

11-1-2016

To:

Koninklijke
Nederlandse
Akademie van
Wetenschappen

To the attention of:
A. Korbijn

Subject: Submission
full proposal KNAW
Agenda
Grootschalige
Infrastructuur.

Health RI - Personalised Medicine & Health Research Infrastructure

Dear reader,

Attached you will find the specification of the proposal Personalised Medicine & Health Research Infrastructure "Health RI" in 2025. The Personalised Medicine and Health dream is introduced to you by means of this letter.

Today life sciences and medical research in the Netherlands encompass several outstanding basic and translational research programmes directed towards personalised prevention, prognosis, as well as prediction, guidance and monitoring of precision treatment in numerous diseases. In this vision we set course for the medicine and health research infrastructure in the year 2025; with an eye on what will be achieved by the year 2040, and strongly rooted in programmes of today.

Today, medicine has only just left an era that was characterized by treating diseases after the fact, decision making on certain population average and physicians making decisions for their patients. This approach is not future proof: we will move towards a new medicine and health paradigm. This paradigm will be predictive, preventive, personalised and participatory¹; healthcare will be focused on improving health and striving to help people function as good and long as possible despite potential (chronic) diseases.

Biology and biomedicine as science fields will adopt a systems approach focussing on health and diseases: understanding how biological processes interrelate, how perturbations in a healthy 'personal system' arise, and how interventions (e.g. lifestyle-related, high-precision medication or regenerative medicine) can restore homeostasis. Systems biology (i.e. the knowledge base) and advanced read outs of biology will help transform medicine from reactive into a P4 mode. Combining advanced genetics with non-invasive imaging and longitudinal physiological monitoring locates disturbances in the body at a very early stage, and with great precision. Any intervention still needed is conducted with the highest level of precision and tailored to the needs of the individual. The change to the P4 mode and the rise of personal data collection creates the opportunity to radically shorten the period between clinical and/or scientific investigation and intervention.

By 2040, medicine and health are a fully pro-active, integrated, predictive, preventive, personalized and participatory science *and* healthcare is at affordable cost levels for society. Preventive self-management of citizens as part of their everyday life focuses on improving health and functioning as good and long as possible despite potential (chronical) diseases. We will provide personalized treatment for every patient and empower patients and healthcare workers in clinical decision-making based on full utilization of systems biology based knowledge of mechanisms of disease. Science will have brought the knowledge and the resources needed to do so and made it easily accessible and applicable in society.

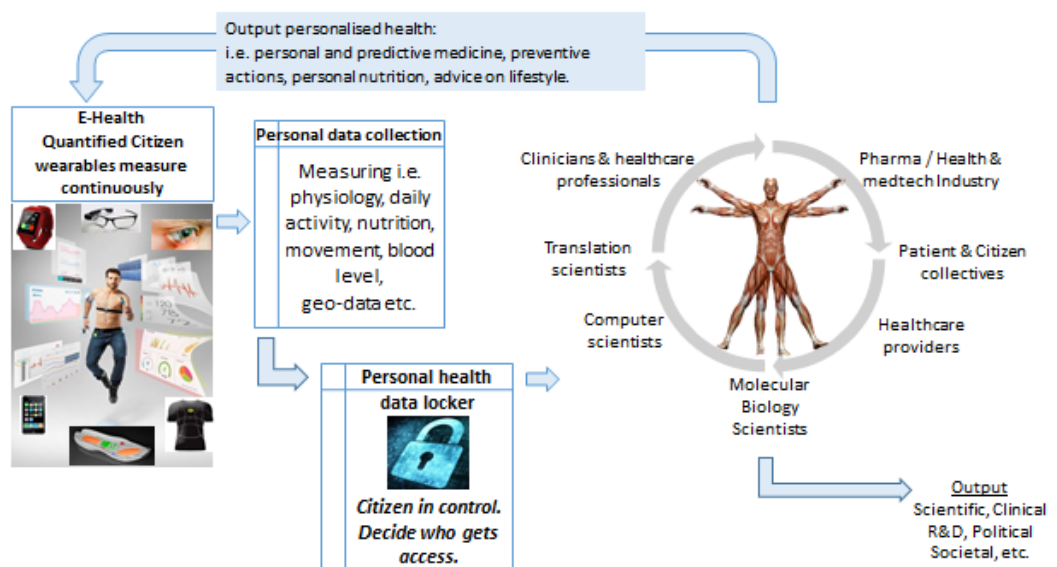
To fulfil this ambition, **by 2025** the medical research community should have access to a research infrastructure that will accommodate all researchers active in areas such as systems genetics, -omics and molecular biology, image sciences, epidemiology, preventive health and clinical medicine. It will have to be common national platform as a strong hub in the international biomedical research network across scientific disciplines, across different types of users and across users-questions.

¹ P4 Medicine Institute (2012). *P4Medicine*. Accessed on the 8th of January 2016, taken from: <http://p4mi.org/p4medicine>.

This is our perspective on the future

In 2025, Dutch citizens all have their own personal digital biobanks. With help of the available smart and wearable technology, these biobanks continuously collect personal health information (figure 1). Each individual is unique in health and functioning).² Thus, the 17 million personal biobanks represent 17 million personal health profiles, influenced by intrinsic and external factors such as genetics, nutrition, lifestyle and (socio-economic) environment. Combined with the information gathered in the biomedical research field on individual patients and the international knowledge base will create a globally unique resource.

In 2025 we will have aligned all major biomedical and health research initiatives in a large-scale unified infrastructure for combined genotyping and deep phenotyping of human diseases *in situ*. Such an infrastructure will combine high-quality molecular and imaging pipelines with nutrition and lifestyle research resources, and feature the ICT and e-infrastructure for sophisticated data integration and systems analyses. By 2025, the infrastructure has assembled the technologies for complete genome analysis combined with detailed phenotyping of the participants based on metabolic and genomic parameters, imaging data, lifestyle information, insight into their microbiome, and information from both electronic patient records and personal health files. Increasingly the research process will depend on direct involvement, data collection and sampling by and from healthy individuals and patients, as well as providing these participants to receive direct feedback on analyses performed with support of mobile electronic devices (e-Health).



In 2025, Dutch bio-medical scientists have massively moved beyond the classical mono-disciplinary and population-based approach into an integrated interdisciplinary systems medicine and personalised health approach. They not only try to understand and model the generic mechanisms underlying health and disease, but also explore the genetic and phenotypic variation, the dynamics of life, and the physiological bandwidth that can help to model the 'health system flexibility' of an individual at (sub-)cellular, organ and organismal level. The technological revolutions in bioimaging, multi-omics molecular profiling of samples, high-tech precision interventions and the availability of longitudinal quantified self, e-health and daily functioning measurements have turned life science

² Huber, M. (2011). How should we define health? *BMJ* ; 343 doi: <http://dx.doi.org/10.1136/bmj.d4163> (Published 26 July 2011)

into a truly multi-disciplinary and big data-driven science field. This has resulted in a strong connection among medical, life science, technology and computer science communities. They effectively combine their know-how and skills in scientific exploration with social development and business development capacities.

In 2025, scientific data should be stewarded in interoperable form and actively shared among scientific groups and disciplines in a fashion that accelerates the construction of a collective knowledge base of rapidly growing value. Dutch citizens massively make their self-collected data available, not only to support their personal self-monitoring and self-exploration, but also to expedite scientific exploration, assured that their privacy is well respected. As full owners of this personal information they remain in control of their personal health data, which will not even need to leave the secure environment of their personal health data locker.

Towards 2025, integrative analysis of multifactorial big data has strongly advanced research into diseases and health. The Netherlands has an infrastructure that offers easy access to (international) sample and data resources, and facilitates scientists to work efficiently in cross-disciplinary studies towards understanding biological complexity and creating the evidence-base to interpret variation among individuals in terms of personal health. Scientists daily use specially designed research-workflows that search the open access data web for information or resources relevant to their particular research question. The results delivered by these 'data-trains' is processed and validated on the spot and the results are integrated in the research at hand with information retrieved from international reference data collections. Hypotheses are thus produced and tested in real-time with high reproducibility.

In 2025 Dutch clinicians and health professionals have strongly sped up evidence-based medicine and health. In the classical approach of 2015, pre-clinical research, clinical trials, meta-analyses and guidelines ruled. This innovation process simply took too long and could not keep up with the speed of knowledge and technology changes. Rather, a form of health care has taken over that is based upon high-precision, non-invasive and continuous health monitoring, mostly by citizens themselves, and combined with data-driven rapid learning technology available to both professionals and citizens. In many cases where remedies as drugs and surgery are already available, this approach has reduced the care and cure innovation lag time from years to timeframes of weeks or even days, all to the benefit of (daily) functioning for individual persons (patients).

By 2025, health professionals have adopted an integral health approach to offer personalized health management solutions to their patients, based upon a combination of quantified self data collected by the patient, their personal genome profile, and (if required) additional clinical and societal information. Professionals thus guide citizens in their social context to optimise their personal health, easily tapping into pre-selected health models suggested by the international health and disease knowledge base. As health professionals, they make sure the information is correct and that the decision meets patient values and preferences. The 2025 clinician is a translational expert, including the latest research insight to coach their patients in optimising their health.

In 2025, the Dutch field of personalised medicine & health research closely involves all of the above stakeholders, and many more. A ground-breaking research infrastructure connects all these people, citizens and experts, scientists and health professionals. It involves all certified lab facilities and clinics, and all biobanks and data collections. Started as an exclusive life science research infrastructure it has become an invaluable part of the public health domain. As an initial step this proposal is aimed at creating the roadmap towards the ideal infrastructure based on the current and potential strengths of the Dutch life sciences and addressing the emerging needs to sustain and strengthen our scientific leadership position in this sector. It will bridge a broad range of technology and infrastructure initiatives across UMCs, universities and other biomedical research institutes, as well as connect different scientific disciplines: basic sciences, clinical sciences and engineering. The infrastructure is provides the stepping stone towards citizen science participation. This proposal refers to the creation of nation-wide biobanks, state of the art – omics and imaging technology as well as an overarching linked-data infrastructure.

This is the integration and elaboration of the initial proposals “Kring”(Dekker), “Personalized Precision Medicine Research Infrastructure” (Wijmenga, Meijer & Luijten) and “Integrated Life Science Research Infrastructure” (Kok et al) and is brought to you with contributions and endorsements from:

- [Dr. Jeroen Belien](#) (VUMC)
- [Prof. Bas Bloem](#) (Radboudumc)
- [Dr. Jan-Willem Boiten](#) (Lygature)
- [Dr. Luiz Olavo Bonino da Silva Santos](#) (VU)
- [Prof. Dorret Boomsma](#) (VUMC)
- [Dr. Rolf Bos](#) (TIFN)
- [Mr. dr. Jasper Bovenberg](#) (Legal Pathways)
- [Prof. Edwin Cuppen](#) (UMCU)
- [Prof. André Dekker](#) (MUMC+)
- [Dr. Ingrid Dillo](#) (DANS/RDNL)
- [Dr. Peter Doorn](#) (DANS/RDNL)
- [Prof. Cornelia van Duin](#) (EMC)
- [Prof. Chris Evelo](#) (Maastricht University)
- [Prof. Dorus Gadella](#) (UvA)
- [Dr. Celia van Gelder](#) (Radboudumc, DTL)
- [Dr. Richard Finkers](#) (Wageningen UR)
- [Prof. Alain van Gool](#) (Radboudumc)
- [Prof. Thomas Hankemeijer](#) (LU)
- [Prof. Frank van Harmelen](#) (VU)
- [Prof. Wilco Hazeleger](#) (eScience Centre)
- [Prof. Jaap Heringa](#) (VU)
- [Dr. Peter-Bram 't-Hoen](#) (LUMC)
- [Dr. Rob Hoof](#) (DTL, NLeSC)
- [Prof. Hilleke Hulshoff](#) (UMCU)
- [Prof. Bart Jacobs](#) (Radboud Universiteit)
- [Dr. Connie Jimenez](#) (VUMC)
- [Prof. Folkert van Kemenade](#) (EMC)
- [Prof. Judith Klumperman](#) (UMCU)
- [Prof. Joost Kok](#) (LU)
- [Prof. Wessel Kraaij](#) (TNO/Radboud Univ.)
- [Dr. Aad van der Lugt](#) (EMC)
- [Prof. Peter Luijten](#) (UMCU)
- [Prof. Nico van Meeteren](#) (Topsector LSH Health~Holland)
- [Prof. Gerrit Meijer](#) (NKI/AVL)
- [Prof. Barend Mons](#) (LUMC)
- [Dr. Iris Nagtegaal](#) (Radboudumc)
- [Prof. Wiro Niessen](#) (EMC)
- [Prof. Ben van Ommen](#) (TNO)
- [Prof. Gert-Jan van Ommen](#) (LUMC)
- [Prof. Anwar Osseyran](#) (UvA/SURFsara/RDNL)
- [Prof. Marcel Reinders](#) (TU Delft)
- [Dr. Marco Roos](#) (LUMC)
- [Dr. Hans Roubos](#) (DSM)
- [Dr. Jeroen Rouppe vd Voort](#) (ENZA Zaden)
- [Prof. Eline Slagboom](#) (LUMC)
- [Prof. Ronald Stolk](#) (UMCG)
- [Dr. Morris Swertz](#) (UMCG)
- [Prof. Cisca Wijmenga](#) (UMCG)
- [Dr. Michel Wouters](#) (NKI/AVL)
- [Prof. Gerhard Zielhuis](#) (Radboudumc)

The proposal is submitted by Prof. Cisca Wijmenga. The operational contact is dr. Ruben Kok. We look forward to the expert committee's feedback. We are of course available to provide additional information to the committee upon their request.

Kind regards, on behalf of Prof. Wijmenga,

Ruben Kok

