project. The summaries requested in the final form are used for the purpose of publication in a final utilisation report.



Discontinuation

STW may discontinue a project before the official termination date if the obligations and/or General Conditions 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.

Drawing up and submitting the research proposal

ISAAC

An application can only be submitted to STW via the online application system ISAAC. **Applications not submitted via ISAAC will not be considered.** A principal applicant must submit his/her application via his/her own ISAAC account. **It is advised to take sufficient time early on to familiarise one-self with ISAAC.**

If the principal applicant does not have an ISAAC account yet, then this should be created **at least one 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:

1. Entering several additional details online in ISAAC.
Make sure you allow enough time for this.
2. Submitting the application form
 - 2.1 Download the application form from the electronic application system ISAAC or from STW's website (on the grant page for this programme).
 - 2.2 Complete the application form.
 - 2.3 Save the application form as a pdf file and upload it in ISAAC.

Appendices

Accompanying appendices should be submitted separately in PDF format (without protection). The application form together with appendices is regarded as the research proposal.

The following appendices are obligatory:

- Form 'Financial planning'
- {Optional} Letters of support from 'users'

No other appendices (e.g. publications, figures) are allowed.

Technical questions about the use of ISAAC

For technical questions about the use of ISAAC please contact the ISAAC helpdesk, see section 'Further Information'.

Reference suggestions may be submitted in ISAAC.

Format

The application should be in English, and applicants have to make use of the format provided at the Programme website of STW.

The **full proposal** should not exceed twelve pages in A4 format (minimum Arial 10 point or similar font), excluding references and appendices. If there is more than one participating research institute, the limit is fifteen pages. In Section 4.1 of the application form, additional sub-chapters may be added.

The information entered should be complete and correct. Applications that do not make use of the prescribed format, incomplete forms or forms that exceed the maximum permitted length may lead to your application not being considered.

Timeframe Call 2

Full proposals	
Information & Match-making Event	15 September 2016
Deadline full proposals	6 December 2016; 14:00h
Check adherence to formal requirements	December 2016
Assessment by (international) referees	January/ February 2017
Primary applicants' rebuttal	End of February 2017
Advice Assessment committee to STW board	March 2017
Decision by STW board	Mid April 2017
Ultimate project starting date	1 October 2017

Programme Meetings	
Mid-term Programme Meeting	September 2019
Final Programme Meeting	September 2021

Contact

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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 research including the utilisation plan. 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:
 - Dutch universities (or with comparable positions at the university medical centres)
 - KNAW and NWO-institutes
 - the Netherlands Cancer Institute (NKI)
 - the Max Planck Institute for Psycholinguistics in Nijmegen
 - Dubble beamline at the ESRF in Grenoble
 - NCB Naturalis
 - Advanced Research Centre for NanoLithography (ARCNL)
- Researchers with a tenure track appointment. STW 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 and funded from structural resources. STW will verify that the appointment meets these conditions and that it is guaranteed for the term of the project.
- Assistant, associate and full professors with a tenured position at foreign research institutes can act as partners in the project consortium. Up to 40% of the project budget may be allocated to possible foreign partner(s). Foreign partners will not receive their funding directly from STW. The budget requested for the foreign partner will be transferred to the main (Dutch) applicant who is then responsible for a correct transfer of funds to the foreign partner, as well as adequate and timely reporting on the use of those funds by the foreign partner.

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 STW research while they are working for the research institute. If this is not the case, STW should be contacted and further arrangements should be made.

Who **cannot** apply? (Applies to main and co-applicants)

- Personnel with a zero-hour appointment
- Personnel with a temporary employment contract (e.g. postdocs)
- Emeritus professors



- 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

Guidelines for applicants

Project-specific costs

The Programme 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,
4. equipment (durable scientific equipment in respect of which economic value is depreciated).

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 applicant/co-applicant cooperates with other institutes not eligible for STW funding, such as TNO or a foreign university, the non-eligible institutes are responsible for their own costs.

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

Temporary personnel positions can be requested for:

- PhD student
- postdoc (PD)
- other SP (scientific personnel, including additional researcher, holders of a masters degree, medical graduates)
- NSP (non-scientific personnel, including technical assistant)

Notes on temporary personnel positions

Temporary personnel positions can be requested for up to four years in the case of a full-time appointment. State the job group, the length of the appointment, the part-time percentage and the associated amount. For each position, STW uses a predetermined fixed maximum rate per year of appointment (see www.stw.nl). In determining these rates, STW 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. The rates which apply at the time of award are maintained for the duration of the STW project. If the personnel rates are changed during the evaluation procedure, STW will apply the new rates at the time of award.

Personnel appointed to additional personnel positions during the course of the project (e.g. in the event of continuation or extension) are subject to the rates which apply at that time.

For postdoc, scientific personnel and non-scientific personnel positions, STW 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 STW 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 rates at the expense of an STW project. The scientist concerned may not be registered as an applicant or co-applicant at STW/NWO. STW 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 STW 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 STW in advance. A secondment agreement shall be concluded. Where the need arises, an applicant can submit a reasoned request to the STW 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.

2. Notes on costs of materials and domestic travel

STW funds consumables, small instruments and aids, and domestic travel expenses.

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 STW, only the consumables costs can be charged to STW.
- Costs of domestic travel.
- Costs of project-specific courses for STW researchers which are necessary for the conduct of the research.
- Posters for disseminating knowledge at conferences and symposia.
- Pre-clinical trials. A condition in this respect is that the project workers themselves are responsible for the majority of the work (e.g. sampling, analyses).
- Costs for the use of cleanrooms insofar as these fall under the cleanroom regulation (see www.stw.nl).

Costs which **CANNOT** be charged to material credit

- 'Miscellaneous' or 'unforeseen' items, unspecified bench fees.
- Patent costs. Where appropriate, STW will consider the extent to which it will bear such costs.
- Costs of publications or costs of purchasing books and/or journals.
- Costs of publications or books.
- Costs of printing a thesis. A separate reimbursement scheme exists for this (see www.stw.nl).
- Costs of general courses which form part of researchers' generic education and the generic education of a PhD student (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. STW 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).
- Clinical trials.

3. Notes on costs of foreign travel

The foreign travel credit is intended to cover costs associated with participation in conferences and symposia in other countries. Extended visits may also be applied for.

Notes on short travel abroad

For temporary project workers, STW applies a maximum standard amount (2000 euro/year/fte) which can be claimed as short travel abroad. Foreign travel costs of applicants and co-applicants can also be claimed up to the maximum standard amounts, provided those costs are directly related to the conduct of the proposed research and a convincing argument is put forward in this respect. In principle, travel costs cannot be claimed for non-scientific personnel (NSP). If the sum claimed exceeds the maximum standard amount per year it cannot be accepted unless clear arguments are put forward on which STW and the referees can base their verdict.

Notes on exchange visits

Temporarily appointed project workers may carry out research at a foreign research institute for a limited period (up to six months) in the context of an STW project. A foreign researcher may also be temporarily appointed to an STW project; he or she visits the research institute and participates actively in the conduct of the project.

Conditions relating to foreign travel of up to six months' duration:

- STW must be aware of this type of foreign travel when considering the application, and it must form part of the research planning and budget so that referees can include it in their review.
- A condition for an exchange is that the knowledge acquired as a result of the visit is not present, or is not sufficiently available, at the research institute where the research is being conducted. In

the event of acceptance, STW verifies whether this actually results in a strengthening of the knowledge base for the project.

- STW reimburses the travel expenses, research costs and a standard amount for accommodation expenses. No (additional) salary costs are reimbursed. For the list of standard amounts for accommodation costs, see www.stw.nl.
- Any intellectual property matters are covered by a separate agreement (waiver/confidentiality) before travel takes place.

4. Notes on costs of investments

Investments are defined as the use of durable scientific equipment in respect of which economic value is depreciated. Investment costs are entered in the budget inclusive and exclusive of Dutch VAT.

Notes on investments

- The equipment is and remains the property of STW. After the end of the project the equipment remains at the research institute. Formal transfer of ownership of the equipment without further payment is possible. A time limit of five years after purchase is applied in this respect.
- STW assumes that the research institute applies a tendering procedure for the purchase of durable equipment and takes account of government procurement guidelines.
- If second-hand equipment is purchased, the original bill must be submitted.
- STW may be asked to co-fund an item of equipment in proportion to its use. This should be put down in writing after the award.
- The research institute is responsible for the connection, operating costs and maintenance of the equipment purchased (service charges and repairs).
- STW distinguishes between operation of existing facilities within the research institute and investment in new facilities specifically for the purposes of an STW project. In the case of operating costs and small-scale investments, STW pays only the costs of consumables. These costs can be claimed as material credit. STW will however pay the full cost of capital goods supplied by internal services in those cases where a disproportionate burden is placed on the service in question, provided that a convincing argument is put forward in this respect. STW will be the judge of this.
- Computers belonging to scientific equipment and specific software used exclusively for the project may be claimed as investment.
- Computing capacity which demonstrably exceeds the normal capacity required for the research in question can be claimed as investment.
- If, in the course of time, it emerges that the costs of the investments described in the proposal are lower than estimated, the remaining funds will revert to STW.
- STW may refuse expenditure not estimated in advance.

Notes on Users and letters of support

Users

Users of research are defined as natural or legal persons (at national or international level) who are able to apply the results of the research. A distinction is sometimes drawn between direct users of the knowledge generated, usually companies, and end users, who buy the products from those companies. To ensure the applicability of the project results, relevant stakeholders as users have to be involved in the project from the start, and preferably earlier (i.e. during the application phase). In every project a representative of the Dutch Ministry of Infrastructure and the Environment (the sponsor of the Research Programme) will be part of each user committee. After the research proposal has been awarded, a minimum of three additional users should sit on the user committee.

Additional users may include, but are not limited to:

- government (e.g., Dutch Ministry of Health, Welfare and Sport, Dutch Ministry of Economic Affairs);
- Biosafety officers (in Dutch: '*biologische veiligheidsfunctionaris (BVF)*')
- non-governmental organisations with relevant societal goals (e.g. patient organisations, animal welfare organisations, environmental organisations);
- organisations who require permits to be able to perform activities creating and/or making use of genetically modified organisms (e.g. knowledge institutes, hospitals, industry).

Research proposals from a medical faculty or university medical centre should have potential users, just like other proposals. It is not sufficient in this case to state merely 'the patient' or 'a clinic'.

Due to the specific goals of the Programme and the intended use of the project results, no financial or material contributions from private parties are allowed, with the exception of (access to) research data.

Letters of support

Letters of support are not obligatory, yet may be considered valuable by the Assessment committee as well as the external experts engaged in the assessment procedure. Should you choose to provide support letters with your application, STW advises applicants to ensure that the users pay particular attention to endorsing the importance of the utilisation plan 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 user.
- Letters of support must be recent (i.e. preferably not older than 6 months).
- Letters of support are addressed to the project leader with a copy to STW.
- Letters of support must be written in English.
- The address on the letter is correct.
- Letters of support must be signed by an authorised signatory.



B. Specific requirements

- Brief description of the organisation or company and the core business (type of organisation, size, which service, products).
- A statement explaining why the organisation is interested in the research described in the proposal.

C. Declaration and signing by the User

- The organisation states that it has read the proposal and signs for this.
- The organisation states that it will actively participate in the User Committee (UC) and signs for this.
- The organisation states that it agrees to the General Conditions of the Programme and signs for this.

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

A copy or scan of the letter will suffice for the submission of a research proposal.

STW will not approach persons or organisations who have signed letters of support to act as referees (code of conduct on conflicts of interest).

After the research proposal has been awarded funding, STW will request a confirmation of the participation to the User committee and in relevant cases will record any further arrangements in an agreement.



Open innovation policy for Intellectual Property and Publication

This Programme intends to stimulate the utilization of the outcome of the research projects. Users and third parties will have open access to all results (without any requirements for financial compensation), which in many cases will consist of knowledge and data on top of which value-adding protocols, tools, products, applications and services can be built.

For this reason STW and the Ministry of Infrastructure and the Environment require the applicants and the other parties involved in the project to agree on making all results of the research publicly available. Resulting software will have to be made available as open source software. The applicants are asked to detail in their project proposal how this public availability will be implemented in their project.

Deviation from this policy is only possible if valid arguments require so. Research based on patents, data or background knowledge that is not free of use by the applicants will be excluded from the Programme, unless a plan is provided as to how to deal with these issues in order to make the results publicly available.

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

STW and the Ministry of Infrastructure and the Environment will conclude separate agreements with all parties involved in the granted projects (a template will be made available) in which the above mentioned topics as well as the following issues are addressed:

- All results deriving from the research projects are jointly owned by the Ministry of Infrastructure and the Environment and the knowledge institute that has generated the result.
- The project leader reports in writing on the progress of the project at least two weeks before a user committee meeting. The project leader sends this report to STW. The project leader reports at least on the aim of the research, the work plan, milestone planning, results, utilisation, cooperation and contacts with users, conferences and publications.
- During the project all parties shall maintain confidentiality regarding the results and shall not disclose these to third parties. This confidentiality requirement does not apply to:
 - results which are disclosed in a publication after approval of the project parties;
 - results which are disclosed as a result of the formalities for the protection of results;
 - reporting of results to the user committee;
 - results which must be disclosed pursuant to a decision of a Court or a body governed by public law, on the condition that the recipient notifies the provider in writing about such disclosure.



- The project leader submits all proposed publications to STW at least thirty days before its intended disclosure. STW then submits the publication to the users in the users committee, asking them to inform STW within thirty days whether, in their opinion, the publication contains information that would hinder the proposed publication. Within thirty days after the publication has been submitted to STW, STW informs the project leader in writing whether there are any objections to the publication. If no objections have been raised before that deadline, the project leader may disclose the publication. STW may decide to suspend the publication for up to nine months if any objections are raised. STW takes this decision following consultation with the project leader.

- All data generated within a project will remain available, on request of the Ministry of Infrastructure and the Environment, for a period of four years after the project has ended.

Notes relating to the proposal application form

1. Details application

1.1. Further details main applicant

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

1.2. Further details co-applicants

State the name and address of the co-applicants. Also state the additional information, including % of full-time appointment and confirmation of permanent employment. Provide these details for each of the co-applicants. Please be aware that Users will be listed in a different section of the proposal.

1.3. Title

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

1.4. Key words

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

2. Summaries

Summaries should be clear to potential reviewers and non-specialists, such as committee members. Committee members will base their verdict primarily on the opinion of the experts as laid down in the protocol, summaries and utilisation section. It is therefore vital that these sections are worded clearly and concisely, so as to be convincing to committee members.

In addition, these sections may be used by STW for publication purposes; the confidentiality of the data will be taken into account at all times.

2.1. Research summary

On a half-page of A4, describe the research question, the research and the anticipated results.

2.2. Utilisation summary

On a half-page of A4, describe the utilisation. State what the committee needs to know about utilisation, the approach taken to it and the likelihood of it being achieved.

2.3. Summary STW's website and online in ISAAC

Add a general summary in English for STW's website. Use this summary online in ISAAC.

3. Current composition of the research group

State the composition of the team which will realise the research and the distribution of tasks and responsibilities.

- 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.
- If an international consortium partner is involved in the project, state here what expertise is brought to the research team by this partner.

- The project leader is responsible in all cases for coordination and communication between the participating institutes/research groups/ researchers.

4. Scientific description

This section should contain sufficient information to enable an expert reviewer to assess the quality of the research proposal.

4.1. Research contents/Introduction

Describe the underlying scientific basis and the content of the project. Indicate the methods and techniques to be used to tackle the problem, the knowledge already available, the state of the art, 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.

4.2. Fit into the Programme

Describe to which Call topic, i.e. to which safety issue(s) and biotechnology development(s), your research proposal is submitted, and how the proposed research will contribute both to reaching the goals of the Programme and the specific goals set for that particular topic. When addressing more than one safety issue and/or biotechnology development, indicate to which topic the proposal will contribute most.

4.3. 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.

4.4. Time plan and division of tasks

Describe the proposed research planning over the years. For each line of research, indicate the phasing and give a clear description of the step-by-step plan (subsidiary aims and/or ultimate aims) and the intended results. If different lines of research are dependent on each other, indicate this. A schematic representation of the research planning is compulsory. The overall duration of the research plan may not exceed five years.

5. Utilisation plan

The utilisation plan must be clear to people without specific prior knowledge. Give sufficient details to enable referees and committee members to assess at what point any potential application outside science may be possible.

5.1. The problem and the proposed solution

- Describe the problem that you propose to solve and indicate for whom it is a problem. Indicate the social and economic consequences while the problem remains unresolved.
- Describe how the intended research results contribute towards solving the problem.
- Describe how you will ensure public availability of the project results (e.g. through Open Access publication, Open Source software development).
- Indicate how long after the start of the research it will be before the intended research results lead to an entirely new method or new product, process or service. Describe the market for this. This relates to non-scientific applications.
- Indicate whether the research results can be incorporated into standards or norms. If so, describe.

5.2. Potential users

State the contact details (name of organisation/company and person to contact, address, telephone number, e-mail address) of companies and institutes wishing to participate in the user committee.

Indicate the step-by-step plan you intend to use to ensure that the results of the research are effectively applied by users, and how you will comply to the Programme's demands on open access publication of the project results and/ or development of open source software code. If third parties are necessary in the course of the project, it is important that they have pledged their cooperation. Also state whether users have already undertaken to accept an invitation to join the user committee or to cooperate in another way.

5.3. Past performance

Indicate whether the research team has achieved successful **utilisation** in the past. Indicate whether scientific results have been commercially or otherwise utilised. Indicate whether the applications were achieved in an STW context or otherwise. Design and construction disciplines can also include the strength of their design portfolio, prizes, awards, prize questions won and relevant advisory positions.

6. Intellectual property

State all information relevant to the research proposal in relation to the IP and open access publication policy of the Programme. Providing the requested information is compulsory.

6.1. Contracts

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.

6.2. Data / Patents

- 1) Give a summary of data and/or patents held and/or patent applications made by intended parties to the project in the field of the research proposal. Indicate whether the data and 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.
- 2) Indicate whether there are any needed data or patents and/or patent applications which obstruct the utilisation of the intended research results. If such an obstacle exists, explain whether there is still sufficient likelihood that the intended research results can be used.

7. Positioning of the project proposal

Describe the extent to which the research proposal differs from ongoing research initiatives. Consider both the national and the international context. Also state the relevant collaborations with other national or international research groups.

7.1. Uniqueness of the proposed project

Indicate what it is that makes the research proposal original and innovative.

7.2. Embedding of the proposed project

Provide further information on the embedding of the research plan described here within ongoing initiatives of the research group and/or section.

Indicate whether the research proposal is part of or related to a research programme in which the applicant or applicants' research institute is participating. If so, indicate the research programme in question.

7.3. Request for support elsewhere

State whether funding has been requested elsewhere for this research 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 STW.

8. Financial planning

Justify the need for both the personnel credits requested and the necessary materials and investments in equipment.

8.1. Personnel positions

State the necessary temporary personnel positions. Temporary personnel positions can be requested for:

- PhD student
- postdoc (PD)
- other SP (scientific personnel, including additional researcher, holders of a masters degree, medical graduates)
- NSP (non-scientific personnel, including technical assistant)

8.2. 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 and exclusive of Dutch VAT.

8.3. Travel abroad

State the costs of foreign travel. The foreign travel credit is intended to cover costs associated with participation in conferences and symposia in other countries. Extended visits may also be applied for.

8.4. Investments

Specify the investment costs and give a detailed summary of the equipment required. Investments are defined as the use of durable scientific equipment in respect of which economic value is depreciated. Investment costs are entered in the budget inclusive and exclusive of Dutch VAT.

8.5. Cost Breakdown

Complete the Financial Planning (FP) form available at www.stw.nl.

- If a project is to be realised at more than one (international) research institute, give a breakdown of the budget for each research institute on page 2 of the FP.
- Please note that in the case of an international consortium, up to 40% of the subsidy may be allocated to the international academic partner(s).
- The form should be submitted together with the proposal, as a separate appendix in PDF format.
- Each research institute concludes a funding agreement with STW for its share of the budget.
- It is not possible to break down the budget for each research group within a single research institute in view of the administrative burden on STW.
- STW does not transfer funds directly to international parties. Any funding to be spent by an international partner in the project will be distributed via the main (Dutch) applicant.
- Due to the specific goals of the Programme and the intended use of the project results, no financial or material contributions from private parties are allowed, with the exception of (access to) research data.

8.6. Letters of Support

Optional. Letters of support may assist in convincing external experts and the committee that the consortium of consisting of applicant(s) and users build the best team to address the questions raised in the specific Call topics.

9. References

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. Design and construction disciplines can, if so wished, provide an overview of designs realised (selected works).

9.2. List of publications cited

State the publications cited. Identify those in which members of the research group(s) submitting the application are involved, by the use of a bold font. Design and construction disciplines can, if so wished, include a list of publications from other people about their designs (Avery Index to Architectural Periodicals, Columbia University, New York).

10. Abbreviations and acronyms

It is important that both experts and 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.

11. Declaration and signing by the applicant

After completing the information requested, please sign the application as truthfully completed, on your own behalf and on that of the co-applicant(s). This is a compulsory element of the application and should be submitted with the application form.

Finally

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

Annex 1: Developments in modern Biotechnology

The six developments in modern biotechnology that are distinguished in this Programme are explained briefly below, including several focus areas relating to these developments that may be important for safety issues.

1 Advanced gene editing techniques

The technology for altering the genome of an organism (gene editing) is developing very rapidly. Techniques such as CRISPR/Cas9 (but also zinc finger nucleases, TALEN and meganucleases) make it possible to remove, replace or add genetic material with much greater efficiency and precision than before, and on a larger scale. Moreover, it is now theoretically possible to make these alternations in all organisms, and with CRISPR/Cas9, multiple simultaneous interventions in the genome have become possible.

These new editing techniques are developing quickly and will be applied widely, in any case in industry (white biotechnology), the medical sector (red biotechnology) and the agricultural and food sectors (green biotechnology)⁶.

Focus areas

- New applications of gene editing such as gene drives and base editing.
- Far-reaching interventions in the genome such as making multiple simultaneous changes, or incorporating or changing biosynthesis routes.
- Developing and using either new editing tools and mechanisms (other than CRISPR/Cas9, zinc finger nucleases, TALEN and meganucleases), or endonucleases that have new functionalities.
- Off-target effects and their potential impact on organisms in relation to the environment.
- Use of genome editing techniques outside the academic circuit (amateur biologists).

2 Targeted regulation of gene expression

Biotechnologists are looking for new ways to make targeted interventions in gene expression. Previously, researchers focused on influencing gene expression by removing or adding coding sequences. Alternatively, the level of expression was regulated by removing or permanently adding genes that directly affect the regulatory sequences of the target gene (promoters, enhancers).

However, gene expression can also be influenced in other ways that do not involve direct intervention in the coding sequences. Examples of these approaches include using RNA interference, or external factors such as light or magnetic fields to regulate gene expression (optogenetics), or modified CRISPR/Cas systems that can act as enhancers or suppressors. A shift is clearly taking place towards these new approaches.

Focus areas

- Influencing gene expression using double-stranded RNA.
- Influencing gene expression using external triggers, such as light or magnetic fields.
- Influencing gene expression using modified CRISPR/Cas systems.
- Off-target and unexpected effects, for example on the germline
- Stability and duration of the effects, and the effects in the longer term (e.g. multiple generations).

⁶ These reports are available as downloads (PDF) from the STW website dedicated to this Programme.

3 Modularisation

Synthetic biology, a sub-discipline of modern biotechnology, essentially uses engineering principles to design and assemble biological components. This has led increasingly to concepts and approaches such as the chassis (minimal living cell), modular genetic building blocks, and standardisation and abstraction (modular organisation of building blocks into systems). Developments in synthetic biology are ongoing. For example, work is taking place on a minimal organism (organism with a minimal genome) that can be used as a chassis to which genetic building blocks with predefined characteristics can be added. The building blocks themselves are being developed and used under the name BioBricks® in student competitions such as iGEM. Discussions are now taking place in the USA about the standardisation of these biobricks.

The engineering aspect of biotechnology becomes more reliable if the functionality of the building blocks can be defined in advance. Recently, a step was taken in this direction with the design of a programming, compilation and testing environment. In this approach, a computer-generated design for a specific functionality ('design') is translated into the most suitable DNA code ('compilation'), and its effectiveness can be tested with special software ('testing').

Focus areas

- Using modularisation (minimal cells, building blocks, modules) to help determine the impact on humans and the environment.
- Using minimal genomes/complex metabolic routes/biobricks.
- Using complex genetic switches. Such a switch could, for example, allow a biosensor to be used safely.
- Integrating safety in all disciplines: incorporating a safety-based approach in the various development phases of the product, including the design phase and in the corresponding tools that are under development (software).
- Integrating safety aspects in the standardisation process, in aspects such as agreements, protocols, standards and software.

4 New forms of life

Work is taking place on new forms of life (protocells: self-organising and replicating units that are based entirely on chemical building blocks) or components of life (such as cell organelles) that are distinct from the DNA-based systems on which all life is based (tree of life). Work is also taking place on artificial ribosomes – the 'factories' which in a classical biological cell synthesise proteins, but in artificial cells can be made to produce a wide range of polymers.

Another development is the use in existing organisms of non-natural (xenobiological) building blocks. Examples include the use of these xenobiological building blocks for constructing the backbone of DNA, the coding information in DNA (the nucleotides), or proteins (non-canonical amino acids). These applications could result in new life forms that are not compatible (orthogonal) with life as we know it.

Focus areas

- Evolutionary impact (a new tree of life?) – How does a protocell relate to existing life forms from a safety perspective?
- Safe use of xenobiological building blocks for DNA or proteins
- Use of xenobiological building blocks as a safety mechanism.
- Impact on humans and the environment of these xenobiological building blocks and/or protocells.

5 Converging technologies

An increasingly visible aspect of recent developments in biotechnology is the integration with other technological developments. This is sometimes referred to as the NBIC convergence (nanotechnology, biotechnology, information technology and cognitive science). For example,



nanotechnology and biotechnology have joined forces in a new field that involves for example the development of nanostructures using biomolecules as building blocks.

Commercial applications of these developments are conceivable, in batteries for example. Another development is 3D printing of biomaterials, which could be used to print organs or biofilms of genetically modified bacteria. Information technology and neurobiology have also become more closely integrated with biotechnology.

Focus areas

- Deeper understanding of the consequences of converging technologies for the safety of humans and the environment.
- Engineered biomolecular structures at the nanoscale.
- Integrated risk analysis methods for converging technologies.

6 Safe and sustainable modern biotechnology

New applications of modern biotechnology can be specifically aimed at contributing to a sustainable and healthy society. For example, organisms such as algae are being cultivated on a large scale to produce biomass and oil for sustainable energy and chemicals and other substances could also be produced sustainably. To make production cost-effective, this cultivation has to take place on a large scale in open, semi-open or closed systems.

Sustainable modern biotechnology applications can also be developed for use in new settings such as the home. Prototypes of biosensors are already being developed for use in meat packaging or in dressings for burn wounds.

Focus areas

How to assess and safely achieve:

- large-scale production in open or semi-open systems;
- sustainable applications to be used in new settings;
- sustainable applications for use by the public.

Annex 2: Evaluation items

1. Scientific quality

- 1.1 To what extent is the proposed research original and how would you rate the innovative elements?
- 1.2 What is your assessment of the design of the project, including the goals, hypotheses, research methods, and scientific feasibility?
- 1.3 What is your assessment of the coherence and time schedule of the proposed lines of research?
- 1.4 Is the research group competent enough to carry out the research? Does the group have a relevant position in the international scientific community? Is the available infrastructure adequate?
- 1.5 Are the number and category of requested personnel, budget for materials, investments, and foreign travel adequate?
- 1.6 What are the strong and weak points of the scientific part of the proposal?

2. Utilisation potential (the application of the results of the research by third-parties)

- 2.1 What is your assessment of the description of the applicability of the research to further adapt and develop the risk assessment methods?
- 2.2 What is your assessment of the research with respect to the contribution of the research to further elaboration and application of the concept 'inherent safety'?
- 2.3 What is your assessment of the contribution, involvement and/or commitment of the users and the proposed composition of the user committee?
- 2.4 Do you expect the application of results to be hampered by security issues, confidentiality, commercial propositions, or existing patents?
- 2.5 What are the prospects for collaboration with the potential users and knowledge transfer and/or dissemination, assuming the project is successful? Please address both aspects.
- 2.6 What is your assessment of the research group's competence regarding the transfer and application of research results?
- 2.7 What are the strong and weak points of the utilisation plan?

3. Fit in the programme

- 3.1. What is your opinion regarding the strategic contribution of this project to the aims of the Programme (see Programme description)?

Annex 3: Evaluation scales

1. Scientific quality

1. Excellent

- An excellent researcher or outstanding research team.
- A well-chosen problem.
- The method is especially/pre-eminently effective and original.
- Very urgent.

2. Excellent to very good

3. Very good

- A competent researcher or competent research team.
- A significant problem.
- The method is original and effective.
- An urgent approach is important.

4. Very good to good

5. Good

- An average researcher or average research team.
- A routine problem.
- With the method, which has some original details, the project can be addressed, although other possibilities are conceivable.

6. Good to moderate

7. Moderate

- It is far from certain that this work is within the capacity of the researcher and / or the research team: the proposal itself contains no obvious errors.
- The problem is moderately interesting.
- Whether the project can be successfully tackled with this standard method, is questionable.
- The project may well be postponed.

8. Moderate to poor

9. Poor

- The competence of the investigator or research team is inadequate.
- The proposal contains serious errors or mistakes.
- This old method is not good for this project.
- Not to be executed, even if there is money left.

Utilisation

1. Excellent

- This will certainly lead to important new techniques or to very important applications in industry, society and other sciences.
- This research is urgently needed to make an estimate of the consequences of the use of this technology or technique.
- The utilisation is very well thought out and the approach ensures the greatest likelihood of an effective use of the results.

2. Excellent to very good

3. Very good



- This research will likely lead to important new techniques or to important applications in industry, society, or in other sciences.
- This research is highly desirable to make an estimate of the consequences of the use of this technology or technique.
- The utilisation is well thought out and the approach makes it plausible that the results of this work will be used well.

4. Very good to good

5. Good

- This work will possibly lead to new technologies or applications that might be useful for industry, society, or other sciences.
- This research will be needed to make an estimate of the impact of this technology or technique.
- The utilisation is sufficiently thought through, it can probably be improved during the execution of the work. The results of this work will probably be used.

6. Good to moderate

7. Moderate

- Technically this work could possibly be useful at some time or it is conceivable that in due course another science, industry or society or of the results could make use of it.
- The results of this research are not exactly awaited, but they may be useful in the future if an evaluation is made of the consequences of using this technology or technique.
- The utilisation is very unsatisfactory. This should certainly be improved, otherwise it is likely that the results of this work will not be used.

8. Moderate to poor

9. Poor

- Technically the work is bad and redundant, i.e. different, better or similar techniques, which are cheaper are already available.
- This study does not evaluate the consequences of using this technology or technique, moreover, it increases the confusion.
- The utilisation is completely wrong.

Fit in the programme

1. Excellent

- The project fits the programme exactly.
- It is in the heart of one of the topics of the programme, or
- More than one cross-cutting safety issue and/ or biotechnology development will be addressed.
- This is a key project for the topic of the programme.

2. Excellent to very good

3. Very good

- The project fits the programme very well.
- It is a very good elaboration of one or more of the cross-cutting safety issues and/or biotechnology developments addressed in the programme.
- This is very important project for the topic of the programme.

4. Very good to good

5. Good

- The project fits the programme.
- It is a good elaboration of one of the topics, but some parts are outside the scope of the programme.



- This project could give an important contribution to the topic of the programme. For this, it is important to focus it on the topic of the programme during its execution.

6. Good to moderate

7. Moderate

- The project partly fits the programme.
- The described work has some relation with the topic of the programme, but the main activities are outside scope.
- This project can only have a minor, indirect contribution to the topic of the programme. Its main focus is on a different topic or it focuses on a minor and/or insignificant part of the topic.

8. Moderate to poor

9. Poor

- The project does not fit the programme.
- The described work is not in any of the topics of the programme.
- The vocabulary of the programme is used but in the wrong context or without substantiation in the research activities.
- This project will have no contribution to the topic of the programme.



Further information

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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 directly from Monday to Friday between 10:00 and 17:00 hours CET on +31 (0)20 346 7179. In addition, you can submit your question by e-mail to isaac.helpdesk@nwo.nl. You will then receive an answer within two working days.

Links

- Ministerie van Infrastructuur en Milieu (Dutch):
<https://www.rijksoverheid.nl/ministeries/ministerie-van-infrastructuur-en-milieu>
- Ministry of Infrastructure and the Environment (English):
<https://www.government.nl/ministries/ministry-of-infrastructure-and-the-environment>
- RIVM / Bureau Genetisch Gemodificeerde Organismen (BGGO, Dutch):
<http://www.ggo-vergunningverlening.nl/>
- RIVM Gene Drives: Policy Report
http://www.rivm.nl/en/Documents_and_publications/Scientific/Reports/2016/februari/Gene_drives_Policy_report
- SCENHIR Final Opinion on Synthetic Biology I Definition:
http://ec.europa.eu/health/scientific_committees/emerging/docs/scenihir_o_044.pdf
- SCENHIR Final Opinion on Synthetic Biology II Risk assessment methodologies and safety aspects:
http://ec.europa.eu/health/scientific_committees/emerging/docs/scenihir_o_048.pdf
- SCENHIR Final Opinion on Synthetic Biology III: Risks to the environment and biodiversity related to synthetic biology and research priorities in the field of synthetic biology:
http://ec.europa.eu/health/scientific_committees/emerging/docs/scenihir_o_050.pdf
- CBD Report on Synthetic Biology:
<https://www.cbd.int/doc/publications/cbd-ts-82-en.pdf>
- Trendanalyse COGEM (Dutch):
<http://cogem.net/index.cfm/nl/publicaties/publicatie/trendanalyse-biotechnologie-2016-regelgeving-ontregeld>
- Technology Foundation STW
<http://www.stw.nl/>
- Netherlands Organisation for Scientific Research (NWO):
<http://www.nwo.nl/>
- Code of Conduct on Conflicts of Interest:
<http://www.nwo.nl/en/documents/nwo/legal/nwo-code-of-conduct-on-conflicts-of-interest>
- Fixed rates in salary tables:
<http://www.stw.nl/en/content/applicant>
- Standard amounts for foreign accommodation expenses:
<http://www.stw.nl/en/content/applicant>
- NWO information on Open Access:
www.nwo.nl/openscience-en
- Nagoya Protocol
<https://www.cbd.int>
- ISAAC:
<https://www.isaac.stw.nl>
- How ISAAC works:
An ISAAC manual can be found in ISAAC (tab 'Help')
- ISAAC helpdesk:
isaac.helpdesk@nwo.nl