European priorities in health research

The Dutch perspective
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Executive Summary

This position paper presents the vision of the NFU, the representative of the Netherlands University Medical Centers (UMCs), on the added value of Dutch medical and health research towards the development of the European research agenda. The NFU does so in view of:

• The grand challenges of healthy ageing and preserving health, and
• The implementation of the European Research Area aiming to ensure the coherence, synergy and added value of national and regional research programmes

Thus joint efforts at national, regional and European level are required to realise the knowledge-based economy and to successfully address the challenges ahead. The NFU supports the outline of the ERA and the importance of the Knowledge Triangle of education, research, and innovation for the future of Europe. With this position paper, the NFU acknowledges that progress can only be achieved by true collaboration, harmonization of efforts and strong commitment.

In view of these challenges, it is the opinion of the Dutch UMCs that a real contribution to the needs and demands of the European citizens and policy makers and other stakeholders can be achieved by prioritizing the following topics on the European research agenda:

• Improving health in an ageing population
• Neurodegenerative diseases, with the main focus on Alzheimer disease
• The metabolic syndrome and obesity, specifically focusing at a systems biology approach
• Regenerative medicine (including stem cell technologies and tissue engineering)
• Collective action for health improvement

Preserving health in an ageing population – by prevention and treatment- is of great importance and requires not only specific knowledge, but also the development of and investment in pan-European research infrastructures. Both European Commission and the Member states need to take the lead in establishing research infrastructures. The NFU has prioritised and committed itself to the following research infrastructures:

• Bio-banking
• Bio-Imaging
• Clinical research

The NFU strongly supports setting strategic (5 to 10 year) research agendas at a European level in a transparent, interactive and open way to tackle the major societal questions. Furthermore, sustainable funding mechanisms to assure maintenance and future access to the pan-European research infrastructures are pivotal. In addition, the NFU endorses actions to foster talent, to stimulate excellence, and to create a barrier free space for European researchers. Finally, the NFU looks forward to more coherence between European policies and initiatives and to a multi-level governance approach.

This position paper is to be presented to and discussed with members and representatives of the European Commission and the European Parliament on April 15th 2010 in Brussels. Its drafting should be taken as the first step in a dynamic and interactive process to demonstrate the position of the Netherlands Federation of University Medical Centers and its contribution towards Europe.
1. Introduction

This paper presents the Dutch position of the Netherlands Federation of University Medical Centers (NFU) and its possible contributions to strengthen the research in Europe.

The NFU is aware of the European grand challenges and the way in which the European Research Area (ERA) is taking shape and will be further implemented also in conjunction with the European Cohesion Policy. Development of the European Research Area as an interactive research ecology in which regional-, national- and European-level processes interact in a coherent and optimal fashion, and wherein the ERA is the totality of European research irrespective of its source of funding, is endorsed by the NFU and the Dutch University Medical Centers.

At the same time, the NFU realises that it has to respond to these developments by further elaboration of Dutch strengths in health research (infrastructures), investigating complementarities to other national or regional research bases, and true collaboration and harmonization of efforts. That process started with this position paper, which should be taken as the first step in a dynamic process.

The NFU has thus taken on the responsibility to prepare itself for 2020 by reaching out for Europe, the European Commission, European policy makers, and European parliament representatives. We invite them to engage in an interactive discussion, to further sharpen our vision and define our specific contribution to the realisation of the ERA.

In the next chapters we present the NFU and the unique position of the eight UMCs; the Dutch added value in view of the grand challenges and the instruments to shape the ERA; and the eight specific areas in which the Netherlands has a key position in health research. These eight areas are described in more detail by departing from the European context, specific topics for the European research agenda, and the Dutch contribution and strengths in these areas. The last chapter addresses future steps and the way in which this position paper has been realised.
2. NFU and the Dutch University medical Centers

The NFU endorses collaboration between the eight University Medical Centers (UMCs) in the Netherlands. NFU’s general objective is to represent the UMCs shared interests. Considering the current developments in the national research landscape and in the European Research Area, the NFU has identified the major Dutch research areas in health research that can contribute significantly to a shared European strategic research agenda. In this position paper we describe these areas, and the choices in more detail, while acknowledging that this is a kick off and that the NFU, will be part of a dynamic process that has only just begun.

In a UMC the Faculty of Medicine, with its responsibilities for the initial training of physicians and for scientific research, has merged with the university hospital, with its responsibilities for tertiary care, clinical research and innovation. All medical faculties and university hospitals in the Netherlands are now joined into UMCs. The Dutch UMCs have positioned themselves at the intersection of medical education, (bio)medical research, and patient care. The added value of UMCs is thus that they integrate three core functions, thereby bridging the gap between three worlds and being a true knowledge triangle.

Research

UMCs have both clinical and basic science research groups. The combination of the two under one roof creates powerful groups specialised in translational medicine. UMCs collaborate both internationally and nationally with other universities, research institutes and biotech companies in solving mechanisms of disease, developing new methods for diagnostics or therapeutic interventions and evaluating the results in clinical trials. Each UMC has a research infrastructure in which they are jointly building prospective patient cohorts for which both clinical data and biomaterials are collected in a standardised fashion.

Patient care

Although all UMCs provide basic hospital services, their public function is primarily determined by the top clinical services they provide together with their last resort function for referrals from other hospitals. Such tertiary care builds on the knowledge infrastructure that the UMC provides, with clinical research, innovation, and a multidisciplinary approach. It provides continuity of expertise, and serves as centre of excellence.

Results of research are taken further, either as direct innovations in patient care, after thorough evaluation studies or through patents, spin out companies, SME’s, large public-private partnerships, or other forms of “valorisation” of science. Innovation in clinical therapeutics or diagnostics has always been important in academic hospitals.

Teaching

UMCs offer all specialties for physicians including family practice and public health. Medical students are exposed to patients as well as basic research from day one of their curriculum and they become part of the UMC community. Almost every doctor and nurse is involved in the teaching process. The modern curriculum includes a mix of clinical and basic science around a specific disease, and therefore both clinicians and scientists often lecture together. All UMCs also have at least one degree programme in biomedical sciences (around 500 student a year) and all participate actively in the training of nurses and nurse specialists.
3. European health priorities, instruments and Dutch added value

3.1 European challenges

Europe’s response to a number of major global challenges will shape its future in the decades to come as stated in the Lund Declaration (2009). In the health sector, these challenges include:

• Dealing with the needs of its ageing population and the challenges of immigration;
• Preserving human and environmental health.

At the same time, European citizens expect solutions to these challenges to be found through science and technology. To address these challenges, it is imperative to:

• Bring together supply and demand-side measures to support both business development and public policy goals, e.g. the patient demands and innovative health care (research);
• Support excellence and well-networked knowledge institutions;
• Contribute to the creation and maintenance of world-class research infrastructures in Europe.

3.2 Instruments to tackle the challenges

In the context of the European challenges, the instruments that have been developed to create a competitive knowledge base include for instance:

• Cooperation (e.g. in the FP7 Health programme)

Trans-national cooperation is required for all types of health research activities carried out by UMCs and aimed to gain or consolidate leadership in key science and technology areas. The NFU supports European cooperation between universities, research centers, industry, SME’s and, other stakeholders like health care providers, health insurers, regulatory bodies, and government's etcetera.

• Joint programming initiatives (JPIs)

Joint Programming (JP) is about optimising public R&D-investments with the support of European, national and/or regional budgets with the objective of achieving greater socio-economic impact. It is an evolutionary process where countries and regions gradually take coordinated initiatives on a voluntary basis regarding the allocation of their budgets for research and innovation. The NFU and the UMCs have embarked on this process, they are committed to the strategic research agenda’s, and they are aligning in some key areas with ZonMw, the Netherlands organisation for health research and development.

• Capacities (e.g. the research infrastructures)

World-class research infrastructures constitute the backbone of European research. It is important for Europe to maintain and develop new large research facilities in order to carry out excellent research and to attract the best people worldwide, which, in turn, can make a difference in a global competitive world. The NFU endorses this vision as shown by their involvement in setting up UMC based research infrastructures. The NFU is aware that continuous investment (both at the national and international level) in research infrastructures is crucial.

• Excellence

Despite the short existence of the ERC, the award of an ERC grant is already perceived as a label of performing high quality research. A particularly attractive feature of the scheme is that it operates on a “bottom-up” basis across all research fields, without
predetermined priorities. Therefore, the NFU recommends and supports application for ERC grants to ensure the focus of health research on excellence.

3.3 NFU and the Dutch added value in 8 areas

Joint efforts at national, regional and European level are required to make the ERA and the knowledge-based economy a reality and to be able to respond to the grand challenges. Here we present the Dutch strengths in health research that will contribute to meeting these challenges and that will further shape the implementation of the ERA.

A major socio-economic challenge in Europe, the developed world in general but also in the emerging countries is the tendency that we are living to an older age but not necessarily in good health. Therefore improving health in an ageing population is of great importance and requires specific knowledge. The need for public health approaches and prevention will increase with the ageing population as well and also asks for research and innovation. Major threats and challenges are lifestyle-associated disorders and neurodegenerative diseases, especially Alzheimer disease. Innovative technologies can contribute to solving these challenges. Together, preserving health throughout the life span is a key mission of the NFU.

Therefore, NFU has set the following priority areas:

- Improving health in an ageing population;
- Neurodegenerative diseases, with the main focus on dementia and Alzheimer disease;
- The metabolic syndrome and obesity, specifically focussing on systems biology approaches;
- Regenerative Medicine (including stem cell technologies and tissue engineering);
- Collective action for health improvement.

To meet the challenges in health, the creation and maintenance of world-class research infrastructures in Europe is imperative. Several Biological and Medical Science (BMS) infrastructures have been identified by ESFRI. The synchronised planning and implementation of these infrastructures create a huge potential to structure and stimulate the European Research Area in biomedical research. To tackle the above-mentioned priority areas, the further development of and investment in research infrastructures is of the utmost importance. Therefore, the NFU has set the following research infrastructure priorities:

- Bio-banking;
- Bio-Imaging;
- Clinical research.

The figure below presents the intricate links between these areas and infrastructures. Because they are partly overlapping, they can create synergy at the national level. At the same time, the specific strengths of the Dutch UMCs and the NFU can contribute significantly to the European context and the health challenges.

In summary, Dutch medical science, innovation, and technology offer great added value to the European Research Area. In addition, the NFU supports the outline of the ERA and the importance of the Knowledge Triangle of education, research, and innovation for the future of Europe for which the UMCs are well suited by design.

The priority areas and research infrastructures mentioned above will be explained in more detail in the next chapters.
European priorities in health research

Figure 1 NFU priorities area’s and research infrastructures

- **GRAND CHALLENGES EU**
  - Healthy ageing
  - Preserving health

- **Dutch contribution NFU**
  - Improving health in an ageing population
  - Neurodegenerative diseases
  - Metabolic syndromes and obesity
  - Regenerative medicine
  - Collecting action for health improvement
  - Bio-banking
  - Biomedical imaging
  - Clinical research (incl. translational research)
4. Improving health in an ageing population

4.1 European context

Ageing is one of the ‘grand’ societal challenges for the forthcoming decades. Due to the post-war baby boom, the ever-increasing life expectancy and dropping birth rates, the proportion of elderly people is steadily increasing. Although healthier than previous generations, tomorrow’s elderly will ultimately require (complex) care for chronic disorders and multi-morbid states. Ageing will exert its influence on the economy (healthy workforce) and prosperity, and set challenges to our healthcare system, individual well-being, and profoundly change society as a whole. The effective prevention, diagnosis, and treatment of chronic age-related diseases are of key importance to meet these challenges. Moreover, development of the Lead Market Initiative on eHealth could contribute significantly to this challenge in terms of care and cure.

The EC has responded to the challenge of ageing. In the 7th Framework Programme (FP7) “dealing with the needs of an ageing population” was labelled as one of the grand challenges. FP7 supports ageing-related research in selected priority areas such as ‘Optimising the delivery of healthcare to citizens’ and ‘Enhance health promotion and disease prevention’ and Translational research areas such as Human Development and Ageing. The EU also supported an ERA-NET in FP6 (ERA AGE, ERA AGEII) with the aim to network funding agencies within ageing research.

4.2 Topics for the EU research agenda

In order to address the challenge of an ageing population, we need to strengthen our knowledge base of determinants and mechanisms of ageing and age-related disease and disability. An international, combined European and integrated effort is needed. An example of the need for a European integrated programme on ageing is the lack of a Pan-European research infrastructure on fundamental ageing research.

More basic research is needed to unravel the underlying mechanisms of the ageing process and how to influence this process; otherwise methods of prevention and new therapies cannot be developed. The organisation of healthcare and the actual care and services offered do not appear to meet current demands, let alone future demands. Accordingly, (new) clinical medicine needs to adapt and adopt. Research on the application of newly developed tools and devices to compensate the loss of function is required. Also the role of informal care, community care, and social services must be assessed by more applied research. Therefore, the NFU recommends the following topics for future strategies on ageing research:

• Strengthening our knowledge of the ageing process;
• Development of new tools and strategies for prevention of disease and disability;
• Development of evidence-based medicine for the elderly (i.e. for chronic diseases);
• Maintenance of functional autonomy of the elderly;
• Research on lifestyle patterns.

4.3 Dutch contribution

The Dutch added value is shown by the fact that a number of UMCs in the Netherlands have focused their attention on (healthy) ageing. They have built a strong track record and participate in a number of international cooperation’s. Examples of Dutch Healthy Ageing initiatives: The Netherlands Institute for Healthy and Successful Ageing (Ti-go), Netherlands Consortium for Healthy Ageing (NCHA), National Program Care for Elderly (NPO, European Research Institute on the Biology of Ageing (UMCG/RUG) and Leiden Academy on Vitality and Ageing (LAVA).
5. Neurodegenerative diseases – Dementia and Alzheimer

5.1 European context

Dementia is one of the most important causes of disability of the elderly. Currently, more than seven million people are diagnosed with Alzheimer’s disease and related disorders such as dementia in Europe, and this number is expected to double by 2040 due to the increase of patients of 80 years and older.

There is an increasing awareness in Europe that investments in care for and research in neurodegenerative disorders are urgently needed. The EC developed a Work Plan for the implementation of the programme of Community action in the field of public health in which a specific reference is made to the need of information and definition of indicators on the prevalence, treatments, risk factors, risk reduction strategies, cost of illness, social support, and what constitutes a "healthy brain lifestyle" related to Alzheimer disease (AD) and other dementias.

Furthermore, the European Council, has called in 2008 for public health strategies to combat neurodegenerative diseases associated with ageing and in particular Alzheimer’s disease and dementia. Moreover, Member States have identified neurodegenerative diseases in general, and Alzheimer’s disease in particular, as an area in which a common initiative (joint programming) would offer major added value compared to fragmented efforts in the European Research Area. In 2009, the EC reported to the European Parliament and Council on a European initiative on Alzheimer’s disease and other dementias that the EU would support national efforts in four key areas.

5.2 Topics for the EU research agenda

Alzheimer’s and dementia bring about several major societal and scientific challenges and needs, such as a large socio-economic burden, the need to understand the mechanisms of the disease better to develop effective treatment, and the need to develop prevention strategies or any intervention that leads to the delay of dementia. Because of these challenges the NFU considers it crucial to plan, invest, and cooperate in this field, both on a national and on the European level, both in order to control the social costs of these diseases as well as to improve the quality of life for patients and their families. The NFU therefore recommends the following topics for the European agenda:

• Establishing a cohort study of people with early onset dementia;
• Executing an pan-European intervention study in lifestyle factors involved in neurodegeneration;
• Establishing very early markers for Alzheimer’s disease and dementia pathology;
• Understanding the multifactorial road of cumulative damage in mixed dementia.

5.3 Dutch contribution

The Dutch added value is shown by the strong involvement of the Netherlands in European initiatives and research. Examples are the involvement in joint programming and the Framework Programmes. Furthermore, Dutch researchers are involved in various FP6 and FP7 projects, both as coordinator as partner, such as the FP7 project ‘the BrainTrain: Integrative neuroscience school on brain function and disease’ and the LiPiDiDiet project on the impact of Nutritional Lipids on Neuronal and Cognitive Performance in Aging, Alzheimer’s disease and Vascular Dementia. In scientific quality, the Dutch UMCs score above average in clinical neurology in publications and citations (CPP/FCSm 1.35) and average in the field of neurosciences (1.02). Furthermore, the Netherlands has substantial expertise in dementia research: UMCs combine care and research in Alzheimer and memory Centers, bio-banks and cohort studies, and a research focus on early onset dementia and biomarkers.
6. Obesity and metabolic syndrome

6.1 European context
Governments across Europe have recognized obesity and the metabolic syndrome as one of Europe’s most pressing public health challenges, particularly for children. They constitute a major threat to economy and human well-being in Western society. It is expected that by 2030, about 33% of the total population in the EU-27 will be obese, and many of them will suffer from one or more co-morbidities. Overweight and obesity are major risk factors for a number of chronic diseases, including diabetes, cardiovascular diseases, and cancer. Although obesity used to be a typical problem in the developed world, it has now become an issue in low- and middle-income countries as well, particularly in urban settings. Both obesity and metabolic syndrome have crucial effects on (labour) productivity and social participation. The cost of obesity has already reached 5% of public health expenditure in several European countries.

The EU can play an important role in dealing with the grand challenge of preserving health through its public health and research policies. Several projects have started in FP6 in the Health theme to study obesity and the metabolic syndrome. FP7 specifically mentions the importance of research on major diseases within the domain ‘translating research for human health’

6.2 Topics for the EU research agenda
The metabolic syndrome is a cluster of conditions such as increased blood pressure, elevated insulin levels, excess body fat around the waist or abnormal cholesterol levels. This condition leads to an increased risk of developing cardiovascular disease and diabetes. The pathophysiology is very complex and has been only partially elucidated. As lifestyle illnesses are strongly related and dependent on several factors, research must take a multidisciplinary and integrated approach by means of concerted actions. The NFU therefore recommends the following topics for the EU research agenda:

- A large concerted programme to unravel the pathophysiology of obesity and its metabolic and cardiovascular consequences as well as its biological origin. Including basic, translational and clinical research using a systems biology approach.
- An international cohort study with intensive phenotyping to enable comparison of relevant factors across cultures;
- Identification of biomarkers to discover those individuals at greatest risk;
- Development of models (insilico, invitro and invivo)
- Development of targeted prevention and treatment strategies for subjects at risk.

6.3 Dutch contribution
The Dutch government is committed to counteract the increase of prevalence of overweight and obesity and is investing heavily in obesity-related research. The UMCs are in the position to unravel the complex processes leading to obesity and metabolic syndrome, but cooperation with experts from the agri-food sector, the public health sector, and the social sciences are essential to implement research results in effective prevention strategies. Several research programmes on nutrition (connected to diseases and healthy diets) are being executed in the country. Recently, three Dutch Systems Biology Centers were awarded thirteen million euros to perform integrated research, including research to the metabolic syndrome and obesity. CTMM funded a study on development and validation of biomarkers for early detection of diabetes (PREDICT). Finally, research on metabolic syndrome by the UMCs is multidisciplinary and often based on a combination of measurements in biomaterials, imaging data of clinical and population cohorts, and building a joint database and biobank.
7. Regenerative Medicine

7.1 European context
An ageing population and a shortage of donor organs and tissues for transplantation, make regenerative medicine a socially relevant research area. This scientific discipline investigates how the body’s natural ability to repair damaged tissues and organs can be stimulated or imitated so as to bring about functional recovery. Regenerative medicine potentially offers cures for organ and tissue damages and it offers the potential for early treatment and an increased quality of life. It furthermore has a significant potential to benefit industry and SMEs that are active in drug testing and discovery. Responding to the grand societal challenges, the European Commission acknowledged the need to take a lead in the development of enabling technologies such as biotechnology, information technology, materials and nano-technologies. FP7 therefore already focuses on innovative therapeutic approaches and interventions with the 'Regenerative Medicine in Europe' project (REMEDiE). Moreover, funding agencies from thirteen European countries have joined forces to launch a cross-disciplinary Research Networking Programme, REMEDIC, to identify the frontiers and future needs in this complex multidisciplinary high-technology field.

7.2 Topics for the EU research agenda
Regenerative Medicine is a field that requires an integrated approach. Knowledge and expertise in this field is largely spread over the European countries, and several supporting technologies need to be developed, preferably in a joint effort to reduce the costs. Regenerative medicine is applicable to several diseases and is a very broad scientific discipline that is in need of clear European regulations and policy, which incorporate both scientific as well as ethical aspects. The NFU recommends the following topics for the EU research agenda on regenerative medicine:

- Basic research of stem cells, biomaterials and their interactions to understand how to completely regenerate the full complexity of tissues;
- Making in vivo and in vitro (2D and 3D) model systems available to obtain basic knowledge on controlled propagation and differentiation in normal and pathogenic organs.
- Development of gene delivery systems for gene therapy
- Developing enabling technologies such as tissue specific biomarkers, single cell imaging, in-vivo and in-vitro modelling systems, bioreactors etc;
- Technologies for personalised cell therapy and autotransplantation

7.3 Dutch contribution
The Netherlands has a strong position in regenerative medicine. It occupies the tenth position in the world regarding the total volume of publications in the field of regenerative medicine, and within Europe it ranks fifth. The Dutch contribution in this field is greater than the average contribution in all research fields. The level of collaboration between various Dutch knowledge institutions in this domain has increased significantly in recent years, as can be seen from the number of publications by national partnerships. The percentage of publications produced in collaboration with foreign institutions has also doubled. Since 2004, the Dutch government has invested more than 85 million euro in research in regenerative medicine. Both private and public partners have to a large extent matched that sum. These programmes are for example the Dutch Program Tissue Engineering (DPTE), the programme Translational excellence in Regenerative Medicine (TeRM), the Biomedical Material Programme (BMM), the programme Stem Cells in Development and Disease (SCDD), and the Netherlands Initiative of Regenerative Medicine (NIRM).
8. Collective action for health improvement

8.1 European context

Public Health should contribute to sustainable health improvement and protect citizens from (new) threats. Public Health includes a wide range of interventions and policies both within and outside the healthcare system, such as vaccination and screening programs; lifestyle interventions and health promotion campaigns; work site, spatial planning and environmental measures; and other health protection measures. The main challenge is to optimize the delivery of healthcare to European citizens in the light of an ageing population, new threats and increasing costs.

The European Commission 2007 White Paper on Health acknowledges that strategic efforts on Public Health are needed. The Health Strategy of the European Commission (2009) and the first draft Health Work Programme 2011, however, do not refer to Public Health as a key research challenge. The NFU advocates the importance of Public Health research at a European and international level and at public and private level. Public Health research will contribute to the development of evidence-based methods in Public Health practice and policy in the European countries. An international approach is essential. The challenge of optimising the delivery of healthcare to citizens is crossing borders while the research efforts are too dispersed. Furthermore, benchmark studies and sharing best practices are of great importance for Public Health research and require international cooperation.

8.2 Topics for the EU research agenda

The NFU has identified topics for a strategic EU research agenda and suggestions on how to implement this agenda. It is important to stress that challenges should be addressed in a multidisciplinary way. The effectiveness will benefit from focusing at the whole Public Health knowledge chain, including health care, and involving all potential public and private users. The strategic EU research agenda focuses on the following topics:

- Identification and evaluation of strategies on a national, regional, or local level. These strategies should contribute to creating opportunities to make healthy choices, and measures in spatial planning, innovations in the healthcare system, or initiatives from industry to develop products that promote a healthy lifestyle.

- Development of models to estimate and compare the health impact of these measures in EU Member States and Associated States.

- Contribution to global health issues by research on reducing poverty and social inequalities, and the burden of disease by using European knowledge and experience.

- Translation of the findings of basic research, especially in genomics, into the Public Health methodology.

- Establishment of the European Commission as a “Public Health ideas laboratory” or “clearing house” to identify and promote the best Public Health practices in Europe.

8.3 The Dutch contribution

The Netherlands has a leading position in Public Health research in Europe. It has strong research traditions in the scientific fields of e.g. epidemiology, health promotion, health economies, and other contributing disciplines. Scientific productivity in terms of numbers of scientific publications and PhDs ranks amongst the highest in the world. Dutch scientists play a prominent role in international networks, programmes and journals.
9. Bio-banking

9.1 European context

Bio-banking is the collection of biological material and data of large numbers of patients and healthy people in order to enable biomedical and health research. Member States have identified that the major burden of disease for all European health systems comes from diseases caused by a combination of genetic, environmental and lifestyle factors (multifactorial diseases). To increase the insight in the aetiology of multifactorial diseases, access to large amounts of comprehensive data and well-documented biomaterial is crucial. Real breakthroughs can be expected from scaling up, interconnecting and creating networks of existing bio-banks, thereby creating added value, and avoiding duplication of efforts. The preparatory phase of BBMRI, the Bio-banking and Biomolecular Resources Research Infrastructure, funded by the EC is recognized by Member States as a major research infrastructure initiative.

9.2 Topics for the EU research agenda

The Dutch UMCs play a key role in the development of bio-banking. The NFU would therefore like to recommend the following topics on bio-banking that are aligned with and build upon the strategic agenda for the second phase of BBMRI-EU:

- To support initiatives to facilitate the communication and interconnectivity between bio-banks;
- Develop applications for subtracting high quality phenotype/clinical data from existing patient records research files;
- To encourage harmonisation of the ethical, legal, and societal (ELSI) framework;
- To implement sustainable funding mechanisms for long-term maintenance of and access to bio-banks;
- To deliver further coordinating activities to BBMRI-EU.

9.3 Dutch contribution

The Dutch added value as partner is shown by the fact that the Netherlands has played a leading role in the preparation phase of the Biological BBMRI. The Netherlands is therefore able to build upon a solid knowledge base and to maintain a top position in international competition. It already has a coordinating role in the legal questions at stake, and is also developing a prototype of a national 'hub' (BBMRI-NL), funded by the Dutch government. The Dutch could add value through various existing initiatives and experiences, that is coordinated through BBMRI-NL:

- A network of 140 existing clinical and population bio-banks including material and data of over 400,000 individuals, connected through BBMRI-NL;
- String of Pearls: a network of new, prospective clinical bio-banks that collects clinical data and biomaterial on eight diseases, initiated by the NFU in 2007 (Cerebrovascular accidents, diabetes, rheumatoid arthritis, neurodegenerative disease, renal failure, leukaemia, inflammatory bowel disease, hereditary colon carcinoma).
- Lifelines: a national (prospective) population bio-bank that has a unique three-generation design and aims to include 165,000 persons and to follow them for 30 years.
- FP7 project BioSHare-EU: harmonisation of phenotyping and biosampling for human large-scale research biobanks

The UMCs and the NFU are heavily involved in these major activities and several Dutch bio-banks participate in European consortia.
10. Clinical research

10.1 European context
Clinical research is being recognized as a cornerstone in health research and for preserving human health. This is as also shown by the FP7 programme ‘Optimizing the delivery of healthcare to European citizens’ that prioritizes clinical research in its work programme.

Clinical research refers to the testing of diagnostic (e.g. imaging) and therapeutic medical interventions (e.g. pharmaceutical, medical device) in human populations on efficacy, effectiveness, and efficiency, following rigorous methodology. Clinical Trials are at the core of Evidence Based Medicine. Currently, large unexplained variations in healthcare practices exist, and many healthcare interventions are not yet based on solid evidence from research. In view of the rising costs of healthcare, the lack of knowledge on the efficacy, effectiveness, and efficiency of healthcare, interventions become increasingly socially unacceptable. In addition, better use of pharmaceuticals and pharmacovigilance will contribute to patient safety and healthcare efficiency.

The European Clinical Research Infrastructures Network (ECRIN) aims at building a EU-wide research infrastructure for clinical trials and biotherapy. World-class services are provided to users through a network implementing harmonised practice and SOPs, with staff trained to multinational studies, and with high-quality infrastructures, data centres, and GMP facilities in order to enhance quality control and scale. Similarly, the European Advanced Translational Research Infrastructure in Medicine (EATRIS) aims to be a European, globally competitive infrastructure for biomedical translational research to optimise the outputs of both basic and clinical research.

10.2 Topics for the EU research agenda
UMCs have a special responsibility towards the performance of clinical trials, as they are the only partners that combine the necessary expertise with access to patients. Yet, merely international collaboration facilitates a sufficiently large number of participants, which is decisive to the validity and usability of the trial results. The NFU would therefore like to recommend the following topics on clinical research:

• Clinical trials in primary care setting;
• Epidemiological follow-up of prospective clinical trials;
• ICT-applications for (remote) monitoring of patients in trial;
• Methods for individual patient data meta-analytical techniques;
• Evaluation of multiple treatments in cost effectiveness.

10.3 Dutch contribution
The Dutch added value as partner is shown by the fact that the Netherlands takes a remarkably strong position in the field of clinical trials in Europe. Together with Switzerland, the Netherlands is the most productive European country, based on scientific publications (numbers and citations). Three UMCs are in the top-10 European institutions of clinical medicine. Furthermore, Dutch scientists take leading positions in clinical trial networks such as EORTC (oncology), ECCR (cardiovascular disease), ESCMID (infectious diseases) and metabolic disease. The Dutch UMCs will also join the European Clinical Research Infrastructures Network (ECRIN). Academia, regulators, and industry collaborate in the Dutch Clinical Trial Foundation (DCTF) to further improve the clinical trial infrastructure.
11. Bio-imaging

11.1 European context

ESF’s ESFRI Roadmap has led to a number of related Biomedical Sciences (BMS) research infrastructures such as ELIXER, INSRUCT, EATRIS, ECRIN, INFRAFRONTIER and BBMRI. The need for a new infrastructure in the BMS field was identified: Euro-BioImaging – research infrastructure for imaging technologies. The aim of Euro-BioImaging is to provide access to imaging technologies across the full scale of biological and medical applications, from molecule to patient.

Imaging techniques are key tools for scientists to understand living systems at both the molecular and the physiological level, from biological model systems to patients. Imaging allows for the non-invasive assessment of structural and functional changes of organs that may reflect specific pathology. Novel imaging techniques, in particular functional MR imaging and molecular imaging, hold great promise for clinical and etiologic research, but cannot yet be used at the population level.

In order to prevent fragmentation of European imaging efforts, Euro-BioImaging will address the imaging requirements of both basic and medical imaging communities by creating nodes in many ESFRI Member States that will deploy imaging infrastructure in a coordinated and harmonised manner.

11.2 Topics for the European research agenda

An imaging research infrastructure for basic and applied research opens the possibility for population imaging: to investigate specific pathophysiological substrates of diseases in a pre-symptomatic phase, in an epidemiological context, and at the population level. The ultimate aim of population imaging is to help develop the implementation of strategies to prevent disease. The NFU would therefore like to recommend the following topics in the field of bioimaging:

- Focus on cardiovascular diseases, diabetes, rheumatic diseases, and neurological and psychiatric disorders;
- Focus on functional and structural imaging in psychiatry;
- Genetic imaging in which (functional) imaging describes the phenotype for association studies;
- Functional drug studies in which imaging is used to provide biomarkers or surrogate endpoints for new drugs.

11.3 Dutch contribution

The Dutch added value as partner is shown by the support for Euro-BioImaging from the NFU, the Netherlands Forum for Biomedical Imaging (NFBI), TiGO, CTMM, and Medical Delta. These partners have also taken the lead in EPI2. It is expected that the Dutch government will further support the population imaging initiatives and this will position the NFU to become the population-imaging node in Europe. The Netherlands has a high quality and quantity output, with scores of 20-35% above the world average. Dutch medical science has a particular track record in both fundamental as well as applied clinical research using (functional) MRI, even in large population-based studies. This is also the case for the Dutch strong position in the competitive field of advanced light microscopy. Strong biomedical imaging techniques have been established in the technical universities of Delft, Eindhoven, and Twente. The Netherlands invested in specific large and unique imaging infrastructures like the 7-tesla MRI systems (VISTA). There are strong relations with industrial partners who benefit as suppliers or as collaborators in activities and investments.
12. To conclude

The NFU takes this as a first step in strategic research agenda setting. In a wider context of European policies and practices, the NFU strongly supports setting strategic research agendas at a European level in a transparent, interactive and open way to tackle the major societal questions. In addition, the NFU endorses actions to foster talent, to stimulate excellence, and to create a barrier free space for European researchers. Finally, the NFU looks forward to more coherence between European policies and to a multi-level governance approach.

The drafting of this position paper has taken place under the auspices of the NFU and in collaboration with representatives of the individual UMCs. First, the NFU Board authorized the eight priority areas. The further delineation within each area was realised through multiple bilateral consultation sessions to acquire the support of all people involved in the process. In a final meeting, advisors from Technopolis, took over the resulting documents, prepared the one-page summaries and the drafting of the first position paper. This process was communicated to and aligned with ZonMw, the Netherlands organisation for health research and development, that is representing the Netherlands in several joint programming initiatives.

The draft was then authorized by the deans as well, and subsequently discussed with and presented to members and representatives of the European Commission and the European Parliament on April 15th 2010 at an invitational seminar in Brussels. The drafting of this position paper should be taken as the first step in a dynamic and interactive process to demonstrate the position of the Netherlands Federation of University Medical Centers and its contribution towards Europe.