Impact assessment of health research projects supported by DG Research and Innovation 2002-2010

Followed by:

Expert group report recommendations on the future of health research in Europe

Foreword

I am pleased to present this document, an impact assessment of health research supported by the Health Directorate of the European Commission's Directorate General for Research and Innovation under its Framework Programmes (FP).

Consisting of an analysis of the programmes 2002-2010, of the challenges that will inform health research in the short to medium term, and an expert panel report making recommendations for the future of health research in Europe, this document forms part of the evidence base for the ambitious proposal for health research under Horizon 2020 (2014-2020).

The document draws in particular on a survey of participants in FP6 and FP7 Health research projects. I am indebted to those participants, to the members of the expert panel whom I thank for their hard work and stimulating contribution and to my staff, in particular Bernard Mulligan and Antoine Mialhe.

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Executive Summary

- Collaborative research in Health in FPs 6 and 7 is regarded very highly by participants, who identify a tremendous volume of high quality results produced and to progress in the state of the art.

- These results are of direct benefit to citizens with the programmes also stimulating innovation activities and job creation. During the 10 years for which FP6 projects have been ongoing and the first half of FP7, the Health Programme has had a considerable impact on job, small and medium enterprises and knowledge creation.

- Estimates suggest the publication of 70,000 PubMed listed publications, the creation of 50,000 skilled jobs and that one in four participants are listed as an inventor on one or more patent applications.

- Participants value their projects as they provide the opportunity to join research networks with ambitious objectives, and provide access to expertise, resources and infrastructures.

- Participants indicate that without support from FP6 and FP7, much of their own research would not have happened or would have been much reduced in scope.

- Furthermore, EU funding from the Health programme leverages other sources of support to research in the health field**.** Two thirds of participants consider that up to 50% of their current research funding is a result of this leverage effect. Participants also consider that EU health research has a very significant impact on building the future research capacity of their organisations.

- The Programmes' robust networking and long-term structuring effects also demonstrate significant progress towards the creation of the European Research Area.

- Europe is nevertheless confronted by significant health challenges which are exacerbated by an ageing population and which if unmet will render the current healthcare model unsustainable. Research and innovation will play a key role in meeting these challenges, in supporting the competitiveness of European industries and in maintaining an excellent standard of healthcare provision.

- In order to make post-2013 European health research more effective and efficient, and able to respond to these challenges, it should build on the successes above and regroup all health related research and innovation activities are under a single 'umbrella'. In the longer term, a European Institute of Health Research and Innovation is proposed which will consolidate European support to health research and reduce fragmentation throughout Europe.

Table of Contents

Introduction

This section assesses the impact of research and related activities supported by thematic priority 1 "Life Sciences, Genomics & Biotechnology for Health[1]" of the 6th Framework Programme (FP6, 2002-2006), and the "Health[2]" theme of the Cooperation Specific Programme of the 7th Framework Programme (FP7, 2007-2013[3]), which are collectively described as the Health programmes or individually as FP6 LifeSciHealth and FP7 Health respectively.

It presents the aims and objectives of the Health programmes, a summary of funding, the research themes supported and the trends in participation by nationality and organisation type. It introduces two innovative initiatives (the European and Developing Countries Clinical Trials Partnership, EDCTP and the Innovative Medicines Initiative, IMI) and presents the impact of the programmes based on a survey of participants. It subsequently analyses the challenges, both organisational and scientific to which future health research and innovation activities will need to respond, and provides some examples of FP6 and 7 projects as inspiration for the development of the programme after 2013.

1. Impact assessment of FP6 LifeSciHealth and FP7 Health

1.1. Programme objectives and basis for assessment

As part of the Framework Programmes, provided for in the treaties of the European Union (EU), the Health research programmes have two major policy objectives: improving the health of European citizens, and increasing the competitiveness and innovative capacity of European health-related businesses and industry. The detailed objectives of the Health programmes are set out in the specific programmes of FP6 [4] and FP7[5].

The basis for FP6 LifeSciHealth derives from the opportunities for improving human health and industrial and economic activity presented by the sequencing of the human and other genomes. The theme focused on integrating post-genomic research, including research on related molecular mechanisms, on more established biomedical and biotechnological approaches, and aimed to integrate research capacities (both public and private) across Europe to increase coherence and achieve critical mass.

FP7 Health also focuses on research to improve the health of European and global citizenry and the competitiveness of health-related businesses and industry. It is divided into three parts: 1) biotechnology, generic tools and technologies for human health, *i.e.* producing knowledge that will be applied in the area of health and medicine; 2) translating research for human health, *i.e.* ensuring that basic discoveries have practical benefits and improve the quality of life and; 3) optimising the delivery of health care to European citizens, *i.e.* ensuring that the results of biomedical research will ultimately reach citizens.

Support to small and medium sized enterprises (SMEs) and innovation, to clinical research and clinical trials, to child health, and to other Commission policies, taking due

[1] http://cordis.europa.eu/lifescihealth/home.html
[2] ftp://ftp.cordis.europa.eu/pub/fp7/docs/cooperationsp_en.pdf
[3] This report covers only the period 2007-2010
[4] Decision 2002/834/EC; OJ L 294/1 of 29/10/2002.
[5] Decision 2006/971/EC; corrigendum see OJ L 54/30 of 22/02/2007.

account of gender and ethical aspects, has been a feature of both FP6 and FP7 Health programmes, with investigator driven clinical trials, innovation and health of the ageing population receiving greater prominence recently.

The collaborative health research supported by these programmes is characterised by transnational cooperation, the integration of relevant activities and participants, and the concentration of European effort on a carefully selected set of shared priorities. In addition to their headline objectives, they are designed to:

- Remove barriers to research co-operation between countries, provide structures and incentives to establish multinational consortia and coordinate Member State (MS) and associated country national funding programmes.

- Provide structures and incentives for cooperation between, and the integration of efforts of, different types of organisations and disciplines: universities, research centres, hospitals, SME, large companies, foundations, patients' organisations, researchers, engineers, clinicians and industry.

- Focus efforts on issues with a scale which can only be tackled at a European (or global) level, or for which there is significant added value in acting in this manner.

1.2. The programme in context

As a proportion of the total budget allocated to FPs, the Health research programme budget increased from 12.6% of the total in FP3 to 17.6% in FP5. Since then the proportion has decreased to 14.0% in FP6 and to 12.0% in FP7. This is in part due to the fact that the FP7 Health programme does not cover all EU-funded health-related research: areas such as Information and Communications Technologies (ICT) for health, nanomedicine, health and food, health and environment and basic or frontier health research are covered by other programmes (not the subject of this document). The place of health research in the succession of recent FPs is shown in Figure 1.

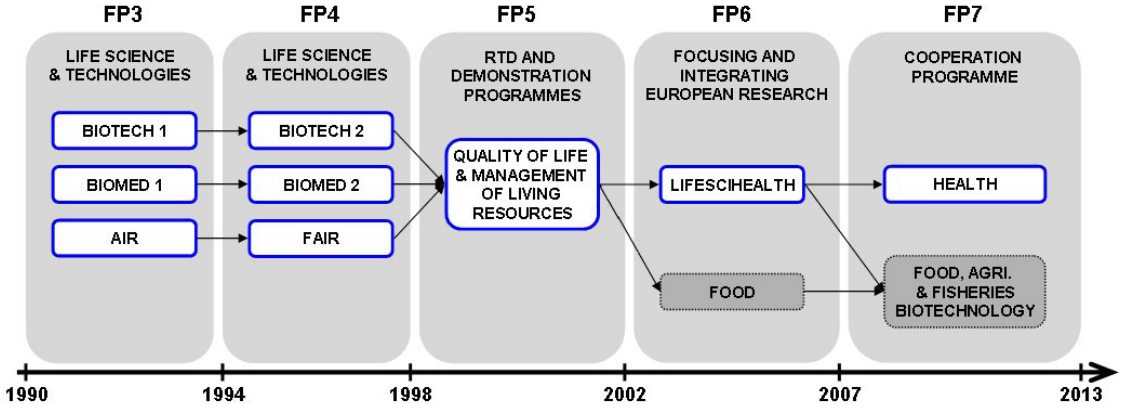

Figure 1: Health research and specific programmes in successive FP

2. Facts and figures

2.1. 1,210 projects funded with an EU contribution of €4.9 billion

From 2002 to 2010, the EU supported 1,210 projects under the FP6 LifeSciHealth and FP7 Health programmes with a contribution of around €4.9 billion. These projects involve more than 14,000 team participations (note that a single team may participate multiple times, creating multiple participations) in 114 different countries.

Under LifeSciHealth in FP6, 10 calls for proposals led to the funding of 646 projects with a total EU contribution of €2.4 billion. By 23 November 2010, €2.5 billion of the €6.1 billion indicative budget for FP7 Health have been allocated to 564 projects. A breakdown according to research domains is given in annex 1 for FP6 LifeSciHealth and annex 2 for FP7 Health.

2.2. New initiatives: EDCTP and IMI

FP6 also saw the launch of the EDCTP[6] and FP7 of IMI[7].

The EDCTP is a partnership between 14 EU Member States plus Norway and Switzerland with sub-Saharan African countries. It aims to accelerate the development of new or improved drugs, vaccines and microbicides against HIV / AIDS, malaria and tuberculosis. It focuses on clinical trials in sub-Saharan Africa. By early 2011, EDCTP had launched 60 calls for proposals and invested an EU contribution of €132.26 million in 163 projects with a total contribution of €311 million, the remainder deriving from MS and 3rd party contributions. These projects bring together researchers from 43 different EDCTP partner countries (29 from sub-Saharan Africa, 14 MS, Norway and Switzerland) and 191 research institutions (140 in Africa and 51 in Europe). 39 non-profit and 20 private/industry organisations also participate. As a result, 54 clinical trials (24 on HIV/AIDS, 18 on tuberculosis and 12 on malaria) are being performed in Africa.

IMI is a public private partnership (established as a joint undertaking) between the EC and the European Federation of Pharmaceutical Industries and Associations (EFPIA) and receives up to €1 billion from FP7 and €1 billion from EFPIA and its member companies as 'in kind' contributions. It aims to significantly improve the efficiency and effectiveness of the drug development process in the pre-competitive stage. The outputs will be used by the pharmaceutical sector to produce more effective and safer medicines, more quickly and more cheaply. IMI has, by the end of 2010, funded 15 projects for a total budget of €246 million. The proposals selected following the second call in 2009 are currently under negotiation for an additional €156 million. The third call, opened in autumn 2010, has a budget of €228 million.

2.3. Trends in participation: organisation type and countries

By comparison with previous programmes, the general trend from FP6 LifeSciHealth to FP7 Health is towards projects with approximately 10% fewer participants and an approximately 20% larger contribution from the EU (annex 3, tables 1, 2 and 3).

[6] Established under Treaty article 185 (ex article 169) http://www.edctp.org

[7] In FP7, the Innovative Medicines Joint Undertaking (IMI), the first EU wide public-private partnership in health established between the EU and the European Federation of Pharmaceutical Industries and Associations (EFPIA), was set-up under Treaty article 187 (ex article 171); http://www.imi.europa.eu/

The main beneficiaries of EU health research funding in FP6 and FP7 are academia and research organisations, which together represent more than two-thirds of all participants. SME participation has increased significantly in FP7, as compared with FP6, as a result of the introduction of specific topics and other actions targeted to them (Annex 3, table 4).

EU-15 countries receive the greatest proportion of the EU contribution (85.0% so far in FP7 Health). EU-12 countries receive a much smaller proportion of the EU contribution with 2.5% in FP7 Health so far. Associated countries together account for 7.0% of the EU contribution in FP7 Health. The United States (US), Russia and China together received 1.2% of FP7 Health EU contribution and the rest of the world shares 4.3% of it (annex 4).

FP6 and FP7 Health are very international programmes with a significant participation of non-EU countries and a correspondingly significant EU contribution going to these countries. This clearly demonstrates the global reach of health-related issues. In FP6, 88 countries participated in the LifeSciHealth programme. In FP7 Health, this figure currently stands at 114 countries, an increase of 29.5%. FP7 Health has seen the achievement of funding reciprocity between the EU and the US National Institutes of Health (NIH); US teams represented 0.3% of participations in FP6 and this figure currently stands at 1.1% in FP7.

A specific call for proposals aimed at strengthening local S&T capacities in Africa has also been launched with an EU contribution to health related projects of about €50 million. Other international co-operation actions have also been initiated and led to the observed increase in the participation rate of third countries.

3. The impact of the programme

3.1. Existing studies on the impact of health research funding

Although there is no easy way to evaluate scientifically the impact of medical research, studies do report positive impacts of public funding for health research. A recent study on publically funded medical research undertaken in the UK between 1975 and 1992 focused specifically on mental health and cardiovascular medicine. The study concluded that the average time lag between research spending in these fields and consequent health benefits was 17 years. For every £1 of public or charitable funding, cardiovascular research produced benefits equivalent to 39 pence per year in perpetuity. The total return comprises 30% in direct returns to the UK economy, including through the pharmaceutical industry, and 9% in gains through new treatments. For mental health research, the total return is 37%.[8]

Furthermore, investment in the UK in prevention for mental health[9] has been demonstrated to provide significant cost benefits from early-year interventions, especially for long-term outcomes, with savings achieved mainly through reduced welfare and criminal justice costs, and higher earnings. Prevention and promotion interventions during childhood and adolescence are particularly cost-effective, with economic returns of early childhood intervention programmes exceeding cost by an average ratio of 1:6.

[8] Medical Research: What's it worth? Estimating the economic benefits from medical research in the UK. Health Economic Research Group, Office of Health Economics & RAND Europe. UK Evaluation Forum 2008.
[9] Royal College of Psychiatrists (2010) "No health without public mental health - The case for action" Position Statement PS4/2010, London, October 2010

Overall, therefore, the steadily increasing body of evidence suggests that public investments in health research pay off. While full impacts may not be immediately apparent in the short term (the period under consideration in this document), timely public investment in medical research in Europe will reap long-term dividends.

3.2. Excellence of the research funded

In the first two calls for proposals of FP7 Health the average total evaluation score received by successful proposals (i.e. those which will be funded by the EU) was 13.47 out of 15, with the average score for "scientific excellence" being 4.51 out of a maximum of 5.00 points. As summarised in the external interim evaluation of FP7[10], these data "provide an objective measure of the quality of proposals" and demonstrate "that only high quality proposals will be funded".

Throughout FP6 and continuing into FP7, independent observers[11,12] have been present at proposal evaluation sessions. They have consistently noted the high quality of the evaluation process, equivalent to high level national and international evaluation boards, and the very high quality of the selected proposals. It should also be noted that EU-12 participation as evaluators of submitted FP7 Health research proposals (as a proportion of total EU-27) has increased from 11% in 2007 to 18% in 2011.

A bibliometric profiling[13] of 'lead scientists' participating in FP6 projects overall clearly challenges "the pervasive and preconceived idea that most top-level scientists do not participate in the Framework Programme". By every indicator examined (for example: authorship of papers in the top 1% cited in the world; level of co-publication with scientists from at least one other country etc), lead scientists from FP6 projects significantly outperformed the overall scientific community. FP6 lead scientists publish more high impact papers than the average population, represented 2 to 3 times more than the general population in the top 1% of most cited papers. Further, lead scientists' highest share by FP6 priority is in life science and health; "FP6 lead scientists have the tendency to publish more than the average scientist in their respective scientific field in journals with a higher impact factor, and this is particularly the case in medical research and fundamental biology".

3.3. Survey of FP6/FP7 Health research participants

In order to assess the impact of FP6 LifeSciHealth and FP7 Health projects, all participants (10,197) in projects funded by these two programmes were surveyed (see annex 5 for a full description of the methodology and annex 6 for the questionnaire). 2,245 questionnaires were analysed corresponding to 22.0% of all participants.

A comparison between the actual gender participation rate, country participation rate and organisation participation rate in the programmes (using the European Commission research database CORDA) and in the questionnaire was performed. The coefficient of correlation r2, used to determine whether two data sets are related and if so, how strongly ranges from +1, indicating a perfect positive linear relationship to -1, indicating

[10] Interim Evaluation of the Seventh Framework Programme- Report of the Expert Group, November 2010 http://ec.europa.eu/research/evaluations/pdf/archive/other_reports_studies_and_documents/fp7_interim_evaluation_expert_group_report.pdf

[11] FP6 Independent Observers' reports, see http://cordis.europa.eu/lifescihealth/src/evaluation.htm

[12] FP7 Independent Observers' reports, see http://cordis.europa.eu/fp7/health/library_en.html

[13] See: http://ec.europa.eu/research/evaluations/pdf/archive/fp6-evidence-base/evaluation_studies_and_reports/evaluation_studies_and_reports_2009/bibliometric_profiling_of_framework_programme_participants.pdf

a perfectly negative linear relationship. In this case r2 is 0.9938, i.e. the data from the questionnaire and the CORDA data are almost perfectly correlated.

Questionnaire respondents clearly stated that – for completed projects - a significant proportion of outputs only became available after the end of the projects (Figure 2). Consequently, as a significant number of participants surveyed are involved in ongoing projects (32%), it can be assumed that the real impact of the FP6 / FP7 Health research will go far beyond what is indicated by the survey and is reported in the following sections.

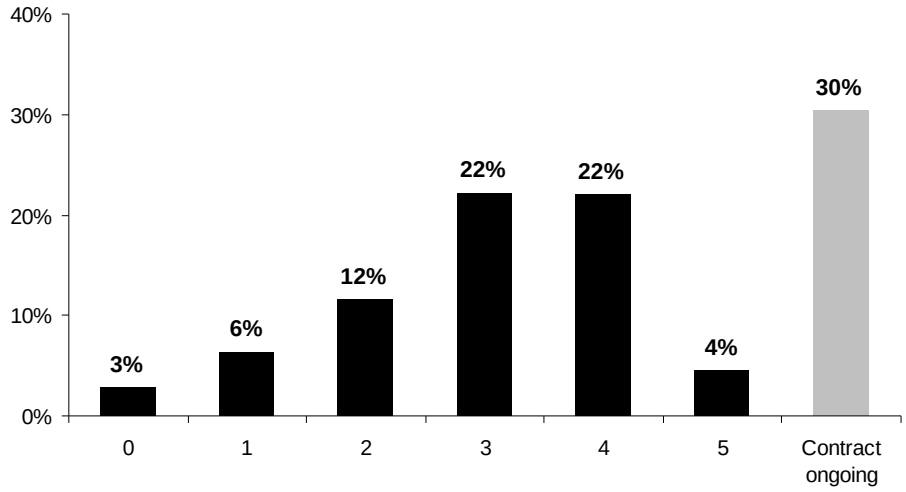

Figure 2: Proportion of project output available after project ends from 0 (none) to 5 (all)

3.4. Survey results

There is very strong agreement among respondents on the four main reasons for joining EU health projects (figure 3): integration in a network, the scale of research, access to multidisciplinary expertise and funding not available at the national level. Access to special resources and infrastructures is seen as moderately important, whilst access to other types of expertise and links to industrial expertise seems less important for the majority.

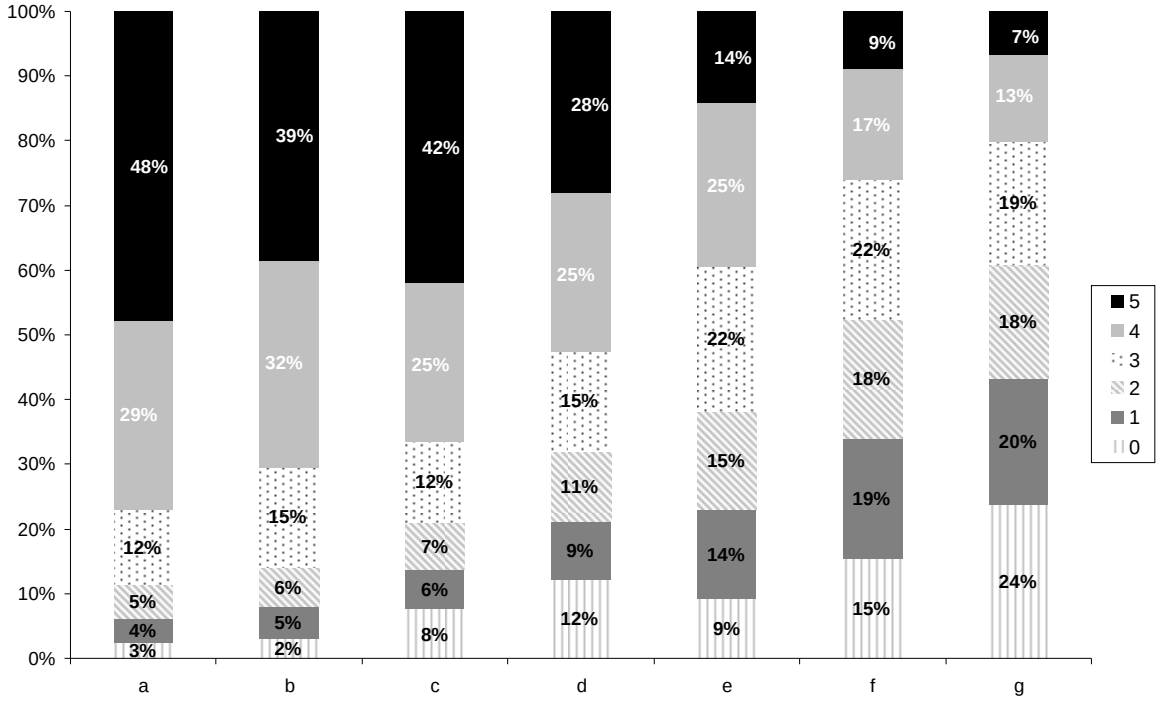

Figure 3: Reasons for participating in an EU collaborative project from 0 (not at all important) to 5 (very important)

a=Integration in an EU network; b=Access to multidisciplinary academic expertise; c=Large scale or scope that cannot be achieved at national or institutional level; d=Funding not available in your country for this type of project(s); e=Access to special resources and infrastructures; f=Access to other expertise (e.g. project management, dissemination); g=Links to industrial expertise

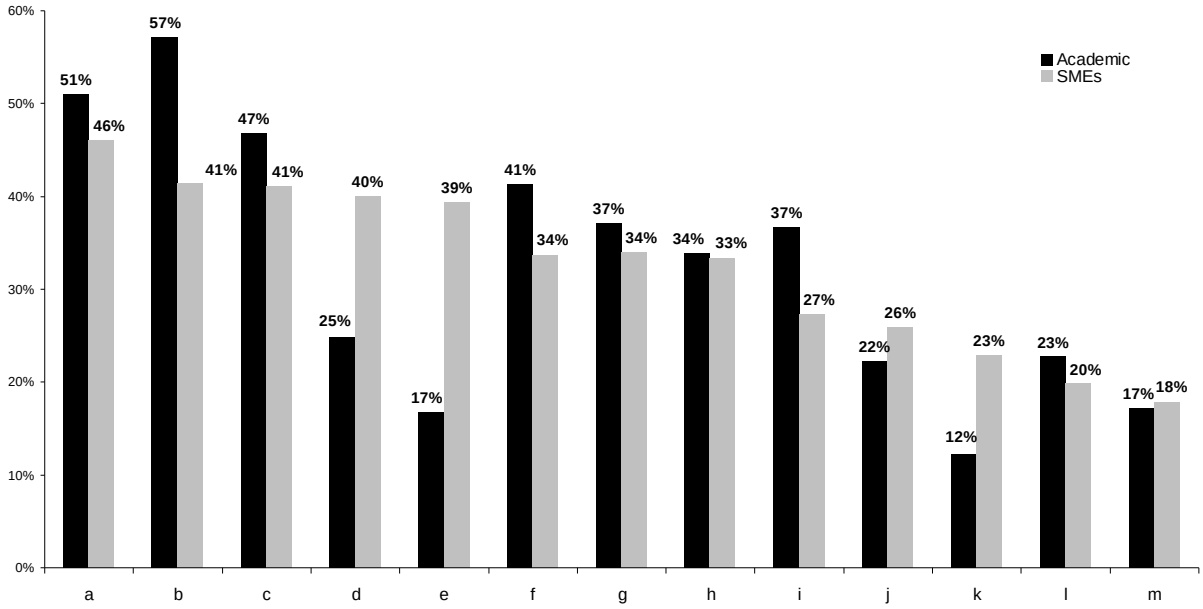

Figure 4: Outputs of EU health research project(s). Each respondent provided his/her 5 major outputs

a=Networking and / or coordination of science; b= Publications in "high impact" journals; c= Significant expansion beyond state of the art; d=New or improved products; e=New / development of companies, new jobs; f=New resources; g=Contribution to international research initiatives; h=Clear benefit to patients; i=Free access to important data; j=New or improved protocols; k=Patents; l=Training programmes; m=Other important outputs

Regarding project outputs, respondents consider that overall; the three most important outputs of their projects are publication in high impact journals, networking and coordination of science beyond the respondent's own institution and the research field significantly expanded beyond the initial state of the art (figure 4).

There are however strong differences of opinion between the two main groups of respondents. Academic researchers (65% of questionnaire respondents) tend to select academic outputs (publications, networking/coordination of science, and progress beyond state of the art), whilst SMEs (10% of questionnaire respondents) select socio-economic outputs (new or improved products, new/development of companies and jobs, patents) twice as often as academic researchers (figure 4).

3.4.1. Publications: a very significant knowledge output

The average number of PubMed-listed publications (figure 5) generated per principal investigator (PI) or by the PI's group with the PI as first author, is about 7 publications per project (though approximately 7% of respondents published 15 papers or more). This figure is in line with, for example, the number of publications (150 or more) typically listed by a consortium in the final report of a health Integrated Project in FP6 LifeSciHealth.

By extrapolation (annex 5), the total number of PubMed-listed publications generated by Health research in FP6 and FP7 up to now can be estimated at more than 70,000. Again, the time lag in this output needs to be kept in mind when estimating impact of research as according to respondents, 42% of scientific publications arose after the end of the project. This volume of research publications indicates a very significant output of original and innovative knowledge in return for public funding of health research in FP6 and FP7.

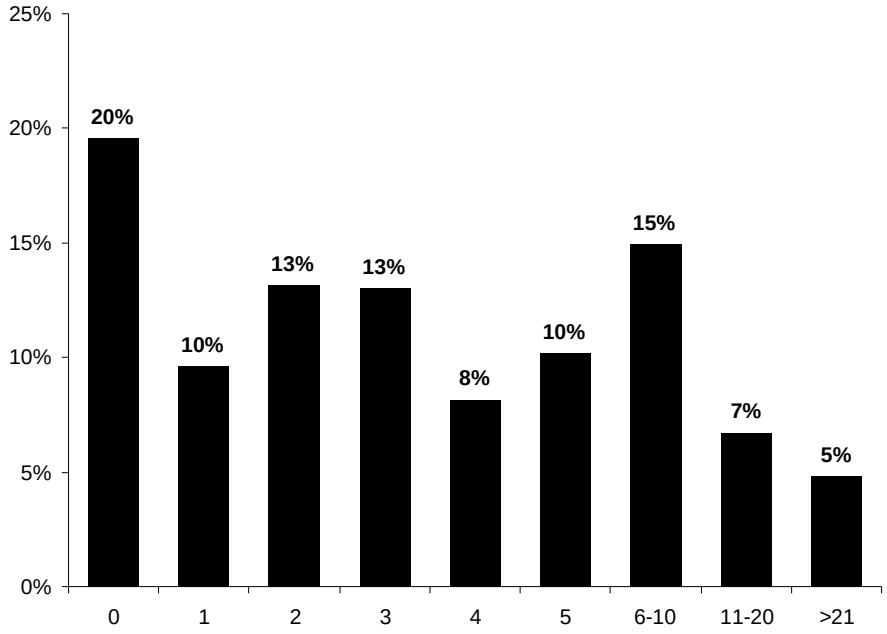

Figure 5: Number of PubMed-listed publications generated per PI

3.4.2. EU health research generates jobs and durable collaborations

The establishment of new, durable research partnerships is a clear outcome from participating in EU funded health research. 60% of respondents declare that their research network(s) formally continued to operate after the end of the project.

PhD, post-doctoral fellowships, technicians and support staff positions are all generated through participation of a team in collaborative research projects of the Health Programme. Around two thirds of respondents claim that they had created new positions in each of these three categories.

By extrapolation, more than 50,000 jobs (about 19,000 PhDs, 16,000 post-docs and 16,000 technicians and support staff) were created in direct relation to the funded projects during the 10 years since the start of FP6.

3.4.3. Research funded would not otherwise take place

53% of respondents indicate that very little (1 out of 5) to none (0 out of 5) of the project output would have been achieved without EU funding (figure 6).

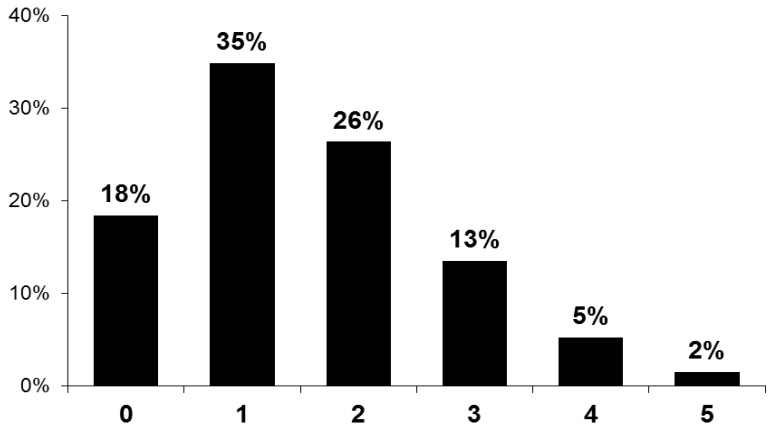

Figure 6: Share of project output that would have been achieved without EU funding (from 0, none to all, 5)

As a further indicator of the importance of EU funding, 75% of respondents acknowledge that EU funding represents up to 50% of their total research budget.

Most respondents also note a significant leverage effect (figure 7): 66% of them, regardless of type of organisation, indicate that EU funding helped them to access other funding to expand or continue their research. It is possible that respondents who do not observe any leverage effect may be reporting projects which have only recently started.

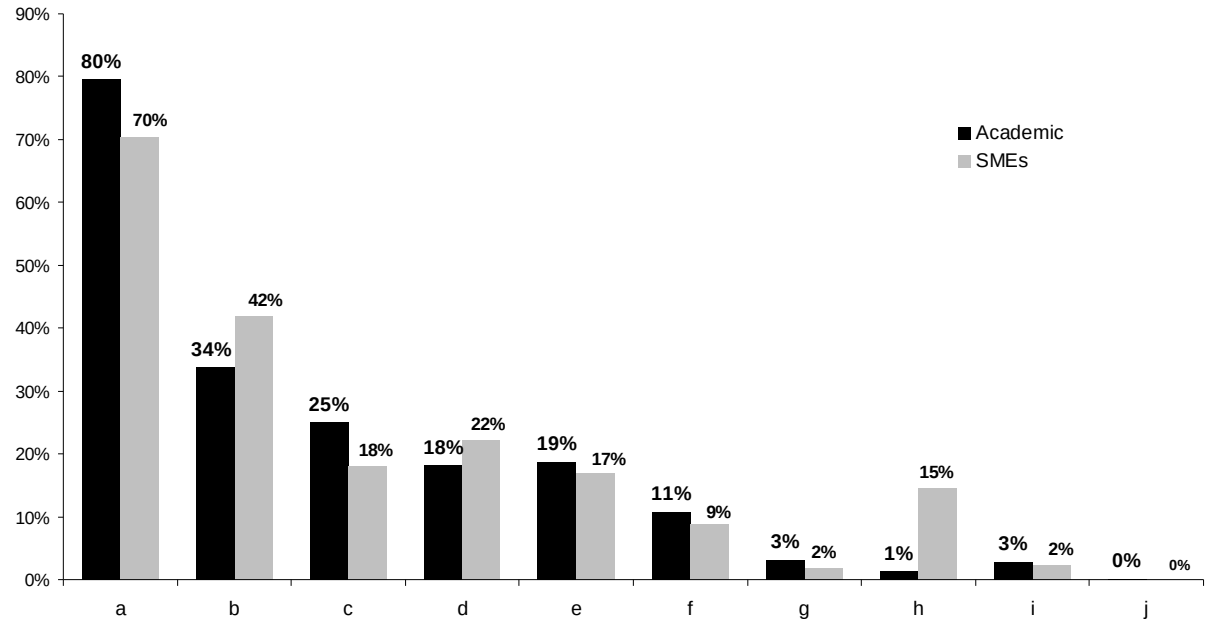

Figure 7: Source of extra funds leveraged by participation in the health programmes (multiple answers possible)

a=National, regional or local agencies in your country; b=EU Framework Programme sources for collaborative research; c=Private foundations or medical charities; d=Industry, such as large pharmaceutical companies, SMEs; e=International programmes or agencies; f=Marie Curie fellowships; g=Other; h=Business angels or venture capitalists; i=ERC grants; j= EU Risk-sharing Finance Facility (RSFF)

The extra funding reported included national or regional sources (70% of respondents had received this), components of the Framework Programme (40%), private foundations and charities (20%), industry (20%) and international programmes and agencies (20%). By contrast, only 3% of all respondents who indicated leveraging by FP funding reported business angel or venture capital sources. 15% of the SMEs which leveraged funds however obtained these from business angels or venture capitalists, compared with only 1% of academia.

3.4.4. A very positive impact on innovation and product development

Approximately 24% of respondents indicated that they are listed as an inventor on one or more patents arising from their project(s). Of these patent applications, 45.5% have been granted, of which 51% have been licensed.

While most respondents in the Health programme come from academia, industry also participates actively; specific incentives in annual work programmes, including SME-targeted topics, have had success in increasing SME participation, which they acknowledge to be of significant benefit to them.

In addition, an average of 7.4% of the respondents created one or more SMEs in relation to their work in the project, of which 94% continued to operate after the end of the project.

As many FP7 projects are not yet completed, even more SMEs are expected to be created: Indeed, 17% of the respondents declare that they envisage creating one or more SMEs in relation to their work in the project.

Type of project outcome		% of respondents
Publications		
PubMed-listed publication(s) with you or someone from your group as first author		80%
Jobs		
Creation of one or more PhD positions		69%
Creation of one or more Post doc positions		72%
Creation of one or more Technician or Support staff positions		65%
Patents		
Listed as inventor on:	Patent applications	23%
	Patents granted	10%
	Patents licensed	7%
Creation of SMEs		
Creation of one or more SMEs		7%
Envisaging the creation of one or more SMEs		17%

Table 1. Summary of the main outcomes from project participation

3.4.5. A significant contribution to the creation of a European Research Area (ERA) in Health research

Responses to the questionnaire point overwhelmingly to the perception that participation brings benefits in terms of ability to tackle more ambitious research objectives in cooperation than alone, the value and sustainability of networking, access to expertise and infrastructures, sharing of data, better coordination of research, leverage of additional funding, job creation, and new products and patents. These are clear indications that the FP6 LifeSciHealth and FP7 Health programmes and their relative research projects directly contribute to the creation of the ERA in health research.

4. Challenges and the need for Europe to intervene

Future EU health research must not only confront ongoing and future health challenges, it must also aim to render the European health research system more effective and more efficient. Necessarily, the challenges will require transnational action and that sufficient resources are allocated for the ambitious objectives to be achieved.

If you think research is expensive, try disease[14]

4.1. Relative underfunding and a fragmented European research and innovation system create the risk that we fall behind

In 2008, 0.222% of US gross domestic product (GDP) was devoted to public funding of health research; this means the US invests approximately US$100 billion a year in health research[15,16], with a three-fold increase occurring between 1994 and 2003. Comparable figures for the EU 27 in 2006 show an average of 0.054% of GDP made available for health research[17]. The GDPs of the US and the EU 27 were roughly similar in 2008, at around US$15,000 billion[18]. Overall, therefore, the USA devotes 3-4 times as much public funding to health research in cash terms as the EU 27. Other estimations reach the same broad conclusion[19].

EU 27 publicly funded health research is not only lower than the US in absolute terms, but also as a proportion of total research funding. EU publicly funded health research, including infrastructures, accounts for approximately 15% of total publicly funded research. The US, Japan, Australia and some MS by contrast allocate 35-50% of total research funding to health research[20].

An additional consideration is that the Framework Programme does not always optimally co-ordinate or catalyse the activities of these various agencies[21], and health research remains fragmented across the EU. Dialogue between FPs and national programmes does not always take place at a sufficiently strategic level during their operation (but at the programme committee level), requires lengthy and repetitive negotiations for each new initiative and time consuming procedures (e.g. co-decision to launch an Article 185 initiative) or remains an isolated activity (e.g. joint programming remains a bottom-up approach that is not part of a common integrated agenda). Furthermore, in domains where European added value is particularly evident, for example in research in rare diseases, the following of long-term cohorts, maintenance of bio-banks, registries or other infrastructures, FP funding is too short term to provide support for the necessary period.

Greater efforts must be made to ensure synergy between the EU health programmes and the 27 MS. Similarly, efforts must be made to avoid fragmentation within the Framework Programme: cooperation, infrastructures, individual grants, training, e-health, environment and health, etc, at present operate as different programmes, creating risks that their internal coordination is ineffective and their external benefit less than it could be (in particular for new MS who lack significant infrastructure). EU SMEs

[14] Mary Lasker 1901-1994
[15] Financing of U.S. biomedical research and new drug approvals across therapeutic areas. Dorsey et al. PLoS One.2009 Sep 11;4(9):e7015
[16] Financial anatomy of biomedical research. Moses et al. JAMA. 2005 Sep 21;294(11):1333-42
[17] OECD Science, Technology and Industry Scoreboard 2009
[18] CIA World Factbook – accessed 1 February 2011
[19] European Council 4 February 2011
[20] OECD Science, Technology and Industry Scoreboard 2009
[21] Towards joint programming in research. Working together to tackle common challenges more effectively, EU COM (2008) 468

and larger industries face a competitive global marketplace, while individual researchers are tempted by superior employment conditions both outside their field and outside Europe.

Our competitors are better able to support more research and more research in the longer term (a necessity since for example, a single drug may take as long as 17 years from first discovery to becoming a marketable product). The unfulfilled potential of this system means that Europeans are missing out on advances in health and on the prosperity which results from a competitive health industry. The pooling of Community and national resources, public and private, towards a common strategic research agenda and objectives is a clear necessity if Europe is to maintain excellence in research and competitiveness.

4.2. Private investment in health R&D

In spite of this fragmentation and relative lack of funding compared with other areas and regions of the world, European health researchers, innovators and companies perform well. The healthcare industry invests in R&D: the pharmaceutical and biotechnology sector and the healthcare equipment and services sector rank 1st and 5th in terms of R&D intensity in Europe and account for almost 19% of total EU private R&D annual investment. The third fastest-emerging industrial pillar, the e-Health industry, is also an R&D intensive sector.

The research-based pharmaceutical industry is one of the few remaining leading high technology industries in Europe, amounting to 17% of EU business R&D investments and about 3% of the total EU manufacturing added-value. The net trade balance in 2009 due to the European pharmaceutical industry was €55 billion. Of the total heath expenditure in Europe in 2007, nearly 48% was on pharmaceuticals and other medical non-durables[22]. In 2009, the pharmaceutical industry in Europe spent €26 billion on R&D, involving some 110,000 R&D employees[23].

The costs of pharmaceutical R&D have soared over the years due to a variety of factors including the increasingly complex nature of science and the size and complexity of clinical trials. Developing a new drug takes years and is estimated to cost from half to over one billion Euros per new entity[24].

In 2009, R&D expenditure by the pharmaceutical industry in Europe and the USA was roughly equal at around €25-26 billion. However, as indicated above, public funding for research is proportionally smaller in Europe. This is a very important deficit: recent research regarding US Food and Drug Administration (FDA) approved drugs during the period 1990-2007 indicates that publically funded biomedical research plays a more important role in providing results for take-up by the pharmaceutical industry than previously appreciated[25]. Furthermore, the same study showed that 90% of new applications (new indications) for already approved drugs originated from publically funded laboratories.

[22] Figures for 2007 show that on average, € 430 was spent on medicine annually by each European, with the market for prescription and non-prescription medicines worth over € 214 billion at retail prices.
[23] EFPIA The pharmaceutical industry in figures 2010
[24] See on this controversy: DiMasi, J.A., Hansen, R.W. and Grabowski, H. (2003a) The price of innovation: New estimates of drug development costs. Journal of Health Economics 22: 151–185 ; and Light D. W., Warburton R. (2011), Demythologizing the high costs of pharmaceutical research, The London School of Economics and Political Science 1745-8552 BioSocieties 1–17
[25] A.J. Stevens et al . The role of public-sector research in the discovery of drugs and vaccines. New England Journal of Medicine 364: 535-41 (2011).

The European medical technology industry is also a major contributor to the European economy[26]. The sector involves nearly 22,500 manufacturers, of which 80% are SMEs (EU + EFTA). Of total sales of €95 billion in Europe in 2009, 8 % was reinvested in R&D.

The European e-Health industry has leading positions in emerging fields such as personalised health systems, medical equipment and in several sectors of integrated e-Health solutions. The e-Health sector has a number of large European-based companies of specialised e-Health solutions that are world leaders in their fields, as well as an estimated 5,000 European SMEs that operate in the various sub-sectors of e-Health.

4.3. Selected health challenges

The Health challenges facing Europeans are many and varied. With an ageing population, the impact of major chronic diseases will become more pronounced. By 2050, 1/3 of Europe's population will be over 60 and taking only one example, estimates suggest that over 115 million worldwide will suffer from Alzheimer's disease or another dementia. Further, the proportion aged over 80 years will rise even faster from 22 million in 2008 to 61 million in 2060[27].

These health challenges are not limited to the older persons, however. Cardiovascular disease currently accounts for 2 million deaths per annum in the EU and imposes costs estimated at €192 billion per year. Of the 150 million DALY (disability adjusted life years) recorded in the WHO European region in 2005, 77% were due to chronic diseases, including obesity, diabetes, increasing mental health disorders, neurodegenerative diseases, infectious diseases musculoskeletal disorders, sensory impairments, rising allergic disease, untreatable rare diseases together with the big killers, cancer and cardiac disease. The scale of this burden of chronic disease is stark: in 2005, more than 150 million DALY (disability adjusted life years) were recorded in the WHO European Region, of which 77% were due to chronic diseases.

These health challenges are also not only European. Though in 2002, infectious diseases, maternal, perinatal and nutritional conditions caused ~7% of deaths in Europe [28,29], 41% of the global estimated 1.5bn DALY were estimated to be due to infectious disease[36]. Poverty related diseases account for 6 million deaths per year with 3 million new HIV infections per year[30], the majority of which occur in sub-Saharan Africa. In the same region there are more than 1 million deaths per year from malaria and worldwide there are more than 1.5 million deaths every year from tuberculosis[36]. In Europe, the infectious disease DALY burden is 8% thanks to improved, hygiene, vaccination campaigns and better living conditions. However, there is no room for complacency as the phenomenon of (multi)-resistance to antibacterial and antiviral drugs demonstrates. Further, globalisation, increasing migration and environmental factors such as climate change are of grave concern in relation to human health, and in addition there are possible risks from emerging or re-emerging infectious diseases such as pandemic flu.

Despite increased prosperity and overall improvements in health in the EU, health differences between and within countries persist and in some case are increasing[31]. There are substantial differences in life expectancy at birth across the EU MS, with

[26] EUCOMED (2009)
[27] 2009 Ageing Report: Economic and budgetary projections for the EU-27 Member States (2008-2060). European Commission DG Economic & Social Affairs, 2009.
[28] Tackling Chronic Disease in Europe. R. Busse, M. Blümel, D. Scheller-Kreinsen, A. Zentner. European Observatory on Health System and Policies, study No 20. 2010.
[29] WHO (2008) The Global Burden of Disease: 2004 Update, World Health Organisation, Geneva
[30] UNAIDS. "2009 AIDS Epidemic Update. Joint United Nations Programme on HIV/AIDS (UNAIDS) and World Health Organization (WHO) 2009
[31] Pages 5 & 9 Background document for press pack - launch of Commission Communication Solidarity in health: Reducing inequalities in the EU, 20.10.2009.

individuals in many new MS living shorter lives than their Western counterparts. There are also large differences (of up to 20 years) in the number of years lived in good health (healthy life years). Recent negative trends have been observed: since 2006 the number of healthy life years has decreased in many countries (FI, AT, ES, IT, IE, BE and all EU12 countries), especially for women who already spend a higher proportion of their lives with limitations.

Healthcare is a key sector in the EU that employs almost 10% of the total work force and corresponds to almost 9% of the European GDP. As the European society ages, and combined with an increasing chronic disease burden, the pressure on healthcare and related social services will increase. Healthcare spending is rising faster than GDP and is predicted to reach 16% of GDP by 2020 in OECD countries[32]. On average, about 75% of health financing comes through public sources (general taxation or social security contributions). Private financing averages around 2% of GDP[33].

4.4. The need for European level intervention

Health and disease do not observe national borders; they are global concerns. The scale of many of these challenges goes beyond that which can be tackled at a single country level. Much research remains to be done in a variety of domains: to understand the fundamental causes of health and disease, to improve existing treatments and discover new ones, to improve healthcare delivery. The nature of biomedical research in the "post-genomic" era, with the drive for personalised medicine based on individual genome sequencing requires collaboration to bring together expertise, resources and infrastructures, such as population cohorts, to achieve the necessary critical mass.

Cooperation beyond Europe will be essential in many disease areas; the case of rare diseases is one obvious example – world wide collaboration will be needed to obtain sufficient patient numbers for proper statistical power of the studies. Tackling the major health challenges for Europe outlined above demands a multifaceted approach. Research is of crucial importance to develop new drugs, vaccines, treatments, devices and new disease management strategies.

This section provides examples of some successful projects or initiatives in FP which confer significant added value. It provides justification that co-ordinated EU level action – rather than MS or other action alone - is required and competent to address the challenges which Health research must confront post 2013.

4.4.1. Critical mass and pan-European challenges

- Some research activities are of such scale and complexity that no single MS can provide the necessary financial or personnel resources, and hence need to be carried out at an EU level in order to achieve the required "critical mass". Similarly, these activities frequently address pan-European challenges.
- One such example of this is in the domain of bio-banking. A number of EU-supported projects (GeonmeEUtwin, ENGAGE, GEN2PHEN, MOLPAGE, Phoebe) have brought together large amounts of data on patients, permitting the identification of susceptibility genes and biomarkers for common diseases. If not conducted at EU level, the studies would not have the same analytical power. Furthermore, these projects bring together European excellence in the field and will develop a pan-European infrastructure for medical research, the Biobanking and Biomolecular Resources Research Infrastructure (BBMRI), through the ESFRI

[32] OECD Heath Data 2010
[33] OECD Science, Technology and Industry Scoreboard 2009.

initiative. BBMRI aims to make European bio-banks more efficient and available for research, to promote the use of research results in a clinical setting and to establish the foundation for personalised medicine.

- Projects such as EUROGLYCANET and the European Network of Rare Bleeding disorders (EN-RBD) developed extensive databases and bio-banks for patients affected by groups of rare diseases, with diagnosis and management capabilities, and an invaluable resource for patients and clinicians alike, with partners in 20+ countries.
- Recruiting sufficient numbers of patients is made easier by trans-European research co-operation. The main project launched under TRANSBIG project is the so called 'MINDACT' clinical trial. MINDACT compares a genomic prognostic test (Mammaprint®) developed with micro-array technology to traditional clinical-pathological methods for assessing the risk of breast cancer recurrence. It is expected that this will help physicians and patients make better decisions about who can safely avoid chemotherapy and its potential side effects. The TRANSBIG project has also developed a bio-bank, extremely valuable for translational research, which allows researchers from around the world to access to genomic data and biological samples.
- The European Clinical Research Infrastructures Network, ECRIN has emerged as a sustainable, not-for-profit infrastructure supporting multinational clinical research projects in Europe. Multinational clinical research is hampered by the fragmentation of health and legislative systems in Europe. ECRIN provides information, consulting and services to investigators and sponsors in the preparation and in the conduct of multinational clinical studies, for any category of clinical research and in any disease area. This is particularly relevant for investigator-initiated or small and medium enterprise-sponsored clinical trials and for clinical research on rare diseases where European and international cooperation is the key success factor.

4.4.2 Leveraging private investment and reduction of research and commercial risk

Other research activities leverage private investment: Through EU research schemes, private companies can collaborate with partners at a scale not possible at national level, in projects tested for excellence, which induces them to invest more of their own funds than they would under national funding schemes.

- One such example of this is IMI. An evaluation performed by a panel of independent experts found that "Europe has succeeded in establishing a new business model between public and private sectors, which unites research strengths across European pharmaceutical industry, academia and SMEs…" and that IMI is "… very important in developing open innovation in the health sector as it has enabled an unprecedented pooling of industrial research assets allowing scientific challenges to be tackled in a manner that could not be done otherwise". Further, IMI is "…an incubator for changing minds on how parties can work together across traditional boundaries and is therefore likely to have an important structuring effect in Europe, fully in line with the Innovation Union objectives".

  After only *two years*, significant activities are underway in IMI which would not otherwise be the case; the number of compounds on which data is being shared is 1,098; the number of patients on whom data is being shared: at least 68,055; the number of clinical trials running: at least 5.
- Added value is also conferred by the reduction of research or commercial risk: working in trans-national consortia helps firms to lower individual risks. Further, it enables the development of EU- and world-wide standards and interoperable

solutions, and offers the potential for exploitation in a market of 450 million citizens.

- One such example is the "BIOMED 2" EU-funded project which resulted in the formation of an SME now listed on the London stock exchange, Ark therapeutics. At the outset, this Anglo-Finnish bio-pharma start-up relied on EU and national grants. Their initial patentable discoveries have arisen from a network of research involving the UK, Finland, Germany and Italy.
- New medicines for tuberculosis: The establishment of an excellent consortium involving 34 research groups from 14 different countries, including partners from the pharmaceutical sector has discovered a new tuberculosis drug candidate, the benzothiazinone group, with prospects for fighting tuberculosis and the extensively drug resistant form of the disease. Co-operation between academic teams and with the pharmaceutical industry across Europe is increasingly necessary if new and effective drugs are to be identified. Similarly, the TB-VAC consortium developed 5 new vaccine candidates.
- ANGIOSTOP proposes an approach to develop a new, safer and more effective anti-cancer medicine. ANGIOSTOP develops an antibody that may constitute a new, safer and efficacious medicine for the treatment of certain cancers, ocular diseases and arthritis. The project has developed TB-403, a humanised monoclonal antibody, and the co-ordinating SME, along with another SME partner is now in strategic alliance with Roche. Roche has a worldwide exclusive license to develop and commercialise TB-403. BioInvent and ThromboGenics retain co-promotion rights for the product in the Nordic, Baltic and Benelux regions. Roche is now funding the development of TB-403. BioInvent and ThromboGenics could receive up to EUR 500 million in upfront and milestone payments, of which EUR 55 million have been received so far, as well as royalties on product sales.

4.4.3. Building the ERA: standardisation, co-ordination and structuring

- Similarly EUROGENTEST provides for genetic testing in Europe, harmonising, validating and standardising test development. It contributes to the improvement of awareness and practice regarding quality assurance in genetic testing, has made many tools available for stakeholders (guidelines, training, databases, etc.) and developed a successful network that has become a reference in Europe and contributed to standardisation and quality assurance schemes for genetic testing.
- The Tiss.eu project has produced a repository of documents concerning the regulation of human tissue research in MS and Switzerland (currently the database comprises about 427 entries of which 362 are accessible by the public). The database is available free-of-charge to the scientific community and the general public. This provides an evidence base for the revision of legislation in this area.
- The structuring effect of EU supported research is exemplified by the establishment of the European Malaria Graduate School, created under EVIMalaR, an FP7 Network of Excellence, as a follow up to BioMalPar (an FP6 Network). The EMG has produced more than 50 European and African PhD candidates in the field of malaria research. It has significantly increased the coordination of new collaborative projects between institutional laboratories within Europe and with African partners. The number of publications released by the consortium's members is around 400 and includes a large number of high profile publications (Nature, Cell, Science etc.). Europe is now recognised as the world leader in the biology of the malaria parasite.
- As a consequence of co-ordination in EDCTP, the initiative is producing important and recognised results (*e.g.* the first African Networks of Excellence for clinical

trials in central Africa have been established; there are new national ethics committees in many African countries; the US FDA has approved an anti-retroviral formulation for HIV infected children in Africa, which was tested in an EDCTP project).

4.4.4. European health research policy and the way forward

If European Health programmes contribute to the co-ordination of national policies, there is still considerable overlap and compartmentalisation of research efforts. EU funded health research still represent a very small percentage of the overall European public funding invested every year in health research. There is however an urgent need for better coordination of national policies to increase efficiency and reduce fragmentation of health research in Europe.

In their report (included in full in the next section of this document) the Expert panel underlined that the main long-term political objective for health research policy in Europe should be the implementation of a European Institute for Health research and Innovation:

"The European Commission has made several efforts to reduce fragmentation of health research funding in Europe. In addition to the FP-specific research funding instruments, some instruments (e.g. ERA-NETs and ERA-NETs Plus) aimed specifically to bring funders to close collaboration have been tested with some success. New initiatives for large scale collaborative programmes, such as EDCTP, IMI (with industry), Joint Programming Initiatives (JPI) for multi-Member State collaborations on specific disease areas such as Alzheimer's disease and private public partnerships (PPP) have served as models for new types of collaboration. Their implementation has sometimes been long and not painless and it is too early to estimate their true impact.

Funding of health research is fragmented within the European Commission. In the DG Research and Innovation, in addition to the Health Directorate, health research receives support from several other Research Directorates: Health and Wellbeing appears in Directorate E, Health and Environment appears in Directorate I. Nanosciences and Nanotechnologies, so important in medicine, is under the responsibility of Directorate G. Furthermore health research is funded through ERC (Ideas programme), Marie Curie (People programme), IMI and infrastructures (Capacities programme). DG SANCO plays an important role in public health and health policy issues. E-Health is managed by DG INFSO, ICT (Information and Communication Technology) programme.

It is, therefore, striking to see how health research is split into many directions and programmes. This diversity has the advantage of promoting multidirectional innovation. However, it also carries significant risks related to its inherent complexity, such as duplication and financial waste, pigeon holing of themes with lack of multidisciplinary interactions, issues relating to accessibility of the programmes and instruments for SMEs, the absence of continuity from idea to market due to the non-implication of practitioners and users and others.

A holistic and integrated transversal organization for health research through a one-stop shop should facilitate more coherence between the three health research sectors (basic, translational and clinical) and between all actors contributing to the success of an innovation to the clinic (academia, SMEs, industry). The recent emphasis made on usability highlights for instance the compulsory need to involve the users (clinicians but also patients) from the early stage of an invention and

their assessment during its whole development and not only at the evaluation phase.

Such a mechanism for transversal coordination and management of FP8 should be simple and user friendly, aiming at optimizing the coordination and coherence among activities that represent a proper response to a global strategy, both within the Commission and with Member States. The budgets and funding instruments dedicated to linking R&D and innovation should be specifically addressed, streamlined and simplified. This new transversal structure should better coordinate EU funded research. This simplified model should encourage SMEs to apply".

Recommendations to improve the efficiency and effectiveness of post 2013 European health research funding may therefore be summarized as follows:

- In the short term, introduce a transversal coordination system for health research, with a "one-stop shop", to encompass all health-related research activities, in order to tackle high impact grand challenges and the innovation-driven health research agenda in a cohesive manner. Subsequently, the panel recommends (by 2020) the establishment of a European Institute for Health, analogous to the US model of NIH but adapted to the European realities and agenda of Europe 2020 and Innovation Union.

- In order to define the scope of the programme the panel recommends a "bottom up" approach engaging the scientific community in identifying areas of truly innovative research to tackle both grand challenges and other areas, such as those with unmet medical need, as well as novel and emerging new research ideas and directions.

- Additionally, post-2013 should provide funding at a sustainable level to secure a European innovation-driven research environment, a critical mass of researchers and better coordination of European funding instruments in health research, including with member states' schemes. In line with the Europe 2020 strategy framework and the Innovation Union flagship initiative, the aim should be to facilitate the development of an innovation culture across Europe, to encourage creative thinking and willingness to explore new ideas, facilitate agility and mobility of ideas and people and support experimentation, calculated risk-taking and questioning of the status quo.

Expert group report recommendations on the future of health research in Europe

Expert Panel report

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Table of Contents

1. Summary

Objectives

In preparation for the forthcoming 8th Framework Programme for research[34], an impact assessment exercise has been initiated by the Health Directorate, to examine the performance of the Health programme in previous Framework Programmes (FP6 2002-2006 & FP7 2007-2013). This independent expert panel has been formed to provide input on the impact assessment with the specific remit for forward looking, to identify and make recommendation on potential directions for Health research in FP8.

This report is based on a large number of documents provided by the Health Directorate to the Expert panel, on other documentation known to the panel members and on interviews with the Director and the Heads of Units of the Directorate. Although the Health programme has been successful in many of its targets, improvements can still be suggested for the remaining period of FP7 and the next FP8 programme. Justifications for the 26 recommendations that are listed below will be presented in the core of this report.

General comments on health research in Europe and its impact assessment

Recommendation 1

The panel recommends that criteria and methodologies for health and innovation impact assessment are carefully evaluated and implemented and a well designed e-based mechanism is introduced for systematic health research data collection, monitoring and evaluation of European health research activities.

Financial considerations and value of health research

Recommendation 2

FP8 should continue to provide funding for health research at a sustainable level to secure a European innovation-driven research environment, a critical mass of researchers and better coordination of European funding instruments in health research, including those of the Member States. In line with the Europe 2020 strategy framework and the Innovation Union flagship initiative, the aim should be to facilitate the development of an innovation culture across Europe, to encourage creative thinking and willingness to explore new ideas, facilitate agility and mobility of ideas and people and support experimentation, calculated risk-taking and questioning of the status quo. In view of the expanded agenda of the FP8 to effectively address the new "grand challenges" and important new emerging directions in basic and clinical research, the panel recommends that funding for health research in FP8 must be increased, accompanied by measures of better use of existing funds.

Thematic prioritization for FP8

Recommendation 3

[34] Note that at the time of writing, the title 'Horizon 2020' had not yet been chosen so the authors referred to the 8th Framework Programme, or FP8. Those terms are left in this document but recommendations should be understood as applicable to Horizon 2020.

The panel supports the value of thematic prioritization based on "Grand Societal Challenges" and recommends a reintroduction of a "bottom up" approach (analogous to a successful Expression of Interest exercise in FP5) that would engage the scientific community, both basic and clinical researchers, in identifying areas of truly innovative research to tackle both the grand challenges and other areas, such as those with unmet medical need, as well as novel and emerging new research ideas and directions. This "bottom up" approach will generate a range of research questions and ideas that will then require a transparent process for in depth and evidence-based ("top down") evaluation, prioritization and final recommendations by panels of impartial experts of high scientific credibility and integrity.

Coordination of European health research and efficient pooling of resources for health research in Europe

Fragmentation of funding to health research

Recommendation 4

Introduce a transversal coordination system for health research leading to a "one-stop shop", to encompass all health-related research activities, in order to avoid duplications and tackle high impact grand challenges and the innovation-driven health research agenda in a simplified, user friendly and coherent manner.

Recommendation 5

In the lifecycle of FP8 and moving towards 2020, design and by year 2020 implement the establishment of the "European Health Research and Innovation Institutes" (EHRII), analogous to the US model of National Institutes of Health (NIH) but adapted to the European realities and scientific strengths, in line with the Europe 2020 and Innovation Union strategies.

Need for simplification whilst promoting research excellence

Recommendation 6

The current administrative and financial reporting and monitoring system is both complex, carrying excessive administrative burden and cost, and is in fact incompatible with the innovation culture of Europe 2020. It must be simplified and become less bureaucratic. Mid-term and final evaluations should be strengthened and based on quality and impact of scientific and innovation output and the cost-benefit ratio.

Recommendation 7

Establish a permanent "FP Outcome evaluation panel" to monitor and evaluate the added value, impact of the scientific outputs and overall performance of FP funding schemes and instruments, based on evidence and proven record of delivering innovation and research excellence.

Working with the European scientific community

Recommendation 8

To invigorate research excellence in countries underperforming in the innovation scoreboard, opportunities for researchers and institutions from such countries to join EU-funded projects and programmes should be enhanced through innovative new

partnership-scheme(s). In this context, calls addressing health problems of high priority to EU-12 countries and their regions should be considered.

New directions in clinical research

Recommendation 9

Clinical research should be strongly supported in FP8 and adhere to the historical aims of improving health, life expectancy and quality of life for all European citizens of all Member States, whilst reducing the burden of diseases for each and every patient. In the new era of translational research and regenerative and personalized medicine, strong academic participation will be key to the success of clinical research and innovation.

Recommendation 10

High priority should be given to observational studies based on European populations aimed at biomarker discovery, the identification of risk factors and causal pathways and a better definition of nosology and disease heterogeneity in prioritized diseases. Such studies should aim at further progressing the concept of personalized medicine. Europe should retain its leadership in the field, leveraging the power of European population and patient cohorts, as well as of medical centres of excellence across Europe.

Recommendation 11

Prevention and public health should be highlighted in FP8, as they represent important angles in addressing the "grand challenges" for Europe 2020, as well as in proactively reducing the burden of common diseases of unmet medical need that are associated with high morbidity and mortality. Mechanisms of effective and rapid communication and translation of results into public health interventions and policy guidance for Member States should be considered.

Recommendation 12

Support science-driven experimental medicine studies, using new evidence based methodologies for "proof-of-concept" of novel small or large molecule therapeutics, cell-based treatments, vaccines, devices and instruments for diagnosis and surgery and novel applications or indications of existing therapeutics. FP8 funded experimental medicine studies should strictly adhere to the highest ethical standards and directives and be truly innovative in their methodologies and/or indications or compounds tested.

Recommendation 13

A new European clinical trials directive is needed to ease the way for clinical research of high quality in Europe, whilst fully protecting the safety of patients, their confidentiality and rights.

Recommendation 14

The medical and scientific EU objective to fight poverty-related diseases in sub-Saharan Africa should be further pursued. The panel strongly supports further funding of EDCTP, but the Commission should work on designing a model of non-bureaucratic but diligent funding mechanism for direct funding of EDCTP by the Commission itself or by pooling contributions of EDCTP member countries or through a "common pot" approach.

The pharmaceutical industry and SMEs

Industry

Recommendation 15:

Set a unique strategic framework ensuring a continuum of actions to facilitate research and cooperation from idea to clinic for academic groups, start-ups, SMEs and large companies in order to increase R&D productivity of innovative diagnostics, medicines and other therapeutic approaches. In the light of the paradigm shift of industry R&D, an emphasis on early-stage drug discovery will be vital for the development of novel "pioneer" drugs and will boost the competitiveness of European academic and SME researchers. Research excellence and an innovation culture across Europe and among the key players (academia, industry and SMEs) must be key considerations in designing future funding mechanisms and calls in FP8.

Public private partnerships (PPP)

Recommendation 16

The panel recommends that a set of measures be put in place, aiming at redirecting the scope of research of IMI towards clinical development. In the new model, the mode of contribution of industry partners should be in cash, with matching public funds from the EU. Thus, industry participation should be based on the financial and strategic commitment of participating companies to the vision and success of IMI. The IP guidelines should be protective of the interests of all parties, without creating layers of complexity, delays or pipeline bottlenecks. Selection criteria and processes should be simplified and clearly formulated. The aim will be to transform IMI into an effective partnership for "risk-benefit sharing" among EU and the pharmaceutical industry, whilst boosting the competitiveness of European academia and SMEs in R&D.

Furthermore, the panel recommends that all revenues generated from royalty and other payments, should be channelled into the creation of an IMI funding programme for open calls for discovery research for new pioneer drugs, among the academic and SME communities in Europe. This funding mechanism may well develop into a powerful and self-sustainable European IMI-led Research Fund that may have an important impact in the discovery of new and effective therapies.

SMEs

Recommendation 17

A unique instrument is needed to ensure a continuum of actions from idea to market for start-ups, SMEs and large companies in order to increase the success of innovative products (i.e from basic and applied research for disease understanding, proof-of-concept, prototype design, patenting, clinical research and trials, venture capital etc.) with the objective to boost the competitiveness of the EU and build world-class innovation leaders in early to late discovery and development. The Commission should modify its participation and financing rules to make it possible to fund proof-of-concept studies by SMEs through a scheme similar to the small business innovation research (SBIR) grants in the US.

Recommendation 18

Establish research priorities covering a comprehensive range of R&D activities, in innovative therapeutics, in vitro diagnostics and health technologies (from medical devices up to e-Health and services) to support SMEs. Set a proactive European policy to

help overcome the barriers faced by SMEs to participate in FPs. Simplification and more flexibility of project descriptions and participation rules, with projects of shorter duration, smaller partnerships, faster approval process and lighter follow-up combined with a thorough final evaluation should strongly encourage SME participation.

Recommendation 19

The expert panel supports the compromise proposed by the European Commission in the context of the Innovation Union, to put forward a harmonized European patenting system and a revision of directives on accounting standards in order to simplify procedures and reduce administration, a particular burden for SMEs.

Research Infrastructures

Recommendation 20

Research infrastructures on the ESFRI Roadmaps should undergo strategic evaluation to determine their scientific rationale, scope of services provided, their running costs and their funding possibilities.

Recommendation 21

Considering the important role of research infrastructures in providing services and access to technologies, repositories and data, develop a model for their sustainable funding through a joint effort of MS and the European Commission; a set of indicators of the utility and performance of such infrastructures must be developed.

Recommendation 22

Establish common rules for research infrastructures to ensure true pan-European access to their services. This should include simplification of governance models and agreed principles on the methodology used for determining national contributions towards joint activities. EU-funded projects should be requested to make their results available to the scientific community through deposition of data and samples in the pan-European research infrastructures.

Recommendation 23

Develop initiatives for public-private collaboration, such as PPP schemes to make research infrastructures accessible to SMEs and industry active in the field of medical diagnostics and drug development.

Gender issues

Recommendation 24

A continuous assessment of the number of women participating in EU funded health research projects and of the gender impact of all health research should be a high priority for any future FP. Our target should be that at least 30% of coordinators (or co-coordinators) of large projects in FP8 are female.

Recommendation 25

Indicators of gender should be included in the Innovation Union scoreboard. We propose that in the New Scoreboard of 25 indicators of the Innovation Union, in the "Human Resources" group, the following points should be added:
(1) Proportion of women PhDs (ISCED6) in the fields of Science and Engineering and in the Medical Sciences, and
(2) Proportion of female full Professors in the public academic sector.

Training and education

Recommendation 26

The European Commission and all MS should cooperate to solve the problems related to recruitment and career development of young graduates, particularly in clinical research and R&D. Harmonization of European training programmes, transparent promotion criteria and removal of the many obstacles remaining in international mobility and in careers of female scientists are urgently needed. Participation of young researchers from EU-12 countries in FP8–funded research should be facilitated through Marie Curie scholarships and other EU schemes.

2. General comments on health research in Europe and its impact assessment

Health research is typically funded by a number of public bodies, charities and industry and involves academic and non academic research institutions, industry research and development (R&D) laboratories and University hospitals. The primary objective of health research is to create new knowledge that will improve health care for the population at the individual and societal levels, through public health measures and recommendations, novel technologies in medical diagnostics and new therapies to combat disease.

In recent years, the introduction of new tools and technologies, termed as translational technologies, such as high throughput genotyping, sequencing, -omics, functional and molecular imaging, as well as bio-informatics and associated IT developments have allowed to directly prosecute aspects of normal function and disease in vivo in humans. Thus, translational research forms bridges between basic and clinical research, allowing to translate laboratory-derived data into the clinic and, conversely, for clinical observations to inform and/or guide pre-clinical experimentation, in a bidirectional way; hence, translational research is often described as "bench-to-bedside". The success of this two-way collaboration and exchange of information between basic, translational and clinical research requires that research excellence and an innovation culture are well embedded in all three sectors of health research and between all actors contributing to the success of an innovation to the market (academia, SMEs, industry). Strong and sustainable financial support, the appropriate culture and environment ensuring access to state-of-art research infrastructures and high-calibre training programmes are, also, key ingredients of success.

Dissemination of research-derived new information to the public domain is usually quite open through scientific publications, open access databases and presentations in scientific and other public meetings. High-impact innovations that arise from this pool of information often have multiple origins and research groups, thus may not be easily traceable to a specific project. Therefore, the impact assessment of health-related research is complex and has some unique aspects, mostly linked to the relatively long time-span from discovery to development to clinic (average 10-12 years); and thus, difficult to establish at short term.

Additional criteria for the assessment include scientific indicators (such as bibliographic and citational) and financial (such as the value of products in the market, size of industry R&D investment, SMEs' productivity, scientific and financial performance).

Recommendation 1

The panel recommends that criteria and methodologies for health and innovation impact assessment are carefully evaluated and implemented and a well designed e-based mechanism is introduced for systematic health research data collection, monitoring and evaluation of European health research activities.

3. Financial considerations and value of health research

Research and innovation are acknowledged key drivers of growth, social and economic prosperity and of environmental sustainability. The EU has set the objective to increase R&D spending to reach 3% by 2020. Evidence of the financial benefits of health research is accumulating. A recent report[35] by the Office of Health Economics & RAND Europe shows that investment in cardiovascular research in the UK produced a stream of benefits thereafter that is equivalent in value to earning 39% per year, in perpetuity. Reports from the US have emphasized that the social benefits of medical research in the US may exceed trillions of dollars[36]. Furthermore, health research has had an impact in the development of some new technologies that go far beyond medical applications, such as the discovery of the GPS system and the microchip. The demographic explosion of the ageing population and the associated increase of the incidence and prevalence of age related chronic (and often debilitating) diseases represent new and significant "grand challenges" for Europe, recognised as such by Europe 2020.

Health expenditure has risen in all European countries, often increasing at a faster rate than economic growth[37]. In 2008, EU countries spent on average 8.3% of GDP on health, up from 7.3% in 1998[38]. On average, about 75% of health financing comes through public sources (general taxation or social security contributions). Private financing averages around 2% of GDP[39]. A strong investment in biomedical research will be essential to help keep a potentially increasing disease burden and the associated health costs in check. However, compared to funding by the National Institutes of Health in the US, Europe is lagging seriously behind in every aspect of health research funding, with a more than 100 % higher funding in the USA compared to Europe[40].
Against this background, the FP7 contribution to health related-research of 6.1 billion Euros represents 12 % of the total FP7 budget. The panel feels that this amount is insufficient, given the scope and above considerations, not withstanding the new "grand challenges" and recommends that the FP8 contribution to health research should increase. The panel also recognizes that, following a series of funding FP cycles, there is scope for potential financial savings and operational efficiencies of its programmes and recommends an evaluation of funding instruments, mechanisms and programmes, based on their proven record of delivering research excellence and their added value.

Recommendation 2

FP8 should continue to provide funding for health research at a sustainable level to secure a European innovation-driven research environment, a critical mass of researchers and better coordination of European funding instruments in health research, including those of the Member States. In line with the Europe 2020 strategy framework and the Innovation Union flagship initiative, the aim should be to facilitate the development of an innovation culture across Europe, to encourage creative thinking and willingness to explore new ideas, facilitate agility and mobility of ideas and people and support experimentation, calculated risk-taking and questioning of the status quo. In view of the expanded agenda of the FP8 to effectively address the new "grand challenges" and support important new directions in basic and clinical research, the panel recommends that funding for health research in FP8 must be increased, accompanied by measures of better use of existing funds.

[35] Medical Research: What's it worth? Estimating the economic benefits from medical research in the UK. Health Economic Research Group, Office of Health Economics & RAND Europe. UK Evaluation Forum, November 2010
[36] Measuring the Gains from Medical Research. K.M. Murphy & R.H. Tope (2003). University of Chicago Press
[37] Health at a Glance. Europe 2010. OECD
[38] WHO Europe/ European Health for All database http://data.euro.who.int/hfadb
[39] OECD Science, Technology and Industry Scoreboard 2009.
[40] EMRC White paper 2007: Present Status and Future Strategy for medical research in Europe, www.esf.org

4. Thematic prioritization for FP8

The funding instruments in place in FP6 and FP7 were generally found to be effective in the health research area. They have been successful in bringing European scientific communities in basic and clinical research together and results derived from FP6 & FP7 funded research have been significant. Analysis of the available reports indicates that high level proposals were received and funded by the Commission in the fields of fundamental genomics and in several disease areas (in the evaluation many funded proposals have received scores of 4.5/5 or higher for science). As scientific excellence has been the accepted prevailing funding criterion, this indicates that the calls of FP6 in these areas addressed key topics for which there are strengths in infrastructures and manpower in Europe.

Overall, the calls in the health domain are heavily oversubscribed. However, some call topics of health research have failed to attract top-level proposals because they may have been restricted in scope and discouraged otherwise excellent research groups to apply. The panel wishes to re-emphasize the well known fact that to reach excellence requires long-term commitment, scientific focus and diverse skills and areas of expertise. In terms of the thematic prioritization of FP calls, the panel has noted that many of the most successful projects of FP6 have their roots in the Expression of Interest (EoI) exercise of FP5, where the scientific community were invited to present projects addressing major basic and clinical research themes addressing health problems. This "bottom-up" process brought up many high-priority themes where strong and competitive research environments exist in several Member States. Subsequently, the Health Directorate developed these themes into several successful research calls.

Through the activities supported by FP6 and FP7 and by Member States, the European health research community is well positioned to tackle the grand societal challenges ahead. The EoI process and a series of workshops and support measures have had, over the last ten years, an important structuring effect on many fast developing, technologically-oriented scientific communities in the genomics and post-genomics areas. Particularly the IP, but probably also the NoE, have been useful tools to support such activities. A majority of the current infrastructures on the ESFRI Roadmaps 2006 and 2008 (and 2010) received support before their Preparative Phase through FP6 (and often through FP7, too), e.g. bioinformatics, mouse genetics, population genetics and bio-banking, structural and systems biology and the different -omics technologies that form their basis. These activities have now been expanded towards translational research with projects on cancer genomics, microbiome and rare diseases (under discussion) but the actual support to infrastructures is now channelled through the Capacities programme in FP7.

As outlined in the Europe 2020[41] strategy and the Innovation Union[42] flagship initiative, health research in the next FP is likely to focus on the grand societal challenges, such as the theme of "improving the quality of life of an ageing population by new innovative solutions, clinical tests, diagnostics and treatments for age-related diseases, deployment of new innovative ICT-based solutions and the development and introduction of novel products, appliances and services specifically suitable for the elderly." Examples of age-related diseases which may have their roots in much younger age groups are: obesity, diabetes, mental health disorders and neurodegenerative diseases, susceptibility to infectious diseases, musculoskeletal disorders, sensory impairments, rising allergic disease, untreatable rare diseases together with the big killers, cancer and cardiovascular diseases. Additional grand challenges that have been identified, with

[41] Europe 2020. A strategy for smart, sustainable and inclusive growth. COM (2010) 2020
[42] Europe 2020 Flagship Initiative Innovation Union. COM (2010) 546

some relevance to health research, include the supply of foodstuffs, water supply and health-related ICT (eHealth). Furthermore, globalisation, increasing migration and environmental factors such as climate change may also have a health effect, in particular in infectious diseases.

The panel feels that, whilst supporting the thematic emphasis on grand challenges, it would be vital to also ensure that innovative and emerging research themes, ideas and disease areas of unmet medical need are not neglected. Therefore, mechanisms to fund research in areas outside the grand challenges should be retained within FP8.

Resources in health related infrastructures and investments in basic research made over the years by the Commission can now form the basis of high-quality research towards new public health and prevention programmes, novel diagnostics and in the discovery and development of new therapies. The concept of personalized medicine will bring huge possibilities for better diagnosis and of differentiated and effective treatments. Bio-banks and large pan-European population cohorts and health-related registries are acknowledged European strengths, which offer great opportunities for innovative collaborative research into the aetiology and risk factors of common diseases, such as dementia, cancer and cardiovascular diseases. Within Europe, the scale of the challenge goes far beyond what can be tackled at a single country level. In fact, the health and disease issues are largely global concerns and emphasize the need for cooperation within and beyond Europe, in many disease areas.

New collaborative research should also be directed towards prevention and public health, a theme that has received relatively little attention during FP6 and FP7. Much research remains to be done to increase our understanding of the complex relationships between the genetic, lifestyle and environmental factors and of the causes and mechanisms of diseases, as well as to discover and develop new treatments and improve existing ones. Advances in molecular epidemiology using large population cohorts are now producing a wealth of information of the relationship between inheritance, life style, nutrition and several other variables on health outcomes and is likely to also result in novel preventive measures. Such results are clearly of major benefit to public health.

Recommendation 3

The panel supports the value of thematic prioritization based on "Grand Societal Challenges" and recommends a reintroduction of a "bottom up" approach (analogous to a successful EoI exercise in FP5) that would engage the scientific community, both basic and clinical researchers, in identifying areas of truly innovative research to tackle both the grand challenges and other areas, such as those with unmet medical need, as well as novel and emerging new research ideas and directions. This "bottom up" approach will generate a range of research questions and ideas that will then require a transparent process for in depth and evidence-based ("top down") evaluation, prioritization and final recommendations by panels of impartial experts of high scientific credibility and integrity.

5. Coordination of European health research and efficient pooling of resources for health research in Europe

The European Commission has made several efforts to reduce fragmentation of health research funding in Europe. In addition to the FP-specific research funding instruments, some instruments (e.g. ERA-NETs and ERA-NETs Plus) aimed specifically to bring funders to close collaboration have been tested with some success. New initiatives for large scale collaborative programmes, such as EDCTP, IMI (with industry), Joint Programming Initiatives (JPI) for multi-Member State collaborations on specific disease areas such as Alzheimer's disease and private public partnerships (PPP) have served as models for new types of collaboration. Their implementation has sometimes been long and not painless and it is too early to estimate their true impact.

Funding of health research is fragmented within the European Commission. In the DG Research and Innovation, in addition to the Health Directorate, health research receives support from several other Research Directorates: Health and Wellbeing appears in Directorate E, Health and Environment appears in Directorate I. Nanosciences and Nanotechnologies, so important in medicine, is under the responsibility of Directorate G. Furthermore health research is funded through ERC (Ideas programme), Marie Curie (People programme), IMI and infrastructures (Capacities programme). DG SANCO plays an important role in public health and health policy issues. E-Health is managed by DG INFSO, ICT (Information and Communication Technology) programme. It is, therefore, striking to see how health research is split into many directions and programmes. This diversity has the advantage of promoting multidirectional innovation. However, it also carries significant risks related to its inherent complexity, such as duplication and financial waste, pigeon holing of themes with lack of multidisciplinary interactions, issues relating to accessibility of the programmes and instruments for SMEs, the absence of continuity from idea to market due to the non-implication of practitioners and users and others.

Recommendation 4

Introduce a transversal coordination system for health research leading to a "one-stop shop", to encompass all health-related research activities, in order to avoid duplications and tackle high impact grand challenges and the innovation-driven health research agenda in a simplified, user friendly and coherent manner.

A holistic and integrated transversal organization for health research through a one-stop shop should facilitate more coherence between the three health research sectors (basic, translational and clinical) and between all actors contributing to the success of an innovation to the clinic (academia, SMEs, industry). The recent emphasis made on usability highlights for instance the compulsory need to involve the users (clinicians but also patients) from the early stage of an invention and their assessment during its whole development and not only at the evaluation phase.

Such a mechanism for transversal coordination and management of FP8 should be simple and user friendly, aiming at optimizing the coordination and coherence among activities that represent a proper response to a global strategy, both within the Commission and with Member States. The budgets and funding instruments dedicated to linking R&D and innovation should be specifically addressed, streamlined and simplified. This new transversal structure should better coordinate EU funded research. This simplified model should encourage SMEs to apply.

Recommendation 5

In the lifecycle of FP8 and moving towards 2020, design and by year 2020 implement the establishment of the "European Health Research and Innovation Institutes" (EHRII), analogous to the US model of the NIH but adapted to the European realities and scientific strengths, in line with the Europe 2020 and Innovation Union strategies.

This new structure would create a powerful strategic framework for multidisciplinary health research, whilst reducing the fragmentation and complexity of funding which now hampers health research in Europe. With a budget comparable to NIH, the EHRII would be in a position to more effectively support innovation in health research, foster collaborative and multidisciplinary research, better coordinate research activities with Member States and also be a vehicle for strategic thinking and planning of European health research. Rather than investing funds and time in designing and building "bricks and mortar", the EHRII should be "virtual", with its central administrative structure within the Health Directorate in Brussels but divided into specific Institutes based on thematic disease areas and distributed among all Member States, thus developing and fostering strong links of scientific cooperation and synergies with the health research structures of each Member State. The EHRII should be inclusive, encompassing the biomedical scientific community in the whole of Europe and promote a better integration of all health research activities and infrastructures. EHRII should be flexible in structures and processes and aim at invigorating a culture of research excellence and innovation within the health research community across Europe.

Need for simplification whilst promoting research excellence

Throughout past and present Framework Programmes, the scientific community has been asking for simplification of the administrative and financial rules and their interpretation. The need for simplification of EU programmes and funding mechanisms has also been highlighted by previous FP evaluation panels, in the Innovation Union Flagship Initiative document, the Green Paper and other strategic EC documents. They all point to the need for lowering the administrative burden and the complexity of financial rules and regulations whilst retaining the utmost diligence but also promoting focus on research excellence (as opposed to the currently prevailing administrative and financial focus). Our panel has identified two disturbing trends that appear to result from excessive bureaucracy of EC-funded projects.

Firstly, the excessive administrative burden requires extensive administrative and financial support in the hosting institution (at an inappropriately high cost) for the co-ordination of research projects. As a result such activities become prohibitive for most research institutions, including SMEs, and tend to be restricted to a select group of large Universities and research institutions in EU15 countries which provide such infrastructure or can afford to subcontract to management companies, at a significant cost to the institutions and the FP programme itself. Such complexity is not compatible with the innovation culture of Europe 2020.

The second observation is the lack of appropriate evaluation mechanisms of scientific performance and output and the paucity of reconciliation of budgets/ research spent to deliverables and scientific output, in spite of the excessive paperwork required for the financial and administrative reporting.

Furthermore, the panel has also noted that, over time, the multiplication of funding instruments and calls may have resulted in potential duplications and risk in potentially funding research activities and areas that may not be state-of-art and /or innovative today and in the lifespan of FP8.

Mid–term evaluation of proposals should aim at an early identification of problems and losers, as well as of high flyers and potential successes. Appropriate and proactive management of both scenarios should be possible. Based on the findings of the mid-term evaluation, more flexible approaches to research funding should be introduced to allow successful and productive research teams to adapt and adjust their research plans towards optimizing results and outputs, based on pre-determined, simple and clearly stated regulations and procedures

Recommendation 6

The current administrative and financial reporting and monitoring system is both complex, carrying excessive administrative burden and cost, and is in fact incompatible with the innovation culture of Europe 2020. It must be simplified and become less bureaucratic. Mid-term and final evaluations should be strengthened and based on quality and impact of scientific and innovation output and the cost-benefit ratio.

Existing funding schemes and instruments must be evaluated based on the principles of added value and proven record in delivering research excellence and innovation. However, the balance of budget between various instruments and FP research programmes seems adequate. ERC and its funding model of supporting "single investigator awards" have been particularly successful. This ERC funding model complements well the funding model of collaborative work of FP. In planning for FP8, an appropriate balance between basic and clinical research, of large long-term collaborative consortia programmes and more focussed and shorter projects should remain an important consideration. Furthermore, whilst promoting the innovation culture, Europe will need to define the balance between what promises to be low-risk and "high impact" –" high risk" research.

The Innovation Union under preparation aims at strongly improving the overall process leading to new innovative products and services to increase the employment rate observed in EU and to provide better quality of life for all people. To reach this objective, EU funding has to be balanced been between fundamental and applied research, whilst fostering research excellence and innovation in both.

Recommendation 7

Establish a permanent "FP Outcome evaluation panel" to monitor and evaluate the added value, impact of the scientific outputs and overall performance of FP funding schemes and instruments, based on evidence and proven record of delivering innovation and research excellence.

Working with the European scientific community

There are several examples where the instruments of FP6 and FP7 have de facto provided sustainable long-term funding for both technology-oriented and major disease-oriented themes, allowing for their progression towards translational and clinical research, personalized medicine and systems medicine; these terms were employed by the Heads of Units in their documentations and during individual interviews with the panel. These success stories have been made possible, to a considerable extent, due to attentiveness of the Health Directorate to the needs and views of the scientific community. The EoI exercise at the end of FP5 was a good example of that, allowing to identify strong European research communities and important health-related research themes for FP6.

The Health Directorate also has a good record of establishing a dialogue with the scientific community in several areas of health research, during FP6 and FP7, to better

understand the needs and directions of research. This dialogue has involved expert scientists directly or through (and with) Member States, such as in the evolving JPI scheme. An example of discussion with the scientific community was the meeting organized by Health Research and DG SANCO in 2006 on BBMRI (the bio-banking infrastructure on the ESFRI Roadmap 2006) and major research projects receiving EC funding. Examples of interactions with Member States were the meetings of the Alzheimer's JPI, organized by Member States but funded centrally. The panel recommends that such interactions with the scientific community should be encouraged but be more inclusive to the wider community, targeting research excellence, as opposed to representatives of professional groups with potential lobbying agendas.

The panel recognizes the need to promote scientific research excellence in EU-12 countries and proposes to expand the opportunities to individuals and teams from EU-12 to participate in FP8 schemes. Innovative ways of supporting young researchers from EU-12 countries in their career and research trajectory should be considered. For example, recipients of the Marie Curie Visiting Fellowship awards could be supported to establish their research projects in their home countries, once they reach the appropriate level of scientific independence and expertise. Collaboration between research groups from EU-12 countries and EU-15 countries and the inclusion of EU-12 researchers in European networks of excellence should be facilitated, subject to peer-review evaluation mechanisms, based on research excellence. Regional collaborations with neighbouring countries should also be supported, based on the same principles, in the Balkans, Baltic counties and the Mediterranean region. Specific calls addressing research themes and health problems of high-priority to these regions should be considered in FP8.

Recommendation 8

To invigorate research excellence in countries underperforming in the innovation scoreboard, opportunities for researchers and institutions from such countries to join EU-funded projects and programmes should be enhanced through innovative new partnership-scheme(s). In this context, calls addressing health problems of high priority to EU-12 countries and their regions should be considered.

8. New directions in clinical research

Clinical research is patient-centric and includes observational and interventional studies. The former are directed towards elucidating the causal pathways and mechanisms of disease and the identification of its risk factors, leading to a more precise definition and diagnosis of disease subtypes, each potentially underlined by distinct mechanisms and more responsive to new treatments targeting the corresponding pathways and mechanisms. This is the concept of personalized medicine, allowing for the right patient to get the right treatment for the right dose, thus carrying the hope of much more effective clinical management in the diagnosis and treatment of human disease. Interventional studies aim at validating developments in novel technological methodologies and procedures and evaluating the safety and efficacy of new therapeutic or preventive interventions.

Clinical research aims at improving disease prevention, diagnosis and treatment and, ultimately, human health in Europe and globally. The European countries have a high and improving average life expectancy but with a West to East gradient for deterioration, with life expectancy in EU-15 still being longer than in EU-12 countries. The main diseases leading to death in Europe are cardiovascular diseases and cancer. Infections and emerging diseases are still threats. The incidence and prevalence of chronic diseases, such as obesity and metabolic syndrome are increasing. With the demographic explosion of the population, the frequency of age-related chronic diseases (such as dementias and cardiovascular diseases) increases rapidly. Improving healthy ageing and combating age related diseases have been identified as a "grand challenge" for Europe, as it moves towards 2020.

Recommendation 9

Clinical research should be strongly supported in FP8 and adhere to the historical aims of improving health, life expectancy and quality of life for all European citizens of all Member States, whilst reducing the burden of diseases for each and every patient. In the new era of translational research and regenerative and personalized medicine, strong academic participation will be key to the success of clinical research and innovation.

During the course of FP6 and FP7, significant progress has been achieved world-wide in the development of new translational tools that now permit to dissect human disease in its subtypes and underlying causal pathways and mechanisms and to discover new biomarkers for a precise diagnosis of disease subgroup, for risk prediction and progression of disease and for outcome measures, thus paving the way for personalized medicine. Significant advances have recently been made in personalized medicine in various forms of cancer and other diseases and this trend is expected to expand considerably in the life of FP8. Such studies require large prospective cohorts and research infrastructures, where Europe has unique strengths. They also require significant investment to overcome some initial bottlenecks in biomarker discovery and development.

Recommendation 10

High priority should be given to observational studies based on European populations aimed at biomarker discovery, the identification of risk factors and causal pathways and a better definition of nosology and disease heterogeneity in prioritized diseases. Such studies should aim at further progressing the concept of personalized medicine. Europe should retain its leadership in the field, leveraging the power of European population and patient cohorts, as well as of medical centres of excellence across Europe.

Prevention and public health research are important areas of publicly-funded health research that are also based on population cohorts and aim at translating research findings into prevention measures, public health interventions and policy guidance that can significant impact European healthcare and the society. Europe has unique resources in large-scale prospective studies, with extensive data and biological sample collections, spanning several decades that can provide excellent material for studies in multiple diseases of high priority, such as cardiovascular diseases and cancer. With the age shift of the population, these cohorts may now by used in studies in ageing and age related diseases, including Alzheimer's disease and other disorders.

A good example is the EU-funded European Prospective Study for the Investigation of Cancer (EPIC). This study, initiated in the early 90s, currently involves 520,000 participants from 10 European countries. EPIC is one of the largest prospective studies in the world, with extensive baseline and follow up clinical data and biological samples collected and stored over the last two decades. The study was initially funded by DG SANCO, jointly with all 10 participating Member States, and has subsequently received FP6 and FP7 funding for disease-specific concerted actions. Through this and other national cohort studies, Europe has a clear competitive advantage for research in healthy ageing and age related diseases. Given the diversity of European cohorts, emphasis should be given in enhancing their value through data harmonization and further utilisation, rather than funding the development of de novo cohorts. FP8 should include targeted programmes in prevention and public health, as part of its strategic objectives to combat the "grand challenges" of 2020 and common diseases of unmet medical need, such as cancer, Alzheimer's and cardiovascular diseases, which are associated with high morbidity and mortality.

Recommendation 11

Prevention and public health should be highlighted in FP8, as they represent important angles in addressing the "grand challenges" for Europe 2020, as well as in proactively reducing the burden of common diseases of unmet medical need that are associated with high morbidity and mortality. Mechanisms of effective and rapid communication and translation of results into public health interventions and policy guidance for Member States should be considered.

The new translational technologies are also transforming early clinical development (phase IIa or "proof of concept") trials into science-driven experimental medicine studies that can now be used for "in human" target validation, evaluation of mechanisms and "proof of concept" for novel therapeutic, diagnostic and therapeutic device and public/ prevention intervention. Such studies may involve small or large molecule therapeutics, cell-based treatments, vaccines, devices and instruments for diagnosis and surgery and novel applications or indications of existing therapeutics. Applying novel statistical designs and evidence-based methodologies, modern-age experimental medicine carries the hope of considerably reducing the very high attrition rates of phase II studies, currently at >90%. In recent years, there has been an increasing trend in new funding schemes for investigator-led experimental medicine studies by ERC, NIH, UK-MRC and funding agencies of other Member States, as these studies are increasingly seen as being at the core of the academia-led translational medicine research. Publicly funded experimental medicine studies will significantly benefit SMEs involved in drug discovery research

Recommendation 12

Support science-driven experimental medicine studies, using new evidence-based methodologies for "proof-of-concept" of novel small or large molecule therapeutics, cell-based treatments, vaccines, devices and instruments for diagnosis and surgery and

novel applications or indications of existing therapeutics. FP8-funded experimental medicine studies should strictly adhere to the highest ethical standards and directives and be truly innovative in their methodologies and/or indications or compounds tested.

The legal framework regulating clinical trials in Europe has received extensive attention in recent years and is thought to be in urgent need of simplification and harmonization. The European Science Foundation/European Medical Research Council Forward Look 2009, Investigator Driven Clinical Trials[43], provides an extensive account of the background, issues and challenges, as well as of potential solutions.

Recommendation 13

A new European clinical trials directive is needed to ease the way for clinical research of high quality in Europe, whilst fully protecting the safety of patients, their confidentiality and rights.

EDCTP was created in 2003 to accelerate the development of new or improved drugs, vaccines and microbicides against HIV/AIDS, malaria and tuberculosis, with a focus on phase II and III clinical trials and to coordinate the European clinical research activities in Africa on these topics. It encompasses 14 EU Member States plus Norway and Switzerland and 46 sub-Saharan countries. After a slow start, EDCTP gained momentum and is now funding several clinical trials (54) and capacity building projects (210). In the meantime, 4 Networks of Excellence have been formed in different African areas in cooperation with European research institutions to foster clinical research and improve research quality. But obstacles still remain, especially due to the unclear and unresolved funding and co-funding system by the EU and the EDCTP member countries.

Recommendation 14

The medical and scientific EU objective to fight poverty-related diseases in sub-Saharan Africa should be further pursued. The panel strongly supports further funding of EDCTP, but the Commission should work on designing a model of non-bureaucratic but diligent funding mechanism for direct funding of EDCTP by the Commission itself or by pooling contributions by EDCTP member countries or through a "common pot" approach.

9. The pharmaceutical industry and SMEs

Industry

The pharmaceutical R&D is undergoing significant change, with a shift of focus from drug discovery to late development and marketing. This paradigm shift has resulted in downsizing of pharma investment, workforce and laboratories in drug discovery research in Europe. This trend has been well documented in the public domain, with several examples in EU countries in the last three years. Increasing financial pressures from the loss of "blockbusters" and a chronic decline in R&D productivity and innovation, as measured by the number of new medicines delivered, may explain these changes. In spite of escalating R&D costs and improving technologies, attrition rates have remained high at all stages of R&D. 50% of high-throughput screens fail and 30% of clinical candidates fail in preclinical evaluation and another 30% in phase I. The greatest attrition occurs in phase II (>90%). The overall attrition for small molecules is estimated at a staggering 97% with a slightly lower rate for (biopharmaceutical) large molecules[44].

[43] http://www.esf.org/fileadmin/links/EMRC/FL_IDCT.pdf
[44] How to improve R&D productivity: the pharmaceutical industry's grand challenge. S.M. Paul et al. Nature Revs. Drug Discovery 9: 203-214 (2010)

Through this paradigm shift, the industry is relinquishing a significant part of their early discovery effort to academia and biotechnology SMEs, whilst they focus on few research areas and in in-licensing promising drug candidates or other discovery programmes (Bountra et al in press). The expectation of industry executives is that academia and public funders will generate more "Silicon valley-like" SME spin-offs to be able to cover the early drug discovery research space and that public funders will support the more successful and entrepreneurial researchers and institutions in doing so. This will not be a new role for the academic health research community, which has a long track record in discovery research of new medicines, albeit somewhat overshadowed in the last two decades by the massive R&D investments of the pharmaceutical industry. In the past 40 years, 153 new FDA approved drugs, vaccines and new indications were discovered through publicly funded research in the US alone[45].

Beyond these purely financial considerations, this trend may also be justified by the limitations of the traditional "animal-based" industry R&D pipeline (usually confined within well guarded research laboratories) to replicate and efficiently study human disease in animal models. Whilst industry has an impressive record of delivering thousands of targets, screens and candidates, the number of new medicines in disease indications has steadily been declining. It is now widely accepted that the new R&D model will require closer links to the human patient and human disease, optimizing the two-way communication between the clinic and discovery research labs, at all R&D pipeline stages: from genomics, pathway analysis and systems biology approaches for target discovery and validation, to biomarker identification and validation through to translational research for early drug development and "proof of concept" studies, to large-scale clinical trials. Therefore, a second paradigm shift is now inevitable in the relative roles of academia, biotechnology SME's and the industry, with an increasingly greater role of the former in drug discovery and development.

These are times of unprecedented challenges and opportunities for the European academic and SME health research. Innovation and high impact research in the new "patient-centric" academia-led model of drug discovery and development will require large, research active, well equipped university hospitals and related research institutions, where Europe has acknowledged strengths. The downsizing of the industry investments in discovery research creates a need for additional public funds, if the European academia and SMEs are to rise to these challenges successfully.

The path will not be free of potential risks and shortcomings. Competition from academic communities outside Europe is expanding. On one hand, US clusters of excellence such as the wider Boston area have a long and successful record in attracting R&D investments and SMEs. However, competition is also now increasing from the east (China, India, Singapore, South Korea) where massive investments have recently been mainly made mainly in large-scale platform technologies. It is noteworthy that over 100,000 Chinese and Indian scientists have returned to their homelands from the US in the last decade and more are expected to return in the coming 3-5 years. Furthermore, the prolonged and worsening current financial environment is proving increasingly unfavourable in securing sustainable research funding in Europe.

In contrast to the pharmaceutical industry, the medical diagnostics- technologies industry has historically retained R&D activities internally, mainly in Europe and the US, with some foci and areas of increasing collaboration with several centres of excellence within the European academic community. An open dialogue and in depth evaluation of the needs and trends of this industry sector may be advisable at this early stage, so that measures to support and facilitate the interactions with the European academic and specialized SME centres may be designed proactively.

[45] A.J. Stevens et al. The role of public-sector research in the discovery of drugs and vaccines. New England Journal of Medicine 346: 535-541 (2011)

Recommendation 15

Set a unique strategic framework ensuring a continuum of actions to facilitate research and cooperation from idea to clinic for academic groups, start-up's, SME's and large companies in order to increase R&D productivity of innovative diagnostics, medicines and other therapeutic approaches. In the light of the paradigm shift of industry R&D, an emphasis on early-stage drug discovery will be vital for the development of novel "pioneer" drugs and will boost the competitiveness of European academic and SME researchers. Research-excellence and an innovation culture across Europe and among the key players (academia, industry and SMEs) must be key considerations in designing future funding mechanisms and calls in FP8.

Public private partnerships (PPP)

The concept of PPP in the domain of health research is now regaining popularity as a possible model to reinvigorate academia-industry collaborations in key areas of basic or clinical research. PPP, if adequately designed, can provide viable funding options with "sharing of risks and benefits" among industry, public funders, charities and academia.

The Expert panel was informed of a new PPP scheme with COLIPA (cosmetics industry association) designed to create a research topic with Commission on repeated dose systemic toxicity testing in human safety assessment. A specific call for proposals was launched in the regular Health 2010 work programme with a proposed COLIPA contribution of €25 million. Normal FP7 rules were applied; the Commission provided a 50% financial contribution and industry topped up funding by another 50% once the Commission had selected and negotiated the projects. The Commission is responsible for project follow up and supervision. The panel feels that this would be an appropriate model of EU participation in PPPs that merits further consideration in the health research sector.

IMI was established in 2008, as a PPP, between the European Commission and EFPIA representing the European pharmaceutical industry. IMI's goal was to increase the competiveness of Europe in the pharmaceutical R&D sector and to address the bottlenecks that were thought to limit the efficiency, effectiveness and quality of the drug development activities needed to bring innovative pioneer medicines to the market. The contribution of EU is in-cash funding (€1 billion), to be matched by in-kind contribution from the pharmaceutical industry. Three calls have been made to date (one under evaluation, two for which projects are now on-going). 23 large consortia have been formed and funded in the first two calls. These involve >200 pharmaceutical R&D groups, approximately 300 academic groups and 50 SMEs and several patient groups, at a budget of more than €400 million. Although too early to assess the impact of these studies at this early stage, preliminary results have been made public and are encouraging. A first interim evaluation of IMI has taken place in 2010 and several observations and recommendations were made. The evaluators identified several shortcomings and challenges: lack of clarity of identified key performance indicators, task responsibilities and accountabilities making the output of IMI vague and difficult to ascertain; difficulties in obtaining and maintaining industry commitment to a given IMI project, given the ever-evolving and changing priorities and internal structures within industry and in clearly demarcating what is precompetitive (thus "open access") or not, and where the competitive element of a project begins. Communication between stakeholders and with the industry, SMEs and the academic community has been suboptimal and partial. The significant changes affecting the pharmaceutical R&D in Europe, as outlined in the previous section, have not been adequately considered or discussed.

Recommendation 16

The panel recommends that a set of measures be put in place, aiming at redirecting the scope of research of IMI towards clinical development. In the new model, the mode of contribution of industry partners should be in cash, with matching public funds from the EU. Thus, industry participation should be based on the financial and strategic commitment of participating companies to the vision and success of IMI. The intellectual property guidelines should be protective of the interests of all parties, without creating layers of complexity, delays or pipeline bottlenecks. Selection criteria and processes should be simplified and clearly formulated. The aim will be to transform IMI into an effective partnership for "risk-benefit sharing" among EU and the pharmaceutical industry, whilst boosting the competitiveness of European academia and SMEs in R&D.

Furthermore, the panel recommends that all revenues generated from royalty and other payments, should be channelled into the creation of an IMI funding programme for open calls for discovery research for new pioneer drugs, among the academic and SME communities in Europe. This funding mechanism may well develop into a powerful and self-sustainable European IMI-led Research Fund that may have an important impact in the discovery of new and effective therapies.

SMEs

The paradigm shift in drug development described above is increasing expectations on academia and biotechnology SMEs to assume a greater role in early drug discovery. This is a significant challenge because technology transfer and funding of proof-of-concept research appears to be suboptimal in many Member States. A major concern is the "valley of death" that SMEs involved in Health research in Europe are facing, as a result of the increasing difficulties to raise venture capital, particularly in Europe. A number of SMEs report that the participation rules and the administrative and financial complexity of current funding instruments are disincentives to apply for funding through FPs[46]. However, the SME field is quite diverse; preliminary results of the Kappa Health study[47] show that 90% of SMEs participating in FP6 and FP7 Health projects consider FP participation a success and 50% of them report generating commercial return.

It appears that despite these results the participation rules and the administrative and financial complexity of current funding instruments are seen by many European SMEs as disincentives to apply for funding through FPs. An average discovery and development time of a drug to the clinic is too long, compared to the time span of current funding instruments for Healthcare SMEs.

The lack of a suitable financing system for innovative SMEs is a serious issue and a major constraint. Only very few European firms grow into worldwide leading companies. There are market gaps which represent real barriers for start-ups and the present EU funding instruments do not fit with their needs. It has been estimated that, in 2010, out of the 266 European private and publicly funded biotech-SMEs with platform technologies or products in the market (thus of proven success), 207 required over €3 billion each to survive, whilst the available capital represented only a small fraction of the needed amount[48]. The Risk Sharing Finance Facility (RSFF), an instrument created jointly by the Commission and the European Investment Bank (EIB) was established to facilitate funding of industry for research and innovation projects through loans and guarantees; however, only two projects in the Health domain have been approved to date.

[46] Interim evaluation of the seven Framework Program, Experts panel report, November 2010
[47] http://www.kappa-health.org/News/196.aspx
[48] Europe's Iceberg 2010: Advancing but frugal", W. Yang *BioCentury*, 18: A15-18 (2010).

Innovative approaches for supporting SMEs should be considered. Ideally, a unique funding instrument covering the entire developmental lifespan of a healthcare product (diagnostic method or drug), with well timed and clearly defined milestones and checkpoints, should be developed for the needs of SMEs. Clearly defined milestones and checkpoints are needed to take into account the fact that currently the overall success rate of new drug development is only about 4%.

Learning from the most effective schemes from outside and in Europe, such as small business innovation research (SBIR[49]) projects in the US and several existing ones in Europe (UK, Germany, Finland, etc.) would be helpful. The provision of small amounts of money and a fast selection process for SME proof-of-concept projects, similar to the US SBIR (without the constraint of a multi-partnership and multi-country involvement), should be examined, and, in case of a favourable outcome, implemented through a second phase project funding. In addition to a SBIR-STTR (small business technology transfer)-like system, a newly designed RSFF specially adapted to SMEs would also have a great value.

The strategic objective for SME participation in EU funded health research has been set at 15%. However, this goal has not been reached so far and SME participation still remains at about 12 % in spite of continuous efforts by the Health Directorate to encourage applications from SMEs. Encouragingly, significant progress in SME participation has been made through a new approach where call topics designed to meet the needs of SMEs have been introduced.

Recommendation 17

A unique instrument is needed to ensure a continuum of actions from idea to market for start-ups, SMEs and large companies in order to increase the success of innovative products (i.e. from basic and applied research for disease understanding, proof of concept, prototype design, patenting, clinical research and trials, venture capital etc.) with the objective to boost the competitiveness of the EU and build world class innovation leaders in early to late discovery and development. The Commission should modify its participation and financing rules to make it possible to fund proof-of-concept studies by SMEs through a scheme similar to the small business innovation research (SBIR) grants in the US.

SMEs play an increasing role in emerging R&D activities of novel therapeutics and technologies that are already starting to have an impact in clinical applications: new

[49] The Small Business Innovation Research (SBIR) program, created in 1982 and regularly prolonged, has a $2 billion budget aimed at financing joint R and R&D projects with potential for commercialization. Up to now, over $16 billion has been awarded by the SBIR program. The SBIR Program aims at stimulating technological innovation, strengthening the role of small business (i.e the PI must belong to the SME) and increasing private sector commercialization of innovations developed through Federal funding. There is a companion program named Small Business Technology Transfer (STTR), set in 1992 and still active, which shares with SBIR the same objectives with, however, the requirement in the early steps of the project to formally collaborate with a research institution. All this process is managed by most of the US Federal agencies.
There are three phases defined in SBIR/STTR Programs:

(1) to establish the technical merit and feasibility and potential for commercialization of the proposed R/R&D efforts and to determine the quality of performance of the SME prior to providing further Federal support in Phase II. Maximum supports are $150,000 for SBIR (6 months operation) and $100,000 for STTR (12 months).
(2) the objective of the second phase is to continue the R/R&D efforts according to the results obtained in phase 1 (scientific and technical merit and commercial potential). Only the awardees of the phase can enter in phase 2. The amount of money for SBIR 2 is no more than $1,000,000 and for STTR 2 $750,000 (total costs for 2 years).
(3) the objective of the last phase is to continue with non-SBIR/STTR funds the commercialization objectives. Private funding search is highly facilitated by the fact that the project was "labelled" by SBIR or STTR in phase 1 and 2.

diagnostic and surgical devices and technologies, in vitro diagnostics, e- health and other IT-based technologies, and novel regenerative medicine approaches. The latter include tissue engineering, gene therapy, cell-based therapeutics, developmental biology and stem cells, biomaterials, nanosciences, bioengineering of cells and tissues and chemical biology. In recent years, some major successes have resulted from the SME sector in these truly innovative, albeit high-risk, emerging fields of R&D.

Recommendation 18

Establish research priorities covering a comprehensive range of R&D activities, in innovative therapeutics, in vitro diagnostics and health technologies (from medical devices up to e-Health and services) to support SMEs. Set a proactive European policy to help overcome the barriers faced by SMEs to participate in FPs. Simplification and more flexibility of project descriptions and participation rules, with projects of shorter duration, smaller partnerships, faster approval process and lighter follow-up combined with a thorough final evaluation should strongly encourage SME participation.

The role of SMEs is becoming increasingly important in Healthcare products, devices and services and is economically and medically strategic for Europe. These markets display a sustainable growth, bring new molecules, high technology and permanent innovation. Biopharmaceuticals SMEs are estimated to comprise approximately 800[50] enterprises' and generate revenues in excess of €21.5 billion in 2006 (Europabio 2006, European Commission 2006). Health technology (representing 60% of the business volume of the pharmaceutical industries) is the second major area in terms of market (the second one after the US with 1/3 of the global market of €187 billion in 2006) and employment in Europe (about 435,000 people with a spending in R&D of €3.8 billion). The European SMEs in this area represent 80% of the 11,000 companies, approximately 5 % of them having a very high R&D activity[51]. These data emphasize the need for a proactive European policy to support SMEs.

The Innovation Union under preparation aims to strongly improve the overall process leading to new innovative products and services, to increase the employment rate in the EU and to provide better quality of life for all people. To reach this objective, EU funding has to be balanced been between fundamental and applied research, whilst fostering research excellence and innovation in both.

Beyond these financing aspects, there is also the regulatory system to consider. Much has been already said on the lack of harmonised regulations for innovations. The level of fragmentation creates a major problem for SMEs as they are not in a situation to re-do an evaluation over all EU countries. The efforts jointly supported by the European Commission and Member States for a common methodology in Health Technology Assessment (HTA) across the 27 members are expected to bring improvements and must be strongly pushed forward.

Recommendation 19

The expert panel supports the compromise proposed by the European Commission in the context of the Innovation Union, to put forward a harmonized European patenting system and a revision of directives on accounting standards in order to simplify procedures and reduce administration, a particular burden for SMEs.

[50] Source: DG Enterprise and Industry
http://ec.europa.eu/enterprise/sectors/biotechnology/files/docs/financing_biopharma_product_dev_en.pdf
[51] See Eucomed: *Competitiveness and Innovativeness of the European Medical Technology Industry*, May 2007).

Intellectual property (IP) and patents remain a strategic tool in the process from idea to market and must be clarified at an early stage. The business models of SMEs are highly dependent on the IP ownership. Unfortunately, Europe is losing its position when compared to the worldwide production. The European countries generated only 37% of the patents submitted to the European Office in 2006 (all areas). This represents a decrease of about 12% from 2001. In the US, the EU as a whole obtained 14.7% of the approved patents.

The creation of a single, unified European patent, the simplification of procedures and removal of bottlenecks for approval and marketing should significantly improve European competitiveness in the SME and pharmaceutical industry sectors. Currently, obtaining a patent protection for all 27 EU Member States is at least 15 times more expensive than patent protection in the US[52]. Simplification, moderate cost and timely response should become the major features of the future European patent as the viability of SMEs is dependent on these.

In a wider perspective, patenting is only part of the story; a key aspect is that these patents must live and be transformed into concrete products. In addition, it is important to ensure that not only a selected "elite" group of SMEs (from the R&D strong countries) participate successfully in the future FP. EU-12 countries lag behind in the development of R&D-oriented SMEs. Also the public-private partnerships in EU-12 countries are underdeveloped. Pharmaceutical companies in EU-12 are oriented into the generic drug market which further reduces the development of the R&D. Steps should be taken to facilitate the public-private partnerships in EU-12 countries.

10. Research Infrastructures

Well functioning research infrastructures form a cornerstone for an innovative research environment in nearly all areas of health research. The important role of infrastructures on the ESFRI (European Strategy for Research Infrastructures) Roadmap(s) is also clearly stated in the Europe 2020 and Innovation Union strategy documents. Six BMS (Biological and Medical Sciences) infrastructures were selected to the first ESFRI Roadmap in 2006, another four in 2008 and yet another three in 2010. Together these infrastructures cover all major repositories and technologies needed in health research from basic research to translation and clinical research, including the drug development process. ESFRI infrastructures for translational research (EATRIS) and clinical research (ECRIN) are good examples of much-needed infrastructures for clinical research. In the future an increasingly important role is envisaged for eHealth-infrastructures.

Although funding of infrastructures is not the primary responsibility of the Health Directorate, it has played an important structuring role in bringing the dispersed scientific communities together (already before the ESFRI process was initiated) and in supporting a number research projects in these areas during FP6 and FP7 (and already during FP5). The Health Directorate has organized a series of workshops and support measures which helped the Commission to identify scientific areas where strong research environments were developing and also had an important structuring effect on the fast developing, technologically-oriented scientific communities in the genomics and post-genomics fields. Particularly the Integrated Projects, but probably also the Networks of Excellence, have been useful tools to support such activities. A majority of the current BMS infrastructures on the ESFRI Roadmaps have received research funding through FP6

[52] Economic cost-benefits analysis of the Community patent, B van Pottelsberghe & J. Danguy (2009). See: http://ec.europa.eu/internal_market/indprop/docs/patent/studies/compact-cost%20-benefit-study-final_en.pdf

and FP7. During FP6 a total of €62 million was directed towards research infrastructure–related activities using the different funding instruments available. During FP7, support to research infrastructures has already reached €168 million (J-E Faure, personal communication).

While the ESFRI process has undoubtedly been productive, the roots of pan-European collaboration on research infrastructures in biomedical research go back to the establishment of EMBL (European Molecular Biology Laboratory) in the 1970's. Supported by 17 EU Member States plus Iceland, Israel and Switzerland, EMBL has developed into a leading research and training institution and provider of key infrastructure services particularly in bioinformatics (EBI, European Bioinformatics Institute) and structural biology. EMBL researchers also participate in ESFRI projects in mouse biology, biological imaging, chemical biology and marine biology[53]. Other pan-European research infrastructures have also been established for structural biology. These include ESRF (European Synchrotron Radiation Facility) and ILL (Institute Laue-Langevin).

Recommendation 20

Research infrastructures on the ESFRI Roadmaps should undergo strategic evaluation to determine their scientific rationale, scope of services provided, their running costs and their funding possibilities.

BMS Infrastructures have been added to the ESFRI Roadmap in 2006, 2008 and 2010. The Expert group feels that the current landscape of infrastructures on the ESFRI Roadmaps cannot be the final one as there is overlap between BMS ESFRIs. Also the national ministries are finding it increasingly difficult to participate in the governance, construction and funding of more than a dozen life science infrastructures. Some condensation of activities is needed. The strategic review should also include an estimation of annual operational costs of BMS ESFRI infrastructures. Many Member States have invested considerable amounts of funds into health-related infrastructures over a long period of time, but the amount of such investments has not been studied in detail. However, such information is needed by the European Commission and the member states for planning future research budgets.

An additional concern has been expressed about the use of structural funds to support construction and equipment of research infrastructures. Such high-cost investments should always be accompanied with plans to increase general research funding to ensure sufficient technical support personnel and the researcher community. Otherwise expensive research equipment will remain underutilized.

Recommendation 21

Considering the important role of research infrastructures in providing services and access to technologies, repositories and data, develop a model for their sustainable funding through a joint effort of Member States and the European Commission; a set of indicators of the utility and performance of such infrastructures must be developed.

The ESFRI process is not without its problems. Importantly, ESFRI was initiated without any clear financial commitment from any party. Although the EC has substantially supported all BMS infrastructures, funding has been project-based or directed to the preparatory phase of limited duration. The only funding to pan-European research infrastructures that can be considered sustainable has been available from Member States to intergovernmental organizations such as EMBL.

[53] The EC and EMBL have signed a memorandum of understanding on cooperation. See: http://www.embl.de/aboutus/communication_outreach/media_relations/2011/110304_Heidelberg/index.html

The BMS infrastructures on the ESFRI Roadmap aim to develop as distributed infrastructures with nodes in many if not all member states and associated countries, thus providing services to the scientific community. In view of the proven added value of such research infrastructures, a request for a joint funding effort by member states and the European Commission is now well justified. Although the member states have made substantial commitments towards national research infrastructures, their willingness to support joint coordination activities outside national borders has not been clearly demonstrated. .

Recommendation 22

Establish common rules for research infrastructures to ensure true pan-European access to their services. This should include simplification of governance models and agreed principles on the methodology used for determining national contributions towards joint activities. EU-funded projects should be requested to make their results available to the scientific community through deposition data and samples in the pan-European research infrastructures.

Currently the participation rules and funding requirements of BMS research infrastructures have effectively ruled out the participation of new and small Member States in the construction phase of such infrastructures. The requirement of many BMS infrastructures to provide equal contributions regardless of GDP and population size makes participation into joint activities (coordination and common services) much more expensive for small Member States than for the EU-15 countries. Subsequently, rather than being inclusive during the preparatory phase, the BMS ESFRIs are becoming an exclusive activity of large and mid-size EU-15 countries during the construction phase. No common rules exist for determining the size of financial contribution to support joint activities.

The expert group considers it important to implement infrastructure initiatives like bio-banking and personalized medicine throughout the EU (including the EU-12 countries). Otherwise the pan-European collaborative dimension will not be achieved. Also the smaller countries need information derived from bio-banks and related health registries for designing knowledge-based national health policies. Furthermore, many EU-12 countries have been suggested to serve as "outdoor laboratories" for diseases caused by life style. To guarantee participation of the smaller and poorer member states in research infrastructures, pan-European agreements and guidelines about financial contributions (taking the size and economic situation of these countries into consideration) are needed to make the infrastructure initiatives truly pan-European.

Recommendation 23

Develop initiatives for public-private collaboration, such as PPP schemes to make research infrastructures accessible to SMEs and industry active in the field of medical diagnostics and drug development.

New innovative public-private partnership schemes should be developed to allow researchers from academia and SMEs as well as diagnostics and pharmaceutical industry to have better access to European research infrastructures for development of new products for health care. Such models are presented in the Business Plans of ESFRI infrastructures preparing to enter the construction phase.

The plan to establish "Expert Centers" within the pan-European Bio-banking infrastructure BBMRI[54] is a good example of applying the PPP model to ensure pan-

[54] See: http://www.bbmri.eu/

European access. According to the draft BBMRI-ERIC business plan, these Expert Centres will become novel non-profit Public-Private Partnership organisations, responsible for the analysis of samples in the country of origin under internationally standardised conditions and the generation of primary data. BBMRI Expert Centres will integrate pre-competitive public and private research and development activities by providing not only access to biological samples and medical data but also to the broad spectrum of medical and scientific expertise related to the samples and data. BBMRI Expert Centres will function as a focal point of contact between public and the private sectors. Human biological samples and medical data are provided as donations and are considered as common goods. Industry and SMEs require access to bio-specimens and data to discover and develop innovative products to keep or gain market leadership. Since commercialization of human bodily materials is forbidden (Oviedo Convention (ETS 164), the PPP-open access model of research collaboration would provide a sound basis for accessing human biological samples and associated medical data. Expert Centres that operate on a not-for–profit basis offer an efficient solution for this problem.

11. Gender issues

The panel strongly believes that the gender dimension and high female participation in science are potentially powerful drivers of change in the economy and society. If, as stated in the Innovation Union strategy, Europe needs at least one million more researchers by 2020, Europe cannot afford to lose female scientists from the career ladder. Innovation, in particular, requires all actors to be involved: a distinctive European approach should reinforce gender equality in all aspects of science and innovation activities.

Europe needs to continue its intervention on gender equality. Progress has been made but we are far from reaching the targets on the two relevant issues: "Research by women" and "Research for women". It is naïve to wait for self-correcting mechanisms, known to be too slow; active measures are still really necessary. This is clearly recognized in the Interim Evaluation Report of FP7[55].

Recommendation 24

A continuous assessment of the number of women participating in EU funded health research projects and of the gender impact of all health research should be a high priority for any future FP. Our target should be that at least 30% of coordinators (or co-coordinators) of large projects in FP8 are female.

The number of female coordinators of large FP7 Health projects is still very low (14.6%; this figure was 12.2% in FP6) and only the NoEs have a high share of female coordinators (42.9% in FP7; 23.1% in FP6). There are large differences between countries in the number of women coordinating projects. In FP7, leading countries are Belgium, France and Italy, where more than 1/3 of projects coordinated by these countries are coordinated by women scientists. Germany, Sweden, Denmark or Finland, however, have less than 15% of women among projects coordinated by their own scientists.

Recommendation 25

Indicators of gender should be included in the Innovation Union scoreboard. We propose that in the New Scoreboard of 25 indicators of the Innovation Union, in the "Human Resources" group, the following points should be added:

[55] See pages 44-46 in http://ec.europa.eu/research/evaluations/index_en.cfm

(1) Proportion of women PhDs (ISCED6) in the fields of Science and Engineering and in the Medical Sciences, and
(2) Proportion of female full Professors in the public academic sector.

If not included in continuous monitoring instruments, gender issues may continue to be considered "dispensable". Results from different questionnaires show that the issue of gender equality attracts less interest or is considered less relevant than other issues related to science and society.

We support the invitation of the Competitiveness Council (May 2010) to the Commission to consider the feasibility of a "Communication on Gender and Research Beyond 2010" and that such a communication should include an emphasis on Health and new technologies.

The ERC will award 427 projects in the third Starting Grant call of FP7; 26.5% of the grantees are women, which is only a minor increase from last year's 23%. The same percentage of women scientists is seen with FP7 Health projects (25%). This demonstrates that progress in increasing women's participation in EU research is slow, even in the youngest group of scientists.

The EU initiatives, activities and policies on the progress of Women in Science are very well described in the document "Stocktaking 10 years of "Women in Science" policy by the EC 1999-2009 (2010)[56]. This document states that the main achievement of these 10 years of activity has been the identification of the problem. In order to get the message out to all concerned, the EC has funded some projects that we consider important: GenSET[57] and GENDERA[58], and is planning a comprehensive communication campaign to be launched in 2011.

The Health Directorate should continue to cooperate with the Unit responsible for gender issues on all gender-related aspects of health research and innovation. Efforts to attract higher numbers of women into research related to health, and not only to clinical practice, should be among the promoted institutional actions at the EU level. There is a recognized need (Competitiveness Council of May 2010) for "reinforcement of the structural change programme for the modernization of research institutions, together with the reinforcement of the integration of the gender dimension in European research".

Training and education

The Europe 2020 and the Innovation Union strategies include an objective to increase R&D spending to 3% of GDP by 2020. It is obvious that if this goal is to be reached, it must be accompanied with a substantial increase in the number of highly trained researchers and support the development of future European leaders in health research. It is estimated that about one million new research jobs are expected. However, surveys show that Europe is running out of well-trained physician-scientists (physicians who have trained in basic scientific research, "MD-PhDs") who are capable of working together and with other clinical trial professions[59]). At the same time patient-oriented research is becoming increasingly multidisciplinary, with new technologies constantly appearing. In many cases young investigators are not being sufficiently well trained to cope with this multidisciplinary environment. In a worst-case scenario this situation leads to a real and damaging decline of patient-oriented research and related studies in Europe and greatly

[56] http://ec.europa.eu/research/science-society/document_library/pdf_06/stocktaking-10-years-of-women-in-science-book_en.pdf
[57] See http://www.genderinscience.org
[58] See http://www.gendera.eu/index.php5?file=12
[59]ESF Forward Look – Investigator-Driven Clinical Trials, 2009; see: http://www.esf.org/fileadmin/links/EMRC/FL_IDCT.pdf

reduces the competitiveness of Europe in the field of clinical research and related research on drug development and diagnostics. Several years ago, the European Medical Research Councils (under ESF) proposed a common training syllabus for clinical investigators[60]), but it has not been fully implemented.

The pharmaceutical and technology industries are also aware of the importance of a critical mass of researchers. Both IMI and EFPIA have recognized the need to train new researchers in all the different areas of medicines research, from basic research, preclinical development and translational medicine to clinical development and pharmaco-vigilance. The IMI is supporting four European Research Training Networks that provide many of the competences needed in medicines research. However, to our knowledge, there is no any equivalent made for medical devices.

Structured training programmes at master's and Ph.D. level, and for clinical researchers (M.D./PhDs) in translational medicine, systems medicine and personalized medicine are particularly important for EU-12 countries to help talented your people in these countries to enter the EU health research workforce. Such training programmes are also needed to attract talented young people coming from developing countries. Thereafter, Marie Curie scholarships should be made available for PhDs from EU-12 and non-European countries to carry out their post-doctoral studies in the leading European and North American laboratories. Harmonization of training programmes is also for importance for EU-wide collaborative projects. Another important element of collaboration is development of research-based treatment guidelines for the use of the entire European medical profession.

Recommendation 26

The European Commission and all member states should cooperate to solve the problems related to recruitment and career development of young graduates, particularly in clinical research and R&D. Harmonization of European training programmes, transparent promotion criteria and removal of the many obstacles remaining in international mobility and in careers of female scientists are urgently needed. Participation of young researchers from EU-12 countries in FP8–funded research should be facilitated through Marie Curie scholarships and other EU schemes.

[60] A European Syllabus for Training Clinical Investigators, 2003; see: http://www.esf.org/index.php?eID=tx_ccdamdl_file&p%5Bfile%5D=4441&p%5Bdl%5D=1&p%5Bpid%5D=3829&p%5Bsite%5D=European%20Science%20Foundation&p%5Bt%5D=1302192401&hash=c553ab6cad55bb63aea37d0bbc69e8dc&l=en

12. Expert Group methodology

The Expert panel was established at the end of November 2010. It comprised eight experts and was chaired by Dr Eero Vuorio. Throughout its work, the panel was supported by a team of EC officials from the Health Directorate.

Six meetings were held in DG Research & Innovation premises in Brussels. A preliminary meeting took place on 10 December 2010; this was followed by five full-day meetings, with the last one organised on 4 April 2011.

As part of the first three meetings, presentations were given by EC officials and key documents provided to the panel in printed form and/or in electronic form on the DG RTD web tool CIRCA to provide on the different issues that the panel might consider relevant for its work. The fourth and fifth meetings were mostly dedicated to interviews of Heads of Unit and Director of the Health directorate in DG RTD, Dr Ruxandra Draghia-Akli.

The outcome from the work of the Expert panel is the present 30 page report including 26 recommendations with justifications for the future of EU-funded Health research. The final version of the report was submitted to the Commission services by the panel chairman in May 2011. This report and the Health Directorate's own 'vertical report' together constitute the Health FP8/CSF Ex-Ante Impact Assessment.

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- BBMRI an evaluation strategy for socio-economic impact assessment, Technopolis, Sept. 2010
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- IMI - Accompanying document to the Proposal for the Council decision on the setting up the Innovative Medicines Initiative Joint Undertaking, may 2007
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- Innovation Union package: rationale, communication & PowerPoint presentation
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Annexes

Annex 1 - FP6 LifeSciHealth: breakdown of projects funded according to subject area, and budget (2002-2006)

Activity field	Project funded	EU Contribution (€)
1. Advanced genomic and its applications for health		
1.1 Fundamental knowledge and basic tools for functional genomics in all organisms		
1-1-1 Gene Expressions and Protomics	32	129.825.626
1-1-2 Structural Genomics	17	84.481.626
1-1-3 Comparative genomics and population genetics	24	103.365.277
1-1-4 Bioinformatics	9	36.126.848
1-1-5 Multidisciplinary Functional Genomics Approaches to Basic Biological Processes	46	250.849.079
1.2 Applications of knowledge and technologies in the field of genomics and biotechnology for health		
1-2-1 Rational and accelerated development of new, safer, more effective drugs	20	97.168.773
1-2-2 Development of new diagnostics	34	106.876.408
1-2-3 Development of new in vitro tests to replace animal experimentation	19	61.054.718
1-2-4 Development and testing of new preventive and therapeutic tools	46	198.904.169
1-2-5 Innovative research in post-genomics, which has high potential for application	29	148.488.483
2. Combating major diseases		
2.1 Application-oriented genomic approaches to medical knowledge and technologies		
2-1-1 Combating cardiovascular diseases, diabetes, and rare diseases	47	234.864.315
2-1-2 Combating resistance to antibiotics and other drugs	21	85.185.973
2-1-3 Studying the brain and combating diseases of the nervous system	44	156.748.673
2-1-4 Studying human development and the ageing process	16	62.996.396
2-2 Combating cancer	68	316.814.517
2-3 Confronting the major communicable diseases linked to poverty	73	229.146.910
3. Scientific Support to Policies		
Horizontal actions across LifeSciHealth	51	24.979.201
Scientific Support to Policies Activity**	50	72.593.780
Total	**646**	**2.400.470.255**
EDCTP	**163**	**311.100.000***

* Includes EC contribution (€132.26 million), Member States contribution (€115.69 million) and third party contributions (€63.15 million)

** Includes 30 Health policy projects and 20 SARS (Severe Acute Respiratory Syndrome) and influenza projects.

Annex 2 - FP7 Health: breakdown of projects funded according to subject area, and budget (2007-2010)

Activity field	Project funded	EU contribution (€)
1. Biotechnology, generic tools and medical technologies for human health		
1.1 High-Throughput Research	15	88.243.375
1.2 Detection, diagnosis, monitoring	33	152.853.178
1.3 Predicting Suitability, Safety and Efficacy of Therapies	6	30.069.413
1.4 Innovative Therapeutic Approaches and Interventions	28	199.632.235
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	16	152.583.489
2.1.2 Systems Biology	36	220.468.643
2.2 Research on the brain and related diseases, human development and ageing		
2.2.1 Brain and Brain-related diseases	29	133.727.405
2.2.2 Human Development and Ageing	9	53.134.518
2.3 Translational research in major infectious diseases: To confront major threats to public health		
2.3.1 Anti-microbial Drug Resistance	15	64.700.136
2.3.2 HIV/AIDS, Malaria, Tuberculosis	45	201.755.473
2.3.3 Potentially New and Re-emerging epidemics	22	95.026.686
2.3.4 Neglected Infectious Diseases	10	38.876.671
2.4 Translational research in other major diseases		
2.4.1 Cancer	47	204.785.503
2.4.2 Cardiovascular Disease	19	119.746.137
2.4.3 Diabetes and Obesity	14	57.282.477
2.4.4 Rare Diseases	27	108.963.806
2.4.5 Other Chronic Diseases	24	133.794.449
3. Optimizing the delivery of health care to European citizens		
3.1 Translating Clinical Research into Practice	26	67.526.756
3.2 Quality, Efficiency and Solidarity of Healthcare Systems including Transitional Health Systems	22	59.507.916
3.3 Enhanced Health Promotion and Disease Prevention	14	43.636.522
3.4 International Public Health & Health Systems	34	77.930.001
4. Other actions across the Health theme		
4.1 Coordination an Support Action Across the Theme	21	17.193.602
4.2 Responding to EU Policy	39	127.989.477
4.3 Specific International Cooperation Actions (SICA)	13	49.359.432
Total	**564**	**2.498.787.301**
IMI	**15**	**281.249.724***

*Including IMI funding derived from FP7 (€109.6 million), EFPIA funding (€132.6 million), and other funding (€39 million)

Annex 3 - Instruments and participants in FP6 LifeSciHealth and FP7 Health research projects

Table 1: FP6 LifeSciHealth projects

Project Instrument	Nb. of projects	Nb. of participants	Average participation	Total EU Contribution	Average EU Contribution per project (€)	Average EU contribution per partner (€)
STREP	347	3,015	8.7	743,953,314	2,143,958	246,750
Integrated Project	123	2,481	20.2	1,195,114,002	9,716,374	481,706
Coordination Action	32	498	15.6	38,346,563	1,198,330	77,001
Support Action	105	568	5.4	42,614,593	405,853	75,025
Network of Excellence	39	1,283	32.9	380,441,783	9,754,918	296,525
Total	**646**	**7,845**	**12.1**	**2,400,470,255**	**3,715,898**	**305,987**

Table 2: FP7 Health projects

Project instrument	Nb. of projects	Nb. of Participants	Average participation	Total EU Contribution	Average EU Contribution per project (€)	Average EU contribution per partner (€)
Focused Project	377	3,562	9.4	1,281,826,868	3,400,071	359,862
Integrated Project	97	1,711	17.6	1,040,088,457	10,722,561	607,883
Coordination Action	45	546	12.1	70,327,223	1,562,827	128,804
Support Action	38	241	6.3	24,566,671	646,491	101,936
Network of Excellence	7	163	23.3	81,978,083	11,711,155	502,933
Total	**564**	**6,223**	**11.0**	**2,498,787,301**	**4,430,474**	**401,541**

Table 3: Comparison between FP6 LifeSciHealth projects and FP7 Health projects

Project instrument	Change in average participation per project from FP6 to FP7	Change in average EU contribution per project from FP6 to FP7	Change in average EU contribution per partner from FP6 to FP7
Focused Project (previously STREP)	+8.0%	+58.6%	+45.8%
Integrated Project	-12.9%	+10.4%	+26.2%
Coordination Action	-22.4%	+30.4%	+67.3%
Support Action	+16.7%	+59.3%	+35.9%
Network of Excellence	-29.2%	+20.1%	+69.6%
Total	**-9.1%**	**+19.2%**	**+31.2%**

Table 4: Type of organisations participating in FP6 LifeSciHealth and FP7 Health

FP6 LifeSciHealth *			**FP7 Health****		
Organisation type	**Total**	**%**	**Organisation type**	**Total**	**%**
Academia	3,609	46.0%	Academia	3,083	49.5%
Research Organisations	2,251	28.7%	Research Organisations	1,729	27.8%
Large companies	584	7.4%	Large companies**	240**	3.9%**
SMEs	584	7.4%	SMEs	738	11.9%
Other	602	7.7%	Other	126	2.0%
Unknown	215	2.7%	Public entities	307	4.9%
Total	**7,845**	**100%**	**Total**	**6,223**	**100%**

* EDCTP initiative is not taken into account
** IMI initiative is not taken into account

Annex 4 – Participation and received EU contribution rate by country in FP6 LifeSciHealth (2002-2006) and FP7 Health (2007-2010)

Country		FP6 LifeSciHealth*		FP7 Health*	
		Participation (%)	EU contribution (%)	Participation (%)	EU contribution (%)
EU-15	Germany	16.9%	18.7%	14.3%	16.2%
	United Kingdom	13.6%	16.4%	14.4%	17.0%
	France	11.5%	12.7%	9.8%	11.2%
	Italy	9.5%	8.7%	8.5%	7.5%
	The Netherlands	6.9%	8.2%	7.2%	9.2%
	Sweden	5.1%	5.7%	4.5%	5.5%
	Spain	5.4%	4.4%	5.2%	4.6%
	Belgium	4.1%	4.2%	4.3%	3.9%
	Denmark	2.9%	3.2%	2.3%	2.5%
	Austria	2.7%	2.4%	2.2%	2.4%
	Finland	1.8%	1.9%	2.0%	2.2%
	Greece	1.1%	0.9%	1.3%	1.1%
	Ireland	0.9%	0.6%	1.2%	1.3%
	Portugal	0.8%	0.4%	0.8%	0.4%
	Luxembourg	0.1%	0.0%	0.1%	0.0%
EU-12	Hungary	1.3%	0.8%	0.9%	0.4%
	Poland	1.5%	0.7%	1.3%	0.6%
	Czech Republic	1.3%	0.6%	0.7%	0.4%
	Estonia	0.6%	0.3%	0.6%	0.3%
	Slovenia	0.5%	0.3%	0.6%	0.2%
	Slovakia	0.3%	0.1%	0.2%	0.1%
	Latvia	0.2%	0.1%	0.2%	0.0%
	Lithuania	0.2%	0.1%	0.3%	0.2%
	Romania	0.1%	0.0%	0.6%	0.2%
	Cyprus	0.1%	0.0%	0.1%	0.0%
	Bulgaria	0.1%	0.0%	0.3%	0.1%
	Malta	0.0%	0.0%	0.0%	0.0%
Associated countries	Switzerland	4.1%	3.9%	4.3%	4.3%
	Israel	1.6%	1.5%	1.3%	1.3%
	Norway	0.9%	0.8%	1.1%	1.1%
	Iceland	0.2%	0.4%	0.2%	0.3%
Rest of the world	United States	0.3%	0.1%	1.1%	0.7%
	Russia	0.5%	0.2%	0.6%	0.3%
	China	0.4%	0.2%	0.4%	0.2%
	Other countries	2.5%	1.5%	7.1%	4.3%
EU-15		**83.3%**	**88.4%**	**78.1%**	**85.0%**
EU-12**		**6.2%**	**3.0%**	**5.8%**	**2.5%**
Associated Countries		**6.8%**	**6.6%**	**6.9%**	**7.0%**
Rest of the world		**3.7%**	**2.0%**	**9.2%**	**5.5%**
Total		**100%**	**100%**	**100%**	**100%**

* EDCTP and IMI initiatives are not taken into account
** Including Romania and Bulgaria which where Associated countries during FP6

Annex 5 - Questionnaire methodology

The survey was carried out from October – December 2010. PI records for FP6 and 7, both of participants and co-ordinators, were extracted from the EC CORDA database. The total number of PI listed was 12,460, of which 6,774 were FP6 and 5,686 were FP7. The data were cleaned for duplicates (a number of PI are participants or co-ordinators in more than one project) resulting in surveys being sent to 10,197 PI.

Data were further cleaned to remove obviously incorrect responses (e.g. an answer of 9,999 to the question asking for the number of patents for which the PI is listed as an inventor). 12 full questionnaires were excluded because of such answers.

A final number of 2,245 questionnaires were analysed. These 2,245 questionnaires account for 22.0% of the total number of unique contacts.

A comparison between the actual gender participation rate, country participation rate and organisation participation rate in our programme and in the questionnaire was performed. The coefficient of correlation r^2, is used to determine whether two data sets are related, and if so, how strongly. The correlation coefficient ranges from +1, indicating a perfect positive linear relationship, to -1, indicating a perfectly negative linear relationship. In this case r^2 is 0.9938, i.e. the data from the questionnaire and CORDA are almost perfectly correlated.

Example of extrapolations:

Number of publications claimed by 2,245 participants (22.0% of all participants) = N_q
Total number of publication for all FP6 and FP7 Health participants = $N_q \times 100 / 22.0 = N_e$

Annex 6 - Questionnaire

FP6 / FP7 IMPACT ASSESSMENT – HEALTH DIRECTORATE - QUESTIONNAIRE	
I. Identification and affiliation	
1	Age group *18-25 / 26-39 / 40-64 / 65 or older*
2	Gender
3	Country where you are currently carrying out EU funded collaborative research
4	Affiliation: *Academic researcher / SME manager or employee / Clinician / Employee of large company / Employee of a patient organization / Other (please specify)*
II. Projects you have participated in and reasons for participation	
5	In how many FP6 and FP7 Health projects altogether have you participated or are you participating?
6	What were you looking for by joining EU collaborative project(s)? Please score each reason below on a scale of 0 [not relevant] to 5 [very important] *1. Funding not available in your country for this type of project(s)* *2. Large scale or scope of the research objectives that cannot be achieved within your own country or institution (such as: number of cases for study of rare diseases, large scale cohorts, or clinical trials)* *3. Access to multidisciplinary academic expertise* *4. Links to industrial expertise* *5. Access to other expertise (e. g. project management, dissemination)* *6. Access to special resources and infrastructures* *7. Integration in a EU network* *8. Other (please specify)*
III. Output	
7	What were the most important outputs of your project(s)? Please rank your 5 most important outputs by order of priority: [1: least important; 5: most important]. - Please comment briefly as you wish. *1. Research results published in "high impact" Journals* *2. New resources, including infrastructures, available to the scientific community* *3. Research field significantly expanded beyond the initial state of the art* *4. Contribution to international research initiatives* *5. Networking and/or coordination of science beyond your own institution* *6. New or improved products (drugs, diagnostics, technologies, tools, etc.)* *7. New or improved protocols* *8. Patents* *9. Training Programmes* *10. New companies (SMEs), development of existing ones, job creation* *11. Outputs of clear benefit to patients, to their health and quality of life* *12. Important (large scale) data sets made freely available to the scientific community* *13. Other important outputs (please specify)*
8*	Brief comments on output
9	On a scale of 0 to 5 what proportion of the project output would have been achieved without EU funding? [0: none of it - 5: all of it]
10	On a scale of 0 to 5, what proportion of the project output became available only after the contract had ended? [0: none of it - 5: all of it; tick N/A if your only contract is currently ongoing]
IV. Publications	
11	How many PubMed-listed publications, with you or someone from your group as first author, did your project generate? (Please give an average per project if you were involved in several projects)
12	How many of these publications were published after the end of the project?

V. Funding	
13	What percentage (estimate) of your total research funding is covered by this (these) project(s)?
14	Did EU funding for collaborative projects facilitate access to other funds to expand or continue your work?
15*	If yes, where did this funding come from? *1. EU FP* *2. ERC grants* *3. Marie Curie fellowships* *4. National, regional or local agencies in your country* *5. International programmes or agencies* *6. Private foundations or medical charities* *7. Industry such as large pharmaceutical companies, SMEs* *8. Business angels or venture capitalists* *9. EU Risk-sharing Finance Facility (RSFF)* *10. Other (please specify)*
16	What percentage (estimate) of your current research funding is derived from this leverage effect?
17	What percentage (estimate) of the transnational activities of your team (e.g., bilateral collaborations, participation in international programmes or initiatives, etc.) do your EU-funded collaborative projects represent?
VI. Jobs	
18	Please estimate how many jobs your project participation generated under the following categories (Please give an average estimate if you were involved in several projects) *PhD students / Post-doctoral fellows / Technicians and support staff / Longer-term jobs created in relation to the project (additional staff hired in view of project exploitation, e.g. in a spin-off company)*
VII. SMEs	
19	Did you create one or more SME(s) in relation to your work in the project(s)?
20*	If yes, how many?
21	Did these SMEs continue to operate after the end of the project?
22	Do you envisage creating one or more SME(s) in relation to your work in the project(s)?
VIII. Patenting	
23	On how many patent applications arising from your project(s) are you (and/or members of your own group) listed as inventor?
24	How many of these patents have been granted?
25	How many have been licensed to outside parties?
IX. Sustainability	
26	Have any of the research networks involved in your finished project(s) formally continued to operate after the end of your project?
X. Overall impact	
27	For your EU collaborative projects, please rank below the 5 most important impacts by order of priority: (1:least important;5:most important) *1. Strengthen the competitiveness of European science* *2. Strengthen the competitiveness of European industry* *3. Significantly advance the state of the art in your field* *4. Contribute to the sustainable development of your field (new funding streams, young scientists to develop the area, infrastructures, etc.)* *5. Foster a spirit of scientific cooperation* *6. Enhance coordination of different funding agencies* *7. Other (please specify)*
XI. Innovation	
28	What would you propose as the best indicator to measure "innovation" in health research?

*Not compulsory

Glossary

Associated Countries: Associated to the Framework Programmes, these are non-EU countries that have signed science and technology cooperation agreements, and which have contributed financially to the Framework Programme budget: Switzerland, Israel, Norway, Iceland and Liechtenstein, Turkey, Croatia, the Former Yugoslav Republic of Macedonia and Serbia Albania and Montenegro, Bosnia & Herzegovina, Faroe Islands, Republic of Moldova.

Member states: Members of the EU. These are sometimes grouped as EU-15 and EU-12 for the purposes of analysis of differing participation in FP (amongst other programmes). **EU-15:** 15 countries: Austria, Belgium, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Luxembourg, Netherlands, Portugal, Spain, Sweden, and United Kingdom. **EU-12:** 10 countries which joined the EU on 1st May 2004 (Cyprus, Czech Republic, Estonia, Hungary, Latvia, Lithuania, Malta, Poland, Slovakia, Slovenia) and the 2 countries which joined the EU on 1st January 2007 (Bulgaria, Romania).

EU contribution: EU contribution received by organisations through their participation in EU funding programmes.

Framework Programme: The Framework Programmes for Research and Technological Development, also called Framework Programmes or abbreviated FP1 through FP7, are funding programmes created by the EU in order, broadly speaking, to support the EU's scientific and technological bases and its industrial competitiveness in those domains.

SMEs: The category of micro, small and medium-sized enterprises (SMEs) is made up of autonomous enterprises which employ fewer than 250 persons, which have an annual turnover not exceeding EUR 50 million, and/or an annual balance sheet total not exceeding EUR 43 million. Commission Recommendation 2003/361/EC.

Third countries: Any country that is neither a Member State nor an Associated Country.