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EU policies in personalized medicine-related technologies

Against the background of a number of first drug–diagnostic co-products developed and introduced into the European market, European decision-makers feel impelled to react and position themselves in the field of personalized medicine. Their reactions cover a broad range, from the analysis of knowledge requirements for market approval to the need for translational activities and the possible contribution of pharmacogenetics to public health. This article summarizes the current positions of European institutions, based on literature review and expert consultation for three items associated with personalized medicine: biobanks, genetic diagnostics and drug–diagnostic co-products, and provides an outlook on requirements for an effective future European policy on personalized medicine.

KEYWORDS: biobanks, clinical utility, clinical validity, drug–diagnostic co-development, effectiveness, European policy, framework conditions, genetic diagnostics, translational research

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Against the background of a number of first drug–diagnostic co-products developed and introduced into the European market, European decision makers feel impelled to react and position themselves in the field of personalized medicine, which aims to use information about a patient's genotype or gene-expression profile to tailor medical care to the individual's needs. Despite a number of regulations already in place, robust scientific evidence on development, use and demand of genomic applications is still lacking. Consequently, reactions of decision-makers cover a broad range, from the analysis of knowledge requirements for market approval to the assessment of translational activities and the determination of expected effects of broad (pharmaco)genetic testing for public health.

This paper presents some results from a report commissioned by the Institute for Prospective Technological Studies (IPTS) of the Joint Research Centre (JRC) of the European Commission [101]. The goal of this report was to identify current gaps in European research and regulation to ensure that emerging genomic applications, including many associated with personalized medicine, will be brought into clinical practice with a high level of evidence available regarding: safety, analytical validity and clinical validity (when relevant), effectiveness, clinical utility and cost-effectiveness. Ethical, legal and social (ELS) issues were also identified, all within the goal to maximize benefits for European patients and contribute to consensus-forming among relevant stakeholders. Furthermore, the report examined similarities in such evidence-generating processes as applied to a relatively broad range of genomic applications, in an effort to mark some common ground for the activities comprised in the ill-defined concept of translational research. A baseline model of this process was provided by Khoury and colleagues [1].

Many authors have highlighted how translational efforts need to strike a balance between generating evidence on the actual benefits, costs and ELS issues of new applications, on the one hand, and promoting and supporting an increased rate of innovation, on the other hand [2,102]. The authors' assessment is that the first goal has been subject of much less research and support (see also [3]).

This article aims firstly to present the technical and institutional barriers to translational research that were identified in the report for a selected set of technologies. A second goal is to provide an overview of the position of European institutions, focusing on how they may affect evidence generation for effective translation of these technologies into practice. It can thereby contribute to the development of an effective European policy on personalized medicine, and the concerted action of different stakeholders in the field. Some of the applications that are particularly associated with personalized medicine are the focus of the current analysis: biobanks, genetic diagnostics and drug–diagnostic co-products. These applications were chosen as

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they have already resulted in personalized medicine products, and seem to be currently under political consideration.

Information on the issues relevant for these different applications was gathered by means of a literature search, using the databases Web of Science and PubMed to identify scientific publications, and an internet search for policy reports. This information was complemented by consultations with 19 experts (researchers, patient organizations, healthcare providers, industry representatives and experts from government-associated institutions). These experts were from Austria, Belgium, Denmark, Germany, Italy, the Netherlands, Spain, Switzerland and the UK. They were asked to identify relevant issues, as well as reflect on the issues apparent from the literature search.

Technological basis

Biobanks consist of repositories of tissue, cell or genome samples with associated molecular, physiological and structural information [103]. They form large systemic ensembles of technologies that are used to allow for high-volume genotype–phenotype associations. These repositories are scheduled to play a central role in providing raw data that is used in fundamental and translational genomic research, and which will form the basis for the development of personalized therapies.

Genetic testing is based on the determination of one or several DNA sequences. It identifies changes in chromosomes, genes or proteins. Genetic testing summarizes the different diagnostic applications of genomic technologies (i.e., DNA- and RNA-based testing, such as diagnostic testing, predictive testing, susceptibility testing, gene-expression profiling carrier testing, prenatal testing, newborn screening, presymptomatic screening and infectious diseases testing). Other applications without a direct link to medicine are in the field of paternity and forensic testing. Whereas some applications, such as genetic screening (both for newborns, and in the case of presymptomatic screening for adults), do not have a direct link to personalized medicine, others, such as diagnostic and susceptibility testing, are clearly associated with, or are even a prerequisite for, personalized medicine. Gene-expression profiling also fits in this latter category, with promising applications for personalized medicine in oncology, and more specifically breast cancer, recently gaining relatively broad use [4,5] and progressively being reimbursed in Europe, according to one developer [104]. Additionally, protein assays and immunoassays often benefit from the development of genetic diagnostics, as once a gene is identified as being part of a disease process, the products of the gene and downstream metabolites can be identified. The resulting tests could also be beneficial for personalized medicine.

Finally, drug–diagnostic co-products refer to drugs and biopharmaceuticals that are labeled for use in combination with a specifically designed diagnostic test, both on a genetic and/or biochemical or immunohistochemical basis (as described above). Such testing may be used to decide whether or not a drug should be prescribed (i.e., whether a drug fits the individual patient's biology) and to decide on the appropriate dosage. Drug–diagnostic co-products are the key elements towards personalized medicine, as has been shown for a number of cancer and AIDS treatments, such as tamoxifen, trastuzumab, cetuximab and others (for a more detailed list, see [6]). While the category of genetic testing can include pharmacogenetic tests, drug–diagnostic co-products can be singled out as a specific technological area in cases of simultaneous development or commercialization of both components.

Barriers to evidence generation & relevant European policy activities

Biobanking

Biobanks are currently perceived in a number of European policy and scientific circles as playing a major role in establishing the knowledge of gene–disease associations that will enable some key advances in preventive and personalized medicine [104]. More specifically, it is often felt that these associations require very large repositories, and networks of repositories, of samples collected in a standardized manner to enable the kind of robust prospective studies that will be required in the case of polygenic, common chronic diseases [2]. A number of technical and institutional barriers have been identified as potentially hampering the establishment of these networks and their full integration into translational research efforts:

- Lack of standardization of complex and vastly differing biobanking systems in Europe;
- Difficulties in standardization and establishment of quality assurance protocols for data collection in biobanks;
- Obstacles in the emergence of the professional field of databank management;

- Uncertainties linked to ethical issues;
- Obstacles to ensuring demographic representativeness of data sets.

Following the rationale presented above, a major scientific and policy concern has recently been the harmonization and standardization of various activities (e.g., sampling, recoding lifestyle and environmental data) in biobanking [105,106], which seems to be the most appropriate way to obtain these large data sets. A number of activities in this respect can be identified at the European level.

A concept paper presenting potential guidelines for the use of biobanks for pharmacogenetics was drawn up by the European Medicines Agency (EMEA) in 2005 with issues concerning procedures for collecting, storing, handling and analyzing samples; 'implications of removing from samples and data identifying information in pre- and post-authorization assessment of medicinal products'; and quality assurance and quality control [107]. Another important source of efforts to establish guidelines for biobanks has been the Organization for Economic Co-operation and Development [103], and the guidelines of this international organization have gained some prominence [7].

The European Commission, through its Seventh Framework Programme (FP7), is set to encourage the increased integration and networking of existing national biobanks in Europe, as well as the use of these biobanks by actors in the field, such as population geneticists [108]. However, in 2006 the following deficits were observed: the lack of a comprehensive inventory of biobanks and disease registries in Europe, as well as the lack of a catalogue on existing regulations pertaining to ethics, confidentiality and security requirements [108], despite previous surveys of biobanks [8]. Recent harmonization initiatives have sought to provide answers to such concerns. One example is the Biobanking and Biomolecular Resources Research Infrastructure (BBMRI), supported by the FP7, which started its preparation phase in early 2008. The initiative involves, among others, institutions such as UK Biobank, deCODE genetics, the Icelandic biobank and the Estonian Biobank, for a total of over 50 participants and external partners, including also other biobanks, national ministries, hospitals, biomolecular biology research institutions, companies, ELS issues research centers, and so forth, distributed across Europe (see [109] for a list). The initiative's goal is to link together European national collections of data and samples that are underutilized owing to fragmentation. It is also interesting to note that the mix of actual repositories and relevant stakeholders in these networks is representative of a number of other initiatives, such as the Public Population Project in Genomics (P^3G), which includes biobanks from Canada as well as Europe, or EuroBioBank, with biobanks focusing on rare diseases. They may hopefully pave the way for increased awareness of some of the issues associated with translational research within what may become foundational activities for personalized medicine.

Efforts to set up biobanks have been subject to many problems and debates [2]. Although there are expectations that biobanks will eventually lower costs for public health systems by improving the prevention and treatment of diseases [2], the enormous cost of setting up these initiatives has caused great criticisms [9,110]. The scientific grounds on which it is expected that biobanks can make a major contribution to establishing associations between genes, environment and lifestyle and the etiology of some common chronic diseases have been disputed, in terms of both scientific soundness and feasibility [9,10] and, perhaps more importantly for the argument developed here, in terms of actual clinical utility of the knowledge generated in a clinical context [2].

Several other potential issues with European biobanks have been identified, notably by Taylor, such as a conflict of current practices with the EU Directive on data protection (95/46/EC) [11]. He argues that these issues will become more acute as biobanks expand and are used more intensively. Concerns have also been voiced that differences between EU member states in the national regulations on biobanks may hamper academic research and industrial development [11,111]. This may also hamper collection of evidence when assessing products for clinical validity and clinical utility [12], and as such it might be worthwhile to conduct research on how to achieve a balance between academic and industrial research interests and needs on the one hand, i.e., the role of biobanks in future fundamental and translational research on genomics products, and privacy regarding personal data and benefit sharing on the other hand [13–15].

Diagnostics

A number of well-defined technical and institutional barriers to evidence generation on genetic diagnostics could be identified for the six dimensions of interest described in the introduction (safety, analytical and clinical validity,

effectiveness, clinical utility, cost–effectiveness). Translational research in this area of applications has benefited from a number of reflections and initiatives, as well as previous experiences with monogenic genotype–phenotype associations, although evidence for polygenic associations is still very much in the early stages. The following points provide a summary of these barriers, which are outlined in more detail in the complete report:

- Uncertainties regarding the safety of drugs rescued with pharmacogenetic testing;
- Lack of participation of physicians/laboratory staff in proficiency testing and quality assurance schemes, and lack of appropriate methods for tests where no gold standard exists;
- Knowledge gaps on genotype–phenotype associations, with associated problems for validation of biomarkers;
- Knowledge gaps in human genome epidemiology and associated results replication, especially for complex diseases;
- Lack of a commonly used validation procedure such as clinical trials to generate practical, premarket evidence for genetic tests;
- Lack of translational research on genetic tests, including complex diagnostic tools such as *in vitro* diagnostic multivariate index assays (IVDMIA) [112];
- Unfamiliarity of actors with the dimension of effectiveness as an important dimension in translational research for diagnostic products;
- Knowledge gaps on penetrance and prevalence of certain genetic diseases;
- Broad dearth of assessments on the clinical utility of genetic diagnostics;
- Lack of coordination and guidelines on the assessment of clinical utility;
- Lack of postmarket monitoring schemes to contribute data for the assessment of clinical utility of genetic diagnostics;
- Inadequacy of current evidence generation for and number of assessments of cost–effectiveness of genetic diagnostics.

Looking at how current European policy activities may impact evidence generation for genetic diagnostics, Directive 98/79/EC on *in vitro* diagnostic devices (IVD) establishes the framework for diagnostics regulation in Europe [113]. It provides the regulatory framework for the examination of analytical validity of diagnostic products and, for those tests deemed moderate or high-risk, their eventual premarket review for CE certification [111]. Despite this directive, EU Members States vary vastly when it comes to the regulation of *in-vitro* diagnostics, as illustrated in the case of inherited genetic disorders [16]. In the USA, there seems to be a more stringent coverage of genetic testing from research to product approval under the authority of the US Department of Health and Human Services (an analysis of these USA–Europe differences, however, exceeds the scope of this article). A number of problems and potential developments for reforming regulation of diagnostics are thus currently being studied in Europe, as will be discussed below.

Collection of data of analytical and clinical validity is made difficult in Europe by the lack of a compulsory systematic premarket review of genetic diagnostic products, harmonized across EU Member States. The IVD Directive does not require most of these tests to undergo review, because the large majority are classified as low risk [102]. The exception is a small number of blood-screening tests considered as high risk and other tests considered as moderate risk. In the case where a test would be classified as moderate or high risk, Conformité Européenne (CE) marking is made following a premarket review, which concentrates on analytical validity and that is accomplished by companies that act as 'Notified Bodies'. Regulations in the EU do not require manufacturers of genetic tests to demonstrate clinical validity if no clinical claims are made [102]. A test can claim to identify a gene with no requirement to explain the clinical relevance of this claim [114]. Hogarth and coworkers reported that the IVD Directive is not limited to analytical validity and does in practice ask for proof of clinical effectiveness when reviewing diagnostic applications [115]. The authors come to the conclusion that, in the end, there is significant ambiguity in what is required by the IVD Directive. At any rate, for the few diagnostics where premarket review must be performed by notified bodies, there would also be little room to ask for data on clinical utility and cost–effectiveness as is currently set out for diagnostic products.

Generating evidence on validity and utility of diagnostics also faces specific problems for homebrew tests, which account for a significant portion of diagnostic services in Europe [111]. The problem of quality control of homebrews developed by individual laboratories – initially

reported for the USA – seems also to be important in Europe, and the way in which quality assurance measures guaranteeing analytical and clinical validity can be put into place [111]. While in principle these diagnostic services would normally need to comply with the safety and efficacy requirements set out by IVD Directive, public health institutions can be exempted from applying the directive when offering homebrews as part of their services [102].

In the face of such gaps in the generation of evidence available on diagnostic tests, certain authors (mostly from the USA) have indeed suggested calling for greater levels of evidence than is currently provided by sponsors when assessing diagnostic products, notably in evaluations conducted to make reimbursement decisions [17–19,116]. A report by Melzer and colleagues mentions interview results with stakeholders in Europe that show a lack of linkage between premarket review of pharmacogenetic applications, health technology assessment (HTA) activities and reimbursement decisions [117]. Improving evidence generation on pharmacogenetic tests, and genetic tests more broadly, and tying this process more closely to reimbursement decisions, would indeed parallel what is being observed in the case of drugs and therapeutic products in Europe [20]. The PHGEN network [118] has for its part proposed to establish:

- Platforms and processes for generating data and evidence to support the evaluation of tests;
- Mechanisms to set and agree standards for the clinical validity and utility of tests;
- Methodologies and facilities for the epidemiological evaluation of their clinical validity and utility;
- Policies for test evaluation that will set out the respective roles of government, industry and academia [119].

Perhaps as a move to address some of these gaps, the Directorate General for Enterprise of the European Commission (DG Enterprise) has recently consulted with relevant actors of the sector for a potential revision of the IVD Directive, as well as other medical devices directives [120]. Eventual changes of particular interest could include a modification of the risk classification of IVDs [102], providing the EMEA with jurisdiction over the regulation of IVDs and medical devices, and merging the IVD directive with the two other medical devices directives. Both measures could result in more widespread and more harmonized (or indeed centralized) premarket review of diagnostic products. They may also prove to be appropriate vehicles for increased evaluations of clinical validity, effectiveness, clinical utility and cost–effectiveness of diagnostics. These proposals have, however, been subject to debates, as some fear that they may also entail additional regulatory burdens for product sponsors in an industry that relies on fast market entry [121], or that the EMEA's expertise lay in medicinal products and not medical devices, which could be considered a very different type of product [122,124].

In view of the additional burden that such an approach may put on test developers, other potential avenues for stimulating the generation of evidence have also been proposed, such as the use of the patent system to promote clinical studies that provide data on the clinical validity of the genotype–phenotype associations supporting genomic diagnostic applications [21]; or using a responsive, risk-based regulatory approach that would, for example, call for refined labeling schemes for genetic tests [22,23]. Clarifying the roles of actors who have been responsible for generating evidence on diagnostics in Europe (Notified Bodies and Competent Authorities, reimbursers and professional bodies) may also contribute to translational research [102]. EuroGentest [123] has also been active in sponsoring workshops to find solutions to improve European provisions on genetic testing [102,125]. This organization has also been very active in ongoing efforts to improve standardization and external assessment schemes for genetic testing products across Europe. Finally, the US Secretary's Advisory Committee on Genetics, Health, and Society (SACGHS) has recently produced reports on pharmacogenomics [126], which may prove to have a certain impact on reflections on evidence generation for these applications in Europe, as the success of the ACCE framework seems to indicate [16].

Drug–diagnostic co-products

Drug–diagnostic co-products pose a unique challenge in terms of evidence generation, with each component belonging to very different innovation and regulation frameworks, as will be explained below. The technical and institutional barriers and knowledge gaps for translational research on drug–diagnostic co-products include, in addition to the barriers mentioned for diagnostics:

- Knowledge gaps in analytical validity and clinical validity compromising safety in the use of co-products;

- Insufficient numbers of epidemiological studies and replication studies performed in pharmacogenetics;
- Increased complexity compared with the drug and diagnostic parts.

Despite the fact of clear regulations for (bio) pharmaceuticals [127] and biosimilars [128,129] in the EU, experts observed the lack of a framework for drug–diagnostic co-products in Europe [24]. As mentioned above and in an earlier report [111], developments related to drug–diagnostic technologies may prove problematic for the EMEA since these two product types fall under two separated legislative frameworks. While drugs can be approved either by a national examination followed by a mutual recognition process or by the centralized European process, diagnostic products are examined for their analytical validity and their compliance with CE regulation (IVD Directive, see [111]) by national authorities. This has led to drugs being approved by the EMEA but not the relevant pharmacogenetic test, for which the EMEA has no competence to do so [114]. In the case where a diagnostic might be envisaged as compulsory or strongly recommended before the prescription of a drug, the EMEA would only be able to act on the drug's label, and could not make the test mandatory. With the whole field of genetic testing attracting attention at the European level, however, EMEA experts have for a certain time recognized that there may be a possible need for a formal communication channel between the EMEA and national authorities in order to improve regulation of drug-diagnostic co-products in a pharmacogenetic context, for example [111].

The Pharmacogenetics Working Party of the Committee for Medicinal Products for Human Use (CHMP) has established briefing meetings that allow applicants for regulatory approval of medicines to hold informal discussions with EMEA experts regarding the technical, scientific and regulatory issues arising from the inclusion of pharmacogenetic tests in the development of these products. These meetings have no impact on the regulatory process, but are intended to reduce obstacles in the use of pharmacogenetic tests, while providing the Working Party's experts with more data about the rationale and circumstances in which pharmacogenetic data are generated [130]. Such meetings can also be organized with both US and European regulatory bodies in joint FDA–EMEA voluntary genomic data submission (VGDS) briefing meetings [131]. The impact of these meetings is intended to be both in specific product guidance as well as in future guidance on pharmacogenetics. From the standpoint of translational research, these meetings offer the potential to generate further data on drug–diagnostic co-products, most probably in the aspects of analytical validity, clinical validity and perhaps clinical utility of the diagnostic component. From the US side, the aforementioned SACGHS report on pharmacogenomics does contain recommendations on evidence generation specific to drug–diagnostic co-products that may have impacts in Europe [126].

In the case of drug–diagnostic co-products, however, current policy-makers may be more concerned about lagging behind in the rate of new innovations. As previous studies have reported, pharmacogenetics, for example, is only slowly gaining ground in clinical practice [111]. Aside from a certain reservation in the context of use, development of drug–diagnostic co-products is also complicated by the fact that the drug and diagnostic components each belong to different innovation and regulation systems. Philips, Van Bebber and Issa provide an analysis of some of the problems faced in the diagnostic pipeline (although regulatory issues are situated in a US context) [25].

On this front, the Innovative Medicines Initiative, set up by the European Commission and the European Federation of Pharmaceutical Industries and Associations (EFPIA), is an initiative that may have a positive impact on the development of personalized medicine in Europe [132]. With a budget of €2 billion, its goal is to reinvigorate the European pharmaceutical sector through the development of research consortiums. One scientific priority of the initiative is to develop pharmacogenetics in order to increase the safety and efficacy of new drugs, and to allow for reduced scope and duration of clinical trials, as well as to allow for preventive trials [133].

Future perspective

With scientific and technical progress in genomics and its application in diagnostics and drugs, the need for a clear and consistent European policy towards personalized medicine becomes obvious. As the case of genetic testing for inherited disorders illustrates [16], current policies provide a rather fragmented framework that will not be adequate to cover all relevant issues mentioned above.

In order to overcome the obstacles resulting from the aforementioned barriers and promote the efficient uptake of personalized medicine-related technologies, EU-level policies are being

considered to establish a research framework for improved translational activities. Some potential goals of these research activities identified were:

- The production of more evidence in clinical validity of tests performed in clinical settings and the genotype–phenotype associations they are based on (when relevant), effectiveness, clinical utility and cost–effectiveness of genomic applications, accompanied by the development of improved methodologies to assess the aforementioned dimensions;
- The development of clear guidance on data handling with respect to informed consent, securing confidentiality and security of the individual but also with regard to fragmentation of knowledge and professional management of biobanks.

It is expected that the biomarker-associated knowledge/technology basis will increase the understanding of biological processes relevant for complex diseases. This will lead to new hypotheses and thus accelerate the pharmaceutical research and development process. However, the majority of these biomarker-based findings will not lead automatically to personalized medicines. In fact, only a small number of companies are currently active in the field of systematic research in personalized medicines. This lack of interest may be explained by the fact that the assessment of the benefits and risks of personalized medicines among stakeholders from industry, policy, academia and healthcare providers is contradictory. A systematic foresight of future developments in a scenario or roadmapping process initiated by European decision makers could be beneficial to overcome uncertainties.

The barriers identified in personalized medicine-related technologies showed that there is a lack of evidence of clinical validity and utility, effectiveness and cost–effectiveness. This knowledge can only be generated in a multi- and inter-disciplinary approach to international collaborations. In the European context, this is especially important considering how such evidence will most probably be generated at national levels rather than at the EU level. Continued coordination of evidence generation and diffusion activities may thus be desirable. More to the point, it may be expected that evidence generation for translational research will take the form of a loose style of governance centered around infrastructure for the diffusion and pooling of evidence produced by a variety of actors. These efforts may be achieved by the development of specific research infrastructures and the implementation of standards, proficiency testing and quality assurance schemes, for example. Additionally, it will be essential to link separate platform- or biomarker-specific competences with an integrated knowledge base that works from a problem-oriented rather than a technology-oriented angle.

A high volume of monogenic and polygenic tests acting as companions to drugs are expected to reach a development stage that allows market launch in the next years. However, according to expert opinion, positive public health effects can only be realized if sufficiently validated tests are broadly marketed in the health sector. Thus, it will be crucial within the next 10–15 years to set the appropriate framework for an efficient uptake of validated tests from basic research into the health sector. This involves the provision of adequate resources for clinical research and health technology assessment, the development of methodologies for evidence generation and the feedback between clinical research, basic research and strategic research funding.

Personalized medicine is a field with a high degree of individualization in the meaning of customized design for specific preferences or features of the individual person or group of persons. Against this background, it is remarkable that little research was carried out in the past on patient preferences and patients' expected utilization of personalized medicine. It seems important to integrate these issues in EU research policies and address the user perspective in the design of the technology and the framework conditions, by involving different stakeholder groups in the process of policy and research development [26,134].

Active and self-determined utilization of a new technology such as personalized medicine implies the availability of commonly understandable information [27–29]. Thus, part of future activities in personalized medicine should be the development and distribution of neutral, comprehensible and targeted information on applications in personalized medicine in an early phase of market penetration. An avenue for further research might be to check the possibility of an internet-based registry that contains all information submitted during the approval process, in the wake of a similar initiative for registering information on clinical trials [30,31]. However, this would require the adjustment of present legislation, as dossiers that are submitted for product approval are kept confidential under currently applicable law.

Executive summary

Introduction

- Biobanks, genetic diagnostics and drug–diagnostic co-products are an important knowledge and technology basis of personalized medicine.

Barriers to evidence generation & relevant European policy activities

- The European Commission FP7 framework programme has encouraged the increased integration and networking of European biobanks, but comprehensive inventories and disease registries in Europe are still lacking. The Biobanking and Biomolecular Resources Research Infrastructure may contribute towards closing this gap.
- The majority of genetic diagnostics are classified as low risk. Thus, they do not undergo compulsory premarket review.
- Drug–diagnostic co-products are not handled within one regulatory body.

Future perspective

- In order to promote the efficient uptake of personalized medicine-related technologies, the generation of more evidence in clinical validity is required both of tests performed in clinical settings and the genotype–phenotype associations they are based on (when relevant), also effectiveness, clinical utility and cost–effectiveness of genomic applications. Thus, it will be crucial within the next 10–15 years to set the appropriate framework in place for an efficient uptake of validated tests from basic research into the health sector.
- Evidence generation should be supported by the development of improved methodologies for the assessment of clinical validity, clinical utility and (cost)-effectiveness.
- Current barriers in the use of biobanks should be overcome by the development of clear guidance on data handling with respect to informed consent, securing confidentiality and security of the individual, but also with regard to fragmentation of knowledge and professional management of biobanks.
- Only a small number of companies are currently active in the field of personalized medicine. A systematic foresight of future developments in a scenario or roadmapping process initiated by European decision-makers could be beneficial to overcome contradictory assessment of the benefits and risks of personalized medicines.
- It will be essential to link separate platform- or biomarker-specific competences to an integrated knowledge base that works in a problem-oriented rather than technology-oriented manner.
- Patients' preferences should be included in EU research policies; the user perspective should be addressed in the design of the technology and the framework conditions by involving different stakeholder groups in the process of policy and research development.
- Active and self-determined utilization of personalized medicine implies the availability of commonly understandable information. It could be an option for decision makers to check the possibility of an internet-based registry that contains all information submitted during the approval process.

Acknowledgements

The authors thank all people who took the time to participate to the interviews. This research was set up on the initiative of the Institute for Prospective Technological Studies (IPTS) of the European Commission and conducted within ETEPS AISBL – the European techno-economic policy support network. The views expressed here are those of the authors and do not necessarily reflect the views of the European Commission.

Financial & competing interests disclosure

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

No writing assistance was utilized in the production of this manuscript.

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