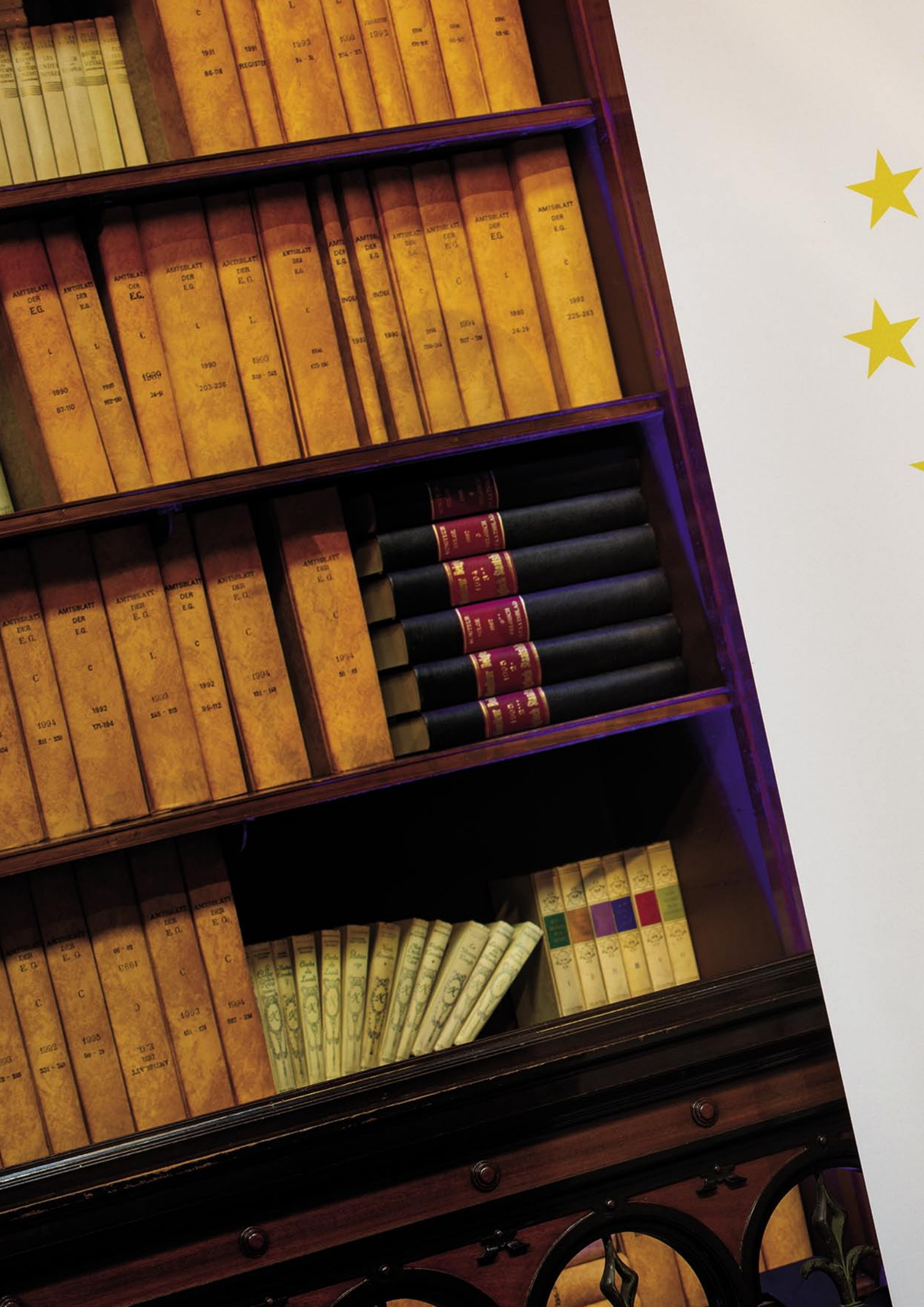
European Alliance for Personalised Medicine

Integrating Personalised Medicine into EU Strategy

EAPM Annual Conference Report
Bibliothéque Solvay and the
European Parliament, Brussels
9-10 September, 2014

SIEPS


AMTSBLATT DER E.G.


SIEPs
Specialised
Treatment
for Europe's
Patients

EXECUTIVE SUMMARY

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More than ever, health is a key policy instrument for sustaining the EU's economic growth. Health has been a key driver of the recovery of the European economy since the crisis, with health a sizeable proportion of EU GDP.

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.

Personalised medicine is a tool to generate prosperity, stability and long-term quality of life for patients. However, 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. Because 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. EAPM provides this platform that brings all these stakeholders together.

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.

Personalised medicine is an exciting, innovative way to improve citizens' quality of life and produce better patient outcomes using the best science available. Yet, despite its many tangible advantages, the take-up in Europe has been relatively slow. This is not because personalised medicine doesn't work – it does, and very well - but it is because the components and interactions involved in bring individualised medicine and treatments to Europe's citizens are complex.

But bring it we must, as a healthier Europe will mean citizens spending less and less time in hospitals undergoing expensive treatment regimes, often at a direct cost to the taxpayer, and it will also mean that patients will be more able to continue working, thus generating wealth rather that whittling it away. By the same token, a shift towards preventative medicine will reduce costs still further.

Meanwhile, a focus on research into new medicines and cutting-edge treatments will also create jobs – whether they be in research itself, education, design and manufacture of in vitro diagnostic products or within the pharmaceutical industry.

Such a focus will clearly benefit society and, if Europe is in the vanguard of developing new ways of keeping citizens healthy, it will inevitably attract investment from other continents.

However, there is an urgent requirement in many areas for reworking and rethinking in order to bring the practice of medicine up to speed in a fast-changing world.

EAPM has begun this process but much remains to be done to lower the barriers currently blocking the ability of PM to give the right treatment to the right patient at the right time, thus ensuring equal access to the best treatments available for all of the EU's 500 million citizens across 28 Member States.

The Alliance has identified the barriers as follows:

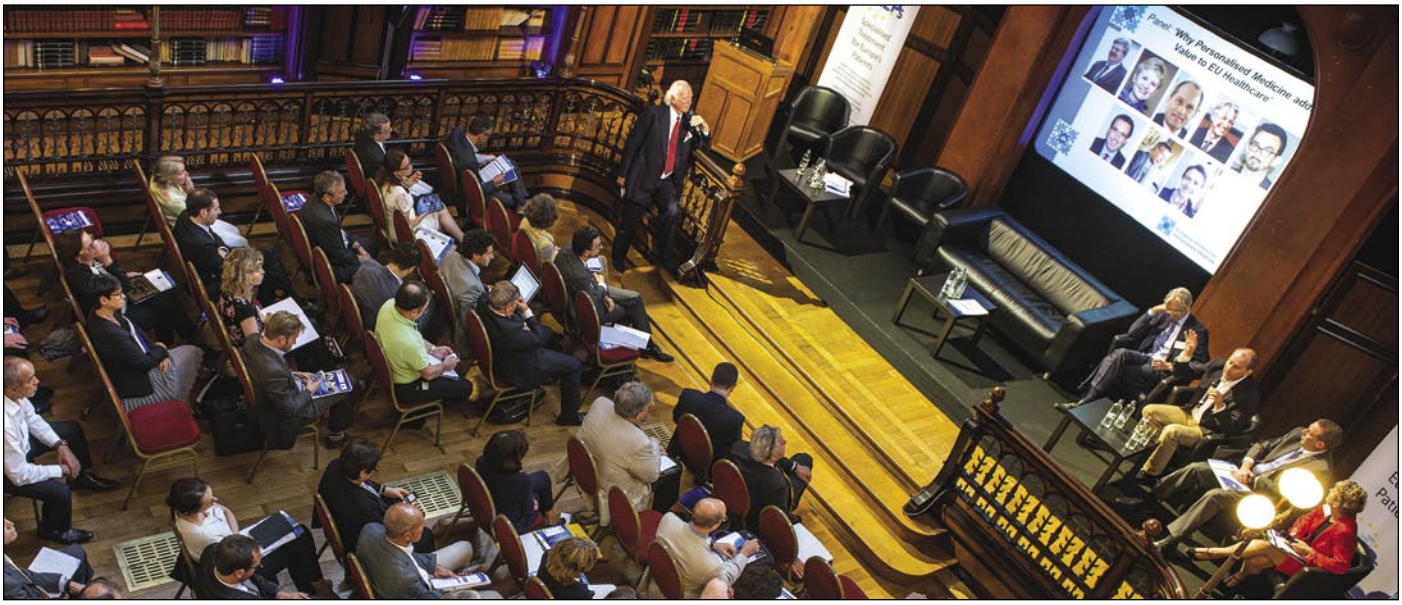
The awareness level of PM – its potential and its current application - needs to be raised, specifically among doctors who either do not know what it is, do not know enough about it or simply do not know whether it is available for their patients.

Up-to-the-minute and continuous training for healthcare workers is urgently required. Any new knowledge needs to be clearly transmitted to the patient as this will greatly assist in bringing about their empowerment.

Europe's patients must be more involved in every aspect of their own health - from clinical trial remodelling to legislation to all other issues that affect them.

Stakeholders across all disciplines must learn to leave their 'silos' in order to interact. Cooperation and cross-disciplinary collaboration needs to improve markedly.

Biomarkers based on genetic data lead to ethical issues concerning the leaking of data. Legislation should take into account the specifics of PM and create an infrastructure in which genetic information is available in a regulated context. National and EU policies currently focus on data protection and privacy, while it is more desirable to focus on empowerment of the patients and



ensuring access to their own data.

Assuming that satisfactory ethical and workable legislation is put in place so that patients are comfortable with sharing their personal information, it then has to be collected, disseminated and, crucially, understood.

There is a huge education gap when it comes to PM, even among some doctors, nurses and patients

The healthcare industry is perceived as slow to produce IT solutions and there are interoperability concerns in some areas that need to be dealt with. For example, interoperability between biobanks is hampered in the EU since different national frameworks exist, increasing the complexity of merging datasets. The national differences in legislation and regulations not only cause interoperability issues, but also have an impact at a financial level, in terms of reimbursement evaluation.

A PM-centric Europe needs to focus more on the verification of biomarkers at a high standard and with the consensus of relevant stakeholders. A lack of consistent evidence currently exists, which results in clinical uncertainty and presents a need for more targeted research.

A successful and efficacious chain that connects PM-research to PM-care and PM-treatment will require changes in healthcare infrastructure, clinical trials are run and organised, and how current diagnostic models are approached.

The research approaches used in basic science do not meet the expectations of evidence needed to implement PM. This necessitates an improvement in the knowledge transfer between basic research and clinical research through the development of enforceable best practice guidelines.

Moreover, as research into treatments takes a great deal of time - largely because treatments are often combined therapies, negotiations etween therapies. Negotiations between companies could be facilitated.

There is a need for stakeholder-agreed standards on everything from validating biomarkers to definitions of 'informed consent' to the use of IVDs. Best-practice guidelines must be formulated and enforced.

PM needs to be regulated centrally to ensure its safe and effective use, because a lack of consensus in guidelines on interpretation and use currently exists.

Regulations need to be robust and consistent while being flexible enough to adapt to a fast-moving field. At the moment regulations are not up-to-speed with the developments in science and industry. This results in outdated and inappropriate regulation. As an example, regulatory processes in respect of biomarkers need to be adapted.

A new rewards and reimbursement model for technologies needs to be put in place, and for their part technologies must have proof of viability on a fiscal level. Whether the promise of PM can be realised depends, in part, on the existence of consistent evidence, a lack of which results in clinical uncertainty and a knock-on effect of scepticism, especially among payers. Conversely, confidence will grow with every successful validation, intervention and effective treatment.

There is a need to create an up-to-date and fit-for-purpose reimbursement model which encourages and rewards investment in good research, which lies at the heart of the future of EU healthcare. Without adequately funded and targeted research, the goal of true personalised medicine will be unattainable.

The above barriers can and must be successfully tackled if we are to create a healthier and, thus, wealthier Europe for this generation and those that will follow.

The recent EAPM conference in Brussels discussed all of the above and the key points are outlined on the following pages.

EAPM CONFERENCE, BRUSSELS 9-10 SEPTEMBER, 2014

The conference heard that health is a top priority for citizens at a 'crunch time' for Europe. When European citizens are asked about their priorities for the next 15 years, health and medical care emerge as the number one concern.

European citizens also believe that the greatest impact of science and technological innovation will be on health improvement through, for example, having tailored treatments for their conditions.

Health-oriented policymaking must therefore become a clear priority. The coming decades will see major simultaneous changes – an ageing population and the growing chronic diseases burden, urbanisation, pollution or climate change – that will increase the health and wealth vulnerability of Europe's society.

The conference was told that many stakeholders have argued that personalised medicine is too complex for the realities of today, too costly for society to pay for and the research needed to bring the idea to life is too far away. But for all its complexity and distance, the reality is simple - either Europe finds a way to create new opportunities for cooperation and coordination between all stakeholder or it will fail.

This is crunch time for Europe. The clock is ticking for patients. But there is time. Time to allow the patients to be put at the centre of their own care. But it also means prioritisation is the order of the day.

Better health for citizens and patients is essential to Europe's prosperity. It cannot grow without healthier citizens that can contribute to the Member State and EU project.

Delegates heard that, to help push the agenda further, EAPM launched its STEPs campaign in the Brussels seat of the European Parliament.

STEPs stands for Specialised Treatment for Europe's Patients and aims to highlight, to MEPs and the European Commission, the possibilities surrounding PM and the advantages for their constituents.

The campaign outlines five STEPs towards a healthier Europe by aiming to secure patients' quality of life through PM. The goals are to ensure a regulatory environment which allows early patient access to novel and efficacious PM; increase research and development for PM, while recognising its value; improve the education and training of health care professionals; support new approaches to reimbursement and HTA assessment, required for patient access to PM, and; increase awareness and understanding of PM.

The conference was assured that, despite scepticism of the EU across parts of Europe, as shown by the election results, there is still added value to be had in Europe, and in particularly in the area of health. Many of the illnesses which affect Europeans are illnesses of older people who are ageing at five hours per day. They are living five hours longer each day. That is the benefit of previous investment in preventive medicine and in healthcare.

But there is now an issue of how to cope with this large number of citizens who will suffer from several illnesses, because co-morbidity is part of the challenge.

It is quite clear, delegates heard, that having done a stocktake of the individual nations in the EU that not one of them can handle this multi-faceted problem alone. It is just too big. It requires all the skills of all the people in all of the Member States.

REGULATION AND POLICY

The conference heard that, what the European Union needs to do, without delay, is to create a regulatory environment which allows early patient access to novel treatments. Europe can no longer rely on a one-size-fits-all model for 500 million as it patently does not work.

The European Parliament and the new Commission are in a unique position to push the health agenda forward and work towards building a healthy and wealthy Europe – not only for our current citizens, but for generations to come.

Health and well-being for all EU citizens is an aspiration for all politicians across all political groups. However in these economic times it is notable that the cost of good health is continuously rising in all Member States and with varying quality and effectiveness of the health care outcomes of citizens.

So key to the EU having an effective health care strategy will be to invest in innovation, particularly through the Horizon 2020 framework so that it can deliver better health solutions for all EU citizens. This will assist the EU in achieving greater growth and competitiveness going forwards.

Advances in technology and science are leading to increased personalisation of treatments but the challenge is always how to allocate resources in a smart way.

EU policy needs to facilitate smarter use of finite resources to treat the health care needs of citizens, so policy makers and legislators need to facilitate advances in diagnostics and treatments and strive for innovative solutions.

First of all they need to do this by ensuring that EU policy does not inadvertently limit the development or application of certain technologies.

Secondly there is a need to actively promote policies that enable innovation in health care delivery.

The EU has a history of strong innovation and diagnostics and pharma and bio-tech and needs to ensure that it can remain in that leading position. This can only be done through continued investment, particularly through programmes like the Horizon 2020 but also through adequately funded health care budgets.

There is also a need to share best practice and ensure efficiency in medicinal use.

The new Commission should be forward looking and, despite financial constraints, it must try and deliver new, more cost-effective treatments as a priority. It should learn from past inefficiencies in legislation but also make sure that, in implementation, it works on the ground.

Delegates also heard that the European Commission adopted a report on personalised medicine which highlights a range of different challenges and opportunities.

Challenges include the translation of research into medical applications, while on the benefit side there would be increased safety of medicines and better disease intervention.

One particular challenge may be affordability of new products and therapies. Of course, the EU may hope that the costs for personalised medicine can be compensated by efficiency gains for public health budgets. Nevertheless, efforts and cooperation between Member States are needed to design and, where appropriate, implement relevant reimbursement policies.

Another challenge is the ability to use the data generated. Europe is already able to generate a lot of molecular data from large populations for relatively little money. On the one hand, this can help to improve knowledge about the causes of diseases and the response to medicines. On the other hand it is often hard to understand such enormous sets of data and it can be difficult to assess their clinical validity.

Therefore, before genomic research achievements are translated, for example into population screening strategies, it must be ensured that the evidence for such interventions is strong enough and that the general public and health professionals are properly informed and ready to accept it.

Regarding the Commission proposal for a revision of the EU in vitro diagnostic legislation, the conference heard that, once adopted, the revised legislation on such medical devices would be a major step forward for personalised medicine.

First of all, the proposal seeks to clarify the scope of the legislation regarding tests intended to select patients as eligible for a targeted therapy, the so-called 'companion diagnostics'.

These tests will be better controlled according to strengthened safety and performance requirements and via the introduction of a new risk-based classification system, built on international guidance. This reinforced classification system will require the systematic involvement of a notified body before any companion diagnostic can be placed on the market.

The proposal foresees a mandatory consultation process with the EMA or with a national pharmaceutical competent authority to assess the suitability of the companion diagnostic in relation to the medicinal product concerned.

Therefore, the European Commission will continue to support voluntary cooperation between Member States on health technology assessment as set up by the directive on cross-border healthcare.

Attendees also heard that it is clear that personalised medicine does have a huge potential to offer new treatment opportunities for the benefit of patients, including better-targeted treatment, avoiding medical errors and reducing adverse reactions to medicines.

However, Europe is just at the beginning of a longer journey and some of the high expectations will have to stand the reality check in the future.

Personalised medicine should be seen as an evolution of

medicine, rather than a revolution, and quite some work has to be done concerning the challenges associated with its successful entry in healthcare systems.

Efforts by the pharmaceutical and medical devices industries need to be stepped up, and collaborations and partnerships between academia and industry enhanced.

To this end, the Commission (DG Research) co-funds a project called EuroBioForum aiming to create an interactive platform for life sciences performers and funders in the field of personalised medicine.

Since 2007 the EU has committed over €1 billion of health research funding underpinning the development of personalised medicine through its Seventh Framework Programme for Research and Technological Innovation. Going forward, funding under Horizon 2020, the EU's new framework programme, continues to support this field.

The European Commission is committed to continue to monitor the developments of personalised medicine in the coming years and maintain a fruitful dialogue with stakeholders.

During the past years, the Commission has worked actively to engage with all major stakeholder groups involved in PM - the academic, industry, practitioner and patient communities as well as policymakers, regulators and payers, in order to identify the main research challenges. This exercise has shown how complex and interlinked the area is and that progress will depend upon an unprecedented level of collaboration amongst all these players.

The European Commission published a staff working document which takes stock of the progress made in the field of personalised medicine - looking specifically at omics technologies - and the opportunities and challenges associated with its implementation in the healthcare systems.

This outlined four overarching challenges that would need to be addressed to advance personalised medicine in Europe. Since the field is so complex, these challenges do not provide an exhaustive list of what needs to be done but they give a good overview of some of the most important elements.

First of all, there is a pressing need to break barriers and to start speaking the same language. There is a need to break silo mentalities and create interfaces that facilitate the collaboration between different scientific disciplines and to enable the rapid integration of knowledge about relevant novel technologies and new scientific approaches in education and training curricula.

Secondly, there is a need to get better at generating knowledge and developing the right research tools. Efforts to translate enormous amounts of data generated by novel scientific approaches such as 'omics' technologies into new and improved scientific tools constitute the foundation for addressing this challenge. It will lead to a better understanding of the fundamental nature of diseases and their determinants.

Thirdly, new knowledge needs to be translated into medical applications for patients, including qualifying and validating biomarkers and developing new designs for clinical trials adapted to stratified patient populations.

Finally, there is a need to fully understand the value and economic aspects of personalised medicine so as to reward innovation and ensure the uptake of PM into healthcare.

At European level, the Commission has already invested considerable amounts in research underpinning the development of personalised medicine and this needs to continue to address all these research challenges in an integrated and coherent way.

Through Horizon 2020 and the Health, Demographic Change and Wellbeing Challenge, the Commission will invest over 7 billion euro in health research and innovation during the next seven years – a formidable resource and investment in better health for all.

The new programme is driven by broad problems (or challenges) and focuses on whatever innovation is best to overcome them. And this is a good thing, if Europe is to overcome 'innovation blockages' and to bring about real health benefits.

Health research calls for proposals for the period 2014-2015 has a budget of 1.2 billion euro with 'personalising health and care' as its main theme. This focus will likely continue in the next funding period for 2016-2017.

In the currently open 2015 call there is a topic dedicated to pilots of new models of care, based on the concept of personalised medicine. These pilots should be conducted in existing healthcare environments and should take into account Europe's national and regional diversity in health system organisation.

Meanwhile, the Innovative Medicines Initiative – IMI 2 - will have an expanded scope compared to IMI 1 as it will address the entire health-related life sciences research and innovation value chain.

As an important novelty compared to IMI 1, the partnership will this time be open to industries beyond large pharma, such as medical technologies or diagnostics. But the principle of all EU funding going to academia, SMEs, patient organisations and regulators is maintained.

The Strategic Research Agenda for IMI 2 is based on the WHO report "Priority Medicines for Europe and the World" and developed by the members of EFPIA, after a period of extensive public consultations.

Personalised medicine sits at the very heart of the IMI 2 Strategic Research Agenda which is focused on "delivering ' the right prevention and treatment for the right patient at the right time'.

For instance, it is expected that the new partnership will deliver a 30% better success rate in clinical trials of priority medi-

cines identified by the WHO and at least two new medicines which could be either new antibiotics or new therapies for Alzheimer's.

The audience heard that, on basic guidance, the Commission's philosophy is that it does not see personalised medicine or a personalised approach to medicine as a stand-alone topic, but sees it as a horizontal issue that needs to be completely mainstreamed in every aspect of public health and every aspect of healthcare.

Everything from prevention to treatment has to become more personalised, that is clear, so the Commission's approach as policymakers responsible for a number of regulatory areas was to ensure as much as possible that all areas that the Commission is responsible for are prepared for the challenges of PM.

The conference heard that the adaptive licensing project that was launched in March 2014 is linked to personalised medicine. The concept is to build on advances in medical science, to bring new innovative medicines early to a targeted group of patients with characteristics linked to the pharmacologist's product.
It is envisaged that if a specific group of patients is targeted, then the benefit will be so large that it will outweigh the risk early in the developments.

For this expansion the focus should be on real-world data, on registries, on observational studies, on studies where the protocol can be changed, not only randomised clinical trials with a fixed protocol. Europe needs to be flexible to use the other data for efficacy, not only for safety.

Another aspect of this concept is involvement of many stakeholders, notably health technology assessment bodies and patients, early on in the development, but also throughout the life cycle of the product.

There is a real problem leveling these issues in the educational system. One of the problems is that the Commission doesn't have all the prerogatives to do something about it so is a little bit handcuffed in this respect.

When it comes to how the Commission can do more, there should be objectives for the Commission in the health sector, but not per directorate-general. There is a need for a real transversal objective in the health sector involving clusters of DGs acting in certain areas.

Attendees heard that healthcare in the past was focused purely on the treatment side, but now there is much more emphasis on prevention and prediction. This is something that national policymakers and European policymakers should take on board, which requires a change in mind set. The old systems, devised over the past 100 or 200 years, do not adequately function anymore. Europe needs to move to capture the true potential of these new therapies and new diagnostics.

Regarding overall survival, the regulatory attitude is moving gradually away from this towards clinical response - response which is linked to clinical benefit. `Obviously, response is a softer end point. So the effect on response must be large enough to outweigh the uncertainties, that is the general regulatory view.

The conference heard that EAPM calls on MEPs and the European Commission, but also on national health ministers, to look at developing and harmonising the citizen-focused personalised medicine research agenda, enable efficient and effective translation of that research and scientific innovation into real benefit for patients.

LITERACY AND TRAINING

Patients as partners must be involved in all stages of the personalised medicine continuum, they can be strong champions of pan-European and national levels to underpin PM integration. EAPM is planning to develop a series of patient advocacy forums in different European countries, really to engage, to inform, to empower.

Literacy is a very important aspect in actually making people aware. Not only patients and patient advocates but healthcare professionals. That includes particularly general and community practitioners, because PM is not just new drugs, or new therapies or new devices, it is also prevention. So there is a need to engage with the various stakeholders who are involved in the different aspects of healthcare practiced today.

The conference heard that four pillars of knowledge have been highlighted. The first one is compatibility. It is necessary to identify the needs for current and future personalised medicine skills, to identify who needs to be educated - healthcare professionals and the population.

The second pillar is keeping pace, ongoing training during a career. Personalised medicine is a fast-moving science, so knowledge needs to be updated with continuous medical education and continuous professional development. It is important to have multi-platform learning with real-time access to an information repository.

The third pillar is interdisciplinarity. Here there is a need to collect input from all medical and non-medical specialties through a string of interdisciplinary networks.

The fourth pillar is the need to coordinate this networking and to set up an educational programme to develop infrastructures, curriculum development, management and more with the support of the European institutions.

The audience heard that, in Zurich, there are two universities, a federal technical school and a university with a medical faculty. This represents a joint competence centre to unify both universities in activities concerning personalised medicine. The federal technical school has all the bio-informaticians and engineers, while the university has the medical faculty.

There will be a new generation of biologists and of medical students at this competence centre with a PhD programme. Around 200 people have applied for this PhD in personalised medicine but there are only 30 places. There is a big interest.

One issue is that the federal technical school argues that all the Big Data people, and the biologists should move to the medical course after the second year and become doctors. It is not easy to convince a medical faculty of this, but it is necessary to educate the young personalised medicine people who come from all sides - the biology side, from the engineering side and from the medicine side. This is also a task that Europe must take on.

Delegates heard that, two years ago, a working group on PM in laboratory medicine was formed to forge a specific understanding of the evolution of the involvement of professionals in this area.

48 laboratories in 18 different European countries are taking part. More than 90% of these professionals believe in the importance of personalised medicine and all wish to improve the health of citizens.

These professionals believe that, alone, they are not enough, so they are ready to collaborate and interact with other disciplines to produce results. However, only 10% decided that they were ready to do this - because the others explained that they do not have a high enough level of PM knowledge.

These said they needed new technological facilities, additional training and new competences to be included in the area of laboratory medicine. But PM is the medicine they would like to give to their communities and it seems that Europe not only needs to work on funding, but also on training and the integration of different competences.

Attendees were also told of plans to develop an educational programme in personalised medicine - starting small with a workshop aimed for 2015 – as well as an online educational platform on PM.

PATIENTS, ACCESS, CLINICAL TRIALS

Failure to achieve the delivery of PM in the health arena will be a huge lost opportunity for patients.

There is a compelling need to develop and implement a coherent strategy that puts patients at the centre but that will require prioritisation in terms of selecting how Europe goes about doing things.

Better health for citizens and better health for patients is essential to the whole sustainability of Europe's future.

In the context of the EU, a lot is talked about equality, 28 States, 500 million citizens, but in the healthcare arena there is a huge divergence between nations.

On patient empowerment, delegates were told of the fundamental importance of quality information related to personalised medicines being given to patients in a way that is accessible to them. This is very much linked to health literacy, enabling patients to understand the information and utilise the information to navigate their health environment.

Attendees heard that it was a considerable disappointment that the EU decided to omit the opportunity in the Clinical Trials Directive to involve patients and patient organisations in the early development of clinical trials.

Patients and patient organisations are not just the end product, they need to be involved in the discussion at each national level. To achieve this, patient organisations need to be regarded

as professional. They are not always patients, most of them actually work for an organisation as a professional, they come from a professional background. They are not there in order to simply get the best medicine from the pharmaceutical company, they need to be treated as professionals.

In fact, delegates were told, it is often the regulatory environment - not the medicines regulatory environment - that causes the pharmaceutical companies to create a number of barriers to their engaging with patient organisations in a way which would allow for much more free access.

The conference heard that, for the Commission it is important to facilitate the conduct of clinical trials throughout Europe. This is the aim of the recently adopted regulation on clinical trials.

The new regulation streamlines the authorisation procedure for clinical trials applications and reduces unnecessary bureaucracy for industry and academia.

The new regulation is expected, in particular, to facilitate clinical trials for personalised medicines, which, because of the small patient populations, might often require multinational clinical trials to reach recruitment targets and thus produce robust and reliable results.

The European Reference Networks between healthcare providers and centres of expertise in the Member States can be focal points for medical training and research and hence could support multinational clinical trials.

Regarding clinical trials, the conference heard that Europe will need special network and clinical study groups that work together. But, in general, there needs to be a better understanding of how stakeholders can work together and how patients can be switched from one centre to another.

Meanwhile, there is a need to harmonise diagnostics, to find a good balance between things that are publicly available and those that companies undertake privately.

The conference also heard that PM has both similarities and differences with the rare disease field, the challenges that are common to both fields are those linked to small population issues and all that goes with it. These are mainly difficulties in gathering critical mass of sufficient numbers of patients to organise clinical trials with a recognised statistical significance.

Within the rare disease field, there are orphan medicinal products targeting all the patients from one rare indication. But not all orphan drugs are geared for all patients within the same indication. Some of these drugs are only for specific sub- target populations, for the ones with the same genetic profile and the same genetic mutation. So this implies another area of common focus, PM will be produced and given together with the appropriate genetic test.

The marketing authorisation is granted for a specific sub-group of one rare indication, based on the genetic mutation. Then there is the hope of expanding to other target groups if clinical studies prove that the same medicine is also safe and efficient and has a positive benefit-risk ratio for other groups.

Meanwhile, the conference heard that, in Vienna, a 26-year-old patient, referred by a small hospital, had resistant lymphoma. A biopsy was undertaken and the DNA of the tumour sample was sequenced. There turned out to be just a single mutation in this tumour, with just one centre in Europe open with an inhibitor targeting this particular mutation.

The patient was accepted for clinical trial in another country, paid for by an Austrian insurance company.

A patient, or a patient's samples, have to be mobile, in order

to send them to specialised centres that will not exist in every country. A problem is that patients like to be treated in their own region. There is a need for rapid exchange of patient data involving a centralised hub.

The conference heard about a test relating to breast cancer. For patients with breast cancer, there is a lot of interaction, and a lot of physicians involved. Patients will not understand which treatment is going to work best for them.

Typically they will receive surgery to remove the tumor and most patients will ask first is whether the surgery or treatment is going to save them and whether they will need chemotherapy.

A lot of the developments in PM need to start with the clinical question that is important to patients. It is important for physicians and society to understand which patients are going to benefit from which treatment. The test identifies which patients are likely to benefit from chemotherapy.

However, there is a strong inequality of access throughout Europe, despite the test also having an economic benefit.

The attendees heard that something as common as breast cancer is now actually at least ten different cancers, so even common cancers are going to be sliced into maybe twenty, thirty, forty, or fifty different sub-types by this kind of diagnostics.

On a broader note, PM is a development that is particularly astute in cancer medicine because of the fact that cancer is a disease of genetic instability - over the course of time mutations accumulate and lead to the derailment of cells, which become independent in their behavior, and do not listen to the normal rules within the body anymore.

The fact that there is genetic instability leading to activation of certain pathways in cells that now are out of control, and the fact that these pathways can have certain altered key proteins that put this pathway in an activation mode and that this protein may be able to be targeted, brings a possibility - but not always – of developing a drug against that key protein for that particular pathway. This gives drugable mutations.

When it comes to tumours, about 50% of the tumour is actually the host immune response to those cells because they express something that the immune system can recognise as 'not self', and one of the biggest revolutions now is happening in the development of immuno-modulatory drugs that can handle and reset the immune system.

Despite this, it does not necessarily mean that there will be a drugable/actionable target for every sub-classified tumour.

HTA

Attendees heard that the EU has set up a new HTA network for carrying out health technology estimates together, but the money side will stay at the Member State level.

Delegates were reminded that all drugs have toxicity. Fortunately, there are some drugs giving fantastic benefit with a good toxicity profile. However, there are many ineffective drugs on the market on which Europe spends billions per year.

These do not bring any benefit to the patients. These drugs and treatments simply fit into an economic model based on the relevant healthcare system. So, Europe must stick to knowledge-based and goal-oriented approaches.

The conference heard that the rare cancer community has always had to cope with the problem of small numbers. Now the more common cancers are splitting in to sub-groups and becoming rare so the same problems are occurring.

There is an issue in validating all the information, even if it is not a large clinical trial. There are methodological problems in that, the more these methodologies fall outside the conventional criteria of clinical studies, the more they will be interpreted differently by regulators across Europe.

Meanwhile, when the EMA approves a drug, the HTA and reimbursement bodies make different decisions across EU countries. Affordability is quite different between the countries in Europe, which is a challenge, when medicines have just one price. There are cultural values that make technology differently attractive across healthcare systems and an HTA assessment has to bring these to the table.

The local burden of diseases may be quite different, depending on technology, and there may be different local health priorities in the Eastern part of Europe than there are in, for example, Germany.

There are also legal constrains in a healthcare environment, which is essentially regulated locally. The biggest challenges are that certain domains of this are not appropriately captured.

Also, Member States' systems are often not ready to adopt what is produced. There needs to be a focus on the methodology of HTA. Much more than going straight into the assessment activity, which cannot be adopted.

That's the construction side, certainly for the years to come. Not only in Brussels but also in Member States, who have to articulate a lot more strongly why they are interested in a European-level HTA.

COLLABORATION

The EU is now extending IMI to IMI 2 and there is another three-billion-plus euro to spend. There should not be a problem finding the money or projects because the big trend is towards externalisation of research and partnerships.

Europe must deliver on this now and it will happen faster with collaboration. Some of the latest thinking in IMI has seen the announcement that four, five or six competitors are going to work together and do Phase II proof concept studies for Alzheimer's. It is possible that five successful products, all

different and all targeted, will emerge from this collaboration.

Europe must create a variety of opportunities for all the different stakeholders, from patients, industry, academia, the regulatory community, the political community and so on to collaborate in a sustainable framework.

And it is a hugely important issue for Europe because only by working at a European level can the critical mass of engagement be generated to bring this about.

BIG DATA

Delegates heard that 'Liberate the data but do no harm' means exactly what it says. It deals very much with accessibility to the data, the governance of the data. This means in reality that scientists need labs, patient population-related data to create drugs and therapies. So which policies are in place, are those the right ones, do we need to change those that exist, which activities, which financing?

'Bring it now' means that Europe needs to be invested by a sense of urgency, to bring this knowledge to the worksite today. It is to do with adoption, and has to do very much with Member States, take-up and their own healthcare policies locally, regionally and nationally.

Which policies, which programmes, which investments should be placed for this to happen today? Today's future is tomorrow and areas such as education - not only from the patient/public point of view but also from the carers, the healthcare providers, the skills, inter-partnership, research and development, high performance computing and other technology.

Delegates heard that, according to the European Commission, Big Data is one of the currently most sensitive issues concerning the public acceptance of personalised medicine.

The current and future development of PM is strongly related to the increasing possibility to capture, store and analyse big amounts of data. Whether it concerns genome sequencing or the collection of behavioural information through lifestyle apps on telephones, the analysis of data patterns is what makes this information valuable.

The trend is very clear. The amount of data gathered is exploding. Better imaging, lower costs for genome sequencing, more mobile medical devices. All contribute to a growing amount of medical data.

And over the past few years, nearly all major IT businesses have started their own Big Data projects. And also in research Big Data plays an increasingly important role. Not only in genome therapy, but also in areas like cancer research and disease prevention.

The use of Big Data in healthcare, however, has important challenges. Data governance and trust are among the best known. Assurances must be given that the data will be used appropriately, in the context of the intended uses and abiding by the relevant laws. The fragmented and overly complex legal environment, the shortage of healthcare data experts, and the lack of cross-border coordination, are barriers to the full potential of Big Data in health.

Big Data seems to allow for great opportunities in patient empowerment, personalised medicine, predictive analytics and in the achievement of greater efficiency in healthcare systems.

These are all main issues in the current EU policy agendas. However, it is still not clear how Big Data will interconnect the promises, and how exactly efficiency will increase and costs will reduce.

Therefore, a better understanding is needed on what Big Data will mean for the national healthcare systems, how the rights and data confidentiality of citizens can be protected, and what actions the European Commission can take to increase the value of Big Data for PM. Pending a final decision, a study is planned under the Public Health Programme to assess the use of Big Data in public health policy and research.

The Commission's intention is to clarify and further harmonise the Data Protection rules across Europe. By introducing specific provisions related to health and research areas the Commission underlines the value of the use of medical data for research. In the longer term, clearer data protection rules in health will increase the quality, safety, and efficiency of the healthcare systems.

Currently the text of the proposed Regulation is discussed in the Council under the lead of the Italian Presidency. The objective is to finalise these complex negotiations by 2015.

However, the conference heard that, concerning the Commission proposal for a Data Protection Regulation, many EAPM stakeholders fear that the changes as proposed in the report of the European Parliament could harm research and make clinical trials more difficult.

Regarding Big Data, its collection, storage and use, which are essential to effective healthcare, attendees were told that the EU needs to be aware that the data concerns should be accommodated by the politicians but should not obstruct development of new initiatives. The Commission should ensure a regulatory environment that facilitates patient access to new innovative medicines and treatments.

PM requires huge amount of data, aggregations of different sets from millions of people, but health data is almost exclusively personal data and it should be controlled and owned by the citizens.

However, current healthcare systems are national, and don't address global needs. The only people who have an interest in the global promotion of healthcare are the citizens themselves. How can we empower citizens to control their own health data while allowing contributions to medical research in order to improve outcomes of research and evidence-based medicine?

The World Economic Forum has called personal data a new asset class. Many big companies live on the secondary use of personal data. It has been argued in Europe that the citizens themselves should decide on the secondary use of their data and not multi-national companies. To do this, citizens have to have the right to control their data and access it in a way in which they can decide what to do with it.

Personal data is a huge economic driver, it is an asset. Individual genomic data and health data is not worth very much until it is aggregated with millions of other data sets but, at this point, it becomes increasingly valuable.

Attendees heard that a data cooperative is the ideal structure in which to operate personal data banks. This is because cooperatives are owned by participating members. The vision is of national personal data cooperatives in which members own all medical data received from their doctor, their nutrition data, the click streams and so on.

Each individual should have a legal right to be able to access his or her data and at which point he or she can decide which data to share with clinical research. Citizens would be able to decide whether they want to participate in research and trials potentially beneficial to them and society as a whole.

There is, of course, a need to be transparent and informative about the opportunities and the risks, thus leaving it up to the individual to decide how much sharing he or she wants to do.

The biggest hurdles are how to get people thinking in a cooperative way about data ownership and the value of personal data, for themselves and society.

The conference also heard that u is vital to protect people's personal data but Europe also needs to work out how to share this knowledge.

There is an immediate concern about the wording that was approved through the European Parliament on the data protection regulation. Many leading scientists and patient organisations have warned that, as it stands, it would be impracticable and make running large-scale clinical trials on things like cancer research extremely difficult, if not impossible.

The conference was told that EAPM would like to see a European-wide data ecosystem for PM. If it is accepted that this is a multi-disciplinary area that means that this policy - at the highest level - should be sustained and should cross-cut a number of areas, regulatory areas, research, innovation, partnership and many others. If Europe is to be a place for world-class computing and world-class scientific research for PM, there needs to be political focus on it.

Computing is very well advanced but it is not totally there yet depending on the computation load. There is a need for sophisticated and advanced computing environments in order to process, interpret, analyse and help the decision-makers at the point of decision with support tools.

RESEARCH AND DEVELOPMENT

The audience heard that personalised cancer medicine is 'one big research project' and that, so far, science is only scratching the surface of what is going to be one of the biggest research - and integration of basic translational and clinical research - projects ever undertaken.

Regarding medical imaging in relation to PM, attendees heard

that there are some tools available nowadays in the field of molecular imaging, nuclear medicine. Although imaging cannot replace biopsy, it can be used to avoid taking a sample of tissue.

And with imaging it is possible to look at cells throughout the whole body of the patient. Unfortunately, there is currently no equal access to this technology - in some countries there is a lot of imaging available but, in some others, there remain access difficulties.

The conference also heard that there is a way to secure spending in Europe. The pharma industry spends 100 billion euro every year on research and development, a third of which is in Europe. Clinical research in numbers of trials is going down but money is up and it is possible that the quality of the types of research is better in Europe,

There are some unmet needs that must be addressed and these are forefront in the strategic research agenda adopted for IMI 2. IMI has, in effect, become the playground for projects that could not be done before.

However, delegates also heard that Europe has a lack of research funding, a lack of strong scientific evidence in some fields,

plus communication and training issues.

There is a lack of knowledge among professionals and Europe eeds to break the barriers between the two worlds of patients and these professionals.

Meanwhile, over the last 5-10 years, Europe has moved from a situation of trial and error medicine, a lot of what was done in the past was not based on evidence at all, it was based on something that worked or seemed to work and then it was done to death.

And that is not the way in which to try and move forward. There needs to be much more of an approach that is actually thought out, considered and is looking to give not incremental change but transformational change.

In order to embed personalised medicine into European health systems the Commission must develop a patient-centered European translation research platform. This in order to empower patients because they are the most powerful advocates for PM and its integration.

There is a need to increase literacy and that is very important across the personalised medicine continuum. It is also necessary to provide solid evidence, not only for the clinical advantage of personalised medicine but also the health, economic and societal advantage. And a more agile but also more pan-European regulatory framework will enable more rapid translation of PM into clinical practice.

What Europe needs to do is convert that excitement in new research discoveries into real meaningful new diagnostic tests, new processes, new procedures that benefit European citizens, that benefit society, and that benefit industry.

The European translation research platform proposal links to the pipeline that has been envisaged by the recent Horizon 2020 advisory group who produced a paper on the implementation of PM in Europe. So this is a response to what is being asked for in the context of Horizon 2020.

The translational research platform has a number of different parts to it. It is necessary to try and link infrastructures and technologies and those infrastructures and technologies need to be across the board. They are not just in academia, not just in industry.

Europe must convene expertise where its needed to work together, but most importantly to develop a patient academic clinical industry partnership, and an equal partnership, because only by working together can Europe achieve something that is going to have a lasting benefit.

HEALTHCARE SYSTEMS

The attendees heard that life expectancy has increased much faster than healthy life years. There has been an improvement in healthy life years but there has been a much bigger increase in life expectancy, which means the years spent in ill health have increased. This is one of the main factors causing the problems in health systems because they were designed with a different population distribution in mind.

However, it was argued that health systems are becoming more efficient. While healthcare expenditure has been increasing, Europe is getting more for its money, so more patients have been treated. The EU is spending more money but the increase in patients treated is greater than the increase in the budget.

Nobody has really defined what sustainable health systems mean. Nobody has actually defined at what point a health system explodes, or implodes. Is it European health systems getting to the point of US spend? Is it US spend plus 5%? Nobody knows and whenever there is an increase in expenditure the question must be asked - what are we getting for the money?

There is a dynamic which goes on in medicines markets all the time. Year on year there will be new innovations, new products which will drive cost, at the same time each company will be losing a share of its portfolio through products that will be l osing patent exclusivity, that would be subject to competition.

The prices of those medicines go down usually dramatically after the loss of exclusivity of patents and data protection, and that efficiency from the lowering price of older medicines yields huge benefit.

There is a situation of growth over a period that has been attributed to new products versus the value of the market that has been attributed to market efficiency of older products becoming much cheaper. These cancel each other out broadly speaking.

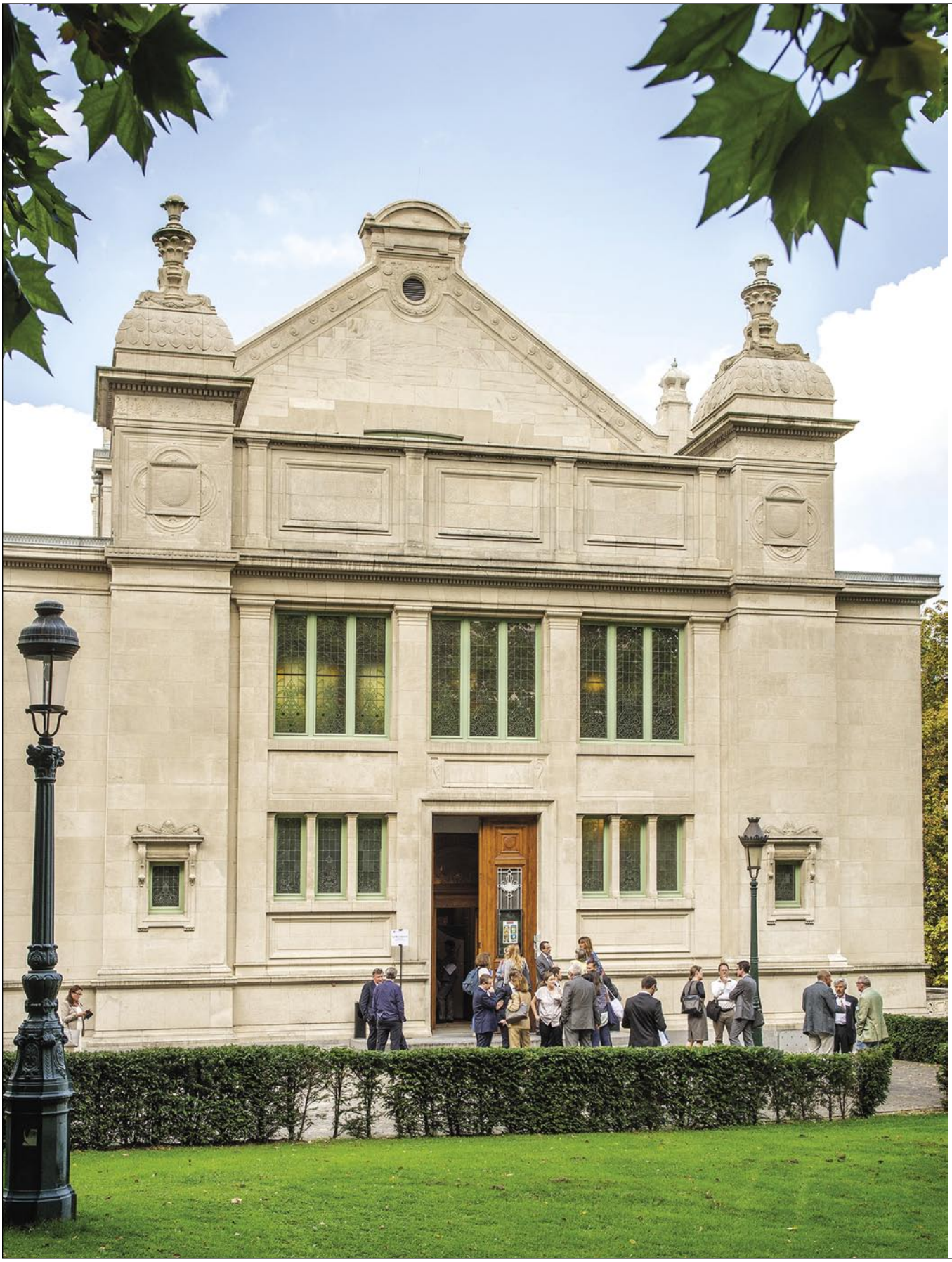
In oncology, Europe is dominated today by a generation of very impressive high- cost cancer medicines, but in the next few years, Europe will start to see some major cancer medicines losing patent exclusivity. This will change the competitive practices within oncology markets, leading to efficiency and thus affordability improvements in oncology markets.

The increased scrutiny on providers of products and healthcare services to demonstrate value for money is absolutely right and should be expanded into other areas to drive smart decision making in healthcare systems.

Europe needs to invest in the right infrastructure to make sure that decision makers are operating in an information-rich environment.

When Europe is able to more cheaply, efficiently and effectively capture patient outcome data; this will open the door to doing many things in a very different way - including the pricing of personalised medicines and the commercial deals that companies can strike with payers.

Generally speaking, the conference heard several opinions that 'the French system is the best', and that other national healthcare systems should look at the French model. The model is being provided free, so is a challenge. But, at the same time, there is a return on investment. While it does not deal with fur-



European Alliance for Personalised Medicine

ther development of personalised medicine, it does, at least, set the first set of rules and bring the first set of benefits. Therefore, it is a good model to look at.

More broadly, there are many healthcare systems in Europe struggling for survival because they are dependent upon state revenue, and state revenue in many parts of the EU is shrinking rapidly. The idea that these systems are identical is far from the truth. Systems of social security have to be careful in order to survive.

Healthcare systems across the EU are also struggling to integrate their citizens and to give care according to certain standards. And these systems are moving apart, not coming together.

EU-US TRADE

The Transatlantic Trade and Investment Partnership could benefit patients in both Europe and America.

Delegates heard that, in both continents, two key issues in the health arena are patient access to high-quality, personalised medicine and free trade.

At first glance, there may seem to be little in common between these issues. Few things sound more "local" and private than the care of patients. And few things sound more "global" and public than the negotiation of a free-trade agreement between countries or in this case between continents.

But the conclusion of the Transatlantic Trade and Investment Partnership, or TTIP, while benefiting all Europeans and Americans in some way, would benefit patients in particular.

At present, neither the US nor the EU economies are growing. Unemployment is stubbornly high. Both are feeling pressure from aging populations and rising health-care expenditures. In response, both economies need to create jobs and growth and TTIP is a great way to do that.

Healthcare market access and reimbursement remain in the purview of the EU member states. But TTIP could establish an important benchmark. Industry recommends a "pharmaceuticals annex" to TTIP similar to the one included in both the US and EU trade agreements with Korea, enshrining principles that reward innovation and promote fair, predictable and transparent processes for deciding which medicines patients can have access to.

The biopharmaceuticals industry would benefit from a TTIP focused on these areas. But so would its hundreds of thousands of employees and suppliers in the EU. So would the cities and regions in which it operates. So would the universities, research hospitals, and other partners with whom it collaborates.

And so would patients if the continuous-innovation pipeline flows more rapidly and with a higher volume of improved, personalised treatments.

It is time for political leaders on both sides of the Atlantic to push forward with TTIP negotiations and emphasise the role of free trade in improving health. Personalised medicine and free trade belong together.

The conference also heard that TTIP will allow innovation in all sectors but in the medical sector too to be encouraged on both sides of the Atlantic at a time when both we and the US need to encourage innovation.

It will make it easier for items like new medical devices to be approved in one country and marketed in another, it will make it easier to share best practices and learn about how both can better come up with new ways to deliver high quality affordable healthcare. If both sides get this right it could unlock huge benefits.

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Angela Brand. Founding Director, Institute for Public Health Genomics at Maastricht University.
Christine Chomienne, President of the European Haematology Association (EHA). Panel: Holger Moch. European Society of Pathology
Mario Pazzagli, European Federation Laboratory Medicine
Paul De Raeve. Secretary General, European Federation of Nurses

European Alliance for Personalised Medicine

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.

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