Health research 2010 – suggestions

Working document

19 December 2008

1. BIOTECHNOLOGY, GENERIC TOOLS AND MEDICAL TECHNOLOGIES FOR HUMAN HEALTH

1.1. High-throughput research

1. Harmonisation of phenotyping and biosampling for clinical research biobanks: To harmonise the characterisation of multivariate phenotypes associated with complex diseases including environmental and life style exposures, and develop evidence-based standards for the collection, processing, storage, management and quality control of human biospecimens.
Funding scheme: Collaborative project (Large-scale integrating project)
Justification: Harmonisation of phenotyping was identified as one of the key strategic priorities for the development of the biobanking field in Europe in the Networking Meeting for EU-funded Biobanking Projects organised in Brussels on 20-21 November 2008. Also suggested by PC (NO, CH). The concept has a major research component and therefore collaborative project is suggested as the funding scheme.

2. Genomics and Genetic Epidemiology of Multifactorial Disease. To bring together national programmes on genomics and genetic epidemiology of multifactorial diseases. This should also create synergies by uniting vast amount of data, resources and know-how which exist in different member states.
Funding scheme: ERA-NET Coordination and Support Action (Coordinating Action)
Justification: In a workshop as recently organised in the context of EUROBIOFUND 2008 in Strasbourg, several funding agencies from several member states (>10) have indicated their willingness to set up an common European programme in Genomics and Genetic Epidemiology of Multifactorial Diseases. This member states initiative will contribute to establish the European Research Area in this important research field. In addition, joining the research efforts taking place in different member states will increase substantially the probability in identifying the key factors involved in these diseases. The concept is also supported by PC delegates' comments

1.2. Detection, diagnosis and monitoring

Diagnostic Biomarkers

Suggestions for two-stage submission and evaluation procedure

1. Tools for the identification and the detection of biomarkers in clinical samples and patients: Proposers are invited to consider at least one of the following areas; integration of more than one area is encouraged.

- **Multimodality biomarker analysis:** Development of workflows, methods and devices for multiplex analysis of multimodality biomarkers (RNA, DNA, proteins or others in parallel) with the potential for high throughput analysis in routine diagnostics. The focus should be on analytical tools and methods but not on the search of new biomarkers. Participation of the industry, including SMEs, is expected.
- **Tools for detection, isolation and functional characterisation of complexes of interacting molecules for diagnostic purposes:** Tools for detection, isolation and functional characterisation of complexes and robust methods for isolation and quantification of interacting complexes suitable for detection in patient samples should be developed. Research should focus on interactions among proteins with each other and with other classes of bio-molecules like DNA and coding or non coding RNA molecules in disease states.
- **Development of new quantitative imaging biomarker(s) for monitoring therapeutic effects and safety in chronic diseases:** Research should develop new quantitative imaging biomarker(s) that should provide surrogates for monitoring treatment response or safety at an early stage. The imaging biomarkers considered here can be newly developed molecules, novel technological approaches, or established imaging technologies with novel applications. Results should have the potential to be translated into clinical use. The concept should address validation of the biomarkers in major chronic disease, such as cardiovascular or neurodegenerative disease.
- **High throughput molecular diagnostic imaging:** The research should develop the integration of high throughput molecular testing with detailed cellular imaging for advanced diagnosis and monitoring of disease. The goal is to integrate sophisticated sample selection and handling technologies (e.g. microfluidics, micro cell culture, arraying and/or conditioning) with powerful, innovative imaging technologies (e.g. scanning probe, electron or fluorescence microscopies), including advanced image analysis, in a quest for new powerful clinically-relevant biomarkers.
- **Development and implementation of Quantum Imaging of X-rays/Y-rays for Diagnosis:** The research should develop and implement quantum X- or Y-ray detection for a diagnostic imaging setting. Potential applications should concern major chronic disease, such as neurological or cardiovascular disorders, or cancer. The developed method(s) should be tested at least pre-clinically.

Funding scheme: Collaborative Project (Small or medium-scale focused research project)
Justification: This research should lead to new non-invasive prediction, diagnosis, monitoring and/or prognosis of disease, in view of a benefit to the patients. This field is also of interest for European diagnostics industry, including SMEs. There is an interest for biomarkers from ES and UK PC members.

2. Stratification approaches and methodologies to select from a wide range of biomarkers relevant candidates for clinical validation: The number of potentially clinically relevant biomarkers is increasing tremendously. There is a need for standardised and superior approaches that would allow discrimination of the best candidates for diagnostic purposes before bringing them to clinical trials. Participation of the industry is expected.
Funding scheme: Coordination and Support Action (Supporting Action)
Justification: A pipeline problem exists for diagnostics biomarkers. The number of potentially clinically relevant biomarkers is increasing tremendously. Current validation strategies do not allow coping with the inflation of candidate biomarkers. There is a need for standardised and superior approaches that would allow discriminating the best candidates for diagnostic purposes before bringing them to clinical trials.

3. Harmonization, validation and standardisation in genetic testing: Outcomes should be validation of methods and technologies, training, counselling, quality procedures and guidelines.
Funding scheme: Coordination and Support Action (Coordinating Action)
Justification: The demand for genetic tests has increased spectacularly over the last years. Unfortunately, genetic services in Europe still suffer from a high level of technical errors and poor reporting, caused by insufficient harmonisation, heterogeneous quality schemes, need for reference systems and fragmentation of services. A major and continuous effort towards quality assurance of the different aspects of the testing is deemed urgent and necessary.

1.3 Suitability, safety, efficacy of therapies

1. Towards the replacement of animals in safety testing in repeated dose systemic toxicity: The full replacement of animals in safety testing is the most challenging long-term target in the implementation of the Three Rs principle. Relevant legislation, regulations and directives require urgently a phasing out of animal tests thus putting a high pressure on research, validation and regulatory acceptance. The present call focuses on the construction of a solid foundation of this long term task. It reflects the research strategy for the next years aimed at the development of 'human safety assessment strategies'. Emphasis should be put on exposure routes relevant for cosmetic products (skin, inhalation).The research plan for the first phase should include the specific building blocks: development and use of functional human-based target cells, identification of intermediate biomarkers and endpoints with clinical relevance, construction of advanced organ-simulating devices, and the development of biological models with emphasis on systems biology, QSARs, PBPK, and TTC.
Funding scheme: Collaborative Projects (Large scale integrating projects)
Justification: Existing legislation (cosmetics directive, REACH, revised directive 86/609 EEC,) require the full implementation of the Three Rs (refinement, reduction and replacement) principle. There is a very high political pressure due to fixed deadlines for the full replacement of animal tests in the cosmetics directive.

1.4 INNOVATIVE THERAPEUTIC APPROACHES AND INTERVENTIONS

The focus is on cell-based immunotherapy. This approach offers hope for sufferers of diseases which are currently untreatable and where life is at stake. It also offers possibilities for addressing problems of an ageing population and has potential for combating rising healthcare costs. It is a high-value new technology offering Europe competitiveness and this opportunity is enhanced by the recent adoption of a European Regulation on advanced therapy medicinal products.

Cell-based immunotherapy has possible applications in autoimmune diseases, allergies, infectious diseases, blood disorders (leukaemia, hereditary diseases), cancer, or improvement of engraftment of transplants.

To meet the challenges and promise of cell-based immunotherapy, large Collaborative Projects should be supported. In particular they should focus on translational research coupled with supporting research on adapting the treatment to particular needs and on improving understanding of mechanisms.

1. Translational research on cell-based immunotherapy: The main objective of this suggestion is to develop cell-based approaches to modulating or rebuilding the immune system for therapeutic purposes. Research should be multidisciplinary, go beyond the means of single centres and include SMEs in consortia. Consortia should be constructed so that results can be exploited by clinical or industrial sectors as appropriate.
Funding scheme: Collaborative Project (Large scale integrating project)
Justification: This suggestion complements the third call on regenerative medicine where haematopoietic/immune reconstitution was excluded. The suggestion corresponds to the request of several delegations (CH, ES, HR, IE, NL and UK) and the recommendations from the EC Workshop on "Cell-based immunotherapy" of 27 November 2008. It is an important area of SME involvement, particularly in supporting technology.

2. TRANSLATING RESEARCH FOR HUMAN HEALTH

2.1. INTEGRATING BIOLOGICAL DATA AND PROCESSES: LARGE-SCALE DATA GATHERING, SYSTEMS BIOLOGY

2.1.1. Large-Scale Data Gathering

CLOSED in WP 2010

2.1.2. Systems Biology

Suggestions for two-stage submission and evaluation procedure

1. Tackling Human Diseases through Systems Biology Approaches: Multidisciplinary research should use the holistic approaches of systems biology to gain knowledge on the

mechanisms of diseases (e.g. cancer, infectious diseases). These approaches, based on quantitative data sets, should generate reliable and validated disease models using computational and mathematical modelling. The research should cross the borders of different disciplines including basic and clinical research, mathematical and computational modelling.
Funding scheme: Collaborative Project (Large-Scale integrating project)
Justification: PC delegations have supported the concept of broader topics and a 2-stage submission & evaluation procedure in fields such as systems biology. Actions in systems biology of basic mechanisms of diseases (e.g. cancer and other major diseases) are supported by several delegations. The need has also been highlighted in a recent EC-NIH workshop on Cancer Systems Biology, in ESF policy papers and so on.

2. Creating European multidisciplinary networks to address systems biology of basic biological processes relevant to health: These should demonstrate a multidisciplinary joint programme of activities and encourage the cross-fertilization between different disciplines needed to implement ambitious challenges in systems biology approaches to address basic biological processes. Networks should aim at durable integration potentially via the establishment of a virtual European Research Institute in the respective field.
Funding scheme: Network of Excellence
Justification: The NoE expert group set up in the beginning of 2008 by the EC, has highlighted the important role NoEs do and should play in realizing ERA objectives. Systems biology is an emerging area and its success depends on the cross-fertilization between different disciplines i.e. basic and clinical research, mathematics, engineering, This need of multidisciplinarity and especially the dry-lab/wet-lab collaborations has been repeatedly emphasised in recent DG RTD-sponsored workshops (e.g. joint workshop with the NIH on cancer systems biology; ICT-BIO conference). The networks should facilitate the cross discipline interaction via the establishment of common research strategies, tools, resources and training programmes, to catalyze progress in the field of systems biology.

3. Coordination and support actions in large-scale data gathering and systems biology: A strong international aspect should be ensured by inclusion of participants from third countries. Appropriate stakeholders, such as academic or industrial partners, journals, regulators and/or funding agencies should be included.
Funding scheme: Coordination and Support Action (Coordinating Action)
Justification: Definition of criteria for data quality as well as promotion of open access policy should facilitate the use of results obtained through publically funded studies. The concept reflects suggestions from the PC (GR, NO).

4. Developing new and improving existing mathematical algorithms for systems biology: The research should focus on the design of algorithms for modelling complex biological systems. These algorithms should be of general applicability for the field of systems biology and should be thoroughly tested using suitable health-related models. Cooperation with other related projects from the EECA region should be ensured and a part of the budget should be set aside for this cooperation.
Funding scheme: SICA Collaborative Project (Small or medium-scaled focused research projects) with focus on EECA

Justification: This suggestion arises from the conclusions of the EU-Russia Workshop on cooperation in health research held in St Petersburg in October 2007.

2.2. RESEARCH ON THE BRAIN AND RELATED DISEASES, HUMAN DEVELOPMENT AND AGEING

2.2.1. Brain and brain-related diseases

The Council adopted on 2 December 2008 Conclusions on "Joint Programming". These Conclusions refer to the Conclusions adopted on 26 September on a common commitment by the Member States to combat neurodegenerative diseases, particularly Alzheimer's. Council considers it necessary to launch a pilot "Joint Programming" initiative on combating neurodegenerative diseases, particularly Alzheimer's. The Commission services currently explore how best to support such initiative via support actions for the development of a vision and a strategic research agenda and structuring research projects.

1. Validation of strategies for treating addiction: The research should explore strategies to prevent and/or reverse craving and relapse mechanisms in animal models and patients (addicts). In particular, in addition to pre-clinical studies in animals, it is expected to include a clinical longitudinal observation study for the evaluation and validation of preventative and/or therapeutical strategies (eg: pharmacological, psychological) on large cohorts of subjects (addicts and controls). A cooperation should be required with similar activities from the EECA (Eastern Europe and Central Asia) region.
Funding scheme: Collaborative Project (Large scale integrating project)
Justification: Across Europe the burden of addiction is high, and for many addictive drugs the magnitude of the problem is increasing. Cocaine use in 16-24 year olds has doubled in the last seven years, and a recent rise in methamphetamine use brings a new concern for this highly addictive and easily made drug. Alcohol usage has similarly doubled and the economic cost of abuse is as high as 6% of GDP for individual member states.
This suggestion has been repeatedly requested by PC (UK, PL, HU, DE, IS, ES). Research on addiction was also highlighted as priority by the Consensus Document on European Brain Research (J Neurol. Neurosurg. Psychiatry, 17 Feb 2006) and the Workshop on "Perspective for Future Brain Research" of 8 May 2007.

2. Actions to support dissemination of scientific knowledge in neuroscience: Scientific data need to be communicated rapidly and effectively to the scientific community to guarantee a timely translation of results into diagnostic tools and therapies. Support should be given to international, broad scope initiatives (conferences, workshops, networks) that promote the dissemination of results from both basic and clinical brain research to a large mass of scientists, clinicians and industry people.
Funding scheme: Coordination and Support Action (Supporting Action)
Justification: Scientific results need to be communicated rapidly and effectively to the scientific community in order to foster translation of results into new diagnostic and therapeutic tools for brain diseases, and new brain-machine interfaces. In addition, actions to support dissemination of results in brain research are instrumental to make Europe a knowledge-based society. This suggestion has been highlighted as priority in the Consensus

Document on European Brain Research (J Neurol. Neurosurg. Psychiatry, 17 Feb 2006) and the Workshop on "Perspective for Future Brain Research" of 8 May 2007.

2.2.2. Human development and ageing

Suggestions for two-stage submission and evaluation procedure

1. Role of early-life developmental processes in longevity determination: This suggestion aims to capitalize on knowledge acquired in the fields of biology, in particular developmental biology as well as in gerontology and research on ageing, gathering research groups with the relevant know-how and expertise. Studies of the role of epigenetic mechanisms should be part of the research approach.
Funding scheme: Collaborative project (Large-scale integrating project)
Justification: Recommended by Portuguese Delegation under "General issues" and by Delegations from Germany, Latvia, Poland and The Netherlands under "2.2"; Emerging as important priority of the Workshop: "A roadmap for the future of ageing research in Europe" Brussels, 11-12 July 2007; Studies aiming at understanding human longevity and its mechanisms have traditionally focussed on adult age, thus neglecting the role of early-life events

2. Homeostasis in human development and its effects on lifespan: Longevity should be studied in terms of the capacity to ensure and maintain good homeostasis and networking between various body systems and functions, and of the entire organism. In addition to internal control mechanisms of homeostasis, the research should also take into account external influences, as for instance, lifestyle and environmental exposures.
Funding scheme: Collaborative project (Small or medium-scale focused research project)
Justification: Malfunctioning and failures of the homeostatic balance result in cellular malfunctions and disease implying that the well-being of the person depends upon the well-being of all the interacting body systems. Knowledge acquired in this area should pave the way to therapeutic interventions. Recommended by Delegations from Germany, Poland and The Netherlands under "2.2"; emerging as important priority of the Workshop: "A roadmap for the future of ageing research in Europe" Brussels, 11-12 July 2007. One of the existing theories defines ageing as the result of a series of defects and damages occurring and accumulating. Healthy ageing would therefore coincide with the capacity of the human body to successfully overcome defects, repair damages or eliminate metabolic toxic by-products. The human body should be considered here as a "System".

3. Integrative systems biology and comparative genomics for studying human ageing: Focus should be on genes and pathways more likely to be involved in ageing, on their interactions and how these give rise to an ageing phenotype. This should enable integrating and making optimal use of resources available for research in bio-gerontology and paving the way to unravelling the genetic and molecular mechanisms of ageing.
Funding scheme: Collaborative Project (Large-Scale integrating project)

Justification: Attention should be devoted to aspects of data collection, storage, sharing and dissemination as well as development of the ability to analyze multisystem and multilevel interactions in the dynamic state. Recommended by Delegations from Cyprus and Greece under "2.1"; emerging as important priority of the Workshop: "Data collection, standardisation, compatibility and accessibility in European Projects on Ageing research" Brussels, 10 – 11 June 2008. Ageing research aims at studying multiple mechanisms and needs several experimental models as well as human studies. Researchers face a clear need for data and systems integration and recognize that the added value of data co-ordination justifies the effort for data integration and sharing.

4. Telomeres and telomerases in cellular senescence and human ageing: The shortening of telomeres represents one of the basic aspects of ageing and diseases, by contributing to the accumulation of DNA damages. The concept would be to investigate the role of telomeres and telomerases have in ageing.
Funding scheme: Collaborative Projects (Small or medium-scale focused research project)
Justification: The shortening of telomeres represents one of the basic aspects of ageing and diseases, by contributing to the accumulation of DNA damages. Important applications include cancer research (most cancer cells have regained the ability to synthesize high levels of telomerase and thus are able to prevent further shortening of their telomeres).

5. Frailty and its implications in modern society: Suggested workshop to be carried out through collaboration between clinicians, geriatricians, health care professionals, carers and patients on "frailty": definition, causes, determination and impact in present day societies. The aim should be to establish a common definition of "frailty", enhance communication between representatives of the various domains and raise awareness of the older population.
Funding scheme: Coordination and Support Action (Supporting Action)
Justification: This will be of direct benefit to older patients as well as a tool for health managers and policy makers. Recommended by Finnish Delegation under "General issues"; priority issue for research highlighted at the 6th European Congress of Biogerontology 2008. Frailty is considered highly prevalent in old age and is associated with high risks for falls, disability, hospitalization, and mortality. Although many studies define frailty, a standardized ascertainment of frailty is needed. The output of this suggested activity would have potential for clinical assessment and for future research to design interventions for frailty. The determination of frailty is of relevance to the quality of care.

2.3. TRANSLATIONAL RESEARCH IN MAJOR INFECTIOUS DISEASES: TO CONFRONT MAJOR THREATS TO PUBLIC HEALTH

2.3.2. HIV/AIDS, malaria and tuberculosis

1. Target characterization and hit-to-lead progression in TB Drug development: The research should concentrate on the target-to-hit phase and contribute in filling the pipeline of new TB drug candidates with the potential of shortening of treatment and being effective against multidrug-resistant TB. Hit-to-lead progression should be done effectively by

academics and partnering industry. Essential elements of the research could include assay development, structural biology, virtual screening, high-throughput screening, fragment-based screening and rational drug design. Participation of players from NMS is encouraged and could increase impact of this research.
Funding scheme: Collaborative project (Large-scale integrating project)
Justification: Many SMEs are involved in this field and some of them are in the new member states. This suggestion would not only strengthen the pipeline, but would also integrate players from Eastern Europe and Russia to the main EU academic groups who are considered to be world leaders in the field. Pharmaceutical industry is likely to be interested in this type of research. This suggestion corresponds to what was requested at the recent "Challenges for the future" Conference on HIV/AIDS, Malaria and Tuberculosis, and suggested by several PC delegations. In addition, this area was recognized as one of the bottlenecks in TB Drug research in the "TB Drugs workshop", which was organized by the Commission services in October 2007.

2. Lead optimization and late preclinical development in TB drugs: Research should aim at optimizing the drug-like properties of lead compounds and generate a pharmacological, safety and biopharmaceutical profile of the compounds. It is expected to take at least one lead compound closer to clinical phase. As an alternative to lead optimization, the concept could concentrate on other aspects of late pre-clinical and/or early clinical development, like manufacturing information and clinical protocols. Active involvement of industry, especially SMEs and/or Product Development Public-Private Partnership organisations, could lead to an increased impact on the research proposed.
Funding scheme: Collaborative project (Small or medium-scale focused research project)
Justification: Investment in TB Drug discovery has already produced a number of lead compounds. Some of them are good candidates for shortening the current standard treatment of TB and also to be effective against multidrug-resistant TB, which is becoming a major problem in Eastern Europe. To ensure and integrated and continuous drug discovery portfolio, funds should be available to take promising compounds generated in FP6, and elsewhere, through preclinical development into Phase I. It is expected that there will be at least on drug candidate coming from FP6 projects on TB. This is an area where NMS can contribute and should have a structuring effect on European TB drug research. This suggestion corresponds to what was requested at the recent "Challenges for the future" Conference on HIV/AIDS, Malaria and Tuberculosis, and suggested by several PC delegations. In addition, this area was recognized as one of the bottlenecks in TB Drug research in the "TB Drugs workshop", which was organized by the Commission services in October 2007.

3. European Network of Cohorts Studies on HIV/AIDS: Such a network should be able to efficiently coordinate multi-disciplinary efforts to prevent and treat HIV infection in Europe, both in adults and children. The inclusion of cohorts of patients with HIV-related co-infections (mainly hepatitis and tuberculosis) will be considered as an asset.
Funding scheme: Network of Excellence
Justification: EU Member States and the European Commission have been financing cohort studies on HIV-infected patients since the very beginning of the pandemic. As a consequence, many different cohorts, including infected children, mother to child transmission, seroconversion, co-infections, long-term non-progressors, etc. have been supported with little or no pan-European coordination. Despite all this fragmentation, the study and follow-up of

these cohorts have allowed increased knowledge on new therapeutic options for these patients, including the publication of European guidelines for HIV treatment.

COORDINATED CALL WITHIN THE COOPERATION PROGRAMME THEMES HEALTH TOGETHER WITH THEME ENVIRONMENT (INCLUDING CLIMATE CHANGE)

Changing distribution of vector-borne diseases: Environment, transmission and vector control measures

The distribution, density and ecology of disease-transmitting vectors are particularly sensitive to environmental change caused in part by changing climatic conditions. The resulting spread of human vector-borne diseases will likely have major health impacts on vulnerable populations in Africa and – with vectors spreading beyond their original tropical habitat – also in Europe. Under an interdisciplinary coordinated programme funded in parallel from the FP7 Health and Environment collaborative research themes, resources are pooled to address in an integrated manner key issues related to the spread of vector-borne infections in Africa and Europe, ranging from the impact of environmental and climate factors to a better understanding of vector biology, population dynamics and research for new vector control tools. The project(s) selected from ENV.2010 will synergistically interact with the corresponding complementary project(s) selected from the Health theme.

4. Controlling Malaria by Hitting the Vector: New or Improved – Vector Control Tools: The major focus of this suggestion is on vector control in Africa, where the disease burden is highest and the need for malaria control most pressing. Inclusion of African research groups is essential to ensure needs and realities of the target countries are met. This suggestion forms part of a cross-cutting coordinated research effort on Climate Change impacts on the distribution of vector-borne infectious diseases, and thus on the spread of these diseases. It is expected to closely cooperate with corresponding complementary projects selected under the Environment theme.
Funding scheme: SICA Collaborative project (large scale integrating project)
Justification: Controlling malaria trough vector control is a research contribution to MDG 6. It also contributes to the EU's "European Programme for Action to Confront HIV/AIDS, Malaria and TB through External Action" (2007-2011), and to the recently launched "Global Malaria Action Plan" (BMGF in September 2007) as well as to the continuing Roll Back Malaria Initiative by WHO. Malaria eradication efforts in the 50ies were largely successful as far as they used insecticides to control the mosquito vector, until resistance to DDT and environmental concerns undermined this path. The Stockholm Convention calls for new insecticides to replace DDT in controlling disease-transmitting insect vectors. A recent international conference on PRD research in Brussels ("Challenges for the Future", November 2008) identified vector control as a research priority for malaria control. Vector-borne diseases have also been highlighted by delegations of the PC.

2.3.3. Potentially new and re-emerging epidemics

1. Biology and control of vector-borne infections in Europe: The emphasis should be on the infection's natural cycle, including basic biology of vectors and diseases reservoirs, and approaches to control it. Given the distribution of vector-borne diseases, participation of researchers from Eastern EU member states is encouraged. Public Health actors and decision makers will be important users of potential results and interaction with these stakeholders should be addressed. Malaria vectors are not addressed under this suggestion, since they are others covering it (e.g. under 4.).
Funding scheme: Collaborative project (Large scale integrating project)
Justification: Vector-borne diseases represent a growing threat to the health of European citizens. This is true for diseases already well established in Europe whose geographical distribution is changing and/or whose incidence is increasing (such as tick-borne encephalitis, nephropathia epidemica, Crimean Congo Haemorrhagic fever) as well as for diseases who are just starting to emerge or have caused single outbreaks in Europe (such as West Nile Virus infections or Congo-Crimean Haemorrhagic Fever) or for diseases who might emerge and pose a major threat to Europe (such as Dengue). Even more than other infectious diseases, vector-borne diseases have long been considered as a phenomenon of the past and research in this area has been neglected. This is especially true for research into the disease transmitting vectors, with disciplines such as medical entomology having almost vanished from university departments and courses. These conclusions and research in this area have the strong backing of the European Centers for Disease Control and Member States' public health institutes and are based to a large extent on the outcome of a recent workshop and study commissioned by the ECDC on the "Magnitude and importance of vector-borne diseases in Europe". A suggestion on this subject was also the strongest recommendation of an EC-organised workshop on the funding needs and priorities in the new FP7 area of "Emerging Epidemics" in 2007. Vector-borne diseases have also been highlighted by delegations of the PC.

2. Drug lead discovery against RNA viruses: Major viral infections with established antiviral drug discovery programs, such as HIV, hepatitis C or influenza are not targeted by this suggestion. The milestone of proof-of-concept in animal studies is considered to be an important outcome. Issues like exploitation plans, route-to-market, intellectual property management and integration of biotechnology SMEs and/or pharmaceutical industry should be explicitly addressed.
Funding scheme: Collaborative project (Large scale Integrating Project)
Justification: Europe currently still has a significant research capacity in this field and is home to some of the most successful research groups in this field, but recent emphasis of funding of biodefense funding in the U.S. has boosted research there and without support of this kind, the European competitiveness might be lost. This subject has been requested by several member states in previous programme committee consultations (DE; FR).

3. Integrated disease-specific research on West Nile Virus infections, Chikungunya and/or Crimean Congo Haemorrhagic Fever: Research areas such basic virology, transmission, epidemiology, diagnostic approaches and/or treatment and prevention strategies, including public health-relevant questions, should contribute to a comprehensive approach to counter the threats from these infections.
Funding scheme: Collaborative projects (Small or medium-scale focused research project)

Justification: Since a first outbreak in Romania in 1996, indigenous human West Nile virus infections have been reported in the Czech Republic, France and most recently Italy. The virus – transmitted by Culex mosquitoes – can cause severe neuroinvasive disease with a significant mortality, particularly in elderly patients. A major outbreak of Chikungunya in 2006 in the French overseas department of La Réunion (with a more severe clinical picture than previously observed) and the recent first local transmission in Europe, leading to over 200 cases in Northern Italy, have highlighted the importance of this disease, which can lead to significant morbidity. It is transmitted by Aedes mosquitoes, which have recently spread over most of Southern Europe. Crimean Congo Haemorrhagic Fever (CCHF) has also been called the "European Ebola" because of its very high mortality rate of 10-30% of infected patients. It occurs in South-Eastern Europe, with a sharply increasing incidence (in Turkey for example from 17 cases in 2002 – the first year it was reported – to 438 cases in 2006) and the first case in Greece was reported in June 2008. Research capacity in these diseases in Europe is so far limited (with Chikungunya research supported almost exclusively in France and CCHF so far affecting only countries with limited resources for research and development). The choice of these diseases as top priorities among vector-borne diseases threatening Europe is based on the results of an ECDC-committed study on the importance and magnitude of vector-borne diseases in Europe in 2008. While some aspects of research on these diseases would be also covered by the "horizontal suggestions 2.3.3-1 and 2.3.3-2, we consider it extremely important to strengthen this first-ever concerted research effort on vector-borne diseases also by a "vertical" disease-specific approach, in order to create synergy and a research capacity that will help Europe to prepare for these threats.

2.3.4. Neglected infectious diseases

1. Vaccines for infantile diarrhoeal diseases: Research should be focused on accelerating the development of vaccine candidates to clinical testing. Testing in vitro and in vivo should form part of the research, which may also include early clinical trials. Priority would on multivalent vaccines that aim to work across different strains of either ETEC or shigella. Vaccines should be suitable for use in endemic regions, and involvement of partners from ICPC countries as well as partners with expertise in industrial vaccine production is encouraged.
Funding scheme: Collaborative Project (Large scale integrating project)
Justification: The estimated death toll from diarrhoeal diseases is four to six million deaths per year, with most deaths occurring in young children in developing countries. Among children under 5, enteric pathogens have a much bigger impact than any of the big three infectious diseases (HIV/AIDS, malaria, TB). Vaccines for diarrhoea is a priority for WHO/IVR, and research into products for infantile diarrhoea was called for by the joint parliamentary assembly between EU and ACP countries According to the WHO/IVR, vaccination against specific diarrhoeal diseases offers the best opportunity for control of infectious diseases. The four main pathogens causing infantile diarrhoea are rotavirus, ETEC, cholera and shigella. Vaccines for rotavirus and cholera are either available or in advanced stages of development. However, vaccines for ETEC and Shigella are still an unmet medical need. ETEC is the most frequently isolated enteropathogen in community-based studies of children aged less than 5 years in the developing world, and probably accounts for approximately 200 million diarrhoeal episodes and 380 000 deaths annually. At a recent

international meeting at WHO the development of new ETEC vaccine candidates was strongly encouraged as well as the clinical evaluation of the available ETEC vaccine candidates in children in endemic regions. (Weekly Epidemiological Record, 17 March 2006, vol. 81, 11 (pp 97-104))
More than one million people are estimated to die from Shigella infection each year. Shigellosis is endemic throughout the world and it is held responsible for some 165 million cases of severe dysentery with blood and mucus in the stools, the overwhelming majority of which occur in developing countries and involve children less than five years of age. The WHO has recommended encouraging basic research on live and subunit vaccine candidates, and supporting the development of a single vaccine for use in people from both industrialized and endemic areas (Weekly Epidemiological Record, 10 February 2006, vol. 81, 6 (pp 49–60). This suggestion was also made by several delegates of the PC.

2. Comprehensive control of Neglected Infectious Diseases: The aim should be at developing an optimised system for prevention, diagnosis, cost-effective treatment, and other health care interventions to be used in disease-endemic countries. This research should further aim to overcome the vertical approach of many disease specific control programmes, and develop methods that are more adapted to a primary health care setting. A majority, but not necessarily be limited to, the NID priority diseases[1], with an aim of developing diagnostic methods and diagnosis-treatment algorithms adapted to resource primary health care settings must be addressed. The proposed treatments should be based on existing and affordable medication. Finally, it is required to develop policy recommendations for use by policy makers and health care managers in disease endemic countries.
Funding scheme: Collaborative Project (large scale integrating project)
Justification: Continued support to operational research from the FP6 INCO programme, but in a joint and coordinated approach across diseases. Operational and implementation research, both in EC and elsewhere, have too often been focused on vertical control approaches to single infectious diseases. This does not adequately address the reality for patients, which often have multiple co-infections and other cross-disease issues (e.g. nutritional). There is therefore a need for operational research on methods that are more adapted to a primary health care setting in resource poor countries. This suggestion has further been developed in consultation with AIDCO and DEV in an attempt to initiate coordinated activities within the field of operational research/public health in developing.

3. Next generation of researchers for Neglected Infectious Diseases: Coordination with ongoing EC activities to support training of researchers in PRD is encouraged. The activities should comprise training of young scientists, and support young researchers to establish independent research activities in disease-endemic countries. High quality science contents, demonstrated organisation and management abilities and clear indications of sustainability and impact should be prerequisites of selected actions. Coordination with ongoing EC activities to support training of researchers in PRD is encouraged.
Funding scheme: Coordination and Support Action (Coordinating action)
Justification: The development of scientific research in Africa is hampered by lack of human research capacity. This coordination action should contribute to fill this gap by providing training to young, promising researchers from Europe and disease-endemic countries, and support them in establishing their own, independent research in disease-endemic countries.

[1] Trypanosomiasis, Leishmaniasis, Chagas, Lymphatic Filariasis, Schistosomiasis, soil-transmitted helminths, Buruli Ulcer, Leprosy, Trachoma and bacterial diarrhoeal diseases.

The coordination action should complement similar activities in the area of poverty-related diseases.

2.4. TRANSLATIONAL RESEARCH IN OTHER MAJOR DISEASES

2.4.1. Cancer

1. ERA-NET on translational cancer research in Europe: ERA-NET to coordinate national and regional translational cancer research activities focusing on the integration of basic, clinical and epidemiological cancer research and funding in Europe with the ultimate aim to streamline EU-wide cancer screening, early diagnosis, prognosis, treatment and care.
Not FP7-HEALTH-2010-single-stage, must be extra ERA net call.
Funding scheme: Coordination and Support Action (Coordinating Action)
Justification: Requested by PC delegates since 2005 (DE, AT, NL, IT, LV). ERA-NETs on translational cancer research, on 'Coordination of Cancer Clinical Practice Guidelines' (CoCanCPG) and on optimisation and standardisation of bioregistries (EUROCOURSE; under negotiation following FP7-HEALTH-2007) could be a first step towards an 'EU cancer platform' requested by the European Parliament and Council.

2. Structuring translational cancer research between cancer research centres in Europe:
A multidisciplinary, investigator-driven network to integrate translational research amongst cancer research institutions and cancer hospitals by careful coordination and prioritisation of investigator-driven, patient-directed joint research on promising therapy strategies. At the same time, this network should define and build on ongoing infrastructure efforts in Europe, design effective joint training/education and coordinate strategic efforts towards long-term sustainability, taking into account and linking ongoing transnational research and partnering activities
Funding scheme: Network of Excellence
Justification: This is a priority as stated by requests from many European stakeholders. Also requested by the European Parliament and several PC delegates (AT, UK, DE, GR, SK, FR).

3. Structuring clinical trials on rare cancers in adults:
To integrate and formalise translational research amongst institutions at the forefront of rare cancers in adults, including furthering joint clinical research on harmonised, clinical evidence-based therapy strategies that increase cancer cure or improve quality-of-life in rare cancers.
Funding scheme: Collaborative Project (Small or medium-scale focused research project)
Justification: This is a priority as stated by requests from the European Parliament[2], the Council[3], and emanating from several public-private partnering events on rare cancers and workshops, including '3rd EC Workshop on Molecular Targets for Cancer'. A clear need to structure clinical trials in this field exists, that depends on close collaboration within several smaller and informal investigator-driven research networks. Cooperation is complicated since rare cancers in adults encompass many different types of cancer whereas only very few national centres/hospitals exist with sufficient expertise and offering optimal treatment and care. The impact of rare cancers on the quality of life of patients and families is very high, as well as the burden on social security schemes. In addition, only few specific drugs are being clinically validated or marketed due to a general lack of industrial interest and public financial support.

[2] 'Combating cancer in the enlarged European Union', P6_TA(2008)0121
[3] 'Reducing the burden of cancer', 9636/08 SAN 87

4. Structuring clinical research in paediatric and adolescent oncology in Europe: To integrate and formalise translational research amongst institutions at the forefront of paediatric oncology, including furthering joint research on (1) harmonised therapy strategies that increase cancer cure or improve quality-of-life in children and adolescents with cancers; (2) clinical epidemiology that should improve early diagnosis and prognosis; (3) development and/or effective sharing of standardised data centres, standardised methodology, tools, technology and equipment. In addition, it should design and deploy effective joint training/education and referral schemes and coordinate strategic efforts towards long-term sustainability, taking into account ongoing transnational partnering activities.
Funding scheme: Network of Excellence
Justification: There is clear need to structure clinical research in this field, that so far has depended on close collaboration of several informal networks and investigators. Cooperation is complicated since childhood cancers are rare cancers and ethical issues with clinical research on children a particular issue. This is a priority as stated by requests from the European Parliament and several PC delegates (AT, UK, DE, GR, SK, FR). Also clearly emanating from several workshops, including '3rd EC Workshop on Molecular Targets for Cancer'.

5. Translational research on common cancers with poor-prognosis: Focusing on either pancreatic cancer, liver cancer, stomach cancer, ovarian cancer or brain cancer, multidisciplinary research should reverse-translate clinical observations concerning treatment failure into better targeting strategies, cancer models closely mimicking the disease and/or any other strategy that stands a chance of increasing patient survival.
Funding scheme: Collaborative Project (Small or medium-scale focused research project)
Justification: For a number of poor prognosis cancers, despite an increased knowledge of detailed underlying molecular characteristics as well as a limited number of clinical trials validating novel therapies to date, 5-year survival rates remain very low. Reasons for this are the absence of reliable and non-invasive early detection and diagnosis resulting in advanced-stage detection for most of these cancers, fragmented research efforts including a gap between basic-clinical research groups. This is a priority as stated by requests on 'difficult-to-treat cancers' from the European Parliament, the Council, and workshops, including '3rd EC Workshop on Molecular Targets for Cancer'. Areas targeting tumorigenic signalling pathways, inflammation, hypoxia, metabolic/energy imbalance, the cancer stem cell, genomic instability and other cancer hallmarks that could be addressed here are requested by several PC delegates (BE, FI, AT, EE, FR, GR, NO, HR).

6. Predicting long-term side effects to cancer therapy: To systematically collect and register data on the incidence and characteristics of late adverse effects to treatment from cancer patients, such as organ toxicity/failure, secondary cancers, late mortality, gender and country-specific issues. It should translate these findings into harmonised guidelines on long-term prevention, risk prediction, training of health care professionals and better management of adverse effects from therapy in cancer survivors.
Funding scheme: Collaborative Project (Small or medium-scale focused research project).
Justification: A majority of cancer survivors suffer from serious late effects of treatment. Detailed information is needed on the exact incidence of side effects, secondary cancers, cohorts and their characteristics as well precise, evidence-based information on best

palliation, treatment options, health care needs and impact on society. Patient quality-of-life issues are a priority as stated by requests from the European Parliament, the Council, several patient advocacy groups and emanating from several workshops.

7. Predicting individual response and resistance to therapy: To integrate relevant clinical data obtained through standardised methodologies from clinical research on pharmacogenetics / -genomics, on genetic variation in the host and the tumour as well as on clinical observation data of cancer patients to improve our understanding of the critical signalling pathways involved, with the aim to achieve validated risk stratification criteria to be used in the processes of early innovative screening methodologies and prediction of individual therapy response and resistance.
Funding scheme: Collaborative Project (Large-scale integrating project)
Justification: Resistance to classical (chemo- and radiotherapy) and targeted therapy regimens in cancer is an enormous and unresolved problem. With recent insight in and translation of the underlying wealth of molecular biology towards the clinic it has become clear that most –if not all- cancers require subclassification. In addition, great diversity exists in response to therapy between patients both because of molecular tumor heterogeneity, but also because of critical differences between patients genetic makeup.

8. Optimising the delivery of radiotherapy and/or surgery to cancer patients: Research with a strong clinical component, should address the optimisation of the delivery of radiotherapy and/or surgery to patients suffering from solid cancers, aiming at optimising treatment efficacy while diminishing/limiting undesired effects.
Funding scheme: Collaborative Project (Large-scale integrating project)
Justification: Local therapy, when favourable TNM staging applies and executed with radical intent, represents the mainstay of therapy in many solid cancers. Furthermore, when the disease stage does not allow treatment planning with intent of radical cure, often radiotherapy is used in a palliative setting for better loco-regional control and amelioration of patients' quality-of-life. However, radiotherapy and surgery (and their combination in a concurrent/sequential mode) do suffer from significant side-effects and morbidity/mortality rates, limiting their full potential in clinical management. Very few public financial incentives exist to improve tailored surgery and radiotherapy in the routine cancer treatment setting, where hospitals are mostly focusing on economically affordable treatments. Patient quality-of-life issues are a priority as stated by requests from the European Parliament, the Council, several patient advocacy groups and workshops.

9. Infectious agents and cancer in Africa: Translational and multidisciplinary efforts should address the aetiology and epidemiology of Kaposi sarcoma, cervical cancer, gastric cancer and lymphoma in the African population with the purpose to identify high-risk factors and design point-of-care diagnostics adapted to local necessities and requirements.
Funding scheme: SICA Collaborative Project (Small or medium-scale focused research project)
Justification: Cancer is an under-emphasised issue in Africa, partly because of the overwhelming burden of communicable diseases. However, cancer is a common disease in Africa with 650,000 people diagnosed annually out of a population of 965 million. Furthermore, the lifetime risk in females (between 0 and 64 years) of cancer is about 10%, which is only about 30% lower than the risk in industrialised countries. In females, the

lifetime risk of dying from cancer in Africa is almost double the risk in industrialised countries (Lancet Oncology 2008). Collaborative research at improving health in Africa is a key challenge for WP2010. Research on the role of infectious agents on cancer initiation and progression, often involving process like inflammation, cancer immunology, is requested by several PC delegates (AT, BE, RO, EE, GR, IT, NO).

2.4.2. Cardiovascular diseases

The focus should be on diagnosis, prevention, treatment and monitoring of heart and blood vessel diseases (including vascular aspects of stroke) using broad multidisciplinary approaches. Hypothesis-driven research with preliminary data available would be supported. The knowledge gained from research performed in this area should lead to an improvement in the prevention and treatment of cardiovascular diseases, which are a major cause of ill health and death in Europe and worldwide.

1. Reducing in-stent thrombosis: The objective is to develop new strategies to prevent in-stent thrombosis combining mechanistic research in platelet biology and coagulation in relevant model studies, with clinical studies using novel imaging technology.
Funding scheme: Collaborative Project (Small or medium-scale focused research project)
Justification: Late in-stent thrombosis remains a major limitation in treatment of ischemic heart disease owing to its high morbidity and mortality. The response to classic anti-thrombotic therapy is limited. The underlying mechanisms are complex and relate to the interaction between stent properties, vessel wall and thrombotic mechanisms. Big industry is unlikely to provide the radically new approaches that are needed and there is a strong need for independent investigation. This research area is identified as a priority in the recent EC organised translational CVD research workshop (October 2008) supported by the Advisory Group and PT.

2. New approaches to reduce ischemic damage to the heart: Implementation of recently developed methods in a medium-scale patient study with extensive sampling for biomarker and annotation of disease variables collection should explore patient-related confounders.
Funding scheme: Collaborative Project (Small or medium-scale focused research project)
Justification: Early thrombolysis and reperfusion at the time of ischemia have increased patient survival but have not reduced the prevalence of myocardial infarction. Myocardial infarction is the leading cause of heart failure. This research area was identified as a priority in a recent EC-organised translational CVD research workshop (October 2008) supported by the Advisory Group, UK for biomarkers and IT.

3. Identifying new therapeutic targets in atrial fibrillation: The objectives are to identify molecular markers for the pathogenetic processes that lead to persistent atrial fibrillation and to identify and validate the potential new therapeutic targets. The study should take advantage

of large-scale patient data sampling, of the potential of animal models for preclinical testing and of small proof-of-concept patient studies.
Funding scheme: Collaborative Project (Large scale integrating project)
Justification: Atrial fibrillation is the most common arrhythmia with an increasing prevalence related to ageing. Its societal impact is large because of the morbidity, predominantly related to stroke as a consequence of embolization from the thrombi in the atrium, but also to heart failure. Therapy, both pharmacological and interventional (ablation), remains suboptimal and carries a high economic cost. This research area was identified as a priority in a recent EC-organised translational CVD research workshop (October 2008) supported by the Advisory Group and IT.

4. Diastolic heart failure: The objective is to define and explore the molecular mechanisms of diastolic heart with the aim to develop specific therapies. A multidisciplinary approach is needed, including molecular marker studies, imaging, cell and systems biology, and including the use of patient data to generate hypotheses to be validated in the experimental setting.
Funding scheme: Collaborative Project (Large scale integrating project)
Justification: Approximately half of all patients who present with signs and symptoms of heart failure have near-normal systolic function but have abnormal filling and relaxation of the heart. Diastolic heart failure has a mortality that is only slightly lower than that of systolic heart failure, around 45% over 5 years. Etiology includes ageing, hypertension and obesity; females are more susceptible. Classic heart failure therapy is unsatisfactory and specific targets remain poorly defined. This research area was identified as a priority in a recent EC-organised translational CVD research workshop (October 2008) supported by the Advisory Group and IT.

2.4.3. Diabetes and obesity

CLOSED for WP 2010

2.4.4. Rare diseases

1. Clinical development of substances with a clear potential as orphan drugs: Support should be provided to clinical studies (including clinical trials up to phase 3 included) of EU designated orphan medicinal products*. Clinical studies should focus on biopharmaceutic studies (incl. bioavailability, bioequivalence, in vitro-in vivo correlation), human pharmacokinetic and pharmacodynamic studies, human efficacy and safety studies. Involvement of industry is strongly recommended. Cancer diagnostics/therapies should not be considered. The orphan medicinal product should need to be granted the EU orphan designation at the latest on the date of the call closure.
Funding scheme: Collaborative Project (Small or medium-scale collaborative project)
Justification: Supporting clinical trials in rare diseases has been identified as a priority in this area (e.g. during EC workshop April 2005 and EC conference on rare disease research September 2007). as many potential orphan drugs are novel chemical entities or biotechnology products, often developed by SMEs.

2. ERA-Net on rare diseases: This action should improve the linking and efficient integration and coordination of national/regional programmes for rare diseases research, building on previous activities in this field. The action should include a strategy leading to the mutual opening of national/regional programmes to the participants and to the implementation of joint transnational calls, as well as activities aimed at fostering the development of rare diseases research programmes in non-participant Member States and Associated States. Extending the consortium of the previous ERA-Net (FP6 E-Rare coordination action; http://www.e-rare.eu/) to new participants, notably EU-12, is a prerequisite.
Funding scheme: Coordination and Support Action (Coordinating Action)
Justification: due to the low number of scattered patients and experts, research on rare diseases needs multidisciplinary, international approaches to be successful, which brings a clear European value added to such research. Developing further the ERA-Net would help exploiting at best the European value added and avoiding the duplication of studies, which would in the end optimise the use of public investment in this area. Such a network would be well in line with the recent Communication of the European Commission on Rare Diseases (http://ec.europa.eu/health/ph_threats/non_com/docs/rare_com_en.pdf) and the proposal for a Council recommendation (http://ec.europa.eu/health/ph_threats/non_com/docs/rare_rec_en.pdf), notably when it comes to the priority of developing European cooperation, coordination, and regulation for rare diseases.

2.4.5. Other chronic diseases

1. Investigation of the mechanisms of initiation of respiratory allergic response, genetic predisposition, biomarkers and identification of targets for therapy: Research should represent a joint effort of clinicians (allergologists and epidemiologists), geneticists, molecular biologists and biochemists with a strong clinical research component, should contribute to the elucidation of the triggering mechanisms of respiratory allergic response including a study of genetic predisposition, characterization of the risk groups among the population, definition and characterization of potential allergens, as well as methodology to establish suitable biomarkers for early diagnosis of allergy.
Funding scheme: Collaborative Project (Large-scale research project)
Justification: In the last decades diseases including allergic asthma, rhinitis, eczema and IgE mediated food allergies have constantly increased. In European countries the prevalence of IgE mediated diseases for children and young adults is about 25 %. The major respiratory allergens are of pollen, arthropod, mammalian and less so of mould spore origin. These areas of research were strongly supported by many Members States through their representatives in the Programme Committee. Out of 15 Member states who provided their suggestions to the Other Chronic Diseases area, as many as 9 MS included recommendation for including research, prevention and therapy of allergic diseases, especially respiratory/pulmonary diseases and asthma (AT, BE, EE, IE, PT, RO, ES, UK, and CH).

2. Infection as the trigger for the development of inflammatory processes in allergies and autoimmune diseases: Research should focus on the investigation of the triggering mechanism

induced by a various pathogens, leading to an inflammation reaction which, under persistent - subclinical- stimulus becomes chronic. Translational research to identify the role of specific pathogens (bacterial, viral, fungal, etc.) and the mechanisms underlying altered host-pathogen interactions in the establishment and persistence of allergic and autoimmune diseases should apply multidisciplinary approach involving immunologists, virologists, bacteriologists, geneticists, molecular biologists, bio-informaticians and the use of animal models and clinical data.

Funding scheme: Collaborative Project (Small or medium-scale focused research project)

Justification: The association and causative role of infectious agents in chronic inflammation, allergy and autoimmune disorders have major implications for public health, prevention, and treatment. Out of 15 Member states that provided their suggestions to the Other Chronic Diseases area, four MS included recommendation for including investigation of a role of infection in triggering and persistence of allergies and autoimmune disorders: LV, PT, UK, and CH. This suggestion is regarded in the recommendations as a cross-cutting issue establishing common mechanisms in allergy and autoimmunity by looking into molecular antigens and specific receptors involved in the initiation of these diseases. Knowledge of the onset mechanisms would allow for identification of targets for treatment of a broad scale of diseases.

3. OPTIMISING THE DELIVERY OF HEALTHCARE TO EUROPEAN CITIZENS

3.1. TRANSLATING THE RESULTS OF CLINICAL RESEARCH OUTCOME INTO CLINICAL PRACTICE INCLUDING BETTER USE OF MEDICINES, AND APPROPRIATE USE OF BEHAVIOURAL AND ORGANISATIONAL INTERVENTIONS AND NEW HEALTH THERAPIES AND TECHNOLOGIES

Suggestions for two-stage submission and evaluation procedure

1. Better understanding of dissemination and implementation strategies: This research should establish the empirically tested theoretical basis for better understanding which factors influence the effectiveness of dissemination and implementation strategies of new knowledge (e.g. clinical guidelines), new products, or new interventions. The objective is to bridge the know-do gap between clinical research and everyday clinical practice.

Funding scheme: Collaborative Project (small to medium scale project)

Justification: To optimise health care delivery we must not only understand how to create the best interventions, but how to best ensure that they are effectively delivered in clinical practice to get the best return on decades of investment in biomedical research. This suggestion is formulated at the area level in order to allow applicants to address key research questions of this area inviting a variety of innovative qualified research proposals as requested by several member states (CY, DK, FR, FI, IT, NO, ES). This approach should be able to address the research questions identified by other member states for this area (AT, CZ, FR, IRL, IT, LV, PL, UK). It is envisaged that several proposals should be funded to achieve acceptable success rates (ES, IT, LV, RO).

3.2. QUALITY, EFFICIENCY AND SOLIDARITY OF HEALTHCARE SYSTEMS INCLUDING TRANSITIONAL HEALTH SYSTEMS

1. Financing systems' effect on quality of healthcare: Models should be developed that take into account the needs of different patient groups in relation to how the treatment is financed. The incentive mechanisms effect on quality of care need to be explored.
Funding scheme: Collaborative Project (Small or medium-scale focused research project)
Justification: This suggestion has been asked for by several Member States in this and previous consultations (CH, ES, PL, RO, MK, NO, UK). The setup of financial mechanisms has an impact on activity, efficiency and quality of care. Both new and old Member States should be able to take advantage of the evidence base resulting from this research.

2. Risk adjustment algorithms for better health insurance coverage: Development of risk adjustment models to better share risks between providers of social health insurance and reduction of the asymmetric information in health insurance. Also the relationship between patients and insurers, insurers and providers and patients and providers should be investigated.
Funding scheme: Collaborative Project (Small or medium-scale focused research project)
Justification: This suggestion has been asked for by Member States in this and previous consultations (CH, DE, NL) and should provide evidence for setting up mechanisms to ensure efficiency in the financing of insurance based health care in both new and old member states.

3.3. ENHANCED HEALTH PROMOTION AND DISEASE PREVENTION

CLOSED for WP 2010

3.4. INTERNATIONAL PUBLIC HEALTH & HEALTH SYSTEMS

(4.3.2: INTERNATIONAL PUBLIC HEALTH & HEALTH SYSTEMS)

This 4th Call foresees an emphasis on collaborative health research with Africa entitled "Better health for Africa". Research activities foreseen in this area is the result of extensive consultations and interaction with stakeholders, in particular WHO for example the 2008 World Health Report on Primary Health Care, the IGWG (**I**nter**g**overnmental **W**orking **G**roup) discussions on a 'Global Strategy and Plan of Action on public health, innovation and intellectual property' (WHA Resolution 61.21 May 2008) , FP6 and FP7 project co-ordinators, a special session hosted in the 2008 Ministerial Forum on Research for Health in Bamako, Mali, the November 2008 EC Conference on poverty-related diseases and other international fora such as the ACP. Furthermore Cluster 6 of the EU-Africa partnership foresees S&T collaboration with an emphasis on capacity building. The lack of reliable evidence on the overall impact and the cost-effectiveness of major health programmes and the need for more impact research has been one of main conclusion from the Ministerial Summit in Bamako

2008. There is a need to provide evidence on the effectiveness of new strategies and interventions to improve maternal and newborn health and should contribute directly to the Millennium Development Goals (MDGs) N°5 - maternal health and N°4 - child health, as about one third of all under-five mortality is related to perinatal causes. At the same time opportunities have to be created to promote evidence-based policy making by involving stakeholders and policy makers, contributing to better access to essential health care and contributing to achieving the health related MDGs.

1. Develop and assess key interventions and policies to address the human resource crisis in the health sector: The deficit in human resources for health should be investigated as well as identifying and analyse the main causes and effects of related interventions and policies to lead to the development of improved or new interventions and/or policies.
Funding scheme: Collaborative Project (Small or medium-scale focused research project)
Justification: This is a concern for all Member States as well as a major EC issue across different areas including health. (DG DEV, SANCO, AIDCO; MARKT)

2. Impact and cost-effectiveness of existing major health programmes: Development and validation appropriate methodologies and application to one or more existing major health programmes addressing priority health issues, such child health, reproductive health, mental health, patient safety, and/or specific disease control programmes.
Funding scheme: Collaborative Project (Small or medium-scale focused research project)
Justification: There is an urgent need for more research on the impact and benefit of established health programmes, as extrapolation of results from small pilot studies are not reliable. This is major concern for the donor community and the international partner countries, as evidenced in the recent Ministerial Summit in Bamako.

3. Feasibility and community effectiveness of innovative intervention packages for maternal and new-born health in Afrika: The focus should be on impact-oriented research on the effectiveness and feasibility of strategies and related interventions to promote the health of mothers and their new-borns and aim at providing evidence on new strategies and interventions that are relevant and applicable in operational health care settings in Africa.
Funding scheme: Collaborative Project (Small or medium-scale focused research project)
Justification: This suggestion addresses directly European and global priorities - MDGs - in maternal and child health.

4. Financing models for accessible health care: Development and assessment of equitable health care financing models that ensure universal coverage and sustainability in low and middle-income countries. Incentive mechanisms to deliver health services to the poor must be taken into account.
Funding scheme: Collaborative Project (Small or medium-scale focussed research project).
Justification: This suggestion addresses the key issue of providing basic health care in the context of the MDGs and the global commitment to universal access to health care.

5. Building sustainable capacity for research for health in Africa: Develop and implementation of mechanisms for the sustainable development of capacity for health

research in Africa in close collaboration with African research institutions that include a substantial element of South-South cooperation and networking.
Funding scheme: Coordination and Support Action (Coordinating Action)
Justification: Building research capacity in Africa is a key element of the Cluster 6 of the current EU-Africa partnership on cooperation in Science and Technology.

6. Assessment of migrants' health, disease patterns and impact on health systems: To be developed further developed.
Funding scheme: Coordination and Support Action (Coordinating Action)
Justification: Related requests have been made by Egypt and SANCO in the context of the neighbourhood policy.

4. OTHER ACTIONS ACROSS THE HEALTH THEME

4.1. COORDINATION AND SUPPORT ACTIONS ACROSS THE THEME

1. Promoting participation of research intensive SMEs in FP7 Health projects: The objective is to promote and support the participation of SMEs in the Health theme.
Funding scheme: Coordination Action or Support Action (Coordinating Action)
Justification: SME participation is a priority of the Framework programme, but attracting research intensive SMEs continues to be a challenge which requires active promotion and support to overcome.

4.2. RESPONDING TO EU POLICY NEEDS

1. Off-Patent Medicines for Children: The aim of this suggestion is therefore to increase the availability of medicines duly authorised for children as well as to increase the information available on the use of medicinal products in the paediatric population. Research will have to develop and test new paediatric medicine formulations in children from older off-patent medicines. In view of many facilities offered by the European Medicines' Agency (EMEA), such as fee reductions, exemptions and deferrals for advice obtained in the context of Marketing Authorisation Applications (MAAs), including PUMAs, the participation of at least one SME in each successful proposal would be considered to be essential.
Funding scheme: Collaborative Project (Small or medium-scale focused research project)
Justification: The updated version of the Paediatric Medicines Priority List (following from the Paediatric Medicines' Regulation) EMEA now contains 55 different molecules. It is necessary to rationalise and simplify the classes of different therapeutic needs and respect those that are the most pressing. As set out above, these include the development of new presentations for existing medications and the need to focus on requirements for specific age-groups. The definition of pharmacokinetic profiles and the need for new knowledge of efficacy and safety in potentially new indication of older molecules cut across all of the above fields.

2. EU-US Transatlantic Paediatric Network: It is both desirable and necessary to bring together European and US stakeholders involved in the joint development and testing of medicines for children. The objective is to foster mutual research activities aimed at better medicines for children. To coordinate European research programmes in paediatrics in order to exchange and benchmark expertise with similar initiatives in the US. Expected stakeholders include industries (large pharma, SME), patient organisations, regulatory authorities, ethical experts. The outcome should be a streamlined transatlantic research agenda to develop better medicines for children.
Funding scheme: Network of Excellence
Justification: Expected stakeholders include industries (large pharma, SME), patient organisations, regulatory authorities, ethical experts. The arrival of the new legislative acts on both sides of the Atlantic, the appearance and growth of new national and international paediatric networks reflect the need for high quality medicinal products for children. These are major public health priorities cutting across all ages groups within the paediatric population and all disease categories. An improved co-ordination of the various research activities, both in Europe and with those in the US is therefore needed.

3. Adverse Drug Reaction Research: The safe use of medicines maintains an even higher profile than before, with often serious adverse events becoming apparent many years after products have been launched and because such events may not be limited to one molecule alone, but to whole classes of products, with similar physiochemical characteristics. Such issues are a matter of grave public concern and further research should generate new knowledge on potentially life threatening drug adverse events that affect different body systems.
Funding scheme: Collaborative Project (Small or medium-scale focused research projects)

- Cardiovascular adverse reactions associated with vascular endothelial growth factor (VEGF) inhibitors
- Neurological adverse reactions, infections and malignancies associated with immunomodulators
- Long-term developmental effects of psychoactive medicines in childhood
- Influence of medicinal products on the health of the musculoskeletal system
- Metabolic disturbances after HAART (Highly Active Anti-Retroviral Therapy) treatment of HIV positive patients.

Justification: The proposed new Pharmaceutical Legislation (Directive and Regulation), due to de adopted at the end of 2008, envisages a more proactive conduct of Pharmacovigilance. This should entail greater reliance on the defining and managing the risk-benefit profile of new and existing medications as well as the need for drug safety studies for these two groups. The industry will face a number of serious obligations in this regard, but since the latter group of compounds are often of a generic nature, obligations on the original innovator to carry out safety studies will be difficult if not impossible to enforce. In addition, safety issues may only emerge when a product or class of products have been on the market for a long time past their patent expiry.

4. International Pluripotent Stem Cell Registry: This should develop an online platform that provides a freely accessible database of human pluripotent cell lines that are available for research in Europe, including adult and embryonic stem cells (hESC) lines and established induced pluripotent cells (iPS) lines. This registry should provide detailed information on

these cell lines including molecular, genetic, phenotypic and functional data. It should network with other stem cell registries established elsewhere in the world with the aim to standardise the available information on these lines.
Funding scheme: Coordination and Support Action (Coordinating Action)
Justification: It is stated in the official FP7 text (article 6), the EU Commission has to support actions and initiatives that contribute to a coordination and rationalisation of hESC research, in particular the EU Commission will support a European Registry of hESC lines. By providing detailed information on all the stem cell lines available, the registry will contribute to maximise the use of existing hESC and may help to avoid unnecessary derivations of new hESC lines. By networking with other registries in the world, it will also contribute to generate standardised information on these lines. The current EU hESC registry (FP6) will end in March 2010.

5. Methodology to evaluate and monitor EU health-related funded projects in developing countries: Develop a sound methodological model for use by EC services and ACP countries, accompanied by evaluation and monitoring tools (indicators), to best assess the impact, implementation and performance of health policy in developing countries as a result of both European Development funds (e.g. EDF) and EU funded research projects in the field of health.
Funding scheme: Collaborative Project (Small or medium-scale focused research project)
Justification: This research is a particular request by EC services (DG AIDCO, DEV) to serve decision makers in the EU and the development partner countries to strengthen monitoring and evaluation of EU-funded projects and consequently base their decisions on the best scientific advice available when they decide on the use of EU development funds, in particular given the trend of sectorial budget support.

6. Impact of EU legislation on health research and related developments and applications: The objective is to evaluate the impact of specific EU legislation and related guidelines on specific research activities within the Health theme.
Funding scheme: Coordination Action or Support Action (Supporting Action)
Justification: Assessing and monitoring the impact of legislation on research activities is vital to ensure good implementation and to identify possible remedial action as soon as possible.

7. International forum for European life sciences funders and performers: The concept aims at organising conferences during which scientists and policy makers would debating strategy to be put in place for addressing large-scale research initiatives in Europe. **Funding scheme:** Coordination and Support Action (Coordinating Action)
Justification: EUROBIOFUND was the "first generation" example of this concept for an international forum. It ended in 2008 after the organisation of 3 successful events. A recent survey organised by ESF on EUROBIOFUND clearly indicated that EUROBIOFUND was a good concept that would need to be re-established in FP7. This international forum would to foster the ERA in life sciences research and be a step towards the identification and establishment of large scale research efforts in Europe that may suited for ERA-NET, ERA-NET+ or joint programming.