Alliance for Biomedical Research in Europe

Consultation on the Advisory group report for the Horizon 2020 Societal Challenge on Health, Demographic Change and Well-being

WHO YOU ARE:	The Alliance for Biomedical Research in Europe (BioMed Alliance) is a non-profit organization representing 22 leading European research and medical societies uniting more than 400,000 researchers and health professionals.
	The BioMed Alliance is committed to promoting excellence in European biomedical research and innovation with the goal of improving the health and well-being of all European citizens.
	BioMed Alliance aims:
	• To provide a platform for our members to speak with a unified voice and interact with EU policy makers on key topics for European biomedical and health research • To provide recommendations for policy and decision makers on facilitating and improving biomedical research in Europe • To advocate for an EU regulatory environment that promotes European excellence and innovation in biomedical research by adopting specific policy statements • To ensure that the European Research Area is supported with sustainable research policies and adequate funding programmes at EU-level to tackle future societal challenges
	The BioMed Alliance has addressed important issues for biomedical and health research in the EU such as: changes to the EU Data Protection Regulation, the EU research budget and European Citizens' Initiatives that could hamper research. BioMed Alliance statements followed by meetings with decision makers have contributed to positive developments on data protection regulation and on securing the budget allocated to Horizon 2020.
	BioMed Alliance's members:
	European Association for the Study of Diabetes (EASD), European Association for the Study of the Liver (EASL), European Association of Nuclear Medicine (EANM), European Atherosclerosis Society (EAS), European CanCer Organisation (ECCO), European College of Neuropsychopharmacology (ECNP), Federation of European Biochemical Societies (FEBS), European Federation of Immunological

Societies (EFIS), European Academy of Neurology (EAN), European Hematology Association (EHA), European League Against Rheumatism, (EULAR), European Respiratory Society (ERS), European Society for Paediatric Research (ESPR), European Society of Anaesthesiology (ESA), European Society of Cardiology (ESC), European Society of Hypertension (ESH), European Society of Human Reproduction and Embryology (ESHRE), United European Gastroenterology (UEG), European Academy for Allergy and Clinical Immunology (EAACI), European Society of Pathology (ESP), European Society of Endocrinology (ESE), European Organisation for Research and Treatment of Cancer (EORTC).

Vertical Themes	YOUR OPINION (on the proposed theme)	'YOUR RATIONALE (i.e. The expected impact of your proposed changes on Health, Demographic Change or the Well-being of European Citizens; the possible impact on businesses - in particular SMEs - on economic growth and job creation; the potential socio-economic outcome or contribution to the definition or the implementation of health policies...)
	Overview The Biomedical Alliance welcomes the report of the Advisory Group. The Biomedical research community is concerned that the document is too general and lacks definition. Key words and ideas included in the report are already widely endorsed by stakeholders. We are glad to notice that the report stress that the establishment of European Reference Networks (ERNs) will allow for enhanced research development beyond health care. Specific calls for European Clinical Research Networks should be fostered to exploit in full the research potential of experts' networking and clustering by disease areas. We would like to point out that research is not the primary aim of ERN in the current legal-administrative framework.	

	Moreover, research infrastructures non involving health care providers cannot become official members of ERN. Therefore, the EU will have to correct the composition of the ERN allowing the full participation of major research actors that bring expertise and resources that health care providers cannot supply. Global recommendation is to avoid duplication of research infrastructures that already exist and have proven records. Existing infrastructures should be better used rather than the wheel being reinvented.	
1. Personalized medicine	Funding has been already invested in numerous projects but the fact is that personalized medicine is not implemented yet. Precision medicine in Europe has not received support as has occurred in the US. Therefore the success in precision medicine is fortuitous, rather than a result of structural solutions. Recommendations for research environment able to support the necessary personalized medicine development steps are lacking. The patient should be put at the center. Currently sponsors create clinical trials and recruit patients eligible for their protocol. This has proven to be inefficient for a number of reasons: rarer subgroups for too few patients overall accessing clinical research. Hence the need for solutions where the starting point is the patient with the full information on the biology of the disease, searching for the matching protocol and treatment. Obviously this needs a completely different architecture and transformation of clinical research. Placing that patient at the center is bringing true solutions for needed therapeutic progress. In many places, the document seems more business oriented than promoting knowledge development. Complex clinical trials targeting genomic alteration may not be useful if these alterations are not connected with health effects and the underlying biological mechanisms. For instance, there are no pragmatic solutions proposed to address the new routes depicted in figure 1. We agree with the report which emphasizes the fact that BBMRI has not solved the issue leaving researchers with	The EU has an essential role in shaping a European environment that is conducive to personalized medicine, including the framework for clinical trials, access to data and human biosamples. Using existing biosample collections is an opportunity to explore personalized therapy in a post hoc, hypothesis-generating fashion. Continued collaboration and further implementation of a strong public – private partnership between academia and research institutes, biotech and SMEs, and large companies are essential in the development of personalized medicine, and require policy support. Implementation of guidelines and outcome studies has uncovered that the diversity in the general population precludes a 'one size fits all' approach to common clinical conditions, and that the current stratification is insufficient. Better definition of patient subpopulations

poor access to biological material, hence the need for alternative solutions. The quality of the research is of utmost importance. External validity is an issue also in the personalised medicine area. Evidence generated by clinical trials is often not generalizable to the entire population.	through better personalized diagnosis in the framework of novel disease classifications can reduce cost and increase efficiency of clinical trials. Subsequent personalized treatments targeting those who are most likely to benefit from a novel therapy can help to reduce the risk of treatment failure and cut unnecessary expenditures. Specific markers may allow targeting new therapies to patients who would benefit most. Existing European solutions are not patient centered and this needs to be changed, this is the next challenge to take. The generation of high-quality data and research material will allow academic, SME and pharma research to progress more rapidly. Anti-data including practices will ensure wide knowledge transfer and access to data for the whole research stakeholders. It will decrease the duplication of research and decrease the costs of treatment development. It will support more efficient drug development. Better drugs will be more rapidly on the market for the benefit of the patients and health systems.

	Common diseases such as musculoskeletal disorders and neurodegenerative disorders are not covered in the report. In the last 5 years a totally new diagnostic and therapeutic approach to these extremely expensive diseases has occurred. The combination of genetics and protein research has led to the area of brain research on disease modifying therapies that could also be applied to other fields of medicine. If properly funded, a major breakthrough here is likely.	
	Specifically, based on the fact that the numerous discoveries in genetics, especially on single nucleotide polymorphisms (SNPs) have not been leading to the elucidation of any impaired cellular functions, it is important to extend these studies by analyzing molecular "on-off switches" on these polymorphisms (functional genomics). After analysis of these genes, so called gene-scissors should be employed to delete the "bad genes" with the novel CRISPR technologies.	
2. Rare diseases	Molecular profiling, biomarker oriented clinical study involving new drug but also other treatment modalities such surgery and radiotherapy are essentials. As outlined in the report Private-Public-Partnership have a role to play when developing new treatments and diagnostic tools in very low prevalence diseases. We would like to stress the importance of fully investigating the biology of the disease prior embarking in expensive clinical development. The lack of knowledge in the biology of rare diseases prevents developing adequate treatments. Therefore, it would have seemed logical that research be the starting point to deliver good care.	Patients with rare diseases deserve high quality research producing safe and efficient treatments. Care can only be delivered if biology is understood and the fact that Europe keeps splitting research and care generate missed opportunity such as exploring solution that develop alongside the continuum of the disease which evolves over time.

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3. Non-communicable diseases	There is no question; we need more basic research and its translation to the clinic.	
	It is also strongly emphasized that we need research into how to sustainably change individual behaviors. However, we already know much about the deleterious effects of negative life-style factors and successful interventions are much dependent on national guide-lines and media support, political measures including taxation. These measures have had positive effects in several countries in, for instance, smoking habits while European holistic approaches as suggested are very expensive and difficult to co-ordinate across different countries.	
	Regular genetic approaches based on large-scale identification of genetic polymorphisms have had very limited success in spite of huge funding efforts. The interaction between genetics and life-style factors is increasingly recognized to involve epigenetic regulations and this novel research field requires a prominent place in future Horizon 2020 programs.	
	Well being and healthy aging is very strongly related to most non-communicable diseases (headache, diabetes, obesity, cardiac dysfunction, respiratory disease, chronic brain disease, rheumatic and musculoskeletal disorders).	
	Translational research is funded by many different streams which makes Europe very competitive. Also novel basic findings and clinical research can be identified and tested and where exploratory clinical trials can be planned and executed. This could radically cut the long delays in translating important basic findings into the clinical setting and strongly improve European competitiveness and delivery of new therapeutic possibilities	
	Hardly anything is in the program which relates to the expensive surgical procedures and the preventive measures for avoiding surgical intervention (orthopedic intervention).	

	What is entirely missing is the interaction of internal organs and the nervous system. **Gastrointestinal system – immunology – nervous system** The identified research questions are relevant, but it will be difficult for research projects to concretely deliver if the goals are too open. Disease specific research is needed to complement research across NCDs (common risk factors & multimorbidities). The report should outline clear deliverables and focus on specific areas. An example could be: *"We want to cure Dementia in 20 years"* *"We want to reduce obesity in Europe in 20 years"* *"We want that everybody in Europe runs every day 1 mile"*	If calls are too open, the eligibility & success rate will be low. Research programmes need to deliver concrete innovative solutions for the prevention and treatment of NCDs. 1) To employ novel strategies to study the molecular and cellular basis of c inflammatory conditions, including rheumatic and musculoskeletal diseases (RMDs) with state of the art technologies. Based on the fact that the numerous discoveries in genetics, especially on single nucleotide polymorphisms (SNPs) have not been leading to the elucidation of any impaired cellular functions, it is important to extend these studies by analyzing molecular "on-off switches" on these polymorphisms (functional genomics). After analysis of these genes, so called gene-scissors should be employed to delete the "bad genes" with the novel CRISPR technologies. 2) To understand the complex interactions between genetic and environmental risk factors, such as obesity - nutrition, hormonal factors, inhaled pollutants and other lifestyle exposures, which together with hereditable predispositions lead to the development of RMDs. 3) To identify reliable prognostic tools, which

		would integrate specific biomarkers, genetic and epigenetic risk markers and environmental exposures into a scale to predict development, disease progression and response to therapy in RMDs.
		4) To develop primary and secondary prevention of inflammatory conditions, which could include lifestyle interventions (i.e. reducing obesity, improving oral health) or medicinal interventions that have demonstrated their effectiveness to reduce the risk of developing specific inflammatory disorders.
		5) To predict the response to different targeted therapies in inflammatory conditions : All targeted therapies, biological or small molecules, convey similar response rates and it is currently unknown if the good responders, which amount to about 15-20% of the patients who start a given treatment after failing conventional therapies, comprise the same or different patient populations. Current decisions are, therefore, based on trial and error rather than stratifying by elements predicting who will respond to which specific therapy. This leads to a huge waste of societal resources, since these therapies are quite costly and used without benefit, waiting for response, or non-response to occur. Finding biomarkers which predict response to specific

		targeted therapies would enable more focused use of treatment choices, decrease societal expense and reduce individual suffering.
4. Public health and prevention including migration	It is important to identify environmental risk factors that have an adverse effect on patient's health. Many of these have already been identified but measures to correct them have yet to be proven. Reducing tobacco consumption as had the desired effect and various preventions programs have been proven. Screening is in its infancy and quality assurance and participation is key in breast and bowel screening programs. Lessons learnt from these can be transferred to other screening potential areas. Tackling obesity and efforts to reduce it has not been proven. Modification of the environment to improve mental health need proof. The environment also includes the gut microbiome. There is no doubt accurate data recording and access to properly biobanks is essential and given patients right to confidentially complete data capture is impossible. The need to collect data needs infrastructure in terms of personnel and IT	

	Migrants have been singled out but the positive contribution that they bring in terms of age and the need to keep them healthy with vaccinations and affordable treatment so they can work and have a quality of life. Fertility and treatment needs regulation. Controlled trials to demonstrate efficacy and assisted reproduction techniques need to be instituted. Healthy ageing and the avoidance of dementia needs to be a priority.	
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1. Big Data	The quality of primary data to be included in big data efforts is fundamental otherwise the big data outcomes will not be reliable. The data quality aspect is covered under the point on personalized medicine. EU should really focus on improving the standardization of data by recommending (imposing) the use of standards like CDISC and DICOM. Furthermore, interoperability between software and other tools should be promoted. Big data process involving complex modelling and other algorithm appear often as black box. Big data outcomes must be clinically validated in adequately designed and powered clinical research projects to prove the reliability of big data exercise. The balance with protection of patient's right to confidentiality and the use of patient data for societal benefits and population well-being need to be balanced and legislations aligned. Today, the opposite is happening.	Reliable big data approaches will allow analyzing and understanding massive and complex datasets. This will support the development of personalised medicine. A real free flow of high quality data supported by big data infrastructure and tools will serve medical and technological development. Candidate new technologies can be identified quickly and their preliminary usefulness assessed based on existing data and simulation. This will allow candidate new technologies to be well prepared before any clinical validation in humans.

	We are supportive of the announced European Open Science Cloud since it would help braking the current data silos and others knowledge secluding practices. However, attention must be paid to the protection of the data by efficient anonymisation methods. Access to data should be controlled. The purposes of these data use should be scrutinized. Misleading or wrong data analysis could harm patients and create false hope. One has to be kept in mind that generating high quality clinical data is a very expensive endeavors and opportunistic use of data should be prevented. Business model should be developed insuring the sustainability of such repository on the side of the repository maintenance as well as compensation aspects for data providers. We need public support to make it happen but political involvement will be critical. Data access and sharing needs technology, but may be more, change of mentality supported by firm pushes from legislators. Private-Public-Partnerships have a major role to play ensuring efficient molecular screening and data collection from longitudinal cohorts independently by academia supported by public funding in collaboration with pharma bringing in new drug. Academias have a major role in maintaining data repositories making them available for research preventing silos and other bottleneck to data sharing. These platforms have the potential to explore solutions placing the patient at the starting point and not the protocol and the drug.	
II. eHealth, mHealth, ICT	Research should focus on the development of solutions, inter-operability, data standards, user and professional interfaces, data linkage, information processing, and assessment of health and healthcare impact and value for money.	Structural and strategic funding is necessary to bring the individual approaches together, increasing the scientific discussion and translating the results into clinically testable concepts. Such funding would have to be supranational and should not so much target individual research projects, but corroborate

		the strength, interaction and visibility of the field by supporting conferences, career options and translational efforts.