European Alliance for Personalised Medicine

Personalised Medicine: New Perspectives for Patients in Europe

Manifesto September 2012
Recommendations by the
European Alliance for Personalised Medicine

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Foreword by Stavros Malas, Cypriot Minister of Health

"I very much welcome the EAPM's Manifesto and its innovative approach towards working with patients and all those involved in the development and delivery of personalised medicine and personalised healthcare by identifying the challenges and opportunities ahead.

Through a better understanding of genetics and increased awareness of environmental factors, a more personalised approach to medicine should allow for improved preventative strategies - as well as the opportunity to stimulete better treatment of chronic and acute disease. Good health remains an important factor in enabling a competitive and successful Europe.

However, in order for European citizens to be able to benefit from personalised medicine there will be a need for a more integrated approach to innovation and healthcare delivery. This will require co-operation between researchers, clinicians, health professionals, industry, regulators, healthcare providers, and funding bodies. This Manifesto provides an essential contribution to creating an awareness and understanding of the key issues.

During the Cypriot Presidency of the EU, we are aiming to promote such collaborative approaches towards innovation with the continued funding of the 'Innovative Medicines Initiative' in Europe which fosters public-private partnerships with a joint budget of €223,7 million.

We will also seek to secure future funding of the EU Research Programme, Horizon 2020 with a planned budget of €80 billion for 2014-20. I am confident that these initiatives will contribute to stimulating innovation and accelerating more personalised pathways in healthcare.

The EAPM's initiative and recommendations provide a good platform for decision-makers at the national and European level to interact with all stakeholders and to address the challenges ahead. Together with successive European Presidencies, I look forward to working with the EAPM stakeholders and promoting Europe's 2020 innovation agenda and to creating a legislative and regulatory environment which enables the development of personalised medicine for the benefit of patients in Europe."

Stavros Malas

Foreword by Máire Geoghegan-Quinn, European Commissioner for Research, Innovation and Science

"Personalised medicine carries the promise of making healthcare smarter, better and more cost-efficient to the benefit of all European citizens. Based on new knowledge on the underlying molecular biological mechanisms that govern health and disease, we should be able to better predict, prevent, and treat disease.

However, we are only at the beginning of an evolutionary process that poses a multitude of challenges. Tectonic shifts in medical research and healthcare delivery will need to take place to usher in the era of personalised medicine. It will require all people with a stake in healthcare including scientists, clinicians, policy makers, industry and patients to collaborate and to listen and learn from one another.

Through the Seventh Framework Programme for Research and Technological Development (FP7), the European Union has already committed over €1 billion to collaborative health research enabling personalised medicine. A multi-disciplinary approach to personalised medicine also features high on the list of health research priorities in the proposal for Horizon 2020 - the next framework programme for the period 2014-2020.

During the past two years, my services in the Health Directorate of the Directorate General for Research and Innovation have organised a series of workshops and a conference providing opportunities for all stakeholders to discuss the research challenges posed by personalised medicine. The outcome of these events provided valuable information that will inform our current and future work and we intend to keep our ears to the ground and continue our discussions with stakeholders as we move on.

Four key challenges can help illustrate the need for further health research efforts at European, regional and local levels to advance personalised medicine in Europe.

Since personalised medicine approaches require an unprecedented level of co-operation and collaboration across the healthcare system, we need to continue to tackle the challenge of breaking barriers and learning to speak the same language. The interaction between different scientific disciplines (such as biology, mathematics, statistics, pathology and medicine) and between researchers working in the laboratory and those working in the clinic needs to be facilitated.

Substantial education and training efforts are needed to ensure that knowledge and good practice concerning novel technologies and scientific approaches are shared. The need for education and training also extends to hospital professionals and to patients, for whom improved health literacy could help make informed and relevant healthcare choices.

New discoveries will not get us very far unless we know how to address the challenge of **generating knowledge and developing the right tools**. Efforts to translate copious amounts of data generated by novel scientific approaches into new and improved research tools constitute a main area of interest for European health research funding. This is equally true when it comes to meeting the challenge of **translating new knowledge to medical applications with patients**, including qualifying and validating biomarkers and developing new designs for clinical trials. These are core challenges where funding on a European and international level can boost innovation and aid the development of internationally recognised standards.

Finally, it should be noted that the uptake of stratified and personalised medicine in healthcare will depend on the benefit for patients and on the economic viability of such approaches in the healthcare setting. We therefore need to address the challenge of fully **understanding the value and economic aspects**. Further information on how to reward innovation and develop more efficient health care systems governed by improved policy instruments would be the measure of success in this arena.

Máire Geoghegan-Quinn

Read more about European Union health research and personalised medicine on:
http://ec.europa.eu/research/health/policy-issues-personalised-medicine_en.html

Foreword by European Parliament MEPs

One of our most important missions as politicians is to ensure that any citizen across the European Union fully enjoys his or her right for access to high quality health care and medical products. We recognise that personalised medicine has the potential to realise the vision of being able to improve overall health, and the prevention, diagnosis, and treatment of diseases.

Since the start of the legislative term in 2009, we have worked to realise that vision with many of the stakeholders in this Alliance. A number of recent developments at EU level have changed the landscape in this area and have further enhanced a policy environment to facilitate access to medical treatments in all 27 Member States, in particular when it comes to increasing the level of human health protection, recognition of health professional qualifications, to accessing healthcare when abroad, or to the availability of high quality safe medicines.

EU legislation has also recently led to redefining the structure of how clinical trials will be carried out in the EU, increasing procedural efficiency in access to treatment and facilitating a more EU collaborative research environment through the Health and Research Programmes 2014-2020. These different aspects and future efforts by the EU, with the support of the stakeholders in this Alliance, will contribute to a suitable environment for increased accessed for better treatment for patients.

The EAPM's integrated approach involving all stakeholders, including researchers, patients, scientists, industry and health care planners, will help to bridge the gap between lay and professional perceptions of innovation, and to deliver practical policy points and case studies, which will contribute towards our efforts in the European Parliament of realising personalised medicine for all patients.

To conclude, this manifesto presents a number of policy initiatives and calls to actions to realise personalised medicine and personalised healthcare for present and future generations enriched by a cross-section of stakeholders from across Europe. We wish every success to the collaborative work of the Alliance for Personalised Medicine in facilitating increased access and the development of personalised medicine in Europe.

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Executive summary

Personalised medicine could transform healthcare, by tailoring healthcare solutions to the individual patient, delivering 'the right treatment to the right patient at the right time' – and helping to get more value from healthcare spending. It will make use of new scientific understanding and new technologies to adapt prevention, diagnosis and treatment of disease to an individual's specific profile.

The concept is already demonstrating benefits in oncology, haematology, cardiology and rare diseases. And new products are being designed to match the approach. However, for personalised medicine to deliver on its potential over the coming years, multiple challenges will have to be met - right across the healthcare sector.

Regulation needs adapting, research needs encouragement, new approaches are needed in assessing the value of personalised medicines, and training of healthcare professionals and awareness among patients and the public need to be boosted. European health care systems will need to take a more sophisticated view of health care that goes beyond merely responding to acute episodes associated with single illnesses.

Above all else, there is an urgent need for engagement of a wide range of stakeholders. As the success of personalised medicine will depend on a shift in thinking across wide areas of healthcare - and a new form of multi-disciplinary engagement.

To take advantage of the opportunities that personalised medicine offers, adaptations will be required to the current approach to healthcare in the following areas:-

- The regulatory environment will have to allow early patient access to novel and efficacious personalised medicine.
- Research and development into personalised medicine will have to be increased and incentives provided for translating laboratory innovation into medicines.
- Education and training of healthcare professionals will have to be adjusted.
- New approaches to reimbursement and health technology assessment will be required.
- Awareness and understanding of personalised medicine will have to be developed among patients and the general public.

EAPM has been created to focus on the need for change, and has developed a vision which this brochure sets out in detail.

EAPM defines personalised medicine as "a targeted approach to the prevention, diagnosis and treatment of disease based on an individual's specific profile."

Views on personalised medicine can vary according to standpoint: for patients, it offers access to life or better quality of life; researchers see potential in their ownareas of specialisation; for industry it offers the hope of developing more effective medicines as understanding advances of specific diseases; a physician sees a new way of treating a patient; for society, it may be perceived as offering scope for an overall improvement of healthcare - or a new cost.

What does personalised medicine promise?

Personalised medicine represents an important evolution from traditional practices in healthcare. It will help tailor healthcare solutions to the individual patient, instead of relying on the "one-size-fits-all" approach that currently predominates.

Through the introduction of personalised medicine, healthcare services will increasingly deliver 'the right intervention to the right person at the right time of the person's life course'. Personalised medicine has the potential to improve the outcomes for patients and cut down the use of unnecessary and expensive treatments. Given the right environment, personalised medicine can contribute to securing more value from healthcare spending, to the benefit of healthcare providers and patients, and in the end of all citizens.

Involving the patient more closely as an individual, with a focus on each person's unique biological make-up and their environmental and lifestyle factors, is central to the concept of personalised medicine. It thus finds its place logically within the move towards personalised healthcare - that broader vision of people taking greater responsibility for their own wellbeing based on the more precise awareness of individual health status and susceptibilities that modern profiling can provide. In personalised medicine, with the introduction of data derived from new technologies ('omics) as a common component of patients' health records, health interventions - for screening, early treatment, or prevention - can be more precisely calibrated for maximum effectiveness by combining precision medicine, imaging and computer technology, as well as other technologies such as sensoring.

At present, there are approximately 200 identified cancers. As understanding develops, latest research is showing that each of these contains a number of sub-groups, so there are actually thousands of different tumour types.

Personalised medicine will go beyond the current broad definition of diseases; it identifies sub-types of diseases and assesses the characteristics of each patient in each situation. In this way, it offers optimal treatment combinations and reduces the likelihood of adverse events. EAPM defines personalised medicine as "a targeted approach to the prevention, diagnosis and treatment of disease based on an individual's specific profile."

Thus, personalised medicine can be achieved through two different approaches: (1) stratification using biomarkers and based on traditional statistics and (2) individualised or truly personalised medicine using 'omics' and related technologies and based on computer models and simulation. It even holds out the prospect of more sustainable healthcare systems.

Personalised medicine will put new tools in the clinician's hands for adapting their therapeutic approach to the individual needs of every patient, through a combination of targeted new molecules and related biomarkers. It marks a shift from reactive medicine to proactive, pre-emptive, and preventive healthcare, promising fewer side-effects and longer and healthier lives.

Ultimately, through compiling data profiles of wider populations, healthcare systems will be able to identify the best course of treatment or prevention for each citizen, introducing radically different approaches to healthcare on a broad scale. The approach will offer medium and long-term gains - to patients and to society - that will heavily outweigh the upfront investment needed.

Current treatments such as chemotherapy or surgery will not disappear overnight, as many are already highly effective. But the shift towards stratified personalised medicine has already started. The approach is used in oncology, haematology, cardiology and rare diseases. And new products are being designed to match the approach. It is also increasingly important to give the right intervention to the right person at the right time of the person's life course[1].

John Bowis & David Byrne, Co-chairs EAPM

How can the promise be realised?

For personalised medicine to deliver on its potential over coming years, multiple challenges will have to be met - right across the healthcare sector.

Regulation needs adapting, policy instruments such as Health in All Policies (HiAP) needs implementation, research needs encouragement, new approaches are needed in assessing the value of personalised medicines, and training of healthcare professionals and awareness among patients and the public need to be boosted by promoting health literacy. European health care systems will take a more sophisticated view of health care, preventing and managing complex multi-morbidity across silos, rather than focusing on acute episodes associated with single illnesses.

Few medicines for truly personalised use are so far on the market, and translating research results into products is still in its early stages. Support is needed, particularly for cross-border and multi-disciplinary collaboration.

But above all else, there is an urgent need for engagement of a wide range of stakeholders, as the success of personalised medicine will depend on a shift in thinking across wide areas of healthcare, and a new form of multi-disciplinary engagement. Currently, the disciplines that contribute to personalised medicine exist more or less in isolation from one another. This is why it is essential to bring all relevant stakeholders together now while planning is just beginning so that the views of all interested parties can be taken into account and a common approach forged. Preventing severe late effects of cancer treatment should be a top priority, since a growing population of cancer survivors worldwide suffer from post-treatment physical limitations and co-morbid conditions in which it is not always easy to identify which treatment (from a multiplicity of drugs or targeted agents) might be responsible. Personalised medicine and rehabilitation could offer the opportunity of incorporating prevention of late effects into the cancer survivor's treatment plan.

The European Commission has already outlined its concept of "smart regulation", The preparations for the Commission's recent proposal to update the EU's clinical trial rules provided a valuable demonstration of the effectiveness of such an approach, with wide consultation and extensive dialogue resulting in draft legislation that has found wide support.

Along with systematic follow-up data collection (including patient reported outcomes), newly designed randomised clinical trials should capture more detailed information about patients before treatment begins, and collect biological specimens for studies of late effects (storage of specimens for future DNA assessment). Evaluation of genetic polymorphisms of DNA should be part of the clinical assessment of potential cancer patients, not only to predict cancer susceptibility, but also to evaluate the biological response to the pharmacological treatments, in order to improve effectiveness of therapy and outcomes. These assessments are often overlooked or incomplete, resulting in poor outcomes and unjustified costs, and impairing the "effectiveness" of the treatment.

It will be possible for patient and professional to discuss options only if a common language and conceptual understanding of genetic and protein signatures and pathophysiology of the disease is available for both - taking account of the individual patient's psychological make-up (educational level, mental state, and attitudes to risk).

Views on personalised medicine vary widely, often focused narrowly around molecular markers for specific treatments rather than taking a broader view of health outcomes, and current discussion is often fragmented. Extensive dialogue and cross-disciplinary consensus will be needed as policy is formulated and practices are adapted. A structure is needed for promoting wider understanding of personalised medicine among health professionals, patients and the public - and, crucially, among payers and policymakers.

All stakeholders, including healthcare providers, payers, industry, regulators, disease specialists, and patients, must participate in defining the future of personalised medicine. And although the challenges will also vary according to the disease specialty, practice setting, and regional context, it is essential to work effectively now on agreeing principles that will permit progress towards a truly personalised approach to healthcare.

Why now?

European healthcare systems were already under huge financial strain even before the economic and financial crisis subjected them to new pressures.

Now health systems have become a routine element in European discussions on the sustainability of public finances - and although medicines are on average only ten per cent of national healthcare budgets, there is a determination to obtain maximum value from spending.

Meanwhile, advances in medical science, coupled with the ageing of European society, leave health systems facing levels of demand that will become insuperable on a business-as-usual basis. At the same time, there is a growing recognition that cuts in health spending, particularly in primary care and early intervention, are a false economy. A healthier population is seen as a contributor to economic growth and as less of a burden on health systems.

Personalised medicine, with its more predictive, personalised and pre-emptive approach, with close patient participation, offers the hope of increasing treatment rates, reducing the impact of treatment on the risk of other illnesses, and positively impacting on the health economy, as well as on the quality of life of patients.

Against this background, new strategies are required.

Calculations on healthcare costs are complex and the complexity must be respected in attempting predictions.

A growing body of evidence shows that 'health is wealth' – health is not only a by-product of economic growth, but one of its key components. For example, 10% fewer deaths at working age due to cardiovascular diseases would give a 1% increase in GDP per capita. Conversely, health inequalities were estimated to have cost the EU around €141 billion in 2004 or 1.4% of GDP, when taking into account labour productivity lost and costs to social security.

"European leaders must realise that cutting spending on essential services such as health, particularly in public health and early intervention, is a false economy. It will drive up long-term costs, leading to the re-emergence of communicable diseases and putting the burden on those people who can afford it least."

Personalised medicine has the potential to generate cost-savings. It will not be the total solution to the challenges of making healthcare systems sustainable, but it provides more efficient use of resources coupled with improvements in public health and quality of life.

Personalised medicine can deliver targeted cost-savings where it is implemented. The French National Cancer Institute (FNCI) is a pioneering example of large-scale implementation of personalised medicine, with molecular testing provided for all French cancer patients before decisions on appropriate treatments are taken. The FNCI spent €1.7 million on testing for EGFR biomarkers in 16,724 lung cancer patients. The tests showed that only 1,724 patients (~10% of the tested individuals) would respond to the available treatments (Gefitinib or Erlotinib). The savings for not treating the 15,000 non-responding patients amounted to €69m based on the median treatment period of 8 weeks.

What needs to change?

To take advantage of the opportunities that personalised medicine offers, adaptations will be required to the current approach to healthcare in the following areas:

- The regulatory environment will have to allow early patient access to novel and efficacious personalised medicine.
- Research and development into personalised medicine will have to be increased and incentives provided for translating laboratory innovation into medicines and other interventions.
- Education and training of healthcare professionals will have to be adjusted.
- New approaches to reimbursement and public health assessment tools including health technology assessment, health needs assessment and health impact assessment will be required.
- Health literacy including awareness and understanding of personalised medicine will have to be developed among patients and the general public.

EAPM has developed its vision of the needs under each of these headings, and this brochure sets them out in more detail.[2]

Regulation

While science has led to major advances - in the understanding of the genomics of disease, the discovery of biomarkers, the development of new statistical methods or the invention of dynamic tools for collecting real world effectiveness and safety data - the basic R&D and regulatory process is largely unchanged.

The EU regulatory environment will have to take account of new science and products to allow early patient access to novel and efficacious personalised medicine. This will require streamlining, simplifying and harmonising the current framework so that it can respond rapidly to emerging personalised therapies and accompanying diagnostics/devices. Ongoing action at EU and national level to tackle the threat of counterfeit medicines will also need to take into account the specificities of personalised medicines.

Clinical trials - Drug registration must be adapted to complex and innovative clinical trial designs which investigate targeted new molecules and related biomarkers with single agents or in combinations, or which deploy nanotechnology or make use of non-invasive data collection such as imaging biomarkers.

As diseases are reclassified into smaller subtypes, smaller patient populations are available for clinical trials.

A new approach will be required to protocols and conditional approvals, and there will have to be greater acceptance of modelling, given the small patient cohorts. The current proposals for new EU rules on clinical trials respond to some of the problems caused by the existing legislation, but are not sufficiently forward looking to react to the future needs. A chapter should be included making provision for trials specific to the development of personalised medicine, including making it easier to conduct the multi-national trials that are essential to allow personalised medicine to become a reality.

Coordination must be improved, to reduce fragmentation of research in Europe.

Guidelines or other 'soft law' mechanisms should ensure that researchers, doctors, pharmacists and patients have better access to information about ongoing trials. This can help avoid duplication, and streamline recruitment, allowing access to the patient numbers essential to speed effective new treatments into daily care practice.

There is a need for coordinated assessment of clinical trials applications – along the lines proposed in the current proposals - in order to make it easier for academia and industry to organise trials.

Co-ordinated pan-European quality assurance must be installed for high-quality molecular testing during clinical trials as well as during routine patient treatment.

Reliable diagnostics are an integral part of delivering a successful personalised therapy.

Disclaimer: The statements on the draft Clinical Trials Regulation and other policy/legislative dossiers outlined in this document do not necessary represent the positions of EuropaBio on these dossiers.

Diagnostics - An agreed level of evidence is needed in the development and validation of biomarkers taking into account their dynamics in time and space, and a regulatory framework is needed for the co-development and development of a biomarker and companion diagnostic.

The regulatory environment for biomarkers needs to reflect the speed with which biomarkers are being developed and clinically validated in order to personalise treatment.

The aim must be to establish European Guidelines for Biomarkers to ensure harmonisation across the EU.

Performance levels must be agreed for clinical evidence in support of diagnostic claims directing specific use of a treatment.

Assays developed by clinical laboratories for in-house use should meet the same quality, safety and regulatory requirements as IVDs in order to ensure they perform to the same level as the companion diagnostics they replace.

The identification and validation of novel biomarkers is essential for the effective implementation of personalised medicine. More quality control to ensure sensitivity and specificity of biomarker tests is needed.

The revision of the In-Vitro Diagnostic Directive must make explicit provision for personalised medicine. It should ensure:

- compatibility of the regulatory frameworks for medicinal products and in vitro diagnostics and medical devices: greater connectivity is needed between national bodies responsible for medicinal products and those responsible for in vitro diagnostics and medical devices.
- an equal level of diagnostic quality across Europe for companion diagnostics by including a rules-based risk-based classification system, and a legal framework supportive of the development of innovative companion diagnostic assays.
- evaluation and reimbursement of all technologies including diagnostics based on the benefit for the single person and the value they provide to the overall healthcare system, and with prices that reflect the expectations of regulators and payers on the level of evidence required for evaluation[1].

Data - A more developed diagnostics industry would enable personalised medicine as there would be more incentives to address clinical questions that can further define subgroups of patients benefited from specific treatment approaches. It is important that diagnostics companies can operate independently and be reimbursed for the tests they develop directly in a timely manner.

The legal framework needs to provide for the giving of broad consent for future studies using stored data, including the sharing of patient data internationally. The proposed General Data Protection Regulation must take account of these needs.

Regulation must also allow for the collection, storage and analysis of biospecimens (biobanks) that are crucial to understanding the causative molecular pathways underlying disease, and for development, validation and regulatory approval of innovative drug-diagnostic pairings. Rules for the handling and management of biospecimens should be

A major regulatory constraint on personalised medicine lies in data protection. Ensuring seamless access to medical data is crucial for prospective, retrospective and past medical research. For instance, personalised medicine relies on the identification of clinically valid biomarkers. In many cases, biomarkers emerge from academic work mid-way through or after a study has closed, and rapid re-analysis of existing data is vital to getting this new knowledge into novel personalised medicines. The legal framework needs to allow the reanalysis of existing data without the need to obtain further consent from patients involved in relevant trials. Similarly, complete anonymisation of data will be an obstacle to innovative research. In many fields of medicine and science, it is crucial for researchers to be able to follow the data of particular patients. Exceptions will have to be made in privacy laws to allow traceability in the case of medical data used solely for scientific, pharmacovigilance and public health research purposes as well as managing patients' own personal health.

standardised and simplified, to allow sharing across Europe and to encourage networks of biobanks. Ethics committees should support the creation and use of biobanks even without detailed future research objectives, so that material in repositories can be used in translational and clinical research other than that for which informed consent was given by the subjects who provided the biological material. Biological assessment of specimens needs to be coupled with analysis of clinical data, so complete anonymisation should be avoided where the patient gave broad consent.

On the other hand, discrimination between patients on the basis of genome-based information must be prevented, and any commercial use of genetic/genomic information must be monitored and regulated. But the mechanisms to assure this must not impede research.

Research

Increased investment and collaboration between European research centres is vital to provide long-term funding and sustainability for the innovative and cost-effective infrastructures needed to exploit personalised medicine. Significant investment is required in radical new technologies for drug discovery and development. To reflect new knowledge about human biology, diseases need to be reclassified in a more detailed manner on the basis of clinical features and biomarkers, to allow different treatment approaches. New technologies for defining and diagnosing disease and directing treatment should be deployed. Standardisation of tissue collection or biobanks will be needed to match the emergence of new technologies.

Collaboration - Strategic co-ordination of health research led by the scientific community but also involving other stakeholders, including patient organisations is essential within the next EU Research Framework Programme, the Horizon 2020 framework, led by the scientific community but also involving other stakeholders, including patient organisations, to avoid overlaps and maximise use of resources.

Strategic action on European health research can accelerate biomedical research and promote Europe as a centre for health research innovation

The EU should encourage new forms of collaboration between academia and industry to discover and validate pre-treatment predictive biomarkers for the stratification of patients for treatment and to use computer models for simulation of treatment options. There is an increased role for bioinformatics and systems biology along with a technological infrastructure in clinical research targeting the identification and validation of predictive biomarkers as well as to develop new tools such as 'virtual persons'. A common platform for biomarker research is needed to deal with its complexity and costs, and to communicate and educate on the value of mandatory and standardised tissue collection. Advanced databases of both biological, clinical and envirionmental data are required as well as clinical databases for outcomes research. Exchange of knowledge and best practice is necessary to harmonise protocols and integrate interoperable data and technologies.[4]

Coordination is needed across the collaborative research networks in personalised medicine, to avoid duplication and to reach critical mass. And multi-centre, international research collaborations should be strengthened to improve access to the required numbers of patients and material for effective research. Close interaction between industry networks, research networks and health-care networks is crucial not only to improve quality of care, but also to foster research, and should be encouraged and properly and permanently funded, since any additional costs will be fully repaid.

Innovative clinical research aiming at personalised medicine requires improved integration of basic/preclinical research with clinical research alongside with public health research. In particular, academia needs to improve collaboration with industries in joint projects to discover and validate pre-treatment predictive biomarkers for the stratification of patients for treatment.

Encouragement should be given to collaboration between the pharmaceutical and diagnostics industries, particularly through partnerships with academic research.

European support for the use of Information and Communication Technologies (ICT) in health, under the rubric of "personalised healthcare" and eHealth chapter, offers possible scope for co-ordination in the collection of patient data for personalised medicine on a scale sufficient to allow stratified as well as truly personalised treatment at the systemic level.

Funding - Research into unravelling the biological complexity of diseases needs funding. Horizon 2020 must allocate sufficient funds for research into the understanding and implementation of personalised medicine by scientists, clinicians and patients.

Funding is required to identify and validate novel biomarkers and develop new simulation tools. Often, for each cancer type multiple markers need to be investigated before one can be found which can be validated to provide a strong clinical utility. Investment in research at this stage thus paves the way for a successful implementation of personalised medicine. Horizon 2020 should initiate a 'European Council for Health Research '(EuCHR) to encourage partnership in innovation and definition of biomedical research and translation programmes.

The public-private partnership in life sciences research and innovation under Horizon 2020 (successor of the IMI initiative) should focus on personalised medicine.

In addition to funding projects on a call basis, research networks across the EU with an outstanding record should be given permanent funding in return for sustained performance, so as to strengthen the EU framework for independent academic research and to assist it in cooperating with industry.

Procedures - The regulatory procedures governing drug approval and reimbursement should be enhanced, to take account of novel trial design, statistical analysis and computational modelling, and there should be greater alignment among the current distinct assessment methodologies and data requirements for the benefit/risk assessment. Special attention should be given to methodological solutions allowing clinical studies in small populations and even single persons (N=1).

Additional incentives should be provided for research, in terms of greater flexibility in conditional marketing approval, or data exclusivity allowance in return for research focused on unmet need.

Healthcare practitioners need to access the right intervention at the right time, and be in a position to correctly interpret a test result in order to identify the right treatment option and communicate the therapeutic rationale to the patient. Healthcare professionals need read-and-write access to patients' medical records to permit identification and prevention of potential medication errors, medicines interactions, duplication of treatments and possible adverse events. Patients need to understand that a test may be necessary to decide on the right treatment, and must be empowered to take decisions on their own therapeutic management.

Training

Because the exercise of personalised medicine will require engagement of so many distinct groups - regulatory officials, healthcare professionals, technologists... - there will be a need for multi-disciplinary training to reduce knowledge and communication fragmentation and breakdowns in knowledge and communication. Training activities on relevant aspects of personalised medicine such as clinical case studies should include participation from all involved professions – biologists, economists, psychologists, nurses, physicians, pharmacologists, pharmacists and so on...

Planning - While funding of training can be left to stakeholders, strategic planning is needed at European level to identify key areas for funding within the H2020 framework, on a public-private partnership basis. Frameworks should be provided for training clinicians, biologists, mathematicians and statisticians in the various stages of research and practice within and between member states.

Communication - Physicians and clinical pharmacologists and pharmacists will face new challenges not only from the complexity of the data that will support decisions, but also in communicating the therapeutic rationale to the patient. They will need additional technological support and education, including from the bioscientists and technologists who supply the data, who will in turn need a sound understanding of patient care. Physicians must also be aware of the psychological aspects involved in communication with patients and in shared decision-making or even own decision-making. Programmes should cover the complete research spectrum of basic, pre-clinical, clinical, public health and outcome research, and should cover not only scientific advances but also the accompanying ethical, legal and psychological aspects. Cross-disciplinary education is the way to ensure that the necessary common ground is established in the short term, to reduce fragmentation and gaps in knowledge and communication.

Evolution - Over the longer term, more profound changes in education and training will be needed as the evolution of personalised medicines drives demand for professionals able to work in a multidisciplinary context. At that point, the focus on technical aspects will be replaced by approaches in which the patient is at the centre of an expert clinical discussion that takes account of numerous factors, including biomarkers, pharmacology, palliation, toxicity, psychology, imaging and statistics.

Training programmes in the use of personalised therapies have been developed within each of the healthcare professions, especially in relation to stratified therapies for groups of cancer patients. But the full value will be derived only with a wider cross-disciplinary approach.

Assessment and reimbursement

The adoption of personalised medicines could ease the burden.facing healthcare systems across Europe. Standard assessment mechanisms will need to be tailored to the specificities of personalised medicines to be able to demonstrate benefit and cost-effectiveness. In particular, broader elements such as quality of life of patients or value of information need to be measured and taken into account, rather than only budget and cost.

New attention to post-authorisation research will be required. Real-life data on the performance of patients and survivors under new treatments are key to continued research, as they widen the information on a new agent that is available when it is authorised. Collecting real-life data needs a collaborative approach between all actors involved to foster clinical effectiveness research and confirm whether effects seen in a clinical trial are relevant to the total patient population.

Cost-effectiveness and cost-benefit - When patient outcomes are taken into account in evaluating cost-effectiveness and benefit, the true value of new diagnoses and treatments will emerge, because it will be possible to demonstrate favourable impacts of new drugs or devices on overall healthcare costs. Late translational research, with its focus on the clinical effectiveness of specific treatments, is a valuable guide to cost-effectiveness. Its use can increase availability of effective treatments (and decrease use of sub-optimal treatments), and help identify priorities in healthcare provision. But comprehensive clinical registries are required to achieve this outcome. Already existing infrastructures must be further explored for this purpose.

Practical reimbursement solutions need to be found to situations where a pharmaceutical is available but its use in treatment is impeded because the relevant diagnostic (or companion diagnostic5) is not yet reimbursable.

Alignment - Current approaches to HTA and other public health assessment tools should be revisited, adapted and further developed to take account of efficiencies offered by truly personalised medicine - such as cost-savings from reduced trial-and-error prescribing or shortened hospitalisation and fewer side-effects, and the advantages of additional quality of life and other patient benefits or value of information. Better coordination and a more standardised approach to assessment is needed among regulators, HTA agencies and payers to ensure the potential value of new healthcare technologies is appropriately recognised and rewarded.

Duplication between EMA and HTA assessments of efficacy need to be addressed, and requirements should be streamlined through an alignment of methodologies and realistic expectations of evidence as well as on what kind of evidence is needed in truly personalised medicine (N=1). Consensus is needed on the aspects of diagnostics to be assessed and the level of evidence for cost effectiveness, clinical validation, analytical validation or value of information. Coordinated assessment at national level is needed to avoid inequalities of access due to regional rules. Models being developed by the rare disease community should be considered, and there should be greater acceptance of alternative endpoints. Efficacy should be de-linked from cost and reimbursement discussions as well as concepts such as disinvestment need to be considered in order to reduce costs and side effects.

Transparency and consistency are needed in post-registration requirements to assure even reimbursement treatment. Even a drug recommended for reimbursement may still not reach the patient because payers restrict its prescription - sometimes delaying treatment until the disease has progressed to a difficult-to-treat level.

Integration - A more integrated reimbursement policy is needed to coordinate reimbursement decisions of the drug and companion diagnostic. Mismatches and inconsistencies in the reimbursement processes for drugs and drug-diagnostic pairings must be overcome. Patients and their evidence ('narrative evidence') should be involved in HTA, prioritisation and reimbursement processes at national level.

Awareness

If personalised medicine is to deliver its full contribution to healthcare, it will have to be adopted by the entire health care and patient community. So awareness and understanding of personalised medicine must be increased, through education and health literacy.

Interpretation - Healthcare practitioners need to access the information at the right time and be in a position to correctly interpret a test result or other information to identify the right intervention or treatment option. Therefore, it is

important to consider the training needs of all health professionals so that they feel empowered by the additional information rather than overwhelmed by it.

Understanding 'omics - Educated and empowered patients will understand that a test may be necessary to decide on the right treatment, one that respects individual differences between people and molecular differences between diseases. There is a need to build links between the scientific community and the general public regarding the use of 'omics to stratify medicines, while ensuring that flows of information do not breach privacy or lead to genetic discrimination. Models are needed for shared decision-making as well as own decision-making, and for tackling wider societal concerns related to personalised medicine.

Empowerment - Patients will be empowered to take decisions on their own therapeutic management. Effective information is essential for successful partnerships, and for the patient to make informed choices that lead to compliance with prescribed treatments.

A patient-centred structure for risk communication should be developed in order to enhance patients' awareness, competence and adherence to medication. Health professionals will commonly be called upon to explain risk profiles or computer models to patients in a manner that fosters clear understanding and can be acted upon appropriately. Patient adherence to treatment must be ensured, as this will govern effectiveness.

Recent developments in the legal framework for the reporting of adverse drug reactions by patients should be exploited in this context - effective pharmacovigilance will be essential as the use of personalised medicines becomes more widespread, and health professionals such as physicians and pharmacists should also ensure they maximise their contribution to effective reporting.

One patient's view: it is all about the patient

Prof. Patricia Garcia-Prieto is the Chair in Organisational Behaviour at the Solvay Brussels School of Economics and Management, Université Libre de Bruxelles in Belgium. She was diagnosed with melanoma on European Melanoma Day in 2008, when her sons were 3 and 8. She has been stage IV since November 2009. She fought for access to clinical trials. After a long struggle, she obtained the E112 form to allow her to participate in one of the first BRAF inhibitor trials in Paris. She was assigned to the chemotherapy 'arm' of the phase-III randomized non-blind trial, but given her low disease burden was allowed to leave the study. She has also been blocked from a cancer vaccine study in the UK for not being a UK citizen. After this she decided to found the Melanoma Independent Community Advisory Board (M-ICAB) (http://www.m-icab.org) in Brussels to establish a political voice for all EU melanoma patients.

"I am alive thanks to personalised treatment - and my experience convinces me that the patient perspective has to be more closely integrated into the discussion of personalised medicine. The radical changes to healthcare that personalised medicine promises will happen only if patient involvement is given greater priority. As I enter my third year of life with stage IV melanoma thanks to personalised treatment – which is very costly and which I had to fight tooth-and-nail to access – I have seen at first hand the limitations of the current regulatory, industry and health system models for personalised medicine in Europe.

Under the current fragmented system:

- a patient wanting to cross a border to access a trial can be denied by the hospital or by the health insurance provider;
- a phase III randomized trial can assign some patients to chemotherapy (with a response rate of 5-7%) compared to personalised therapy (70-80% response rate);
- a ground-breaking monoclonal immunotherapy with demonstrated benefits in unmet need and fully authorised can be denied reimbursement in most countries;
- even when a national reimbursement body agrees to reimburse 95% of the approved immunotherapy, an oncologists might choose not to prescribe it;
- compassionate use of a targeted therapy can be denied to end-of-life patients because of the "risk of toxicity" even though no other alternative exists;
- a patient in Poland needs to take part in a clinical trial in Italy – despite the fact that the drug he needs is approved by his country, because it is not yet reimbursed nor supplied by the company.

This situation deserves to be changed, so that personalised medicine is perceived just in relation to costs, but as a way of giving patients additional productive life-years."

Patricia Garcia-Prieto
Co-Founder of the Melanoma Independent Community Advisory Board

The view from the Eurocan Platform

Personalised cancer medicine is in its infancy. Its development is dependent on availability of pre-treatment predictive tools and anticancer agents. Clinical activities and research should be structured to optimise availability of treatments for patients, and collection of clinical data and biological materials for research, including clinical effectiveness of anticancer agents and health economy. Advanced clinical trials for validation of biomarkers is an issue for international collaboration: funding and regulatory authorities must support international research collaborations. It should be possible to recruit patients from any geographic area.

Ulrik Ringborg,
Director, Cancer Center Karolinska, Stockholm

The view from EURORDIS

Personalised medicines derive from recent knowledge in the field of genomics. This trend will transform the approach towards therapeutic intervention which will target population-subsets with a genetic profile making individual patient responsive to the proposed treatment: this will be true for both common and rare diseases. Even if the experience

gathered in the rare disease field on studies in small populations will be useful for the reflection on personalised medicines, the confusion of concepts should be avoided: in fact, the genetic profile used to define population subsets for treatment response may be a necessary criterion to define a rare disease – but is not a sufficient one. Rare diseases are conditions with coherence of symptoms, as observed by clinicians in their practice.

Yann Le Cam, Chief Executive Officer, EURORDIS

The view from the European Society for Medical Oncology

As the leading European professional organisation committed to advancing the specialty of medical oncology and promoting a multidisciplinary approach to cancer treatment, ESMO is committed to good science that leads to better medicine and determines best practice. ESMO supports oncology professionals in providing people with cancer with the most effective treatments available and the high-quality care they deserve. When speaking about personalised medicine, good model of the challenges confronting this topic is rare diseases, particularly in clinical research, where trials methods will be required which can generate good evidence from small numbers of subjects. Regulators and payers will then be expected to endorse the innovative methods emerging from the evolution of clinical medicine. The slight increase in uncertainty from new methods will influence the patient-physician clinical decision-making process, and will require more consensus-based collaborative work by the disease-based communities of researchers, and by patients. But there will be huge gains from personalised treatment of the single patient, far beyond the small benefits which are observable from the use of many of today's new oncology drugs which are designed for the average rather than a highly selected patient.

Prof. Paolo Casali
Executive Board Member, European Society for Medical Oncology

The view from Ecancer

Personalised medicine means personalised to each individual patient or groups of patients with similar or the same characteristics. To achieve this aim, personalised medicine exploits the science of genomics to enable tailored approaches to prevention and care. The furore caused by the unravelling of the human genome and the excitement of the subsequent possibility of targeted therapies (and prevention opportunities) has left the "human" in the human genome behind. Inevitably the discussions are technical, but this can be no excuse for failure to communicate the new opportunities to the patient population, and to the "pre-patients" going about their daily lives. Most of those folk already assumed that treatment was particular to individual patients, thanks to the wide scale "professional cover-up" of the essentially empiric nature of modern medicine. And there's more to the patient or the person than their illness. What about the reaction of the non-physical parts of the person? Their psyche, their fears, their expectations, and their comprehensive failure to understand the plethora of complex "informative" messages from the professionals. To face the fascinating challenges of personalised medicine, we need to focus back on the individual, and tailor information and interventions to their educational level, needs and expectations, in order to empower people to become active participants in their own healthcare.

Gordon McVie and Prof. Gabriella Pravettoni

The view from the European Association of Urology

Personalised medicine is the future, because it will allow the treatment of patients with a maximum chance of efficacy and a reduction of toxicity. But it will reduce the number of patients per treatment, which will oblige clinicians to perform European or worldwide clinical trials, and will render the use of a control group unethical in many situations. For example if in a phase 2 study a subgroup of patients selected with a biomarker discovered during the study have a much better result than the others, it will become unethical to embark on a phase 3 study with a control arm in which patients will have less chance of effective treatment. Better communication and organisation of healthcare professionals will be needed, with coordination at the national and EU level.

Didier Jacqmin
Chairman SPO EAU

The view from the European Centre for Public Health Genomics

Truly personalised healthcare facilitating the management of personal health drives a fundamental change not just in what is known but also in how we think of ourselves and the way we are living, thus redefining our society. We have to prepare in time for all the various organisational changes ahead of us. The political will is there. However, the real paradigm shift depends on the willingness to restructure our current policies, to support knowledge transfer to maximize benefit to public health, and – most importantly – to change our minds. We have to define today what type of (policy) guidelines we need for tomorrow – the future is built today!
The Public Health Genomics European Network (PHGEN) has been asked by the European Commission to fulfil this task and to produce the first edition of "European Best Practice Guidelines for Quality Assurance, Provision and Use of Genome-based Information and Technologies" assisting all EU Member States, Applicant and EFTA European Economic Area (EEA) countries with evidence-based guidance on the timely and responsible integration of genome-based information and technologies into healthcare systems for the benefit of population health.

On 19 and 20 April 2012, key European and national organisations and institutions from policy-making, academia, and the private sector came together at the final PHGEN meeting in Rome – among them the European Society for Pharmacogenomics and Theranostics (ESPT) and the European Medicines Agency (EMA) – to discuss the future of public health genomics and to endorse the Declaration of Rome on 19 April 2012, a summary of the "European Best Practice Guidelines for Quality Assurance, Provision and Use of Genome-based Information and Technologies ".

The next steps for PHGEN will now be to ensure the implementation of the European best practice guidelines in the different European countries through the efforts of the PHGEN National Task Forces. PHGEN is therefore working towards a Joint Action in 2013 with the support of the EU Member States, WHO Europe and the ECPHG. By bringing together all stakeholders under one umbrella, EAPM plays a crucial role in helping to forge constructive links between the EU institutions and society.

Angela Brand,
Coordinator PHGEN and Director ECPHG

The view from the Organisation of European Cancer Institutes

Personalised Medicine, previously based on clinical and histological staging, is increasingly based on the use of biomolecular targets with the aim of optimising several aspects of patient care, such as early diagnosis, prediction of prognosis, drug targets, prediction of response to therapy and minimisation of therapeutic toxicities.

These aspects involve many professional disciplines, amongst whom biologists, pathologists, clinicians, psychologists and nurses; for this reason education and training in Personalised Medicine is a complex matter.

The key to improving the training of healthcare professionals in the area of personalised medicine lies in multidisciplinary training programmes. The Comprehensive Cancer Centre (CCC) is the ideal environment for developing such programmes. CCCs cover the complete research spectrum of basic, pre-clinical, clinical and outcome research, so therefore are in an optimal position to offer multidisciplinary training.

Networks of CCCs already established in Europe have the necessary critical mass (both healthcare professionals and access to large patient cohorts and biological samples) to implement both successful PM research projects and training programmes on a pan-European level and to ensure that results are amply diffused. The OECI is committed to

collaborating with all public, private or such organisations that pursue goals of improving the quality of life of all cancer patients in the EU, and offers its full support to the EAPM initiative.

Wim van Harten, OECI President
Angelo Paradiso, OECI Education and Training WG Chair

The view from the European Brain Council

Personalised medicine starts with the patient. Today, many medicines do not work effectively for a large number of the patients they are supposed to treat. Personalised medicine has the potential to provide solutions that are better tailored to the individual patient than traditional "one-size-fits-all" medicinal products. It is essential that the EU's role in developing am environment for personalised medicine is coordinated so as to allow better delivery of treatments for European patients'

Dr Mary G Baker, MBE
President, European Brain Council

The view from industry

Personalised medicines offer a more scientific approach to diagnosing and classifying diseases and, therefore, will lead to more effective treatment decisions for individual patients. It offers a possibility to predict to which medicines patients will respond and what doses are needed to tackle the disease with the least side effects. Over the last years, promising 'targeted' drugs that address an underlying molecular mechanism linked to the disease have been developed with oncology being a front runner in this field. Personalised medicines could provide more value for money because of improved drug effectiveness and reduced toxicity. It could also decrease the average research and developments costs for new medicines.

However, we still have a lot of work to do, namely we need tools to identify patient profiles. Therefore we have to understand diseases better than we do now and we have to identify biomarkers: indicators on a molecular level that provide information on - the physical state of a person. Biomarkers can be used diagnostically and predictively. Therefore, we need to perform research on biomarkers and turn them into diagnostic and predictive tests. The development of personalised medicines is very complex and difficult.

Against this background, we should remain realistic and understand that the expanding on the current successes of personalised medicines will take a major effort from all parties involved, including financial and organizational resources, as well as a need for further collaborations in this - field.

A structural change towards personalised medicines development requires a solid science base, basic science and medical expertise. Furthermore, the current science base needs to be expanded in order to encourage a structural change towards personalised medicines development. For example, private public partnership initiatives can significantly contribute to this process.

The difficulties to overcome include: the costs of diagnostics are not easy to describe; the evaluation of cost-effectiveness is difficult and the regulatory pathway is fragmented. Changes to the system evaluating cost-effectiveness might be needed to adapt to personalised medicines. Health organisations, companies and government institutions alike, will need to rethink, recalibrate and change their standard operating procedures to allow personalised medicine approaches to be adopted by the European healthcare system.

EuropaBio & European Biopharmaceutical Enterprises

EAPM Call to action

Through the introduction of personalised medicine, healthcare services will deliver 'the right intervention to the right person at the right time of the person's life course'.

Personalised medicine will improve the outcomes for patients and cut down the use of unnecessary and expensive treatments as well as side effects. As a result, we will see a more value based system with a higher level of acceptance by the healthcare provider and patients. The European Alliance for Personalised medicine is therefore calling on the European Commission, Members of the European Parliament and Member States to help encourage the introduction of personalised medicine. They should:

1: ***Ensure a regulatory environment which allows early patient access to novel and efficacious personalised medicine***

2: ***Increase research and development for personalised medicine***

3: ***Improve the education and training of healthcare professionals***

4: ***Acknowledge new approaches to reimbursement and public health assessment tools including HTA assessment, which are required for patient access to personalised medicine and its value to be recognized***

5. ***Increase awareness and understanding of personalised medicine***

What can you do?

1. ***Ensure a regulatory environment which allows early patient access to novel and efficacious personalised medicine***

- The coordination and recruitment of patients to clinical trials must be dramatically improved.

Improved coordination of clinical trials will reduce duplication and fragmentation of research in Europe. Researchers, doctors and patients should have better access to information about on-going trials. Increased numbers of patients in clinical trials will help speed the best new treatments becoming daily care practice.

- Streamline-Simplify-Harmonize the European regulatory framework

The revision of the clinical trials directive should guarantee more harmonization across the EU by establishing a process for coordinated assessment of the Clinical Trials Application (CTA). This in turn would support Personalised Medicine by by facilitating initiation of academic and industry trials for patients with rare conditions which could be a raw model for all common complex diseases..

- The registration of new drugs must be adapted to complex clinical trial designs, investigating targeted new molecules and related biomarkers, which is the basis of Personalised Medicine.

New drugs in the pipeline require innovative clinical development, as single agents and/or in combinations, supported by computational modelling and simulation tools. Additionally, the co-development of a biomarker and companion diagnostic need to be taken into consideration, adding complexity, time and resources. Registration process should be adapted to allow quicker access to innovative drugs to patients in need.

- The regulations on data protection must recognise the importance of the secondary use of data and sharing patient data internationally.

Personalised Medicine depends on the identification of clinically valid biomarkers and availability of genome-based information and technologies. In many cases biomarkers emerge from academic work mid-way through or after a study has closed, and rapid reanalysis of existing data is vital to getting this new knowledge into novel personalised medicines. The legal framework needs to allow the reanalysis of existing data without the need for re-consent from patients involved in relevant trials.

- There is a need for pan-European co-ordinated quality assurance with respect to high-quality (molecular)

testing as well as an agreed level of evidence in the development and validation of biomarkers.

2. ***Increase research and development for personalised medicine***

The next EU Research Framework Programme, Horizon 2020, must allocate sufficient funds for research into the understanding of Personalised Medicine by scientists, clinicians and patients. Increased investment and collaboration between European research centres is vital to provide innovative and cost-effective infrastructures needed, with long-term funding for sustainability.

- Encourage new forms of collaboration between academia and industry

Academia needs collaboration with several industries in mutual projects to effectively discover and validate pre-treatment predictive biomarkers for the stratification of patients for treatment and truly personalised medicine. Advanced databases of both biological, clinical and environmental data are required as well as clinical databases for outcomes research.

- Strengthen multi-centre, international research collaborations

Looking at the example of cancer: at present, there are approximately 200 identified cancers. As our understanding develops, the latest research is showing us not only that each of these areas contains a number of sub-groups, but also that every cancer in a patient is unique, therefore there are actually thousands of different tumour types. This means that one research centre will only have a few patients of a specific type and international collaborations will be necessary to get the required numbers of patients and material for effective research.

- Research funding is required to identify and validate novel biomarkers.

The identification and validation of novel biomarkers as well as the use of simulation tools is essential for the effective implementation of personalised medicine. Often, for each cancer type multiple markers need to be investigated before one can be found which can be validated to provide a strong clinical utility. Investment in research at this stage thus paves the way for a successful implementation of personalised medicine.

3. ***Improve the education and training of healthcare professionals***

Different professions need to be following a common and multi-disciplinary educational programme in the relevant aspects of a patient's journey in order to reduce fragmentation and breakdowns in knowledge and communication. To achieve this:

- Educational activities on relevant aspects of personalised medicine such as clinical case studies should include participation from all involved professions such as psychologists, nurses and physicians;

- Frameworks for trainings within and between Member States should provide especially clinicians and biologists a better and more complete understanding of the various stages of research and practice.

4. ***Acknowledge new approaches to reimbursement and public health assessment tools including HTA, HNA and HIA, which are required for patient access to personalised medicine and its value to be recognised.***

Personalised medicine is an important strategy to address the increasing burden facing healthcare systems across Europe. The cost-effectiveness and cost-benefit of personalised medicines will need to be acknowledged to overcome payer and government concerns about costs and the value they bring.

- Research has to continue after registration of new medicines and technologies to demonstrate that effects seen in a clinical trial are relevant to the total patient population.

- By linking overall patient outcomes to value, it will be possible to demonstrate the cost-effectiveness and cost-benefit of diagnosis and treatments and the impact any new drug or device or intervention has on the cost burden.

- Practical reimbursement solutions need to be found to situations where a pharmaceutical or any other technology is already available but the barrier to treatment created because for example the diagnostic (and companion diagnostic) is not yet reimbursable.

- Current approaches to HTA should be reassessed, adapted and further developed in order to evaluate the efficiencies offered by this approach to the diagnosis and treatment of the disease. Models being developed by the rare disease community should be reviewed.

5. ***Increase awareness and understanding of personalised medicine***

For personalised medicine to revolutionise care it will require adoption by the entire health care and patient community. Health literacy including patient awareness, education and understanding are key.

- Healthcare practitioners need to access the right infomation at the right time and be in a position to correctly interpret a test result to identify the right treatment option. Therefore, it is important to consider the training needs of all clinicians so that they feel empowered by the additional information rather than overwhelmed by it.

- Educated and empowered patients need to understand that a test or any other technology may be necessary to decide on the right treatment; one that respects genetic differences between people and molecular differences between diseases.

- Patients will be empowered to take decisions on their own therapeutic management.

- A patient-centred structure for risk communication should be developed in order to enhance patients' awareness, competence and adherence to medication.

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1 Preventing severe late effects of cancer treatment should be a top priority, since a growing population of cancer survivors worldwide suffer from post-treatment physical limitations and co-morbid conditions in which it is not always easy to identify which treatment (from a multiplicity of drugs or targeted agents) might be responsible. Personalised medicine and rehabilitation could offer the opportunity of incorporating prevention of late effects into the cancer survivor's treatment plan. Along with systematic follow-up data collection (including patient reported outcomes), newly designed randomised clinical trials should capture more detailed information about patients before treatment begins, and collect biological specimens for studies of late effects (storage of specimens for future DNA assessment). Evaluation of genetic polymorphisms of DNA should be part of the clinical assessment of potential cancer patients, not only to predict cancer susceptibility, but also to evaluate the biological response to the pharmacological treatments, in order to improve effectiveness of therapy and outcomes. These assessments are often overlooked or incomplete, resulting in poor outcomes and unjustified costs, and impairing the "effectiveness" of the treatment.

2 http://www.epha.org/IMG/pdf/FINAL_letter_to_European_Council_SECURED.pdf

3 Besides companion diagnostics for selecting therapies, standalone diagnostics can be used to determine prognosis, pathogenesis, drug resistance or duration, all of which can impact treatment modalities including surgery and overall healthcare costs. A more developed diagnostics industry would enable personalised medicine as there would be more incentives to address clinical questions that can further define subgroups of patients who would benefit from specific treatment approaches. It is important that diagnostics companies can operate independently and be reimbursed for the tests they develop directly in a timely manner.

4 Malignant melanoma is a good example of a tumour disease for development of personalised cancer medicine. There are new anticancer agents with good effects on subpopulations of patients but data on clinical effectiveness on unselected patient populations and cost-effectiveness are lacking. A consequence in the majority of European countries is difficulties for the health care systems to pay for the new treatments. A structure is needed to assay clinical effectiveness on population-based patient groups and cost-effectiveness. For development of personalised cancer medicine large number of patients must be screened for specific tumour characteristics, and research programmes are need for biomarker discovery and validation aiming at treatment predictive technologies. To reach the critical mass for this type of research, collaboration between centres and countries is essential for availability of patients, biological materials and advanced technologies - with changes in regulations regarding sharing of patient data and biological materials accordingly needed. To use resources in an optimal way, new forms of collaboration between academia, industry and health care systems are required. It is impossible to establish this type of research in all countries. Therefore patients must have the right to participate in clinical trials at centres in other countries.

5 If a companion biomarker is established after authorisation, the cost-effectiveness of the drug will change, as will the susceptible patient population. It would be natural to adjust the price accordingly - something that is currently nearly impossible, and a factor that current discourages post-authorisation research, despite potential patient benefits.


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European Association of Urology


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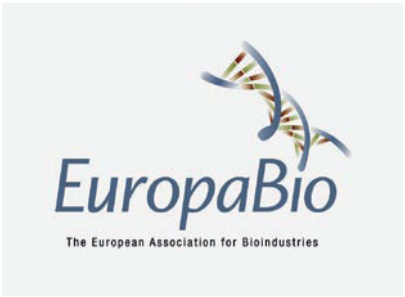
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About EAPM

The European Alliance for Personalised Medicine (EAPM) brings together European healthcare experts and patient advocates involved with major chronic diseases. The aim is to improve patient care by accelerating the development, delivery and uptake of personalised medicine and diagnostics, through consensus. EAPM was launched in March 2012, as the European discussion on personalised medicine gathers pace. It is a response to the need for wider understanding of priorities and a more integrated approach among distinct lay and professional stakeholders. It works on case studies, education, training and communication to deliver practical policy recommendations designed to exploit the potential of personalised medicine to the full.

The mix of EAPM members provides extensive scientific, clinical, caring and training expertise in personalised medicine and diagnostics, across patient groups, academia, health professionals and industry. Relevant departments of the European Commission have observer status, as does the European Medicines Agency. By bringing together all stakeholders, EAPM's aim is to help to forge constructive links between the EU institutions and society.
The EAPM Forum brings all members together every 2-3 months to review activity and to direct political strategy. Working groups develop positions on key topics and make proposals and recommendations to the Forum. The secretariat manages day-to-day operations, prepares Forum meetings, and co-ordinates the working groups).
EAPM is funded by its members.

For more information, please visit www.euapm.eu or contact Denis Horgan on +32 (0)472 535 104

EAPM is bringing together vital and necessary partners for raising awareness about and proposing position so as to develop an environment for personalised medicine for the benefit of patients.

Patient organisations
Members: European Cancer Patient Coalition (ECPC), European Parkinson`s Disease Association (EPDA)
Observers: European Patient Forum, EURORDIS, International Diabetes Federation Europe, Europe

Medical professional organisations
Members: E-Cancer Medical Science, ECP Biobanks, European Association for Cancer Research (EACR), European Society of Medical Oncology (ESMO), European Oncology Nurses Society (EONS), The European Association of Pharmaceutical Wholesalers (GIRP), Pharmacy Group of European Union (PGEU)

Researchers/scientistic organisations
Members: European Organization for Research and Treatment of Cancer (EORTC), Organization of European Cancer Institute's (OECI), European Society of Pathology (ESP), EUROCAN Platform. European Haematology Association (EHA), European Association of Urology (EAU), European Centre for Public Health Genomics
Observers: European Science Foundation

Industry
Members: Amgen, Eli Lilly and Company, EuropaBio, European Diagnostic Manufacturers Association (EDMA), Pfizer, Merck Serono, Boehringer Ingelheim, Novartis, Daiichi-Sankyo

Institutional observers
European Commission: DG SANCO, DG Research, DG Enterprise, European Medicines Agency

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