EuropaBio White Paper

Realising the potential of personalised medicine in Europe
Dear reader,

We believe that personalised medicine can and will be a pillar of a competitive EU healthcare biotech industry, and a significant contributor to the Union’s ambition of becoming the world’s foremost knowledge economy by 2020. Research and development in the personalised medicine field means investment in innovation; it attracts and creates highly skilled workforce and has positive ripple effects on academia, secondary and tertiary care institutions and other sectors. Building on the latest knowledge in life sciences, it kicks off new types of research and clinical trials, contributing to a competitive European Union and making Europe a dynamic place for innovation. Most importantly, personalised medicine has the potential to meet the unmet medical needs of patients.

It is the ambition of EuropaBio’s members to make Europe a world leader in this area, not only as a research hub but also as a place for patients to reap the benefits of personalised medicine.

In alignment with EuropaBio’s 2014 Biotechnology Industry Manifesto, our healthcare policy recommendations call on national and European decision-makers, industry representatives, patients, physicians and payers to rethink and adapt their standard operating procedures so as to integrate personalised medicine approaches into the operating environment for healthcare systems right across Europe.

Our previous publication, the EuropaBio 2012 ‘White Paper on Personalised Medicine: status quo and challenges’ identified the specificities of personalised medicine throughout the value chain and the required adaptations in terms of science, drug and diagnostic development programmes, as well as in terms of valuing and reimbursement.

This publication goes a step further and sets out a series of calls for action and policy recommendations to foster the development of personalised medicine in Europe and help create the right eco-system for it to flourish.

We strongly believe that it is time to make Personalised Medicine a priority in Europe, and we look forward to working together with all stakeholders to realise this paradigm shift.

Yours sincerely,

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Introduction

Traditional medicines have long relied on the ‘one-size-fits-all’ approach, while personalised medicine aims at providing the right treatment, to the right patient at the right time. Based on the combination of diagnostic and therapeutic tools, personalised medicine intends to create more predictable outcomes and tailor medical treatments to the individual characteristics of each patient and of his / her disease.

Recent scientific developments have brought us closer to this concept, which offer both hope and excitement to patients and healthcare professionals alike. However, personalised medicine is a relatively new concept within the healthcare sector. In its infancy, this sector is still a fragile and small market. Moreover, as a relatively new medical approach, personalised medicine will require changes in healthcare systems and practices to reach its full potential.

There is no doubt that the paradigm shift towards personalised medicine will be to the benefit of patients and the healthcare system, however the products themselves are complex and expensive to develop. Indeed, innovative companies face the challenge of discovering and developing medicines while at the same time developing the appropriate companion diagnostics, arduous tasks which are in no way aided by the current challenging economic climate and growing risk aversion on the part of regulatory authorities.

Industry’s R&D programmes are gradually shifting to a more personalised approach, but the success of this shift depends on several impending issues. All stakeholders will have to collaborate to deal with a diverse range of issues: from the consideration placed upon the economic and social value of personalised treatment when compared to a non-personalised treatment, and the consequence of that valuation in terms of government investment in this area, to the willingness of payers to reimburse such products. How much payers will be willing to reimburse these new products, as well as what kind of regulatory requirements will be necessary, will affect the pace of development and of access to market of personalised medicines.

Equally important in the success of this paradigm shift will be the level of trust that healthcare professionals and patients have in personalised medicine, for which accessibility to better information and education is a prerequisite.
The contribution of science to personalised medicine

For years, scientific disciplines taught us that patients with the same symptoms suffer from the same disease. However, more recent clinical experience shows that patients diagnosed with the same disease based on the same diagnostic criteria may respond very differently to the same treatment. We now know that these patients are probably suffering from different diseases caused by different underlying pathologies or react in different ways to the same treatment.

The scientific progress in basic scientific disciplines such as anatomy, physiology and biochemistry has been substantial over the last centuries. However, we still have a very limited understanding of the mechanisms of disease action at a molecular level.

Over the last decades, molecular research and biotechnology have provided new insights in cellular signalling pathways thus helping us to understand some diseases and disease mechanisms more precisely.
In particular, by deciphering people’s genetic code, we are able to learn about rare monogenetic disorders and the underlying genetic alterations that contribute to disease development. The understanding of the role of regulating RNA and cellular signalling networks and other molecular events will lead to new ways of developing treatments.

We can now develop biomarkers into diagnostic tools that are able to identify the specific mechanism involved in a disease affecting a specific patient. These specialised diagnostic tools contribute to classifying diseases based on the underlying mechanisms and pathways of the diseases themselves and aid the development of personalised medicines directly targeting specific disease mechanisms present in a patient.

Although the preliminary results of the targeted approach to treatment look promising, further research on disease mechanisms and cellular pathways is urgently needed in many instances. Moreover, biomarkers alone may not be sufficient to diagnose all diseases. New forms of multidisciplinary partnerships are needed to succeed in personalised medicine, as the complexity and the costs of drug development are nowadays beyond the knowledge and operational capacity of single organisations. Recent studies show that collaborative research platforms have the advantage of optimising the expertise of several partners and combining efforts alongside cost-sharing models for efficient patient selection.

The European Commission has recognised the importance of public-private partnerships (PPPs) in biomedical research in its recent report on the ‘use of -omics technologies in the development of personalised medicine’ published in October 2013. The report recommends exploring new incentive structures and models, such as public private partnerships, to share the cost of new treatment strategies and to speed up innovation in the area of personalised medicine.

**Call for action**

- Streamline access to collaborative multi-stakeholder research projects co-funded by the EU, with a focus on investigating molecular disease mechanisms and cellular pathways via biomarker use.

- Create a trust-based interactive platform in the field of personalised medicine so as to connect life science stakeholders, especially innovative biotech SMEs, with research funders and foster the development of new PPPs in biomedical research.

- Establish a ‘fast-track access programme’ to award funding for research into innovative targeted therapeutic approaches addressing areas of urgent unmet medical need and reduce administrative burden for applicants.
Translation of personalised medicine concepts

The concept of personalised medicine centres around predictive biomarkers: biologic markers that can help select a patient population with a higher chance of a favourable response to a specific kind of medicine. Biomarkers can also help identify patients who might have a greater risk of side effects from specific treatments.

Predictive markers compare intervention effects (i.e. treatment versus control) for marker-positive versus marker-negative patients, and predict differential effect of treatment on the outcome. There are also prognostic biomarkers. This is a signature that separates different populations with respect to the risk of an outcome in absence of treatment.

Predictive biomarkers will increase R&D productivity by determining the biologically relevant dose, range and selection of an optimal target population. Development timelines will be shortened and costly late stage attrition of new molecules in development will be reduced.
However, biomarker research requires a number of changes such as:

- Better model systems that predict drug response. Ex-vivo systems have proven valuable but their application remains to be fully investigated.

- Clinical trials for personalised medicine need to include patients selected on the basis of presence or absence of specific biomarkers. The more homogenous patient populations participating in clinical trials are, the more consistent and predictable response to treatment will be. As a consequence, fewer patients are needed for the detection of a statistically relevant finding.

- Biomarker research activities should run in parallel with the clinical development programme for a specific treatment in order to constantly improve the related biomarkers.

It is difficult, time-consuming and costly to identify and qualify biomarkers, especially those aimed at predicting clinical outcomes. Public private partnerships (PPP) based on continuous open dialogue between the industry, EU and national authorities are the way forward in advancing biomarker research. The flagship Innovative Medicines Initiative (IMI) project, jointly funded by the Commission and industry, now being succeeded by IMI 2, is one such PPP. It encourages development not only of SMEs but also of midsized and larger healthcare biotech companies. Another example of a PPP in this context is the ‘Stratified Medicine Programme’ in the UK, where industry, the national government and the charity organisation Cancer Research UK are working together to establish the foundations for a standard, high quality, cost-effective routine genetic test for tumours and for the delivery of personalised treatments to patients with lung cancer. The project is currently in its second phase.

Industry also needs a regulatory and incentive system that will facilitate innovation in complex diseases where one targeted therapy may not be enough to help patients (novel combinations and multiple companion diagnostic tests). An example of such incentive system is the so-called “adaptive licensing” approach. Adaptive licensing (AL) approaches are based on stepwise learning under conditions of acknowledged uncertainty, with iterative phases of data gathering and regulatory evaluation. This approach allows approval to align more closely with patient needs for timely access to new technologies and for data to inform medical decisions. In order to move science forward and meet medical challenges for patients, new collaborative approaches to testing the efficacy and effectiveness of new improved medicines such as AL should be embraced by regulators in close partnership with patients, payers, and practitioners.

The European Medicines Agency (EMA) has recently launched a pilot project on adaptive licensing, which aims to provide a platform to discuss how future adpative licensing pathways might be designed for different products and indications.

Call for action

- Track, accept and validate relevant IMI results and make them available for usage to all relevant stakeholders;
- Regulators and industry: collaborate to enable more rapid qualification of clinically meaningful biomarkers;
- Facilitate the collaboration among industry and academic institutes by simplified IMI collaboration rules.
From biomarkers to companion diagnostics

Once biomarker tests have been turned into diagnostic test kits, it is possible to routinely classify patients in clinics. However, the development of diagnostic test kits has to be coordinated between two entities – pharmaceutical companies and diagnostic manufacturers – with rather different regulations.

Pharmaceutical and biotechnology companies are working hard on integrating the drug/diagnostic co-development concept. Until now, genuine co-development has been a rare phenomenon for two reasons:

- It is quite difficult to find clinically useful predictive biomarkers early on in a drug development programme, simply because they can only be validated on the basis of the patients’ responses to the drug.
- The worlds of medicines and diagnostics are parallel universes in many ways: they have different development timelines, product lifecycles, return on investment, customers, and regulations.
In the US, the FDA has moved quickly in recent years to build and shape a regulatory infrastructure to help make personalised medicine possible. In particular, the Agency has strived to evolve its regulatory processes in response to – and in anticipation of – scientific developments that are critical for the development of personalised therapeutics and diagnostics. Such regulatory evolutions are well described in a report published by the FDA in October 2013x.

The current EU directive on in vitro diagnostics medical devicesxi (IVDs) is under revision and will probably introduce a number of changes that will definitely impact the development of companion diagnostics:

• A companion diagnostic, on which the selection of a patient’s eligibility for a targeted therapy will be based, appears likely to be classified as high risk test. Requirements may be added on how to demonstrate clinical validity and clinical utility proportionately with the risk level of the test.

• It is likely that both the EMA and Notified Bodies will be involved in CE markingxii of companion diagnostics. Although the roles, responsibilities and detailed process are not yet defined, we hope that the involvement of both these regulatory bodies will ensure higher quality and safety for patients while avoiding work duplicationxiii.

Another challenge relates to the protection of diagnostics tests manufacturers, who go through major financial efforts to develop a biomarker. As soon as the test has been validated, it is quite easy for in-house laboratories to copy the test. Moreover, patent protection for biomarkers is difficult to obtain and increasingly coming under pressure in the USA, the largest healthcare market for these products. This further complicates business models of diagnostic companies and increases the risk profile of investments in the diagnostics sectorxiv.

Call for action

In the context of the ongoing legislative process on the In-Vitro Diagnostic (IVD) Medical Devices Regulation:

• Introduce a conditional CE marking of companion diagnostics and maintain in-house exemption for IVDs in the space of unmet medical needs;

• Ensure a quick review of companion diagnostics technical dossier by Notified Bodies and EMA to avoid any delay of commercialisation;

• Clarify the regulatory post-launch requirements for companion diagnostics; also clarify the post-launch situation of a pharmaceutical product in the event a new companion diagnostic becomes available;

• Initiate a support programme for SMEs to help them to navigate the complexity of the new regulatory environment.
Health economic aspects of personalised medicine

Current health economic research shows that personalisation of treatment has the potential to improve outcomes for patients and deliver efficiencies in healthcare systems and medicines R&D\textsuperscript{xv}. However, conventional Health Technology Assessment (HTA) impedes market access of personalised medicine.

Much of the efficiency gains of personalised medicines depend on the ability to select responders from non-responders before starting treatment. In other words, ‘testing before treating may be economically viable if the savings gained by avoiding ineffective treatment and adverse events are greater than the cost of testing’\textsuperscript{xvi}. Early HTA research shows that these efficiency gains are possible.

Personalised medicine trials often complicate conventional HTA approaches\textsuperscript{xvii}. In a personalised medicine trial, patients are selected by a molecular diagnostic test to enrich for response to a therapy. Hence, all
selected patients are more likely to respond to the treatment compared to a traditional trial and it is more likely that therapeutic benefit becomes substantially evident in an early stage of the trial. In the case of life threatening diseases, patients from the control group are usually moved to the treatment group as soon as their health deteriorates. As a result, personalised medicine therapies are often approved on the basis of more limited, but compelling, early clinical trial data with a positive risk/benefit ratio than traditional medicines.

Another reason why the conventional HTA approach complicates the testing of personalised medicines is that the provided clinical trial evidence for targeted therapies is limited to a defined group of patients who are expected to deliver the most positive risk-benefit ratio. This data cannot be compared with data on ‘unselected patients’ from older ‘pre-personalised’ clinical trials because the targeted subgroup’s response in the older trial might not be reflected very well by the overall results. As a consequence, the relative benefit of the personalised medicine in its specific patient sub-group may not be quantifiable with current methods.

Activities to strengthen innovation in personalised medicine at the HTA level need to take the following aspects into account:

- There is only provisional evidence available at the time of launch;
- There is a need for a new diagnostic step which may not have large quantities of clinical data to demonstrate its value;
- There is a need to fit into health systems that are still configured for broad populations and ‘average’ patients.

**Call for action**

- HTA bodies: be pragmatic in using the available evidence to assess the relative benefit of a new personalised medicine, and understand that there will be potential to misrepresent the benefit of medicines when making indirect comparisons with older trial data;
- Initiate discussions between all relevant stakeholders involved in the assessment process – including regulators, HTA bodies, payers, health professionals and industry – about the clinical utility versus costs;
- Provide guidance on potential quality indicators for prescribing personalised medicine;
- Assist with the design of registries for follow-up studies to capture the value of the combined companion diagnostic and medicine combination in relation to outcome measures relevant for the patients.
Even in an era with intense budget pressure on European health systems, a longer term view on bio-pharmaceutical spending is still needed for managing healthcare systems and meeting unmet medical needs. We need transparent and predictable policy and reimbursement environments in order to ensure that personalised medicine will be able to reach its potential and patients have equitable and timely access to personalised medicine treatments.

Personalised medicine has the potential to improve efficacy, safety and public health. Early evidence from personalised medicines in disease areas such as oncology also shows that targeted therapies are offering significant improvements in care for patients and improving their quality of life. However, a number of concerns have been raised about personalised medicine as regards its financial impact on already strained healthcare budgets. Although this impact is undeniably important, focusing only on short term budget considerations and neglecting long-term cost effectiveness and value to patients would unnecessarily limit
the potential of personalised medicines\textsuperscript{\textcopyright}. ‘BUDGET’ should not translate to ‘Bringing Unnecessary Death/Disability by General Exclusion from Treatment!’\textsuperscript{\textcopyright} Personalised medicine, with its focus on improved effectiveness of treatment, can actually be a key driver in the current move towards Value-based Health Care, where reimbursement is linked to the quality of care and to improved patient outcomes\textsuperscript{\textcopyright}\textsuperscript{\textcopyright}.

Next to the assessment process, valuing of active contribution to society and the available healthcare budget in the individual member state are important factors influencing patients’ access to personalised medicines. In some examples, personalised medicines have been approved on the basis of a retrospective analysis of clinical data identifying the responsive sub-population. In other cases, personalised medicines have been launched under conditional approval mechanisms on the basis of phase 2 data alone (smaller studies, often without overall survival end points).

It is also problematic to evaluate the cost-effectiveness of particular molecular diagnostic approaches. Diagnostics are normally supported by analytical performance data and rarely by clinical or outcome data, but in order to perform a health technology assessment you need the latter. According to a systematic review, only eight studies evaluated the clinical validity, and none of the studies was a prospective evaluation of a test’s clinical utility\textsuperscript{\textcopyright}.

While medicines are valued and reimbursed as products based on clinical outcome, typically of high value, diagnostics are currently valued and paid for as services, typically at a much lower value. Relatively few if any models exist for valuing a drug-diagnostic combination, hence we believe there is a need for adapted approaches in this space.

It is foreseeable that those countries which establish effective regimes for delivering accurate molecular diagnostics and choose to adopt new personalised medicines early and use them in the patients for whom they are intended will see the greatest efficiency gains from important scientific advances.

Call for action

- Provide timely and regular education to health practitioners about scientific advancements in personalised medicine. Public authorities and public funding opportunities, such as for example the EU funding programme for research, Horizon 2020, should play an essential role in educating and raising awareness about personalised medicine among healthcare practitioners and patients pre-to-post launch.

- Decide in an early stage whether care delivery should be re-organised to adopt personalised medicine solutions and whether new quality indicators and registries are needed.
The societal perspective on personalised medicine

Personalised medicine has the potential to make healthcare practices more patient-centred. Patients will become more involved in the decision-making process about their own treatment plan, and they will increasingly discuss therapeutic options and their consequences with their doctor. This requires patients to be provided with appropriate information, and doctors to be capable of explaining things clearly to patients.

Personalised medicine opens up new opportunities for patients and caregivers, such as for example the ability to determine a person’s biological disposition to a wide range of diseases via testing devices at home. Developments in personalised medicine will need to be coupled by an increase in patient empowerment, enabling patients to make better and more informed choices about their treatment options, based on detailed information about their own profile.
In other words, they will be more ‘health literate’, not only thanks to information and forums on the Internet, but also due to the availability of home tests. Health literacy entails people’s motivation to understand health information in order to make judgments and take decisions in everyday life concerning healthcare, disease prevention and health promotion.\textsuperscript{xiv}

Ethical questions arising in the context of companion diagnostics need to be tackled. For instance, while personalised medicine can identify patients who are likely to respond well to a particular medicine, it also offers the possibility to rule out patients for whom the medicine is not likely to be effective or suitable. What happens if there are no alternatives? Should the person still receive the only medicine available, even if that medicine is likely to cause severe side effects or even adverse reactions? What happens if, conversely, the predictive information provided by the biomarker is perhaps not accurate enough and deprives the patient of access to life-saving treatments?\textsuperscript{xxv}

Finally, questions related to privacy issues need to be addressed. For example, biological samples are needed for diagnostic tools, which are pivotal for the personalised medicine concept. What happens with the samples and related information that people provide? Who has access to it? Can individuals be identified? Who owns the data? Should employers or insurance companies have access to it? And also, should “incidental findings” from genetic tests be communicated to patients or not?\textsuperscript{xxvi} These are many questions that the expected regulation on data privacy should address.

These and many more questions require an open dialogue between science, industry, policy makers, patients, and civil society.

**Call for action**

- Invest in health information and communication about the benefits and challenges of personalised medicine and foster multi-stakeholder dialogue by organising workshops involving patients, physicians, industry and payers;
- Give health literacy a higher priority in the health policy agenda and, more specifically, support educational programmes on personalised medicines.
- Promote and support patient participation to personalised medicine initiatives in order to create a pull factor for personalised medicine.
Policy recommendations

Building on the key issues described in the previous chapters, this section looks into policy measures that can drive change towards personalised medicine for the benefit of the patient, healthcare systems and innovation in Europe.

We believe that the environment and market conditions in Europe should be more conducive to the development and delivery of personalised medicines. Only a fair and appropriate reward system supporting valuable innovation would encourage more investments into personalised medicines, and thus offer additional opportunities for employment, economic growth, especially for innovative SMEs, and increased global competitiveness.

More specifically, the following policy areas deserve special attention:

■ The contribution of science to personalised medicine
  - EuropaBio supports the ongoing projects co-funded by the European Commission aimed at creating an interactive platform for life sciences performers and funders in the field of personalised medicine, as well as the Commission’s intention to rely on Horizon 2020 as an opportunity for funding projects for the advancement of personalised medicine in certain well-defined areas.
  - There is a need for a smooth and quick implementation of the various research projects to effectively establish a trust-based interactive platform for life sciences performers and funders in the field of personalised medicine.

■ Translation of personalised medicine concepts
  - We support a framework that stimulates the conclusion of collaboration arrangements between companies, the academic and scientific community, and other stakeholders such as patient organisations, to conduct R&D efforts in personalised medicine.
  - We call on the EMA, the European Commission and Member States to facilitate smaller, streamlined development programmes supported by high-quality patient registries as new model to designing clinical trials.
  - We encourage increased early stage cooperation among all relevant stakeholders, particularly patient organisations, to address patient’s informed consent in relation to biomarker research.
From biomarkers to companion diagnostics

- We hope that the new IVD Regulation will enhance Europe’s leadership with regard to the development and early marketing of novel diagnostics. It is important that regulatory requirements do not hinder the ability of (especially small) innovative companies to discover biomarkers and further develop companion diagnostic tests. The new Regulation should also prevent any delay in the CE marking process and thus patients’ access to innovative diagnostics.

- We recognise the excellent expertise of the EMA and stress the need to ensure specific scientific expertise to assess the potential sensitivity and specificity of new companion diagnostic tests (clinical validity and utility) in collaboration with Notified Bodies. Finally, there is a need to clarify aspects of the consultation between the Notified Bodies and EMA in terms of roles and responsibilities, methods, decision rules and consistent timings between companion diagnostics and pharmaceutical products.

- EuropaBio supports the swift adoption of a new regulation that introduces appropriate levels of clinical validation for diagnostic tests. It is paramount that safety is managed appropriately within a flexible legislative system that encourages innovation. The willingness to meet challenging regulatory requirements can only be counterbalanced with adequate rewards for new health technologies that are able to trigger competition in innovation.

- We support close collaboration between the relevant regulatory authorities for marketing authorisations of a medicinal product and CE marking of the corresponding companion diagnostic to accelerate commercialisation of both products. Timelines for therapies requiring a companion diagnostic should not be slower than timelines for therapies which do not require a companion diagnostic.

- A level playing field must be achieved, by upholding consistent quality standards for in-house tests and companion diagnostics.
Health economic aspects of personalised medicine

- Health economic evaluations need to become more flexible and adapt to early launches based on high confidence of therapeutic mechanism and early promising data. Relevant diagnosis of patients suitable for treatment with personalised medicines needs to become the norm and embedded in routine healthcare pathways and this should not be viewed as an additional separate step and cost, brought about by having a new medicine available.

- We support more creative funding strategies, such as coverage with evidence development as proposed by Ramsey et al. (see above on page 9). However, such an integrated model would require that test manufacturers and clinical trial groups modify their current ways of operating trials and insurers modify their current ways of paying for treatment.

- Health decision-makers should set up systematic evaluations of personalised medicines based on their long term cost-effectiveness. This assessment should consider their clinical and economic value in a long-term (years after their launch).

Market conditions for personalised medicine

- Adaptive licensing: We support the initiation of the EMA’s adaptive licensing pilot and the concept of earlier licensing in a stratified indication(s). The model outlined in the EMA pilot project reflects well the personalised medicine approach. For the model to be successful however, it must include a concept of adaptive pricing and reimbursement and should cover the entire development pathway – from medical product and companion diagnostic through to patient access.

- Expedited pathways: We support improvements to the current early and/or faster approval pathways in the EU (conditional approval) to support the rapid development and uptake of personalised medicines (both drugs and companion diagnostics) in Europe. We welcome dialogue with the EMA on the improvements to the current conditional approval pathway and encourage discussion on conditional approval of companion diagnostics.

- We believe there is a new approach needed to value and reimburse diagnostic tests.

- A pan-European implementation strategy is needed, to ensure the availability and patient access to high quality companion diagnostics.

The societal perspective on personalised medicine

- Health literacy should receive a higher priority in the health policy agenda and, more specifically, educational programmes that provide information about personalised medicines should be supported.

- We believe that patient organisations should be empowered to strongly represent the patient views and needs in personalised medicine debates.
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Notes and references

1 RNA (Ribonucleic acid) is a ubiquitous family of large biological molecules that perform multiple vital roles in the coding, decoding, regulation, and expression of genes.


3 Lacombe et al, European perspective for effective cancer drug development, Nature Reviews Clinical Oncology (2014) doi:10.1038/nrclinonc.2014.98 Published online 17 June.


6 For further information on the project, cfr. http://www.cancerresearchuk.org/funding-for-researchers/how-we-deliver-research/our-research-partnerships/stratified-medicine-programme


12 The CE marking is required for many products. It states that the product is assessed before being placed on the market and meets EU safety, health and environmental protection requirements. If a medical device is correctly CE marked it does not need any additional approval or certification to be marketed in the entire European Union (EU), in the European Economic Area (EEA) and in Switzerland. The CE marking allows free movement of goods in these states and it is applied by on products by the manufacturer after a conformity assessment is performed by Notified Bodies. Cfr, European Commission: http://ec.europa.eu/health/medical-devices/faq/market_en.htm


19 Arnedos M. et al., Personalized Treatments of Cancer Patients A Reality in Daily Practice, A Costly Dream or a Shared Vision of the Future From the Oncology Community?, Cancer treatment Reviews Published Online: July 17, 2014 DOI: http://dx.doi.org/10.1016/j.ctrv.2014.07.002


26 “Incidental findings” are results of genetic tests that sequence all genes from a sample, not just those related to the condition of interests. Whether or not to report incidental findings is a topic of considerable debate. H. C. Mefford, What’s Your Attitude? Sci. Transl. Med. 6, 245ec124 (2014); J.-H. Yu et al., Attitudes of genetics professionals toward the return of incidental results from exome and whole-genome sequencing. Am. J. Hum. Genet. 95, 77–84 (2014).

27 Please note that job titles in this bullet list refer to positions held by authors in 2012.