



Exact and Natural Sciences

## **Call for proposals**

### **CarboBiotics: Pre/Probiotics Mitigating the Antibiotics Burden**

#### **Partnership Programme NWO-CCC**

2017

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# 1 Introduction

## 1.1 Background

The Dutch government has designated the Agri&Food sector as one of the Top Sectors. Within the Top Sectors, the business community, knowledge institutions and the government collaborate financially and based on content to support knowledge and innovation development. The related arrangements are laid down in innovation contracts; see <http://www.tki-agrifood.nl> for details concerning the Agri&Food sector. The [NWO Work Programme 2016-2017](#) for the Top Sector Agri&Food provides an overview of activities carried out by NWO in cooperation with this sector. The NWO-CCC Partnership Programme CarboBiotics is one of these Top Sector activities.

The NWO-CCC Partnership Programme was initiated to stimulate effective collaboration between academia and industry on the role of carbohydrates in human and animal health. The industrial partners of the Carbohydrate Competence Center (CCC) are jointly the industrial partner in this programme. CCC is active at the forefront of innovative carbohydrate research through collaboration of a diversity of food and feed companies with knowledge institute partners, to strive towards a healthy and sustainable society. Based in the Netherlands, CCC has established an internationally renowned centre with national and multinational companies and an extensive network of strong knowledge partners.

Antibiotics are efficient tools to combat infectious diseases, killing pathogenic bacteria via different mechanisms, with positive effects on human and animal performance and health. Extensive and prolonged antibiotic treatments however cause severe side effects, e.g. (1) reduced gastro-intestinal health, less efficient and reduced digestion of food, and (2) a rapid appearance of strains of bacteria resistant to antibiotics. NWO and CCC have decided to join forces to analyse the ability of prebiotic carbohydrates, and combinations of prebiotics with probiotic bacteria, to mitigate the antibiotics burden. Preliminary evidence indicates that prebiotics/probiotics support the maintenance and recovery of balanced bacterial populations in humans and animals. The aim of this programme is to develop in-depth fundamental knowledge about the effectiveness of prebiotics/ probiotics, and to elucidate in detail the underlying mechanisms.

The NWO-CCC Partnership Programme "CarboBiotics: Pre/Probiotics mitigating the Antibiotics burden" was prepared in consultation with the Top Sector Agri&Food.

## 1.2 Preamble

The research in this NWO-CCC Partnership Programme will be precompetitive, yet with a clear view on the applicability of the results for industrial benefits. Research projects to be funded under this call will study the ability of prebiotic carbohydrates, and combinations of prebiotics with probiotic bacteria, to counteract the undesirable effects of antibiotic treatment in humans and animals, and/or to reduce the need for use of antibiotics in animal feeds. The newly gained knowledge may allow application of prebiotic carbohydrates and probiotic bacteria in animal feeds, human food, and medical nutrition, and to reduce the use of antibiotics in animal feed at livestock farms, thus mitigating the antibiotics burden.

### **1.3 Participating companies**

The participating industries AVEBE, FrieslandCampina and Nutrition Sciences, are CCC members and will co-fund this call. To be effective as a programme, project deliverables must be in the sphere of interest of these companies.

### **1.4 Available budget**

The total funding budget available for this call is M€ 2,25 (in cash) for a period of 5 years, funded 50% by NWO and 50% by industrial partners of CCC. The university contributions are additional and implicit on 'in kind' basis, by making available infrastructure, equipment, and guidance/supervision through staff. NWO-CCC programme activities will be combined with other CCC activities as much as possible, offering extensive exchange of information about use of specific research technologies, carbohydrate structural analysis, and new CCC initiatives.

The budget of M€ 2,25 is available for research projects by PhD students and/or postdocs, to be carried out by knowledge institutions in partnership with partners from the private sector. Applications are expected for a maximum project size of k€ 500 (i.e. 2 positions for PhD students and/or postdocs), and it is estimated that a maximum of 5 of these projects can be funded.

### **1.5 Validity of the call for proposals**

This call for proposals is valid until the closing date for submission of full proposals July 6, 2017, 14:00 hours CE(S)T.

## 2 Aim

This call for proposals aims to generate an efficient pipeline of accurate methods to study the effects of antibiotics/prebiotics/probiotics on (in)stability and recovery of gastrointestinal tract microbiota at the strain and population levels, in both humans (specifically infants and elderly) and production animals (poultry, pigs, cows). The existing cross-talk between microbiota and hosts will be studied in detail to elucidate the ensuing (positive/negative) effects on human and animal health. This may result in a better understanding of the mechanisms of functioning of already available prebiotic carbohydrates, and the identification and development of new prebiotics (e.g. psycho- and neurobiotics that interact with host cells and affect mood and behaviour of the host) and "next generation" probiotics (sets of microbiota that will be tailored to interact with a given diet of carbohydrates).

This partnership programme NWO CCC will perform in depth fundamental research at the participating knowledge institutes. The results generated are expected to be of strong and immediate interest for all contributing industrial partners.

### **CarboBiotics: Prebiotics/Probiotics mitigating the Antibiotics Burden**

Antibiotics are efficient tools to combat infectious diseases, killing pathogenic bacteria via different mechanisms. These compounds are mainly produced by microorganisms and are thought to serve as competitive tools in natural environments. Antibiotics clearly are a blessing for mankind, and have saved millions of human lives. However, it has become increasingly clear that especially extensive and prolonged antibiotic treatments cause severe side effects. Most profoundly, the non-pathogenic bacteria on and in our human body are severely reduced in number and diversity. These resident non-pathogenic bacterial populations are very important for our food digestion (intestinal tract microbiota), and our health: maintaining stable ecosystems that serve to exclude harmful microorganisms (intestinal, skin and lung microbiota). Antibiotic treatments may thus result in reduced gastro-intestinal health, in less efficient and reduced digestion of food, and increased risk of infections. The period of recovery from antibiotic treatment may vary between individuals but generally is quite lengthy, involving regrowth of a balanced bacterial population. This is already undesirable for generally healthy persons, because it results in a general loss of well-being, and also in economic losses. For vulnerable patients, for elderly and young (preterm) children, this can be clearly dangerous. **Aim of this call** is to develop in-depth knowledge about the use and effectiveness of prebiotic carbohydrates and combinations of prebiotics and probiotic bacteria (see below) to prevent harmful effects and to stimulate full and relatively quick recovery of the (gastro-intestinal) microbiota during and/or after periods of antibiotic treatment.

Modern livestock farms may house thousands of animals in high densities. In the past symptoms of diseased individual animals were commonly counteracted by constantly providing antibiotics via animal feed, treating the whole population to avoid the further spread of such infectious diseases. It has become alarmingly clear that bacterial evolution during growth under such selective stress results in a rapid appearance of strains of bacteria resistant to antibiotics. Such strains (e.g. MRSA) can cause havoc in hospitals with vulnerable patients, but may also strongly affect weak infants and elderly people. Governments have taken various measures to reduce the use of antibiotics in animal feed at livestock farms. Although antibiotic use has dropped by 60% from 2009-2014, antibiotics are still widely applied

because of their effectiveness. However, given the health risks and costs involved, it is most desirable to develop new effective dietary strategies to prevent health problems because in this way all animals are easily reached. **Aim of this call** is to develop in-depth knowledge about the use and effectiveness of prebiotic carbohydrates and probiotic bacteria (see below) in animal feeds to avoid or at least reduce the emergence and spread of infectious diseases in animal populations by maintaining balanced and stable resident (gastro-intestinal) bacterial populations.

Prebiotic carbohydrates and probiotic bacteria are promising tools to promote gastro-intestinal health and decrease or even abolish the use of antibiotics in livestock and humans. Prebiotics and probiotics may govern the composition of gut microbiota, stimulate the numbers and physiological roles of what are considered healthy bacteria, thereby preventing colonization of the gut by pathogens and reducing infections. Prebiotic compounds are short oligosaccharides that survive the acidic environment of the stomach, and the digestive enzymes of the small intestine, and withstand intestinal absorption. They are considered to induce the growth or activity of bacteria that contribute to the well-being of their host (e.g. Bifidobacteria and Lactobacilli). In the large intestine they are fermented by the microbiota, stimulating the growth of specific groups of bacteria, also resulting in enhanced synthesis of immune active short-chain fatty acids (SCFA), and anti-inflammatory butyrate. Prebiotic compounds also directly bind to immune active receptors and improve immune function in adults and neonates. Prebiotic carbohydrates include human mother milk oligosaccharides and the already industrially produced fructose-oligosaccharides (FOS, derived from inulin) and galacto-oligosaccharides (GOS, derived from lactose). Currently the biggest applications of such prebiotic compounds currently are in infant nutrition with GOS and FOS provided in a ratio of 9 : 1, consumed world-wide by millions of young children, from infants up to toddlers. Also various glucose-oligosaccharides have now been characterized as prebiotics, especially those that present alternative glycosidic linkage types ( $\alpha$ 1-2, 1-3, 1-6 instead of 1-4), after enzymatic (e.g.  $\alpha$ -glucanotransferases) or chemo/physical treatments of starch/ maltodextrins (e.g. polydextrose). Pectin-, mannose- and xylose-oligosaccharides, and Beta-glucans, are also increasingly recognized as promising prebiotic compounds.

Preliminary evidence indicates that prebiotic carbohydrates stimulate a quick recovery of a healthy balanced bacterial population in the human intestinal tract and suppress intestinal inflammation. Ingested via feeds, prebiotic compounds may also be effective in supporting the maintenance of healthy and balanced bacterial populations in the intestinal tract of animals, serving to prevent establishment of pathogenic bacteria, and ensuing infectious diseases. In both cases this may allow a reduced use of antibiotics. **Research projects to be funded under this NWO CCC call aim to develop in-depth knowledge about the use and effectiveness of prebiotics, and to elucidate in detail the underlying mechanisms. This may involve use of currently recognized prebiotic compounds, or newly derived prebiotics either from other natural carbohydrate sources or produced using chemical and/or enzymatic methods.**

Probiotic bacteria are live micro-organisms which, when administered in adequate amounts, confer a health benefit to the host. At present only preliminary evidence exists for most probiotic health claims. Probiotic use during for instance pregnancy has decreased the risk of asthma in the neonate, and it has also been suggested to decrease the risk for complications during pregnancy. Probiotic bacteria are commercially marketed in fermented dairy products (e.g. yoghurts), in probiotic

fortified food, as freeze-dried cells in tablets, etc. Examples are various Bifidobacteria and Lactobacilli, representing groups of bacteria that may have positive effects on human nutrition and health. **Research projects to be funded under this NWO CCC call aim to develop in-depth knowledge about the use and effectiveness of (combinations of prebiotic carbohydrates and) probiotic bacteria, and to elucidate in detail the underlying mechanisms. This may involve the use of the currently recognized probiotic bacteria, or newly identified bacteria, providing clear experimental insights in their mechanisms of action.**

*The newly gained knowledge will provide a firm basis for the effective development and use of (novel) prebiotic compounds and "next generation" probiotic bacteria, and their applications in animal feeds, human food, and medical nutrition, mitigating the antibiotics burden.*

#### **Scientific disciplines**

The disciplines needed to execute the partnership programme include – amongst others -, carbohydrate structural analysis, immunology (as a research tool, using previously developed methods), food & nutrition technology, gut biology, physiology, microbiology, bioinformatics and proteomics.

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## 3 Guidelines for applicants

### 3.1 Who can apply

Each project proposal has one main applicant to whom the [conditions](#) for submission and granting apply. In addition it is required that there is one co-applicant to whom these conditions equally apply.

The main applicant submits the application on behalf of the project consortium and is responsible for the scientific coherency, reporting of the results and the financial accountability. The NWO budget applied for (including cash contribution for the NWO component) is awarded to the institute of the main applicant, who is responsible for allocating the funding to the partners in accordance with the budget of the awarded funding.

Researchers who have been appointed by any of the research institutes listed below are able to act as the principal applicant:

- Dutch universities;
- NWO and KNAW institutes;
- the Netherlands Cancer Institute;
- Naturalis Biodiversity Center;
- the Max Planck Institute for Psycholinguistics in Nijmegen;
- researchers at the DUBBLE-beamline at ESRF in Grenoble;
- Advanced Research Centre for NanoLithography (ARCNL);
- Royal Netherlands Meteorological Institute<sup>1</sup>;
- UNESCO-IHE Institute for Water Education<sup>1</sup>.

Principal applicants, and co-applicants requesting funding, must:

- hold a doctorate and/or be professor;
- have a paid appointment for at least the duration of the application process and the research period for which the grant is requested.

The principal applicant should submit the application and is responsible for the scientific cohesion and reporting of the results as well as for the financial accounting.

Each proposal should have unambiguous participation from at least two different universities and/or institutes.

In this round, a researcher may submit no more than two applications, and may do so only once as the principal applicant. This means that he/she can act as the principal applicant for one application and can act as co-applicant for another application, or may act as co-applicant for two different applications.

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<sup>1</sup> Researchers from these knowledge institutions can submit an application if they are collaborating with a university within the project, which is clear from a personnel or material contribution to the project from this university.

## 3.2 Project consortium

A Consortium Agreement has been agreed upon by CCC, the participating knowledge institutes and companies, in which among others the financial and IP arrangements have been laid down. The Consortium Agreement is similar to the one used previously for the NWO-CCC Partner Programme CarboKinetics. Projects will be carried out under the umbrella of this common Consortium Agreement. The financial commitment of the companies has been settled with Letters of Commitment to the NWO-CCC Partnership Programme.

Prospective knowledge institute applicants are strongly recommended to interact with the participating companies during the writing phases of pre-proposals and full proposals.

Associated industrial partners are stimulated to organize in-house application-oriented research aiming to rapidly convert the new in depth fundamental knowledge into industrial applications (additional 'in kind' contributions to the programme).

## 3.3 What can be applied for

This call for proposals covers projects for PhD students (AIOs) and postdocs. Appointment as part of the project is 2-3 years for postdocs and 4 years for PhD students (based on a full time appointment; full PhD projects only). Researchers must be appointed to the project for a minimum of two years, working at least 50% part time. The total duration of the overall project, with one or two PhD students and/or postdocs, must be at least two years and be no more than five years.

It is possible to apply for grants of a maximum of € 500,000. Project proposals should be scientifically interdisciplinary.

The grant can only be used for:

- Temporary scientific personnel (PhD student (AIO), postdoc) employed by a university or research institute recognised by NWO. Personnel costs are funded in accordance with the most recent version of the Agreement on Payment of Costs for Scientific Research (['Akkoord bekostiging wetenschappelijk onderzoek'](#)). For each PhD and/or postdoc a personal bench fee of € 5,000 is available to partly cover the costs such as travel costs, visiting congresses and the costs of printing a thesis.
- Material costs required in order to perform the research. Costs associated with knowledge transfer, internationalisation, valorisation or instruments for the research may, to a limited extent, be included in the budget to be financed by the grant. Material costs can never be more than 20% of the grant.

Costs related to computers, standard software and other expenses forming part of the standard facilities of the research institute or the partners' research departments are excluded from the grant, as are the costs of management, supervision, coordination and consultancy.

### 3.4 When can applications be submitted

The deadline for the submission of preproposals is **April 6, 2017**, 14:00 hours CE(S)T.

The deadline for the submission of full proposals is **July 6, 2017**, 14:00 hours CE(S)T.

When you submit your application to ISAAC you will also need to enter additional details online. You should therefore start submitting your application at least one day before the deadline of this call for proposals. Applications submitted after the deadline will not be taken into consideration.

### 3.5 Preparing an application

- Download the application form from the online application system ISAAC or from the website of NWO (at the bottom of the funding page of the funding instrument concerned).
- Complete the application form.
- Save the form as a PDF file and upload it in ISAAC.

The application should be written in English in a standard font (at least 11 points with the exception of the references which may be in a 9–point font). References to external documents (with the exception of references to literature) should be avoided. Do not place any bookmarks in the PDF as these will hinder the processing of your application. To ensure a good processing of your application, the PDF documents may not in any way be protected.

When writing your proposal please bear in mind that it will be read by expert referees as well as a more broadly composed international assessment panel.

### 3.6 Specific conditions

General guidelines and conditions:

The '[NWO regulation on granting](#)' and the '[Agreement on Payment of Costs for Scientific Research](#)' apply to all applications.

NWO Code of Conduct regarding Conflict of Interests:

The '[NWO Code of Conduct regarding Conflict of Interests](#)' applies to all persons and NWO personnel involved in the assessment and decision-making procedure for this call for proposals.

Rules for public-private partnerships:

Upon request of the government NWO, KNAW, TO2, VSNU, Vereniging Hogescholen, VNO-NCW and MKB Nederland have formulated [rules](#) for public-private partnerships in the programming and conduction of fundamental and applied research and for intellectual property. This programme is PPS-version 3 (intensive form).

NWO-CCC Consortium Agreement (see Annex 6.1):

NWO and CCC have agreed that a Consortium Agreement similar to the one used for the NWO-CCC Partner Programme 'CarboKinetics' will be adopted for this NWO-CCC Partner Programme CarboBiotics. The Consortium Agreement is in line with the NWO Framework for Public-Private Partnerships. Projects will be carried out under the

umbrella of this common Consortium Agreement. It provides clear arrangements on the consortium's governance, finances, publications, intellectual property and liability as well as disputes. When a researcher submits a proposal, the consortium partners need to confirm that they have read this Consortium Agreement. A start cannot be made on an approved project until all consortium partners have signed this Consortium Agreement. The final version of the Consortium Agreement will have to be checked and confirmed by the Legal Department of NWO before final signature by all partners.

#### Open Access

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 accessible worldwide (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](http://www.nwo.nl/openscience-en).

#### Start of the project

If the proposal is successful, the partners –including the knowledge institutions involved- are required to fulfill certain conditions before the project can actually start:

- All partners should have signed the final version of the Consortium Agreement (after approval of the Consortium Agreement by NWO).
- The companies that provide a 'cash' contribution should have confirmed their contribution for the whole project period to NWO (incl. payment tranches) and should transfer the first tranche of the 'cash' contribution to NWO.
- The project leader fills in the details of the project employees to be appointed to the project in ISAAC and uploads the appointment form.
- A 'data management plan' has to be presented to NWO by the consortium partners within 4 months after the proposal was granted. This plan should be in accordance with the NWO policy on data management, and meet the FAIR standard (Findable, Accessible, Interoperable, Reusable).

Within half a year after award, the partners must have fulfilled these conditions and the project must have been started by appointing the first PhD or postdoc. If it is not possible to achieve this, the awarded research grant may be withdrawn.

#### 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:

##### 1. Data management paragraph

The data management paragraph is part of the research 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.

## 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 will approve the plan as quickly as possible. Approval of the data management plan by NWO 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 at [www.nwo.nl/datamanagement](http://www.nwo.nl/datamanagement).

### 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 ([www.absfocalpoint.nl](http://www.absfocalpoint.nl)). NWO assumes that researchers will take all necessary actions with respect to the Nagoya Protocol.

## 3.7 Submitting an application

An application can only be submitted via the online application system ISAAC ([www.isaac.nwo.nl](http://www.isaac.nwo.nl)). Applications that are not submitted via ISAAC will not be considered. A main applicant must submit his/her application via his/her own ISAAC account. If the main applicant does not have an ISAAC account yet, he or she should create this at least one day before the submission. Then any registration problems that may arise can be resolved on time. If the main applicant already has an ISAAC account then he/she does not need to create a new account to submit a new application.

When you submit your application in ISAAC you will need to enter several additional details online. Make sure you allow sufficient time for this. In ISAAC you can only use ASCII symbols ("plain text"), the use of (structural) formulas, illustrations, italics, et cetera is therefore not possible. These can of course be used in the actual proposal.

For technical questions please contact the ISAAC helpdesk, see Section 5.2.

You can state a maximum of three names of people who may not act as an external referee for your proposal (also referred to as 'non-referees'). These can be researchers as well as representatives from private and public parties. You may state the names of any non-referees in ISAAC.

## 3.8 Additional note for applicants

FrieslandCampina participates in this NWO-CCC partnership programme together with two other industrial partners AVEBE and Nutrition Sciences. Both food and feed are included in this research programme, and therefore it is anticipated that experiments with animals can be part of some research projects.

FrieslandCampina will not participate in proposals and projects that comprise animal experiments, both actively and inactively. By definition, animal experiments require a DEC application.

## 4 Assessment procedure

### 4.1 Procedure

Each prospective applicant is obliged to consult with the Management Team of CCC ([info@cccresearch.nl](mailto:info@cccresearch.nl)) to check beforehand if the intended (pre-)proposal fits within the frame of the programme as laid out by NWO-CCC, to align expectations. Prospective applicants who do not comply with the intended scope of the programme will be strongly discouraged to apply.

It is obligatory to submit a pre-proposal. Pre-proposals will be reviewed by a programme committee with representatives of all participating NWO-CCC CarboBiotics companies and scientific/societal experts appointed by NWO, within 4 weeks after closure of the call for pre-proposals. This selection will primarily be on the fit with the intended programme. It is expected that 10-15 applicants of pre-proposals will be invited to write a full proposal. Other applicants will be strongly discouraged to submit a full proposal. At this stage the programme committee also may stimulate applicants to jointly apply (e.g. in case of clear complementarity or strong overlap of proposals).

NWO will organize the evaluation of all full proposals by a minimum of two external, international reviewers, renowned and independent researchers with a background in the relevant scientific disciplines. The applicants will receive the review reports and have the opportunity to submit a rebuttal.

The programme committee will receive all full proposals, review reports and rebuttals. The assessment committee will issue an advice to the accredited board within NWO<sup>2</sup> about the assessment and ranking of the project proposals. During the realisation of this advice, policy considerations can play a role, such as realising a balance on the content of the programme or a reasonable spread of the projects across the research field covered by the programme, in the case of project proposals that have the same level of quality. The accredited board within NWO will decide about the allocation of funding.

The [NWO Code of Conduct regarding Conflict of Interests](#) applies to all persons and relevant NWO personnel involved in the review and/or decision-making processes.

NWO gives all full proposals a [qualification](#). This qualification will be announced to the applicant together with the funding decision.

#### 4.1.1 Programme management

The CCC NWO programme will be managed by a programme committee (PC). The Programme Committee will be different in composition during the assessment phase and during the management phase once projects have started. The PC will be

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<sup>2</sup> In 2017, NWO will have a new governance structure with a central Executive Board and four domain boards (<http://www.nwo.nl/en/news-and-events/news/2015/contours-new-nwo-announced.html>). More details as to what the "accredited board" for this funding instrument is will be published in due course on the NWO Funding page for this call.

chaired by a chairman appointed by NWO in the assessment phase and by the scientific director of CCC in the management phase. NWO and CCC shall appoint a programme manager as secretary to the PC, who will support the work of the PC in both phases and will manage the daily affairs regarding administration. CCC will appoint an operational manager for daily affairs regarding organization and running of the programme. All members of the PC will sign a non-disclosure agreement (NDA) to protect each idea laid down in the project (pre-)proposals. During and after evaluation, the PC (including the members on behalf of CCC) will not communicate on any of the contents of the project (pre-)proposals or the selection process outside the PC.

#### *Assessment phase*

During the assessment phase the Programme Committee will consist of a maximum of 12 persons. Each industrial partner will have one representative; a maximum of six additional members (independent scientific experts) will be nominated by NWO. The PC will be chaired by a technical chairperson without direct involvement in the assessment. Each member of the PC has the skills and knowledge to assess the project (pre-)proposals. The PC will make the selection of the pre-proposals after the initial call, and invite selected applicants to apply with a full proposal. The PC will prioritize and rank all full proposals, and provide a recommendation about selection of proposals to accredited board within NWO.

#### *Management phase*

During the management phase the Programme Committee will consist of representatives of all industrial parties and knowledge institutes involved and with the scientific director of CCC as an independent chairman. Each member of the PC has the skills and knowledge to supervise the execution of the programme. The PC is responsible for the overall directions and management of the programme during its entire lifecycle. PC meetings will be organized at least once a year unless the PC decides differently. The PC will invite all project leaders to present the progress in their projects. The PC may invite other advisory members to their meetings in the management phase (not during the assessment procedure) who will not have voting rights.

### **4.1.2 Admissibility of applications**

The first step is to determine whether applications are admissible.

NWO shall not process any applications (pre-proposal or and full proposal) in cases where one or more of the following apply:

- the application was not completed correctly or in full and the applicant failed to comply with the request to submit a corrected application by the relevant deadline;
- the application is not in English;
- the principal applicant does not fit the description given in section 3.1;
- the application is not in keeping with the aim and themes of this call for proposals;
- the application was not submitted using ISAAC;
- the application was submitted after the deadline;
- the project cannot start within six months of the grant being awarded;
- the scientific content of a full proposal is not in line with the pre-proposal;
- the project proposed cannot be carried out with the funding applied for.

In cases where it is possible to correct the application, the applicant shall be given

48 hours to modify the application. If the application is not corrected by the relevant deadline, it shall not be considered. Following its approval, the corrected applications shall be considered.

#### 4.1.3 Assessment of full proposals

Assessment of full proposals consists of two phases:

##### Phase 1: Assessment by external referees and rebuttal.

At least two international referees are to issue an assessment report for each proposal, based on the applicable criteria. Applicants shall be given the opportunity to respond in writing to the reports of the referees (rebuttal).

##### Phase 2: Assessment by programme committee.

The programme committee shall use full applications, the external referee reports and the written rebuttals from applicants to make an independent assessment of each of the applications. The role played by the programme committee is different from that played by the external referees in that the committee, unlike the referees, is to see all applications, comments from referees and written responses from applicants. For this reason, the programme committee and the referees may make different assessments.

The members of the programme committee shall discuss all applications during a meeting, using the applicable criteria (see section 4.2) as a basis. The meeting will result in a recommendation on each application and a recommendation regarding the prioritisation of all applications.

#### 4.1.4 Decision

The accredited board within NWO takes a decision about granting based on the recommendation of the programme committee. The board has the right not to use the entire budget available, depending on the number and quality of the applications.

#### 4.1.5 Timetable

January 2017	Publication of call for proposals
February 2017	Match-making
6 April 2017	Deadline for submitting pre-proposals
May 2017	Selected applicants are invited to submit a full proposal
6 July 2017	Deadline for submitting full proposals
September 2017	Applicants are given opportunity to respond to recommendations from referees
October 2017	Assessment and prioritization of applications by assessment committee

October 2017	NWO accredited board decision to grant or reject applications
April 2018	All research projects started

## 4.2 Criteria

Applications are to be assessed on the basis of the following criteria:

- A. Originality and scientific quality;
- B. Potential for societal and economic application.

The two criteria are given equal weight in the assessment procedure and prioritization. NWO makes use of scores on a scale from 1 (excellent) to 9 (unsatisfactory). A separate score is provided for each criterion. To be eligible for funding both the originality and scientific quality of the proposal (criterion A) and the potential for economic and societal impact (criterion B) must score at least very good.

### A. Originality and scientific quality

- Originality and innovative nature, potential for excellent, precompetitive scientific contributions; development of new knowledge and/or concepts, or ground breaking methods and technologies;
- Scientific quality of proposal: objectives, approach and methods, fitness for purpose and feasibility;
- Scientific quality of the consortium: interdisciplinary collaboration within and between subprojects in the research, national and international embedding, publications, expertise, access to the required equipment and facilities.

### B. Potential for societal and economic application

- Potential for societal and economic added value. In this call, with 50% private contribution, the emphasis is on the economic application within the sphere of interest of the participating private partners. In addition there is a societal value as described in the aim of this call;
- The added value and potential for practical application of the envisaged research results in economic and/or social terms;
- Extent to which the application is in keeping with the aim of this call for proposals (see section 2)

# 5 Contact details and other information

## 5.1 Contact

### 5.1.1 Specific questions

For specific questions about this call for proposals please contact:

Drs. Martijn Los, NWO  
T: 070-3440508

Email: [alwccc@nwo.nl](mailto:alwccc@nwo.nl)

For specific questions about the NWO-CCC partnership, please contact:  
[info@cccresearch.nl](mailto:info@cccresearch.nl)

### 5.1.2 Technical questions about the electronic application system ISAAC

For technical questions about the use of ISAAC please contact the ISAAC helpdesk. Please read the manual first before consulting the helpdesk. The ISAAC helpdesk can be contacted from Monday to Friday between 10:00 and 17:00 hours CET on +31 (0)900 696 4747. Unfortunately, not all foreign telecom companies support calling to 0900-numbers. However, you can also submit your question by e-mail to [isaac.helpdesk@nwo.nl](mailto:isaac.helpdesk@nwo.nl). You will then receive an answer within two working days.

# 6 Annexes

## 6.1 NWO-CCC Consortium Agreement

NWO-CARBOHYDRATE COMPETENCE CENTER PARTNERSHIP PROGRAMME (CARBOBIOTICS): CONSORTIUM AGREEMENT

# CONSORTIUM AGREEMENT NWO- CARBOHYDRATE COMPETENCE CENTER PARTNERSHIP PROGRAMME CarboBiotics

between

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**The undersigned:**

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the foregoing entities 1 to .. are solely referred to as "Party" and collectively to as "Parties".

Parties ..... hereinafter, jointly or individually, referred to as "Industrial Parties" or "Industrial Party"

Parties ..... hereinafter, jointly or individually, referred to as "Knowledge Institutes" or "Knowledge Institute"

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**taking into account:**

- A. *that* Parties want to co-operate in the domain of carbohydrate-related strategic-fundamental research and evolving industrial innovation, namely the detailed subjects specified in the approved full project proposals (Appendix 2) submitted within the frame of the NWO – Carbohydrate Competence Center Partnership Programme "Prebiotics/Probiotics mitigating the Antibiotics Burden (CarboBiotics)", its annexes, and future working plans. Assessment and approval of the full project proposals was conducted according to the procedure described in the "Call for proposals" (Appendix 3).
- B. *that* Parties, in that scope, have consulted each other to combine their activities in this field and thereto will jointly set up CarboBiotics (as defined in this Agreement).
- C. *that* the collective aim of CarboBiotics is to generate, develop and share know how in the domain of carbohydrates.

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- D. *that* the Industrial Parties articulate their innovation questions, assume a strong steering role in the research and exert their strengths to commercialize the outcome of research efforts.
- E. *that* the Knowledge Institutes have disposal of, and/or capacities to gain the relevant knowledge, to contribute to the achievements of said aims.
- F. *that* to realize the collective aim as optimally as possible, Parties commit themselves to provide CarboBiotics with the needed information in a timely fashion.
- 70 G. *that* Parties wish to lay down the agreements regarding their collaboration in CarboBiotics in this consortium agreement between the Parties (“Agreement”).
- H. *that* NWO and Carbohydrate Competence Center will jointly be responsible for the management of CarboBiotics.
- I. *that* NWO has granted a research subsidy, including the Contribution of the Industrial Parties, to ... projects in the CarboBiotics Programme, being:
  - a) .....
  - b) .....

**have agreed as follows:**

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**Article 1 Definitions (alphabetical order)**

- *Affiliate*: any legal entity that is under the direct or indirect control of a Party, or under the same direct or indirect control as the Party, or that is directly or indirectly controlling a Party. Control may, in particular, take either of the following terms: (a) the direct or indirect holding of more than 50% of the nominal value of the issued share capital of the legal entity concerned, or of a majority of the voting rights of the shareholders or associates of that entity; (b) the direct or indirect holding, in fact or in law, of decision making powers in the legal entity concerned.
- *Agreement*: this consortium agreement NWO-Carbohydrate Competence Center Partnership Programme Prebiotics/Probiotics mitigating the Antibiotics Burden (CarboBiotics).
- 90 - *Background*: all information, data, materials, know-how, knowledge, methods, techniques, whatever its form or nature (tangible or intangible), including any rights such as intellectual property rights that is/are (i) owned by a Party and/or Affiliate prior to the date of the Agreement and identified by the Parties in Appendix 5 to this Agreement, and/or (ii) developed or acquired by a Party and/or Affiliate after its accession to this Agreement outside the scope of the Programme and introduced by such Party into a Project of the Programme in accordance with the provisions of Article 4.
- *Business Focus Area*: field of application/exploitation for the Industrial Parties of the Programme, to be defined before the start of the Programme. Such definition may be based on type of feedstock, market segment (product type, geographic region), product property et cetera.
- *Carbohydrates*: organic compounds, found in living organisms and composed of carbon, hydrogen  
100 and oxygen, as well as their chemical derivatives. Carbohydrates are classified into mono, di, tri, poly and heterosaccharides. The most important carbohydrates are starches, sugars, bacterial and plant cell wall polysaccharides and gums.
- *Carbohydrate Competence Center (CCC)*: a consortium of public and private parties co-operating in the domain of carbohydrate-related strategic-fundamental research and evolving industrial innovation. University of Groningen is Commissioner of CCC. CCC has the ambition to clearly position itself in the national and international carbohydrate knowledge arena, with the aim to generate, develop and share know how in the domain of carbohydrates. This aim is pursued by setting up and executing various research programmes and projects with combinations of partners of CCC.
- *CarboBiotics*: the consortium established by the Parties in accordance with article 2.

- 110 - *Contribution*: the contribution in cash to the Programme by Parties in the Programme as further described in article 7.
- *Decision*: the letter from NWO in which the subsidy is awarded, including all conditions imposed by NWO in connection with the CarboBiotics Programme, such as, without limitation, Article 2.2.2 of the Community Framework for State Aid (2014/C 198/01), the NWO Regeling Subsidies, Akkoord bekostiging wetenschappelijk onderzoek, NWO Beleid Intellectuele Eigendom and ALW Aanwijzingen voor project- en programmaleiders.
- *Director*: the person(s) appointed in accordance with article 3 and charged with the final responsibility for the day-to-day management of CarboBiotics and with a focus on the scientific and strategic management of CarboBiotics. The Director of CarboBiotics is prof. dr. L. Dijkhuizen of the
- 120 RUG and scientific director of CCC.
- *Evaluation Panel*: the Evaluation Panel is an ad-hoc body installed by NWO at request of the Management Board. The Evaluation Panel is responsible for evaluating the scientific progress and output of CarboBiotics during and after the Programme.
- *Management Board*: The Director together with the Operational Manager and the Programme Manager constitutes the Management Board of CarboBiotics, appointed in accordance with article 3 and responsible for day-to-day management of CarboBiotics.
- *Operational Manager*: the person appointed by CCC, in accordance with article 3 and responsible for day-to-day operational management of CarboBiotics.
- *Programme*: the CarboBiotics research portfolio comprising a well-defined Programme for the years
- 130 2016-2020, as laid down in the approved project proposals submitted within the frame of the NWO – Carbohydrate Competence Center Partnership Programme “ Prebiotics/Probiotics mitigating the Antibiotics Burden (CarboBiotics)”, annexes (e.g. Programme description and budget overview), and future working plans, being attached to, and forming an integral part of, this Agreement, as appendix 2.
- *Programme Committee (PC)*: the Programme Committee is a body of CarboBiotics. The Programme Committee is responsible for supervising (the management of) CarboBiotics.

- *Programme manager (PM)*: appointed by NWO. The Programme manager will act as a secretary to the PC and will support the work of the PC and will manage the daily affairs regarding the financial administration and project reports within the Programme in accordance with NWO-regulations.
- 140 - *Project*: specific research activities to be carried out under this Agreement, characterized by distinct goals as well as activities and budget per Party. The description used in the approved full project proposals submitted within the frame of the NWO – Carbohydrate Competence Center Partnership Programme “Prebiotics/Probiotics mitigating the Antibiotics Burden (CarboBiotics)” will be the basic definition of the project unless agreed otherwise unanimously by all the Parties within the Programme.
- *Project Party/ies*: the two respective Knowledge Institutes involved in the respective Project and the three Industrial Parties. Also described as ‘Parties within the Project’.
- *Project Leader*: The persons within CarboBiotics responsible for the following aspects of parts of the Project: (a) the set-up, (b) the day to day coordination of scientific aspects and (c) progress and  
150 accomplishment of the milestones. Parties involved in the Project unanimously propose a candidate to become Project Leader. This proposal is approved by the Programme Committee. The Project Leader is reporting to the Director of CarboBiotics. In case of malfunctioning of the Project Leader, the Programme Committee is entitled to appoint another Project Leader after consulting the Parties involved in the relevant Project and the Director.
- *Research Results*: all information, data, materials, know-how, knowledge, methods, techniques, expertise, interim and/or end results generated by the Party / Parties under and within the limits of the Programme, including the rights associated with this information, these data, materials, know-how, knowledge, methods, techniques, expertise, interim and/or end results resulting from an  
160 application for or the granting of intellectual property rights.

References to articles are to the articles of this Agreement, unless stipulated otherwise.

## **Article 2 General Clauses (No legal entity; participation of Parties).**

### **2.1 Collaboration between the Parties**

The Parties hereby establish a consortium with the name NWO – Carbohydrate Competence Center Partnership Programme “Prebiotics/Probiotics mitigating the Antibiotics Burden”, in this Agreement referred to as “CarboBiotics”. This Agreement is considered by the Parties as pertaining to their mutual collaboration as well as constituting for each of the Parties the agreement by means of which they participate in CarboBiotics. The office of CarboBiotics is located at the Carbohydrate Competence Center (CCC), Nijenborgh 7, 9747 AG, in Groningen.

## **2.2 Support**

The Parties agree that the Carbohydrate Competence Center (hereinafter ‘CCC’), and legally represented by prof. dr. S. Poppema, president of the University of Groningen, will be involved in the execution of the Programme as member of the Management Board, with the tasks as described in articles 3.1 and 3.2. Herewith, the Parties empower CCC to represent the members of the consortium mentioned in paragraph 2.1 where applicable in the execution of their tasks. In such cases and where applicable, the CCC will sign as ‘director of the consortium’. CCC-representatives, involved in the Programme, will be bound by the provisions of this Agreement, especially the principles of confidentiality as laid down in provisions on Mutual Non-disclosure (Appendix 1).

## **Article 3 Institutes of CarboBiotics**

CarboBiotics will have the following bodies:

- The Programme Committee
- The Management Board
- The Evaluation Panel

Every member of the Programme Committee and the Management Board respectively shall be bound by the provisions of this Agreement. The members of the Evaluation Panel will be bound by the general provisions of NWO, including non-disclosure regulations.

## **3.1 The Programme Committee**

The Programme Committee encompasses representatives of all participating Parties with a maximum of ..... persons, including the chair. Each Party will have one representative. Each member of the PC has the skills and knowledge to supervise the execution of the Programme. The PC is responsible for the overall directions and management of the Programme during its entire lifecycle. The PC will be chaired by the scientific director of CCC, also director of the Management Board CarboBiotics. As a consequence of art. 3.2 the chairman will not have voting rights.

200 The PC meets at least once a year unless the PC decided differently. On written request of at least a number of PC representatives authorized to cast at least one fifth of the votes at meetings of the PC, the chairman of the PC must convene a meeting of the PC.

Meetings will be convened with due observance of a period of at least fifteen working days (a week will consist of five working days), not taking into account the day of the notice nor the day of the meeting. The notice convening the meeting will state the place and time of the meeting, as well as the items on the agenda. If the chairman or the secretary is absent, the Programme Committee will appoint a deputy chairman of said meeting.

In performing its duties the PC of CarboBiotics shall act in accordance with the common interests of the Carbohydrate Competence Center and the activities connected with it.

210 All decisions (to be) taken by the PC will be adopted by a simple majority of the votes cast with a minimum quorum of two third of the votes cast, unless stipulated otherwise in this Agreement. If in a meeting less than two third of the votes cast is present and/or represented, then no resolutions will be adopted and the items on the agenda will be handled in the following Meeting of the PC, to be convened in accordance with this article. Irrespective of the PC members present and/or represented in this following meeting, members can adopt decisions concerning the items on the agenda of the previous and this following meeting by a simple majority of the votes cast, unless stipulated otherwise in this Agreement.

220 Each member has a voting right. For Industrial Parties the weight of the vote will be according to their financial effort, for the Knowledge Institutes the weight will be according to the number of their PhD- or postdoc positions. See appendix 4. Every member may be represented by another member, to be evidenced by a written and signed proxy. A member may represent at most two other members.

The secretary or another person designated by the chairman will take minutes of the meeting. The minutes will be confirmed by the next meeting and signed and dated by the chairman.

The chairman of the PC may invite members of the Management Board and/or other parties to attend its meetings.

230 Resolutions may be adopted outside a meeting if no member objects to passing such resolutions and all Parties take part in such resolution in writing.

### **3.1a Duties and authorities of the Programme Committee**

The PC is charged with the supervision of the Management Board and advises the Management Board when requested to do so or when the PC itself is of the opinion that it should. In the discharge of their duties, the PC will be guided by the interest of CarboBiotics and its activities.

The PC is authorized to inspect all books and records of CarboBiotics and to take cognisance of all acts performed.

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The PC will decide on an application of admission of new Parties of CarboBiotics.

### **3.2 Management Board**

CarboBiotics will be managed by the Management Board. The Management Board will be formed by the Director, the Programme Manager and the Operational Manager, all three natural persons.

In performing its duties the Management Board of CarboBiotics shall act in accordance with the common interests of the Carbohydrate Competence Center and the activities connected with it.

A member of the Management Board cannot be a voting member of the Programme Committee. The Programme Committee can suspend or dismiss a member of the Management Board at all times, which

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suspension or dismissal will not be on unreasonable grounds.

In the event of absence or vacancy of a member of the Management Board, the other members of the Management Board will deputize the concerning duties, unless the Programme Committee decides otherwise.

The Management Board will adopt the management regulations of CarboBiotics, which includes the manner and frequency of holding meetings, the secretariat, decision-making, the duties assigned to each member of the Management Board, the scheduled meetings with the Programme Committee of CarboBiotics, and all other matters that the Management Board deems to be necessary. The  
260 management regulations will be in accordance with the rules of the parties granting subsidies.

The management regulations and any amendments of the management regulations need the prior approval of the Programme Committee.

The Management Board will provide the Programme Committee the necessary information and documentation timely in order to perform its duties.

Every six months the Management Board will evaluate the Programme in accordance with the rules of the NWO. All of these will also be presented to the Programme Committee.  
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The Management Board will submit and provide the parties granting subsidies with all information and documentation with due observance of the relevant subsidy arrangements.

### **3.2a Duties and authorities of the Management Board**

The Director is charged with the day-to-day management.

The Management Board is responsible for:

- correct execution of the Programme with respect to scientific standing, the management regulations and managerial and financial rules;
  - financial matters, in accordance with the rules of NWO;
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- the implementation of all decisions taken by the Programme Committee and carrying out any other duties delegated by the Programme Committee.

Other duties and authorities can be determined in the management regulations of the Management Board.

### 3.3 The Evaluation Panel

290 The Evaluation Panel is an *ad-hoc* body installed by NWO at the request of the Management Board and subject to the NWO regulations for committees, including non-disclosure regulations. The Evaluation Panel is responsible for evaluating the scientific progress and output of CarboBiotics during and after the Programme.

The Evaluation Panel consists of three natural persons and is formed by two independent societal/scientific representatives and a chairman, all nominated by NWO.

The Evaluation Panel will be invited by NWO two times during the Programme lifetime to provide an evaluation of the scientific progress and output of CarboBiotics. A first evaluation will be carried out halfway the Programme (.....) and a second evaluation after the Programme is completed (.....).

300 All decisions by the Evaluation Panel will be adopted by a simple majority of the Evaluation Panel.

No resolutions may be adopted if no majority of the Evaluation Panel is present at the meeting, unless all absentees have been consulted in writing and such consultation has shown that the majority of the members of the Evaluation Panel have expressed themselves in favour of the proposal under discussion. Each member of the Evaluation Panel has one vote at the meeting.

#### 3.3a Duties and authorities of the Evaluation Panel

The Parties agree herewith that, based on the evaluation results, the Evaluation Panel is authorized to provide weighty advice to the Programme Committee and the Management Board with a view to the

310 scientific progress of CarboBiotics and the overall activities connected with it. According to NWO regulations, conclusions and advice of the Evaluation Panel will also be sent to the board of NWO. Members of this board will be bound to NWO regulations on non-disclosure.

#### **Article 4 Ownership and use of Background**

All Background is and shall remain the exclusive property of the Party that has made such Background available. Each Party shall identify its Background prior to disclosing such Background for use in the Programme.

Each Party hereby grants to all other Parties participating in the Programme wherein the Background was introduced a royalty free, non-transferable right of use of its contributed Background, solely for research activities related to the Programme under this Agreement during the term of the Programme.

320 In Appendix 5, the Parties have identified and agreed on the Background for the Programme and have also, where relevant, informed each other that access rights to specific Background is subject to legal restrictions or limits.

Any Party may add further own Background to Appendix 5 during the Programme by written notice to the other Parties. However, approval of the Programme Committee is needed should a Party wish to modify or withdraw its Background in Appendix 5.

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#### **Article 5 Ownership and use of Research Results**

The Project Parties within each of the ..... Projects of the Programme will obtain a joint ownership with regard to the Research Results developed within the Projects of the Programme pro rata to their respective value of their Contribution.

Each Project Party shall ensure that the other Project Parties are informed of any Research Results generated in the Project promptly after the generating Party becomes aware of any Research Results.

340 Research Results within the Business Focus Area(s) as defined in appendix 6, cannot be used, exploited and/or encumbered by any individual Party involved in the Project of the Programme, unless stipulated otherwise in this article. The acquisition of exploitation rights will be in conformity with market conditions, according to EU directives on State Aid Rules as specified in “O&O&I steunkaderregeling (2014/C 198/01)”.

**Exploitation (and revenue sharing) outside the Business Focus Area(s)**

Notwithstanding the foregoing, solely the Parties being Knowledge Institute involved in one of the Projects of the Programme are allowed to use and exploit the Research Results in this Project also outside the purpose of the Business Focus Area(s). In case the Knowledge Institute(s) generate(s) any profit (i.e. revenues remaining after deduction of accountable costs) as a result of any use and/or  
 350 exploitation of the Research Results outside the purpose of the Business Focus Area(s), these profits will be fully ascribed and reimbursed into (the Project of) the Programme. Furthermore, the Project Parties being Knowledge Institutes maintain the right to use the generated knowledge and expertise for academic purposes.

**Exploitation (and revenue sharing) within the Business Focus Area(s)**

In accordance with “NWO Beleid Intellectuele Eigendom” the Industrial Parties will receive a non-exclusive royalty-free exploitation right to the Research Results within their respective Business Focus Area(s). (An) Industrial Party/ies) has/have the first right to obtain the **exclusive** ownership and/or  
 360 exploitation rights of/on the Research Results within their respective Business Focus Area(s). If an Industrial Party waives its right or fails to initiate negotiations (or reach an agreement) within a reasonable period of time (as defined below in this article) after the Research Results have been achieved, the option will also become available to the other Parties within the Project of the Programme. To obtain the exclusive ownership/exploitation rights within its/their Business Focus Area(s), the interested Party/ies will proceed with the buy-out principles set out below. Such reasonable period of time will be 12 weeks after receipt of a written notice and reasonable request of a Knowledge Institute within the Project of the Programme requiring the Industrial Parties in the Project to initiate

negotiations. As soon as (a) Party/ies obtain(s) the exclusive ownership and/or exploitation rights, all (other) rights to use and/or exploit the Research Results (as described in this article 5) related to the obtained exclusive ownership and/or exploitation, i.e. in the relevant Business Focus Area, are terminated immediately, without any right to compensation of costs and/or damages, other than the pro rata compensation resulting from the buy-out outlined below. Parties concerned will cooperate with any actions needed to confirm the termination of their rights in this respect.

### **Buy out principles**

Terms and conditions will be concluded in a purchase agreement, duly signed and agreed upon by all Parties within a Project in the Programme. In this purchase agreement arrangements will be made with respect to the purchase price and/or other relevant arrangements. The purchase price will be contributed and paid to the other Parties in the Project taken into consideration the value of the Contribution of each Party in the Project.

If after negotiations no purchase agreement will be accomplished (“Deadlock”) and if the majority of the Parties involved in the Project agrees with the terms and conditions regarding the buyout, the final offer of the said interested Party should be conclusive and the refusing Party or Parties has/have to accept such offer. The irrevocable decision to either accept the final offer or execute a buyout themselves has to be taken within 10 working days after a Party has declared a Deadlock in writing to the other Parties within the Project taking into account the foregoing procedure.

To avoid any doubt it is explicitly agreed that Background is not included in any (transfer of) ownership of Research Results as mentioned in this article 5. The Party that owns the Background needed for the exploitation of such Research Results shall use its best endeavors to ensure that the Party / Parties that obtain the ownership or license to use the Research Results in accordance with article 5 obtains a non-exclusive license to use the Background against fair and reasonable market conditions, unless it has been stated in appendix 5 that use of such Background is restricted by third-party rights.

### **Patenting**

400 Within 30 working days after having been notified, Parties within a Project of the Programme shall unanimously decide whether they are interested in filing a patent application in respect of such Research Results or wish to rely on know how protection only. If no consensus is achieved within the 30 working days period, the issue will be offered to the Programme Committee for mediation. However, an advice of the Programme Committee concerning the issue will not be a binding advice.

410 A patent application will be filed in the name of, and by, the Party/Parties who generated the Research Results with approval of the patent description by all Parties within the Project. All the costs related to the patent application shall be borne by all the Parties involved in the Project, pro rata to their respective value of their Contribution, except by such Parties that explicitly waive their rights of ownership and/or exploitation rights. If no unanimous support among the Project Parties for the indicated preferences has been achieved within the 30-working day period, the issue will be offered to the Programme Committee for mediation. However, an advice of the Programme Committee concerning the issue will not be a binding advice.

In case a patent is granted and an Industrial Party (or Parties) has (have) obtained an exclusive ownership of the Research Results within its own Business Focus Area, such Industrial Party/Parties will receive an exclusive, royalty free, transferable, irrevocable, sublicensable, worldwide, perpetual license with regard to their own Business Focus Area(s) if applicable.

420 In order to ensure that the research within the CarboBiotics Programme is performed in accordance with European State Aid Rules as specified in "O&O&I steunkaderregeling (2014/C 198/01)" the transferred IPR, licenses and the value for which it is transferred will be reported to the Programme Committee and the subsidy provider NWO. This is done by a report of the Management Board at the end of the research period.

#### **Article 6 Parties' Contributions to the Programme**

The starting points for the research activities within CarboBiotics include:

- The relevant Parties carry out the Programme as laid down in the approved full Project proposals (as described in the NWO decisions to all Knowledge Institutes, Appendix 2).
- Prior to the start of the Programme all Parties have to agree unanimously upon the Background (appendix 5) and the Business Focus Areas (appendix 6) of the Industrial Parties.
- 430 - After the start of the Programme all Parties are allowed to arrange additional considerations regarding ownership of existing intellectual property rights, the Research Results, user rights and conditions in an Addendum. An Addendum has to be approved by the Management Board as well as the Programme Committee.
- Knowledge Institutes will contribute in kind to the Programme by making available personnel, knowledge and research facilities. The Contribution of the Knowledge Institutes will be represented by a pro rata share in the NWO grant.
- Industrial Parties may make personnel and/or research facilities and/or cash available as agreed and specified in the Programme. The Contribution of the Industrial Parties will consist of the in cash contribution to CarboBiotics, as shown in appendix 7.

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**Article 7 Confidentiality and Publication**

Parties commit themselves to the principles of confidentiality as laid down in provisions on Mutual Non-disclosure (Appendix 1). All Project Parties within a Project agree that Research Results in this Project may only be published after written consent of all the Project Parties. If a Party wishes to publish certain Research Results, that Party will inform the other Project Parties and will send a draft publication and written request for approval. Each Project Party has to inform such requesting Party within four weeks after it has received such request whether or not it approves and/or desires modifications of said draft publication. Approval will not unreasonably be withheld. An objection has to include a precise request for necessary modifications. If a Party has not replied within such period of four weeks, such Party is considered to accept such draft to be published.

The Knowledge Institutes have the right to publish the Research Results according to the Netherlands Education Legislation (Wet op het Hoger Onderwijs en Wetenschappelijk Onderzoek (WHW)), but should take into account the confidentiality provisions of this agreement. If one or more Parties oppose to the publication on basis of possible harm to its business interests, because the publication demonstrably contains confidential information of that Party, parties will therefore have “good faith discussions” to overcome the conflicts of interest e.g. by elimination of certain “business sensitive” data. If the Programme Parties are unsuccessful in reaching agreement in such consultation, the issue will be offered to the Programme Committee for mediation. However, an advice of the Programme Committee concerning the issue will not be a binding advice.

In any case, if any Party involved in the Programme wants to seek Intellectual Property protection by filing a patent application, publications can/will be delayed by a maximum period of 6 months from the date of submission of the draft to the other Parties.

### **Article 8 New Parties**

The Management Board will ensure that any third party, of which the Programme Committee decides that it may become a Party, will agree to be bound to the provisions of this Agreement in the same  
 470 manner as the existing Parties and shall comply with all obligations thereof, in consideration of which this new Party can claim all rights of a Party under this Agreement, including any Addendum concluded by the Parties.

### **Article 9 Duration / termination**

- The day all Parties have signed, the Agreement starts and will be entered for a period of five years with the possibility of an extension of this period if Parties should agree thereto in writing. This Agreement may not be prematurely terminated, unless explicitly stipulated in the following provisions.
- Each Party has the right to terminate the Agreement per the end of a contract year, upon one month  
 480 prior written notice, provided at any time at least one month before the expiry of such contract year, by registered mail to the Director. Such terminating Party remains obliged to (i) fulfill its financial obligations towards the other Parties regarding the full Programme period and (ii) to grant access rights pursuant to this Agreement as if it had remained a Party for the whole of the Programme.
- However, when (external) circumstances change (e.g. as a result of newly published knowledge by third parties or change of the research focus within the Programme) the Programme can be changed in accordance with all Parties collaborating in the Programme and NWO.
- The Programme Committee has the right to terminate the Agreement towards one or more of the other Parties with immediate effect if one of more of the following situations is applying to such Party:
- 490 - In the event a Party is in state of bankruptcy or suspension of payment or a petition of that effect is filed by or against that Party;
- In the event the business of a Party will be wound up or closed down;
- In case of force majeure if the force majeure situation will last over ninety (90) days;

- In case a Party is in breach of an obligation resulting from the Agreement, and such Party does not, after having been given written notice of default, meet the obligation within a reasonable term as decided by the Programme Committee.

Such decision by the Programme Committee shall be taken with due observance of article 3, however by a majority vote of 75% of the votes cast, on the understanding that the Party / Parties involved in (a) situation(s) set out above is / are not entitled to vote.

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In case of termination of this Agreement towards a Party (including retirement of such Party), any and all account receivables of the other Parties and/or CarboBiotics towards the Party no longer being a Party to this Agreement will be immediately due and payable by said Party. Access rights granted to a Party involved in (a) situation(s) set forth above and such Party's right to request access rights shall cease immediately upon receipt by such Party of the formal notice of the decision of the Programme Committee to terminate its participation to this Agreement. Such Party shall immediately return any and all other Party's materials, equipment and any other element that can be requested by a Party (including without limitation Confidential Information capable of being returned) in its possession at its own costs.

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In the event of termination of this Agreement, whether in whole or towards a Party, the Parties (including the retiring Party) will remain bound by the provisions of this Agreement that by their nature require to survive the termination of this Agreement, including, but not limited to, non-disclosure, whether the Agreement is terminated by lapse of time/termination or the act of any Party and for any reason.

#### **Article 10 Liability**

The liability of one Party to (an)other Party or Parties is in any case limited to damages with a maximum of the share of that Party in the Programme, as laid down in the budget overview (Appendix 7).

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Parties shall in no case be liable, towards the other Parties, and/or any Affiliates and/or for any indirect, incidental or consequential damages (including without limitation, lost goodwill, economic loss of turnover or profits, loss of revenue, loss of contracts, loss of use, loss of data, loss of use of equipment, cost of removal and reinstallation of goods, interruption of business or other economic loss), provided

that such damages were not caused by gross negligence or wilful misconduct.

Parties are neither jointly, nor individually liable for obligations of CarboBiotics.

A Party shall not be liable towards the other Parties for any claims, costs or damages that may result, directly or indirectly, out of the activities performed within the Programme and/or the use of the Research Results, including infringement of third party rights, unless and to the extent that damage is caused by gross negligence and/or due to wilful misconduct by that Party. If a Party uses or applies any Research Results or enables third parties to use or have used and/or apply the same, that Party shall  
530 indemnify the other Parties from claims of itself and from claims from third parties for damage.

#### **Article 11 General provisions**

- In the event of any conflict between the terms of this Agreement and the appendices thereto, the terms of this Agreement shall prevail over the terms of the appendices thereto and the Parties shall forthwith cause such necessary alterations to be made to the appendices so as to resolve such conflict.
- In the event of any conflict between the terms of this Agreement and a Decision, the Decision shall prevail over the terms of this Agreement and the Parties shall forthwith cause such necessary alterations to be made to the Agreement so as to resolve such conflict.
- 540 - All modifications and amendments to this Agreement shall be made in writing, executed by all Parties or their duly authorized representatives.
- Neither Party shall be entitled to transfer, assign, novate or subcontract its rights and/or obligations under this Agreement to another party without prior written consent from all other Parties by a majority vote of 80% of the votes cast, which consent shall not be withheld or delayed on unreasonable grounds, except to one of its Affiliates by written notice to the other Parties. The aforementioned prohibition in this sub paragraph will not apply in case of transfer by a Party to its legal successor under universal title.
- Neither Party shall have any right or authority to assume, create or incur any liability or obligation of any kind, express or implied, against, in the name of or on behalf of any other Party or CarboBiotics  
550 as a whole, except as provided for in this Agreement.

- No failure by any Party to enforce at any time, or for any period of time, any of the provisions of this Agreement, shall be considered to constitute a waiver of such provisions or of the right thereafter to enforce any and every such provision.
- In the event that any provision contained in this Agreement shall be deemed invalid or unenforceable, the remaining provisions shall be construed as if such invalid or unenforceable provisions were not contained herein, and the Parties shall make a reasonable attempt to negotiate in good faith in order to replace such invalid or unenforceable provisions by valid and enforceable provisions which as closely as possible meet the intention of the Parties when inserting the original provisions.
- 560 - This Agreement may be executed in any number of counterparts, each of which shall be an original, but all of which together shall constitute one instrument.
- Notwithstanding the right to terminate this Agreement subject to clause 10 of this Agreement, Parties hereto waive their right to invoke and/or claim dissolution (“ontbinding”) and/or nullification (“vernietiging”) of this Agreement.
- Any and all notices required to be delivered to any Party pursuant to or in connection with the Agreement shall be in writing and may be delivered by hand, by registered mail with advice of delivery (and with copy per facsimile) to the address of the other Parties as stated in appendix 3, or to such other address or representative as any of the Parties may designate by means of written notice to be send to all other Parties from time to time, taking into account at least one month  
570 notice period before the actual change of address takes place.
- Nothing in this Agreement is intended to or shall operate to create a partnership or joint venture of any kind, between the Parties and/or CarboBiotics, or to authorise any Party and/or CarboBiotics, to act as agent for any other Party and/or CarboBiotics and no Party and/or CarboBiotics shall have authority to act in the name or on behalf of or otherwise to bind any other Party and/or CarboBiotics in any way (including but not limited to the making of any representation or warranty, the assumption of any obligation or liability and the exercise of any right or power).

### **Article 12 Applicable law and disputes**

580 This Agreement shall also be interpreted, governed and enforced exclusively by and in accordance with the laws of the Netherlands.

All disputes in respect of the conclusion, interpretation, performance or the termination of this Agreement or agreements that arise therefrom, are the result thereof or are related thereto, shall be exclusively submitted in the first instance to the adjudication of the competent court in Groningen, the Netherlands, without prejudice to the right of Parties to appeal and cassation.

### **Article 13 Appendices**

The following appendices are added to this Agreement, forming an integral part thereof:

- Appendix 1 Provisions on Mutual Non-disclosure;
- 590 Appendix 2 Approved full project proposals; Decisions NWO;
- Appendix 3 Call for proposals;
- Appendix 4 Distribution of voting rights within the Programme Committee;
- Appendix 5 Background;
- Appendix 6 Business Focus Areas;
- Appendix 7 Budget Overview;
- Appendix 8 NWO-document 'Gedragcode belangenverstrengeling';
- Appendix 9 NWO-document 'Beleid Intellectuele Eigendom'.

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