EPEMED

The European Personalised Medicine Association

Highlights

2010 – 2011

Contents

EPEMED Foreword

Over the next few years, we will see profound changes in medical care due to the unprecedented advancement of break-through innovations in the field of molecular diagnostics, based on new science and technologies that will significantly help clinicians improve the care of their patients. Therefore, it is timely for organisations and individuals involved in personalised medicine and high-value diagnostics to join forces to help shape the policy and regulatory environment and accelerate access to innovation in personalised medicine in Europe.

EPEMED is a recently formed, not-for-profit organisation. The association was founded to address issues in personalised medicine that confront the industry, regulators, payers & insurers as well as governments. The organisation comprises a dynamic and diverse group of leaders in the personalised medicine field, who have great expertise in the application and development of diagnostic tools and stratified medicines to deliver improved patient care.

EPEMED aims to provide a pro-active platform for the harmonisation of personalised medicine development and implementation across Europe, focusing on the crucial role of diagnostics, to make personalised medicine a reality. Its mission is to create a central point of communication for all those involved in progressing personalised medicine; to determine optimal regulatory and reimbursement routes to deliver personalised medicine to patients efficiently and to promote improved development of personalised medicine through the creation and application of advanced diagnostic tests.

Members of EPEMED benefit by harnessing the collective strength of a dynamic collaboration between diverse European parties with the common goal of promoting the concept of personalised medicine and high-value diagnostics to the public, government and private sector across Europe. Together we are providing opinion leadership with a collective view on issues related to personalised medicine and advanced diagnostics in Europe.

Our past and present activities are described in this brochure, and include the publication of a white paper on European market access for high value diagnostics, the broadcasting of webinars, as well as annual conferences on personalised medicine. The 2010 conference was held in the French Senate (Paris, 12 October 2010), the next one is taking place in Luxembourg December 2011.

I hope that you will consider joining EPEMED and work with us to realize the full potential of personalised medicine in Europe and beyond.

Kind regards,

Alain Huriez, MD
Chairman

Webinars

1st EPEMED Webinar, 15 September 2010, "Market Access for Personalised Medicine in Europe"

The webinar was moderated by Ann Bruinvels, featuring several key speakers in the field of biomarkers, healthcare, pharmaceutical and as well as the Chairman of EPEMED.

Ms Rasika Ramachandran (Frost & Sullivan) gave a complete overview of the context of Personalised Medicine. Starting from the different stakeholders, she summarized the different existing models and the needs for Personalised Medicine in the picture. She also gave several examples of the different models including the development of companion diagnostic scenario and the associated key market trends.

Mr Joe Ferrara (Boston Healthcare) intervention focused on the value based payment of Personalised Medicine. Economic and societal forces are driving an increased demand for value in health care. All the stakeholders are trying to assess and capture value. In the US model, the payers recognize the potential of Personalised Medicine. The gap between evidence needed for market launch and market acceptance mirrors differences in stakeholders value expectations. He also gave an extensive view of the key differences between drug and diagnostic for the development, value determination, policy approaches, and reimbursement strategies in the different location US, or EU.

MD Alain Huriez (Founder and Chairman of EPEMED and CEO of TcLand Expression) gave the vision of EPEMED and the need for such organization, given the increasing demand for Personalised Medicine as described in the previous presentation. Alain also gave a practical vision and examples of the situation in several European countries (UK, France, Germany, Italy and Spain).

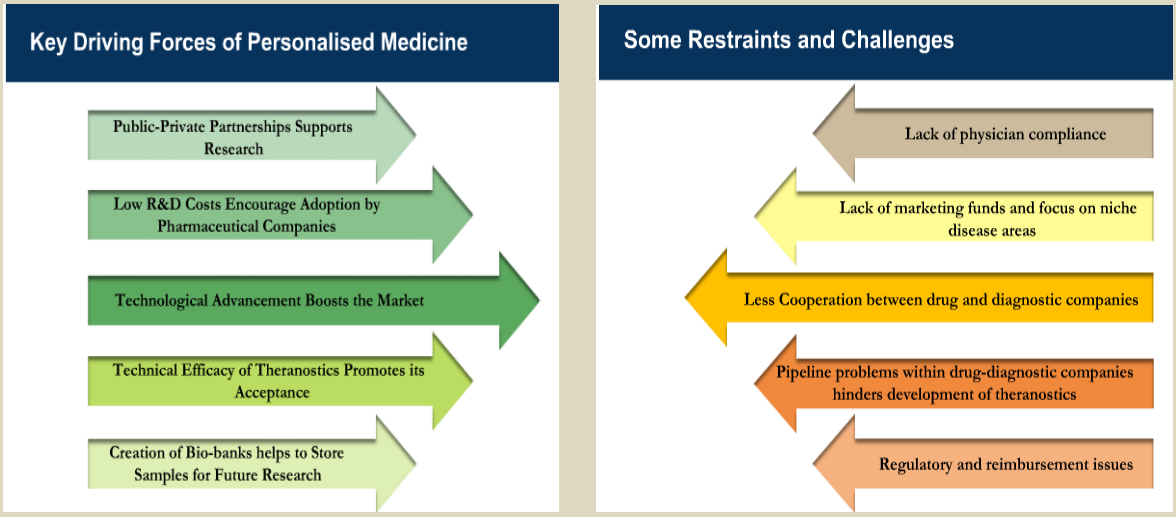


Figure Adapted from Ms Rasika Ramchandran (Frost and Sullivan)

2nd EPEMED Webinar, May 2011, “Building the European Personalised Medicine Market”

This event was chaired by Iain Miller, then Executive Director of Theranostics at bioMerieux (now serving as Global Head, Personalized Healthcare Strategy & Partnerships at GE Healthcare). In addition to moderating the webinar, Dr. Miller gave a presentation titled “Market Access Challenges in EU for High Medical Value Diagnostics Tests”. Other speakers were Nick Crabb, Associate Director, Diagnostics Assessment Program, NICE with a presentation "NICE Assessment of Companion Test Products" and Loic Kubitzka of PWC who discussed "The opportunities and challenges of European market entry for emerging diagnostics companies".

Dr. Miller described the great progress made in recent years, yet highlighted the lack of standardized global products. Most tests remain as Laboratory Developed Test offerings. He noted that this lack of IVD “kit” success stories renders challenging the substantiation of a good business model in this still-nascent market. In particular, modest volume companion test value propositions have to compete with high volume “traditional” IVD test offerings, without an attendant pricing premium. Value capture remains elusive in all markets but Europe presents particular challenges in terms of decentralized diagnostic reimbursement, heterogeneity and lack of transparency. Specific challenges in several major European markets were reviewed.

Loic Kubitzka reviewed European IVD market dynamics and deal activity, with a focus on the Luxembourg accelerator model. Encouraging signs of accelerated partnering between diagnostic and pharma companies was noted, and some specific indicators of European market potential were reviewed. For example, lower regulatory barriers allow more rapid test diagnostic product entry in Europe, versus the United States. PWC efforts to develop a business accelerator in Luxembourg were detailed. (Author note – The 2nd annual EPEMED conference will be held in Luxembourg on December 8).

Dr. Crabb reviews the NICE diagnostics assessment program (DAP), with particular emphasis on methodology challenges and companion test considerations. The general lack of clinical utility studies was noted, and economic modelling proposed as a partial solution. Several illustrative companion test scenarios were reviewed, the most challenging of which, independent development of test and drug, is perhaps the most common scenario in the market today.

While all speakers agreed on the challenges faced in this market, they noted positive signs of market evolution and emergent business models.

Notes prepared by Iain D. Miller, Ph.D.

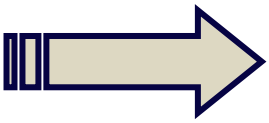
3rd EPEMED Webinar, November 2011, "Nutrigenomics and Health / Personalised Healthcare"

Introduction and chaired by Patrick Terry, Co-founder, Board Member EPEMED with the intervention of 3 keynote speakers:

Prof. James Kaput Nestlé Health Science Program Director, Clinical Translation Nestlé Institute Health Sciences

Prof. Christian Bréchot "*Nutrigenetic Scientific Context"* VP, Medical and Scientific affairs at Institut Mérieux

Dr. Robert Jones "The Business of Food as Medicine Principle", Scientia Advisors Functional Foods Division



Further information and slideshow presented during these webinars may be downloaded on the EPEMED website at :

http://www.epemed.org/index.php/page/webinar_2011

White paper

Market access challenges in the EU for high medical value diagnostic tests

Iain Miller, Joanna Ashton-Chess, Herman Spolders, Vincent Fert, Joseph Ferrara, Werner Kroll, Jon Askaa, Patrick Larcier, Patrick F Terry, Anne Bruinvels, & Alain Huriez

Personalized Medicine (2011) 8(2), 137–148 ISSN 1741-0541

The clinical utility and medico–economic value of several personalized diagnostic tests has been well described in the literature. Development of such tests, including generation of the necessary supportive clinical validation data, is a complex and expensive endeavor. In general, sponsors of such tests lack sufficient clarity on appropriate reimbursement and regulatory pathways to provide the clear development framework necessary to incentivize the required level of investment. In the USA, an imperfect reimbursement paradigm has evolved to accommodate a small number of 'value-priced' laboratory-developed tests, although major structural barriers remain to broader implementation. In Europe, by contrast, there is virtually no precedent for value-based public sector pricing, and even such procedurally based pricing as currently exists is administered by a complex network of largely decentralized bodies. As a consequence, patient access is limited and health–economic savings are not realized. This article explores some of the European market entry barriers, with a focus on reimbursement challenges, and highlights some collaborative proposals to address such.

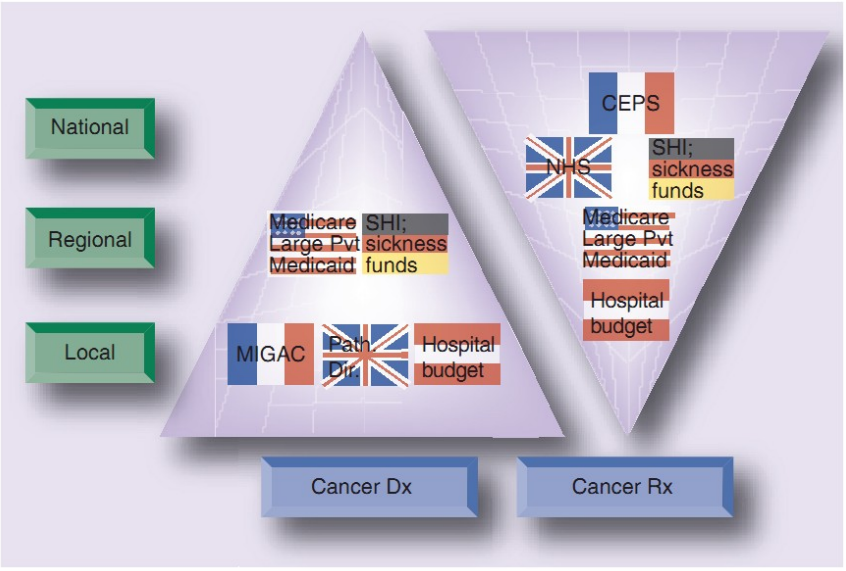


Figure. Key differences in reimbursement policy approaches for oncologydiagnostics and therapeutics. For most countries, drugs are reviewed for reimbursement at the national level while tests are reviewed at the local or regional level. CEPS: Comité Economique des Produits de Santé (Economic Committee for Health Products); Dx: Diagnostics; MIGAC: Missions d'Intérêt Général et d'Aide à la Contractualisation; NHS: National Health Service; Pvt: Private; Rx: Therapeutic; SHI: Statutory health insurance. Adapted with permission from Boston Healthcare, 2010.

1st EPEMED annual conference: Personalised Medicine in France and Europe: a major health economic challenge

Executive Summary, Palais du Luxembourg, Paris, 12 October 2010

EPEMED, the European Personalised Medicine Association, organised its first conference in collaboration with the French Senate in Paris on 12 October 2010. The conference was entitled "Personalised Medicine in France and Europe: a major health economic challenge". The purpose of the meeting was to inform and educate policy makers, industrial players and other interested parties on the broad challenges associated with access to personalised medicine in Europe, with a particular emphasis on France. It was hosted by French Senator Philippe Adnot, member of the Finance Committee, who introduced the conference together with the French Member of Congress Claude Birraux. The conference attracted a diverse group of attendees from Europe and the United States. The meeting was structured as a plenary session presented by EPEMED's chairman Dr Alain Huriez, followed by a series of 3 round tables, together with several presentations followed by a discussion of the role of French industry.

First the concept of personalised medicine and in particular the innovations coming from translational research in the public sector were presented. Professor Fabien Calvo, Director General of INCA (Institut National du Cancer), highlighted INCa's 28-center Personalised Medicine testing network, whereby INCA funds emerging tests while they progress towards standard of care, thereby facilitating early access. A lively discussion of the challenges associated with the commercial development and clinical laboratory provision of complex tests and of the law of Ballereau which limits the sites at which molecular diagnostic tests may be carried out, including the role of corporate sponsors. In particular, the French prohibition of the kind of commercially led activity common in the US and other markets was seen as a force driving French innovation overseas.

The US experience regarding personalised medicine.
Chaired by Patrick Terry, co-founder of Genomic Health, the panel included Ed Abrahams (President of the Personalised Medicine Coalition), Felix Frueh (Vice-President of Personalised Medicine, Medco), and Pierre Cassigneul (CEO of XDx). The panel highlighted the more advanced status of PM in the US versus Europe. Felix Frueh presented Medco's US data illustrating the reduction in hospitalizations (around 30%) following the introduction of CYP2C9 and VKORC1 genotyping before prescribing warfarin in a six month study. Medco's personalised medicine program has already demonstrated improved patient outcomes by implementing diagnostic testing prior to dispensing certain drugs. The company, which can employ such approaches effectively as its data are nationally wired and real-time, has already made significant cost-savings following the introduction of its personalised medicine program. Pierre Cassigneul noted that the XDx AlloMap test used to predict organ transplant rejection is reimbursed by various US payors but, because of Europe's complexity,

the test is currently not being marketed in Europe. However, an advantage for the introduction of personalised medicines in Europe was noted by Patrick Terry who stated that the European single payor systems presented an opportunity for a more cohesive approach to the market than the segmented US system.

From French industry perspective, Christian Parry (Vice-President, SFRL, the French Syndicate of In Vitro Diagnostic Industry) highlighted the size of the European in vitro diagnostic market with around €10 billion in annual sales (in 2008; more than a third of global sales) with Germany, France and Italy representing the largest markets. Although there are a number of companion diagnostic test on the French market, Christian Parry stressed the hindrance of new companion diagnostic development through increasing regulations and quality control processes. Also reimbursement frequently limits new test availability and the initial costs are currently often covered by the industry as a necessary interim step. Mr. Parry suggests that faster market access to novel personalised medicine diagnostic tests may be achieved by 1) collaborations between various parties (In Vitro Diagnostic industry, pharmaceutical and biotechnology companies and academic research groups), 2) adherence to in vitro diagnostic standards and development processes and 3) improvement of reimbursement procedures. Christian Bréchot (Vice-President of Medical and Scientific Affairs, Institut Merieux) noted the considerable challenges and expenses associated with development of novel diagnostics, spanning the need to demonstrate analytical and clinical validity, clinical utility and health economic impact. He did, however, stress the strategic and economical benefits for both pharmaceutical and biotechnology firms to collaborate with diagnostic companies to develop personalised medicines and companion diagnostic tests.

The conference was completed with an excellent overview by Professor Phillippe Amouyel (CEO, National Foundation for Alzheimer's Disease, General Director of Institut Pasteur, Lille) of the latest clinical evidence of how personalised medicine approaches can have great impact on patient outcomes with particular emphasis on Alzheimer's disease and myocardial infarction.
In conclusion, EPEMED's first conference highlighted the recent advances made in personalised medicine but also discussed the difficulties in making personalised treatments available for patients in Europe. EPEMED has edited proceedings of the conference and a white paper which may be downloaded from its website (www.epemed.org).

EPEMED report from the Bruxelles european conference

Key facts and challenges for personalised medicine in Europe; a report of the "European Perspectives in Personalised Medicine" conference

On the 12-13 May 2011, the European Commission brought together around 500 delegates in Brussels for the "European Perspectives in Personalised Medicine" conference. EPEMED was kindly invited by the European Commission and took an active part in the discussion, with a session chaired by Alain Huriez (Founder and Chairman of EPEMED). The association was also present at the conference mini-fair. Here we provide an overview of the conference with focus on the main issues discussed. For convenience, links to the different sources (summary reports, presentations, and references) are provided.

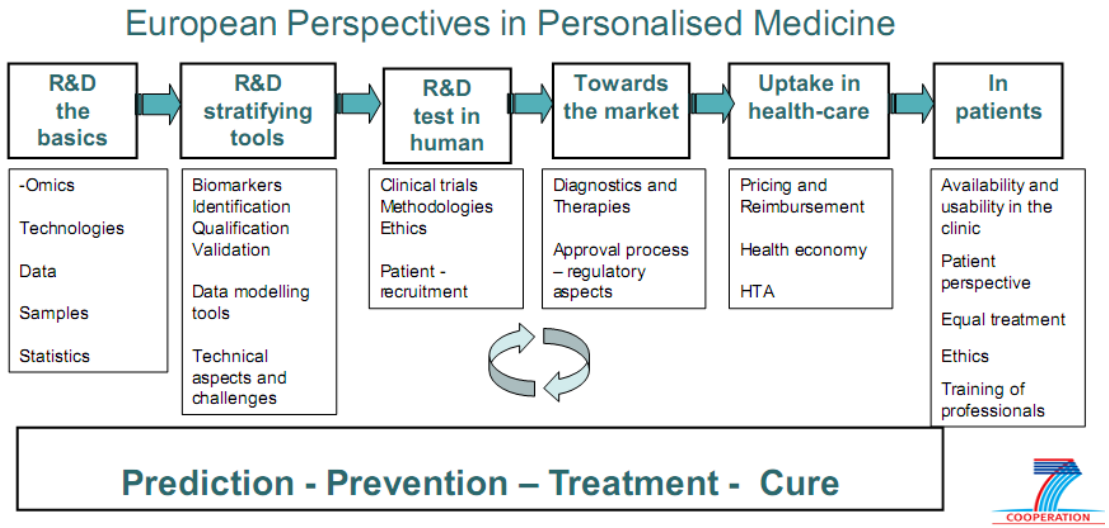
EPEMED stand animated by Pierre Etienne Sado and Alice Le Bars:

Source: Adrien Piron for visualnews

Session 4: Towards the market and patients - approval process, Chaired by Alain Huriez

Representatives of researchers, practitioners and patients shared their points of view on the future paths of personalised medicine. “The conference is dedicated to the necessary research and development aspects serving as the basis for personalised medicine approaches and to the downstream issues of the innovation cycle including the approval processes and the uptake into health care.” said Ruxandra DRAGHIA-AKLI from the European Commission (EC).

Definition of personalized medicine (PM): Personalised medicine aims at better predicting, preventing and treating or curing diseases based on a patient's individual characteristics. (Ruxandra DRAGHIA-AKLI; EC)



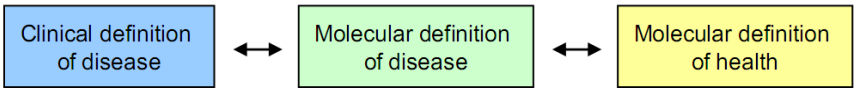
Source: Ruxandra DRAGHIA-AKLI, EC

The use of PM may be seen as an opportunity for Pharmaceutical companies, which have seen an increased attrition rate for their molecules as well as an increase in R&D costs. In 1996, 53 new molecular entities appeared for $17 Bn expenditure in R&D; in 2008, 18 new molecular entities appeared for more than $45 Bn expenditure in R&D. ([1])

The needs vary depending on the type of disease; for example, the efficacy of drug response for analgesics is approximately 80% whereas it is only 20% for cancer therapies. Furthermore, adverse drug reactions still cause 5-7 % of all hospital admissions.
Personalised medicine could also provide the opportunity to redefine a disease at the molecular level, thereby improving:

- Patient stratification as responders and non-responders
- The development of diagnostic tests for treatment and/or dose alternatives
- The avoidance of treating patients at risk of serious side-effects

“PM is the right medicine at the right dose to the right patient at the right time” (European Medicines Agency (EMA))



Source: Ruxandra DRAGHIA-AKLI, Director, Directorate Health, DG Research and Innovation, European Commission

[1] Sources: FDA/CDER Data, PhRMA data, Price Waterhouse Coopers analysis, Pharma 2020. Diap : Knowles, EPFL, Lausanne

At the R&D level, biomarker development has thrived as the result of high throughput techniques, which have recently led to the achievement of several milestones:

- Sequencing of the Human genome (2001)
- Construction of Dense genetic maps (2000-11) (SNP consortium, Hapmap, 1000 genomes)
- Implementation of Ultra-high throughput genotyping methods (2006) (Genome-wide association study (GWAS))
- Development of "Next-generation" sequencing (2008) (Whole genome and exome[2] sequencing)

Nevertheless, one challenge of PM will be the attrition rate of drugs which is still high; only 1 compound out of an initial 5-10 000 passes the regulatory review to achieve marketing approval after 10-15 years of development (Uhlen, KTH).

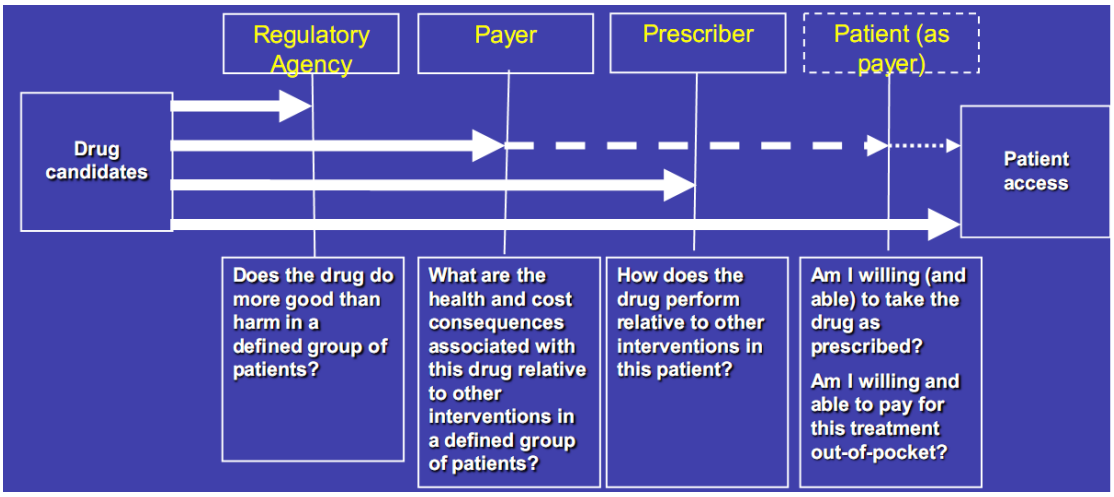
Another challenge for PM is to use biomarkers (BM), which are mainly used in the development phase: "Most BMs are developed for the drug discovery phase, from 30 to 60% of BM used in the development phase to less than 5% commercialized with drugs." (C. Larue). This bottleneck could be caused by difficulties related to patient cohort and biological specimen access.

An example of the widespread use of BM in clinical practice is the device created by the Institut National du Cancer (INCa), which has set up 28 regional platforms to perform analyses. This has enabled the benefit and clinical use of biomarkers to be surveyed and computerized.

Cancer	Drug	Biomarker	% patients with mutation	Nb of tested patients	Number of spared prescriptions	Median PFS for non responders	Cost of treatment/ patient	Spared cost	Public fundings allocated for the provision of the test
lung cancer	gefitinib	EGFR mut	10,3%	16722	15000	8 weeks	4 600 €	€69 M	€1.7 M
	erlotinib				15000	8 weeks	4 600 €		
colorectal cancer	cetuximab	KRAS mut	36%	17250	6 210	8 months	32 419 €	€ 201 M	€2.5 M
						8 weeks	9 263 €	€57 M	
	Panitu-mumab					4 weeks	4 390 €	€27 M	

(Source: Calvo, INCa)

EMA underline the different points of view of market actors

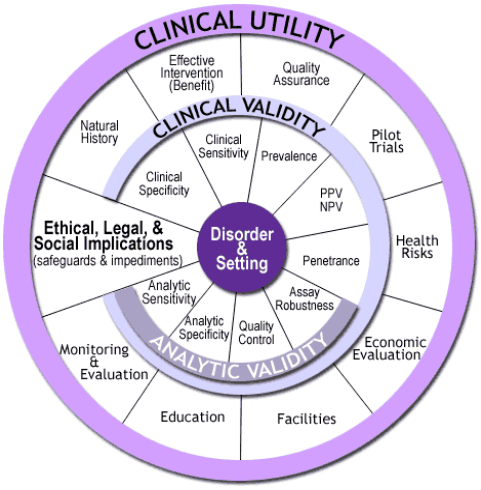


(Source EMA)

[2] Exome: part of the genome formed by exons, coding portions of genes in the genome that are expressed.

The current IVD directive is expected to change to include rule-based classification based on the Global Harmonization Task Force model: GHTF/N045:2008, Class C High Individual Risk and/or Moderate Public Health Risk and Conformity assessment by a Notified Body.

Pharmacoeconomic studies must take into account cost-effectiveness and cost-utility as well as cost-benefit. Considering the ACCE-wheel[3] , the 4 main criteria for evaluating the clinical utility of a pharmacogenetic test are Analytic validity, Clinical validity, Clinical utility and Ethical, legal and social implications.



"Cooperation is key: everyone must work together. From the patients' perspective, Personalised medicine should be seen as one part of the holistic approach to patient-centred chronic disease management. Meaningful patient involvement is key to developing personalised medicine so it will really benefit patients" Anders Olauson, President, European Patients' Forum.

Written and formatted by Alice Le Bars from materials available on the EC website

List of abbreviations

BM: biomarkers
EMA: European Medicines Agency
HTA: Health technology assessment
INCa: Institut National Cancer (France)
IVD: In vitro diagnostic
NICE: National Institute for Health and Clinical Excellence
PM: Personalised medicine

Related references

The summary can be downloaded at: http://ec.europa.eu/research/health/pdf/eu-perspectives-in-personalised-medicine-summmary-report_en.pdf

Prior to this conference, 4 workshops were organised:"omics in personalised medicine", "clinical trials and regulatory aspects", "stratification biomarkers in personalised medicine" and "personalised medicine: opportunities and challenges for European healthcare" (their summary reports can be found at http://ec.europa.eu/research/health/policy-issues-personalised-medicine_en.html)

[3] http://www.cdc.gov/genomics/gtesting/ACCE/

E P E M E D

The European Personalised Medicine Association

Bringing together forces in Personalised Medicine

Recent innovations in molecular diagnostics have played an important role in improving patient outcomes in a range of human diseases. Jointly with personalised therapeutics, companion diagnostics form the field of personalised medicine, where a person's clinical, genomic and environmental information is used to more precisely select medication and dose for each individual patient. The application of personalised medicine is likely to improve patient care as well as lower healthcare costs.

Practical applications of molecular diagnostics, companion diagnostics or personalised medicine are still lagging behind in Europe despite the progress and first successes observed in the USA. In Europe the current challenge is to educate the various stakeholders to improve understanding of the advances personalised medicine may bring, through the delivering of more effective healthcare.

By highlighting these issues and serving as a forum for best practice sharing, EPEMED community can help drive solutions and promote diagnostic innovation in clinical practice.

Alain Huriez

MD, chairman and Founder of EPEMED and CEO of TcLand Expression

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www.epemed.org or email contact@epemed.org

EPEMED focuses on and provides

- Education, awareness and promotion of personalised medicine.
- A forum to share best practices
- Input to policy makers on relevant legislation
- Regulatory guidance on the co-development of diagnostic tests and personalised drug therapy
- Validation approaches for companion diagnostic tests
- Ways to improve market access for high-value companion diagnostics

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