Format rapportage projectinformatie PPS-en Landbouw, water, voedsel

Datum versie: 7 december 2020

Uit projectplan (svp zoveel mogelijk invullen)

1. Projectinformatie

1.1 Organisatie/financiering *(keuze maken)*	TKI A&F ~~/TKI T&U/WR-PPS/overig~~
1.2 Projectnummer	TKI – AF 16035
1.3 Project titel	PhenFlex-based resilience as measure for health effects of diet
1.4 Projectleider *(naam en emailadres)*	Karin Bosch, karin.bosch@tno.nl
1.5 Startdatum (*dd-mm-jjjj)*	01-04-2017
1.6 Einddatum (*dd-mm-jjjj)*	31-08-2020
1.7 MMIP primair (nummer en naam van het MMIP, zie overzicht bijlage 1)	D2 Gezonde voeding een makkelijke keuze Voormalige roadmap Voeding & Gezondheid
1.8 MMIP secundair *(deze alleen invullen als er een 2e MMIP is waar het project aan bijdraagt)*	N.v.t

2. Projectomschrijving

2.1 Samenvatting *Geef een korte samenvatting van wat het project inhoudt en beoogt. Het gaat om een publiek beschikbare samenvatting (doel, bijdrage aan de missie, op te leveren resultaten in termen van kennis voor doelgroep x en de partners in het project).*

Het meten van gezondheidseffecten van voeding en dieet is nog altijd een obstakel in de innovatieve pijplijn van vele voedingsbedrijven in Europa. Het is lastig om de gezondheidseffecten van een dieet of van ingrediënten te kunnen demonstreren. Om het effect te kunnen laten zien, is het noodzakelijk om een verandering in biomarkers weer te geven na een dieet.

Om de multi-target rol van voeding in het lichaam te erkennen, is het doel van dit project om het concept van verbetering van fenotypische flexibiliteit door voedingsinterventie te onderbouwen. Robuust bewijs voor dit concept en de daarmee samenhangende opkomst van nieuwe biomarkers zal naar verwachting de acceptatie van fenotypische flexibiliteit als gezondheidsvoordeel op zich door regelgevende autoriteiten zoals de EFSA verder bevorderen. Het doel van dit project is om proof-of-concept vast te stellen voor de toepassing van het challenge test-concept voor de wetenschappelijke onderbouwing van gezondheidsvoordelen van een optimale voeding in een gecontroleerde interventionele setting (studie 1)

Bovendien zal in een tweede studie de fenotypische flexibiliteit worden gemeten bij een zieke populatie van COPD-patiënten voor en na hun longrevalidatie (een multidimensionale benadering). Deze studie zal een eerste inzicht geven in de toepasbaarheid en geschiktheid van

het veerkrachtconcept in een populatie met suboptimale gezondheidskenmerken (Spruit et al, Eur Respir J. 2016). De resultaten van de challenge-testresultaten zullen worden vergeleken met de resultaten van controles om een indicatie te vinden van verbetering van de veerkracht bij COPD-patiënten na gepersonaliseerde revalidatie (pilot-studie 2).

2.2 Doel van het project *Wat gaat het project bijdragen aan de doelen van de KIA, de missies en de MMIP's?*

Objectives of the study are:

- To demonstrate that a healthy or optimal diet in an intervention study can improve "metabolic age" and "metabolic stress", which are composite biomarkers by quantifying phenotypic flexibility, within a healthy population. These composite markers validate previous findings from other intervention studies using phenotypic flexibility and could be the next generation biomarkers.
- To show additional advantages of personalization / tailoring of dietary recommendations over general dietary recommendations. PhenFlex-2 delivers the scientific evidence that a healthy diet is beneficial for your health specially when this is tailored to the (nutritional) needs of a person.
- To encourage acceptation of the approach by the international scientific community by publications in peer-reviewed journals and discussions with regulatory authorities.
- To learn more about other new biomarkers, (DIY) methods and study-designs that in the future can be used to substantiate health effects of food and nutrition.

2.3 Motivatie *Licht toe waarom dit project passend en nodig is binnen het MMIP*

The measurement of health effects of food and diet remains a hurdle in the innovation pipeline of many food companies in Europe. Nutrition science has difficulty to demonstrate specific health-beneficial effects related to diet or dietary ingredients such as probiotics. PhenFlex represents a new avenue of providing evidence for building health claims and strengthens the importance of resilience-thinking in health research. Robust proof for this concept and the related emergence of new biomarkers is expected to further promote acceptance of phenotypic flexibility as health benefit in itself by regulatory authorities like the EFSA. A next generation health claim based on the concept of resilience could contribute to making healthy nutrition available to the consumer. Furthermore, within this project we will also evaluate the effect of personalised nutrition based on this resilience concept. The expectation is that when consumers are being confronted with feedback on their health (by means of phenotypic flexibility evaluation) as well as on their eating behaviour, it will become easier to make the healthy choice the easy choice. Therefore, the research from the public private partnership "PhenFlex-based resilience as measure for health effects of diet" contributes to mission D2 healthy nutrition an easy choice

Being resilient is a great value for any dynamic system and a prerequisite to maintain sustainable system performance in increasingly complex, demanding and connected societies. Health is no exception to this. The Netherlands, and TNO as recognized party, is a frontrunner in resilience thinking and this project will contribute to strengthen this position.

2.4 Resultaat *Zo SMART mogelijke beschrijving van de beoogde resultaten van het project. Het gaat om zowel de inhoudelijke resultaten (in relatie tot vraag 2.2) als resultaten zoals bijeenkomsten en rapporten. Geef zoveel mogelijk ook de planning per jaar.*

DELIVERABLES (D) & MILESTONES (M)
D1. design of a biomarker for “metabolic age” and “metabolic stress” as primary read-out for intervention studies and agreed by all partners of the consortium. (June 2017)
D2. approved METC protocol agreed by all partners of the consortium. (August 2017)
D3. approved METC protocol for Ciro study. (August 2017)
M1. Completion of the intervention study. (July 2018)
M2: Completion of the intervention study for Ciro study. (January 2018)
D4. Data Analysis Plan agreed by all partners of the consortium. (October 2018)
D5. Two scientific articles describing results of the human intervention study. (April 2020)
D6. An opinion article that proposes an acceptability strategy for the concepts and application of phenotypic flexibility in collaboration with ILSI and stakeholders from different meetings. (April 2020)

OUTPUT (up to and including 2020)
O1. 13 Scientific publications
O2. >14 Conference publications (poster/presentation)
O3. >2 Spin-offs
O4. 2 New projects with industrial partners
O5. 3 Non-scientific presentations (interviews)

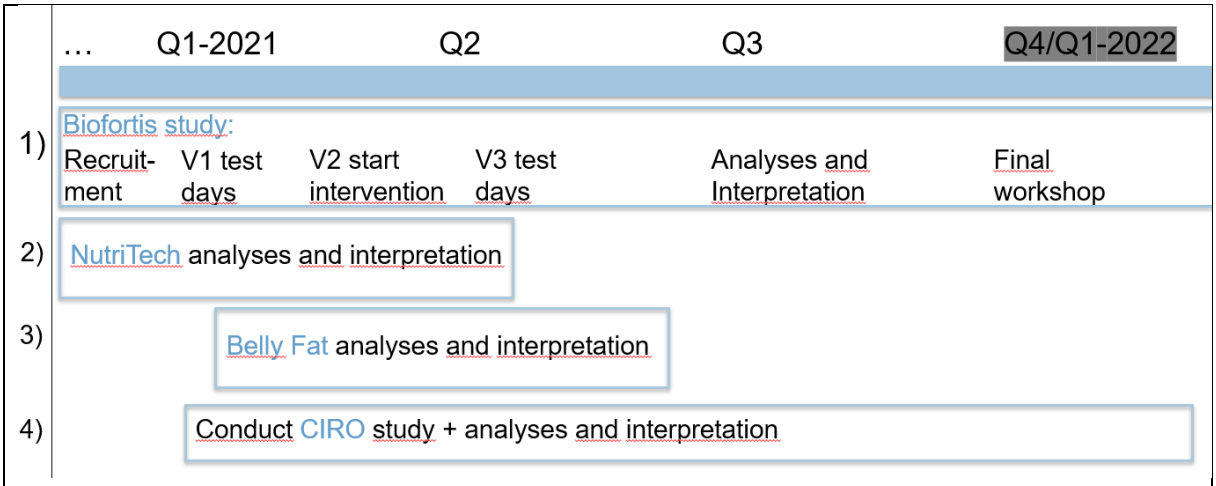
Jaarrapportage (svp ook laatste jaar invullen)

3. Status project

3.1 Status project *(keuze maken)*	~~project loopt op schema~~/project loopt achter/~~project loopt voor/project is niet gestart/project is voortijdig afgesloten/project is afgerond~~
3.2 Toelichting incl. voorziene wijzigingen t.o.v. het oorspronkelijke werkplan	The project is delayed due to: 1. Issues with the drinks necessary for the challenge tests in Study 1, the study had to be repeated. M1. Completion of the intervention study is now expected Q4 2021. 2. The Covid-19 pandemic which put Study 2 behind schedule. M2: Completion of the intervention study for Ciro study is now expected not sooner than Q1 2022. To finalize the entire project, including relevant analyses, workshop and reporting, we will request an extension up to Q1 2022.

1. Behaalde resultaten

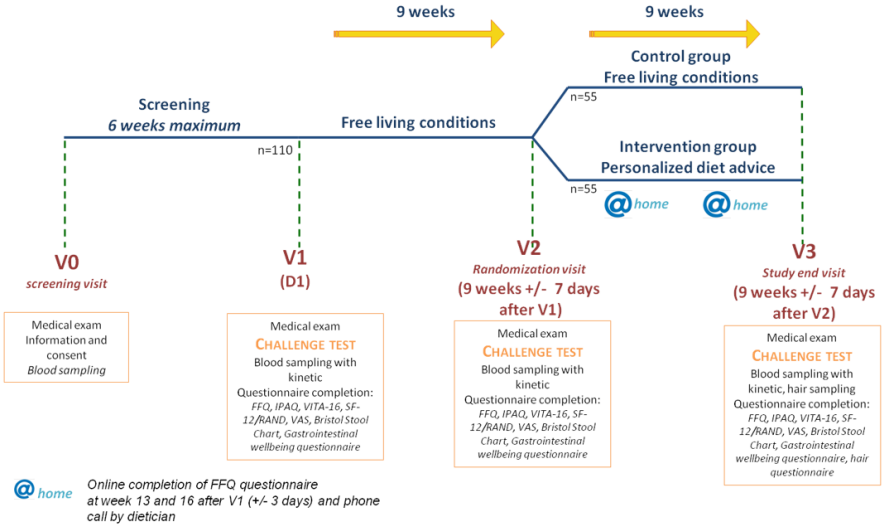
4.1 Korte beschrijving van de inhoudelijke resultaten en hun bijdrage aan het MMIP (zoals beschreven in 2.2)
To obtain the objectives of this project, several project lines are executed.



The current activities are described here:

Biofortis study:

This is a dietary intervention study in which the efficacy of a dietary intervention using next generation biomarkers will be demonstrated in a general and in a personalized intervention strategy in a European population. This study is being repeated, as reported earlier, as the endeavors in 2018 haven't resulted in a successful trial. At this moment we have included almost 100 of the 110 volunteers in this study. The V1 test day has commenced, while the remaining volunteers are recruited.



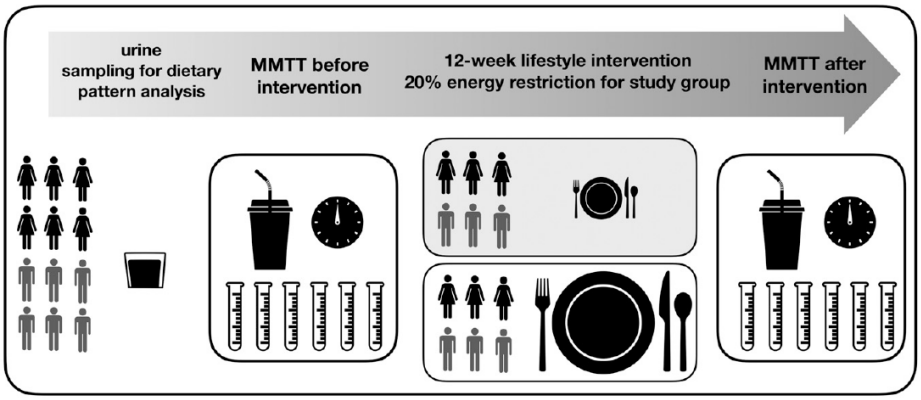
The first intervention study resulted in a paper describing the food-intake behavior:

Evaluation of Food-Intake Behavior in a Healthy Population: Personalized vs. One-Size-Fits-All. Hoevenaars FPM, Berendsen CMM, Pasman WJ, van den Broek TJ, Barrat E, de Hoogh IM, Wopereis S. Nutrients. 2020 Sep 15;12(9):2819. doi: 10.3390/nu12092819.

NutriTech analysis and interpretation:

The goal of this study was to:

- Define set of practical biomarkers for health (maintenance, improvement)
- Evaluate mechanisms of 'phenotypic flexibility' as read-out for health status



We have used the data from this study to explore the metabolic resilience and stress using the health space and the flexscore.

BellyFat analysis and interpretation – due to legal discussion we have not obtained all relevant data yet to perform the analysis and interpret the results.

Ciro study:
This intervention will be a pulmonary rehabilitation program for COPD patients to investigate the potential of the resilience approach for evaluation of health status in a less resilient population. Due to some legal discussions and the Covid-measures in the clinic for patients with pulmonary diseases, this study is ready for start, however not commenced yet.

4.2 Deliverables (bijeenkomsten en andere output, die niet benoemd wordt in 4.3 en 4.4)

WP #/ milestone/ deliverable #	Realised: 1/2/3/4Q 20XX Expected: 1/2/3/4Q 20XX	According to the schedule: Yes/No If not, please explain
DELIVERABLES		
D1. design of a biomarker for "metabolic age" and "metabolic stress" as primary read-out for intervention studies and agreed by all partners of the consortium	Realised	
D2. approved METC protocol agreed by all partners of the consortium.	Realised	Study is being repeated, METC approval obtained for second study
D3. approved METC protocol for Ciro study.	Realised	
D4. Data Analysis Plan agreed by all partners of the consortium	Realised	

D5. Two scientific articles describing results of the human intervention study.	Expected	We have published some results from the first study, but will publish the results from the repetitive study once performed
D6. An opinion article that proposes an acceptability strategy for the concepts and application of phenotypic flexibility in collaboration with ILSI and stakeholders from different meetings.	Realised	Next Generation Health Claims Based on Resilience: The Example of Whole-Grain Wheat. Hoevenaars F, van der Kamp JW, van den Brink W, Wopereis S. Nutrients. 2020 Sep 25;12(10):2945. doi: 10.3390/nu12102945.
Milestones		
M1. Completion of the intervention study	Expected, Q4 21	We have started a repetition of the intervention study due to issues with the drinks in the first trial
M2: completion of the intervention study for Ciro study.	Expected, Q1 22	Behind of schedule due to COVID-19, but ready to start.

4.3 Communicatie (lijsten)

4.3.1 Wetenschappelijke artikelen en hun doi (*Digital Object Identifiers)*

13 Publications:

- The circadian clock, shift work and tissue-specific insulin resistance. JE Oosterman, A Kalsbeek, S Wopereis**.** Endocrinology. 2020;161(12):bqaa180. doi: 10.1210/endocr/bqaa180.
- Next Generation Health Claims Based on Resilience: The Example of Whole-Grain Wheat. Hoevenaars F, van der Kamp JW, van den Brink W, Wopereis S. Nutrients. 2020 Sep 25;12(10):2945. doi: 10.3390/nu12102945.
- Evaluation of Food-Intake Behavior in a Healthy Population: Personalized vs. One-Size-Fits-All. Hoevenaars FPM, Berendsen CMM, Pasman WJ, van den Broek TJ, Barrat E, de Hoogh IM, Wopereis S. Nutrients. 2020 Sep 15;12(9):2819. doi: 10.3390/nu12092819.
- A new randomization procedure based on multiple covariates and applicable to parallel studies with simultaneous enrollment of all subjects prior to intervention. Schoen ED, Wopereis S.BMC Med Res Methodol. 2020 Sep 3;20(1):222. doi: 10.1186/s12874-020-01085-w.
- Measuring health promotion: translating science into policy. Griffiths JC, De Vries J, McBurney MI, Wopereis S, Serttas S, Marsman DS.Eur J Nutr. 2020 Sep;59(Suppl 2):11-23. doi: 10.1007/s00394-020-02359-1.
- From lifespan to healthspan: the role of nutrition in healthy ageing. Wickramasinghe K, Mathers JC, Wopereis S, Marsman DS, Griffiths JC. J Nutr Sci. 2020 Aug 24;9:e33. doi: 10.1017/jns.2020.26. eCollection 2020.
- Associations between Circulating Lipids and Fat-Soluble Vitamins and Carotenoids in Healthy Overweight and Obese Men. Kelly JM, Matuszek G, van den Broek TJ, Huggins GS, Smith CE, Ordovas JM, Wopereis S, Booth SL.. Curr Dev Nutr. 2020 Jun 11;4(6):nzaa089. doi: 10.1093/cdn/nzaa089. PMID: 32550273; PMCID: PMC7290122.
- Plasma metabolome analysis identifies distinct human metabotypes in the postprandial state with different susceptibility to weight loss-mediated metabolic improvements. Fiamoncini J, Rundle M, Gibbons H, Thomas EL, Geillinger-Kästle K, Bunzel D, Trezzi JP, Kiselova-Kaneva Y, Wopereis S, Wahrheit J, Kulling SE, Hiller K, Sonntag D, Ivanova D, van Ommen B, Frost G, Brennan L, Bell J, Daniel H. FASEB J. 2018 doi: 10.1096/fj.201800330R. [Epub ahead of print] PubMed PMID: 29718708. https://www.ncbi.nlm.nih.gov/pubmed/29718708

- A 12-wk whole-grain wheat intervention protects against hepatic fat: the Graandioos study, a randomized trial in overweight subjects. Schutte S, Esser D, Hoevenaars FPM, Hooiveld GJEJ, Priebe MG, Vonk RJ, Wopereis S, Afman LA. Am J Clin Nutr. 2018 Dec 1;108(6):1264-1274. doi: 10.1093/ajcn/nqy204. https://www.ncbi.nlm.nih.gov/pubmed/30541093
- Whole grain wheat consumption affects resilience in a randomized controlled trial in overweight and obese adults with mild hypercholesterolemia: the Graandioos study. Femke P.M. Hoevenaars, Diederik Esser, Sophie Schutte, Marion G. Priebe, Roel J. Vonk, Willem J. van den Brink, Jan-Willem van der Kamp, Johanna H.M. Stroeve, Lydia A. Afman and Suzan Wopereis. Journal of Nutrition. 2019 Dec 1;149(12):2133-2144. doi: 10.1093/jn/nxz177.
- The impact of micronutrient status on health: correlation network analysis to understand the role of micronutrients in metabolic-inflammatory processes regulating homeostasis and phenotypic flexibility. Tim J. van den Broek, Bas H. A. Kremer, Marisa Marcondes Rezende, Femke P. M. Hoevenaars, Peter Weber, Ulrich Hoeller, Ben van Ommen, and Suzan Wopereis. Genes Nutr. 2017; 12: 5. Published online 2017 Feb 8. doi: 10.1186/s12263-017-0553-7 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5299688/
- Multi-parameter comparison of a standardized mixed meal tolerance test in healthy and type 2 diabetic subjects: the PhenFlex challenge. Suzan Wopereis, Johanna H. M. Stroeve, Annette Stafleu, Gertruud C. M. Bakker, Jacobus Burggraaf, Marjan J. van Erk, Linette Pellis, Ruud Boessen, Alwine A. F. Kardinaal, and Ben van Ommen. Genes Nutr. 2017; 12: 21. Published online 2017 Aug 29. doi: 10.1186/s12263-017-0570-6. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5576306/
- Ranges of phenotypic flexibility in healthy subjects. van den Broek TJ1, Bakker GCM1, Rubingh CM1, Bijlsma S1, Stroeve JHM1, van Ommen B1, van Erk MJ1, Wopereis S1. Genes Nutr. 2017 Dec 6;12:32. doi: 10.1186/s12263-017-0589-8. eCollection 2017. https://www.ncbi.nlm.nih.gov/pubmed/29225708

4.3.2 Rapporten/artikelen in vakbladen

- Interview Suzan Wopereis for lifestyle magazine 'Fit met Voeding' entitled "Ik werk vanuit een holistisch perspectief", nr. 3, 28e jaargang (2020)
- Hoe de dingen werken: De belofte van personalized nutrition (video) & interview of VoedingNu with Suzan Wopereis (voedingnu.nl) https://www.voedingnu.nl/voedingswetenschap/artikel/2019/10/hoe-de-dingen-werken-de-belofte-van-personalized-nutrition-video-10113202?_ga=2.237508419.213812988.1581501783-1067504672.1581501783

4.3.3 Overige communicatie-uitingen (inleidingen/posters/radio-tv/social media/workshops/beurzen)

Conferences / presentations on PhenFlex-2:

- Vitafoods 2020, online event, 2020, Challenge test-based resilience as a measure for health, presented by Biofortis. https://www.vitafoodsinsights.com/sites/vitafoodsinsights.com/files/BIOFORTIS%20POSTER.pdf
- Personalised Nutrition Europe Conference, Quantifying Personalised Nutrition, London, 6th of December 2018, https://personalisednutrition-europe.com/events/personalised-nutrition-europe-2018-0
- Precision nutrition from the perspective of phenotypic flexibility. The 3rd China Special Food International Conference, 30 October – 1st November2018, Beijing, China, www.sfic.net.cn/index.php/Homeen/Index/index.html
- Nutrition strategies to maintain optimal health The 5th DHU 2020 Autumn School « New approaches in precision medicine : state of the art and practice », Nantes Thursday 18 ~ 19 october, Nantes, France http://www.dhu2020.org/index.php/en/training/autumn-school-2018

- Precision Nutrition from the Perspective of Phenotypic Flexibility. Korean Nutrition Society Annual Conference, Roadmap to Precision Nutrition, October 18~19, 2018, Pyeongchang, South Korea, http://kns.or.kr/English/index.asp
- Personalised nutrition from perspective of phenotypic flexibility, 4th nutrition-alimentation-metabolisme-sante, 4th October 2018, Rennes, France, https://www.rennes-congres.fr/fr/votre-evenement/l-agenda-des-evenements/4emes-rencontres-nutrition-alimentation-metabolisme-sante
- Phenotypic Flexibility as a Measure of Health Through the Life Cycle, 117th Abbott Nutrition Research Conference, Carbohydrates Through the Life Cycle and Across Tissues, June 20 2018, Columbus, Ohio, USA, https://anhi.org/conferences/117-anrc-carbohydrates
- Personalised nutrition from the perspective of phenotypic flexibility, Experimental biology April 2018, San Diego, USA, https://experimentalbiology.org/2018/Home.aspx
- Showcasing the possibilities of phenotypic flexibility (PhenFlex) testing as a new measure for health status and indicator for personalised dietary advice, Vitafoods educational programme, May 2018, Geneve, Swiss, https://ezone.vitafoods.eu.com/seminars-2018?&filters.STREAM=personalised-nutrition&searchgroup=00000001-seminars-2018
- Personalized Nutrition from the Perspective of systems Flexibility, Personalized Nutrition Guardrails Expert Meeting, ILSI North America, 25 June 2018, Washington DC (USA)
- Personalized nutrition: what is the science? HAS hogeschool Food trend college 'Personalized nutrition: Hoe gepersonaliseerd kan het zijn? 12 June 2018, HAS hogeschool, s'Hertogenbosch, https://has.nl/nl/event/trendcollege-personalized-nutrition
- Meten van gezondheid, NAV (Nederlandse Academie voor Voedingswetenschappen) meeting op locatie TNO, 31 May 2018, Zeist, https://www.voedingsacademie.nl/activities/nav-op-locatie-tno/
- MyNewGut Workshop: MyNewGut's perspectives for innovations, health claims and impact on public health policies Impact of whole grain wheat on the gut microbiome, resilience and health June 4, 2018
- https://www.efsa.europa.eu/en/consultations/call/170306
- Council for responsible nutrition-international (CRN-I's) roundtable on measuring health promotion; translating science into policy, Düsseldorf, Germany
- 13th European Nutrition conference (FENS), Dublin, Ireland
- Human Variability in Response to Food and Nutrients: Building the Bridge to Personalised Nutrition – Challenges and Opportunities for Industry, Public Health and Academia, ILSI A'asia & CSIRO meeting, Sydney, Australia

4.4 Overige resultaten: technieken, apparaten, methodes

D1. design of a biomarker for "metabolic age" and "metabolic stress" as primary read-out for intervention studies, agreed by all partners of the consortium.
D4. Data Analysis Plan, agreed by all partners of the consortium.

4.5 Project website: geef het adres van de projectwebsite (indien beschikbaar)

Nvt.

Bijlage 1 MMIP's

KIA: Landbouw, water en voedsel	
MMIP	A1 Verminderen fossiele nutriënten, water en stikstofdepositie
	A2 Gezonde, robuuste bodem en teeltsystemen gebaseerd op agro-ecologie en zonder schadelijke emissies naar grond- en oppervlaktewater
	A3 Hergebruik zij- en reststromen
	A4 Eiwitvoorziening voor humane consumptie uit (nieuwe) plantaardige bronnen
	A5 Biodiversiteit in de kringlooplandbouw
	B1 Emissiereductie methaan veehouderij
	B2 Landbouwbodems, emissiereductie lachgas en verhoging koolstofvastlegging
	B3 Vermindering veenoxidatie veenweide
	B4 Verhoging vastlegging koolstof in bos en natuur
	B5 Energiebesparing, -productie en -gebruik
	B6 Productie en gebruik van biomassa
	C1 Klimaatbestendig landelijk gebied voorkomen van wateroverlast en watertekort
	C2 Klimaatadaptieve land- en tuinbouwproductiesystemen
	C3 Waterrobuust en klimaatbestendig stedelijk gebied
	C4 Verbeteren waterkwaliteit
	D1 Waardering van voedsel
	D2 Gezonde voeding een makkelijke keuze
	D3 Veilige en duurzame primaire productie
	D4 Duurzame en veilige verwerking
	E1 Duurzame Noordzee
	E2 Natuur-inclusieve landbouw, visserij en waterbeheer in Caribisch Nederland
	E3 Duurzame rivieren, meren en intergetijdengebieden
	E4 Overige zeeën en oceanen
	E5 Visserij
	F1 Verduurzamen en kostenbeheersing uitvoeringsprojecten waterbeheer
	F2 Aanpassen aan versnelde zeespiegelstijging en toenemende weersextremen
	F3 Nederland Digitaal Waterland
	F4 Energie uit water
	ST1 Smart Agri-Horti-Water-Food
	ST2 Biotechnologie en Veredeling

Bijlage 2 TRL-categorieën

De detailcategorieën bestaan uit:
TRL 1 – basisprincipes zijn geobserveerd en gerapporteerd
TRL 2 – technologisch concept en/of toepassing is geformuleerd
TRL 3 – kritische functie of karakteristiek is analytisch en experimenteel bewezen
TRL 4 – component of experimenteel model is gevalideerd in laboratoriumomgeving
TRL 5 – component of experimenteel model is gevalideerd in relevante omgeving
TRL 6 – systeem/subsysteem model of prototype is gedemonstreerd in een relevante omgeving
TRL 7 – prototype van het systeem is gedemonstreerd in een operationele omgeving
TRL 8 – daadwerkelijk systeem is compleet en gekwalificeerd door test en demonstratie
TRL 9 – daadwerkelijk systeem is bewezen door succesvol operationeel bedrijf