

Structure of the PHGEN Interim Report of the Guidelines for

Use/Users

of Genome-based Information and Technologies

- 15 November 2011 -

General remarks:

Since,

- the ultimate objective of PHGEN II is to enable informed decisions to be made at the macro, meso and micro levels regarding emerging genome-based information and technologies with respect to issues of quality assurance, provision and use, and
- the means chosen by PHGEN II is to produce European best practice guidelines to support this decision-making process currently and in the future,

meta-level guidance is needed.

Attention: This guidance is NOT the development of clinical guidelines!

This meta-level guidance can be achieved by ensuring that the different Public Health tasks (the "10 Essential Public Health Tasks" as described within the Public Health wheel or Public Health Trias (Assessment, Policy Development, Assurance) can be adequately fulfilled in each jurisdiction on the basis of a common understanding of best practice standards for each task.

These best practice standards need to be well adapted to the content of Public Health Genomics (PHG), for example, adaptation of existing standards to the specifics of PHG may be more important for some tasks than for others. Guidance is therefore needed for each task of the PH wheel and, for the overall process to be efficient, the link with research is essential and the system management needs to be thought through.

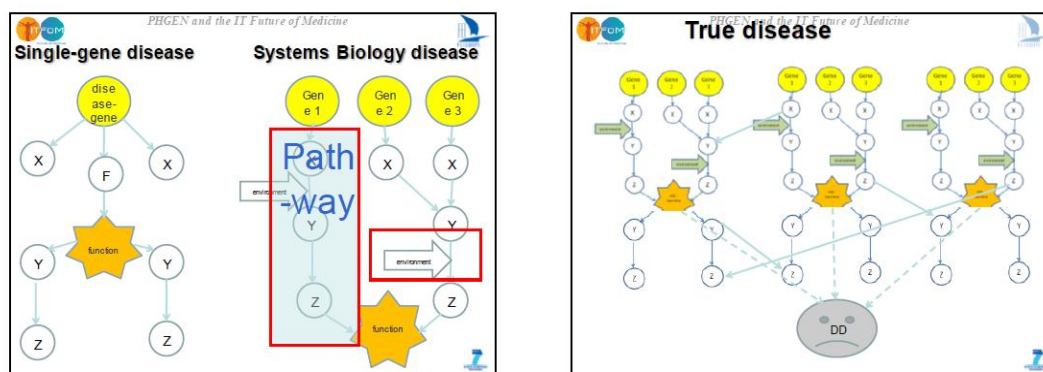
Each pillar will follow the wheel and will fill in the complete template of the guidelines ("10 Essential Public Health Tasks").

Definition of Genome-based Information (GBI) and Technologies (GBT)

PHGEN II builds on the definitions which had been developed and agreed on in PHGEN I such as the Glossary on PHG (WG 1) or the “Status of Genetic Information and Genetic Testing” (WG 2).

In addition, most recent developments in the fields of genomics, systems biology and systems medicine need to be taken into account being essential for the evidence base of the guidelines (task 10: Research for new insights and innovative solutions to health problems).

This task will be provided by the VUA group (Westerhoff et al). The group will provide the other PHGEN partners with a number of practicable blueprint definitions and analyses addressing (i) genetics, genomics, functional genomics, systems biology and systems medicine and the distinctions between them, (ii) genetic disease, genomics disease, and systems biology disease, and the distinctions between them, and (iii) the differences between (a) generic, (b) cohort-based, (c) personalized, and (d) truly individualized medicine. This integrates genetics, genomics, functional genomics as well as systems biology, in a systems medicine perspective (see figures below).



Not cohort based but individualized
Not genomics but systems medicine

**Yes, but a beginning of
Collective but individualized
systems medicine for health**

PHGEN and the IT Future of Medicine
Implications

- 1 SNP per gene
- All individuals are different multiply
- →Every systems biology disease is a rare disease
- Genetic disease and environmental disease merge
- Tests not only for genome sequence but also for functions of state (e.g. proteomics)
- Comprehensive (multi source; network targeting) approaches called for

The highly technology and computational sciences driven dynamics of genomics as a “moving target”, starting from the Human Genome Project (HGP) to the Personal Genome Project (PGP), is currently changing public health research, policies and practice in a substantial way.

Rapid scientific advances and tools in genomics such as in the light of epigenomics, microbiomics and systems biology supported by new ICT solutions not only contribute to the understanding of disease mechanisms, and to the characterization of each person's unique clinical, genomic, and environmental information, but also provide the option of new promising applications in human health management during the whole life-course. In fact, what was little time ago a vision for a new era of public health, in which advances from the -omic sciences would be integrated into strategies aiming at benefiting population health, is now responding to the very pressing need for the development of effective personalized healthcare going even beyond personalized medicine. While the utility of most genetic tests and biomarkers is still not evidence-based, the real take home message stops here and is a different one. For example, in the personalized medicine setting the traditional assessment and evaluation tools just do not work anymore and ask for concepts such as personal utility instead of clinical utility.

Thus, PHGEN II faces the need for a new paradigm understanding that: (1) what we call common complex diseases might be a sum of “rare diseases”, and “rare diseases”, in the sense of Mendelian Disorders and monogenetic diseases, might be indeed very complex; (2) we move from diseases towards “diseasomes” (disease nodes); (3) we move from risk factors to individual pathways or networks; and (4) we move from clinical utility to personal utility.

In the end, the real paradigm shift depends on the willingness to restructure policies, and on the ability to train practitioners from various professions.

The P4 Medicine being predictive, personalized, pre-emptive and participatory serves as a blueprint for PHGEN II to prepare health care systems and policy makers in time.

Important challenges

- Ensure functionality and complementarity of the different tasks within each jurisdiction: PHG system management (guidance on structures and processes needed ?)...
- Ensure harmonisation across jurisdictions and avoid duplication of efforts: PHGEN II best practice guidelines and sustained international collaboration/platform. There can be overlaps between the pillars but this must reinforce the concept rather than duplication.

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Content

1. Executive summary

The USE work package produced a coordinated document to which all partners of the WP could contribute/add comments.

The main points to underline are 1) the deep necessity to take more into account the lay user's perspective in guidance as this is a strong gap and little of existing guidance can be used; 2) the usefulness of the definition of the three levels of users utilised throughout this report (Policy maker level, professional level, lay people and citizen level); 3) the interest of anchoring recommendations and best practices in explicit principles. The assessment of existing guidelines and characterisation of gaps and domains covered, prior to redact this recommendation/best practice part was done in depth.

Regarding the 10 Public Health Genomics tasks (cf. the wheel) we classified domains according to their importance from users' perspective:

- 1) Inform, Educate, Empower
- 2) Mobilise Community Partnerships
- 3) Link to / Provide healthcare
- 4) Develop policies
- 5) Enforce laws

From the perspective of the translation and use of genome-based information and technologies in health the following topics can be classified by importance order:

- 1) Diagnose and investigate
- 2) Link to / Provide healthcare
- 3) Assure Competent Workforce(s)
- 4) Monitor Health
- 5) Develop policies

Recommendations are expressed towards the EU institutions and the Members States (e.g. governments, professional organisations, lay people and non-governmental organisations [NGO's] etc.). Best practices have been somewhat detailed. Evidence informed policies are targeted and the present status and foreseeable developments have been considered. The importance of public health oriented research is underlined.

The agenda for a Public Health Genomics policy fully implemented at national and European level represent a middle-long term approach and could only be envisaged over a several year agenda. As it is moving target and as literacy about genome based information and technologies will probably change over the coming years a specific emphasis has been put on educating professionals and the lay publics. The evaluation of the developments in public health genomics should be regularly performed.

2. Specification of the pillar / working definition

2.1 General objective of the pillar (perspective / definition)

The WP Use covers use and user perspectives in the areas of genetic information (biobanks & genetic databases); services (genetic testing, screening, counselling); user issues related to drug development (pharmacogenetics); and those to marketing (direct-to-consumer offers). Special themes will be chosen as exemplary cases. Thus, the length of developed public health tasks from use / users perspective are varying.

Relevant ethical, legal and social aspects will be tackled, from the patients'/consumers' point of view, through the analysis of existing enforceable regulation, opinions and literature in order to extract common principles and to work on missing issues towards integration of genome-based information and technologies in the public healthcare system and to achieve adequate protection for individuals and society. Likewise, the possibilities to give a sustainable proactive role to individuals involved are systematically explored, which is lagging behind. For example favoring direct democracy in public health activities can imply defined consent possibilities for individuals and populations to certain public health monitoring activities using genome-based information.

2.2. Specific objectives of the pillar (target audience)

The aims include making recommendations and proposing related best practices concerning the use of genome-based information and genome-based technologies that are capable of taking into account users' needs, concerns and expectations in public health genomics and P4 medicine.

Identification of USER levels

Users: Individuals or groups of individuals who may use any genetic service whether they are patients or not, including professionals using genome-based technology and/or genome-based information. Users can be differentiated into categories of individuals or groups.

However, we identified “users” in a broad way of interpretation as targeting three main levels of stakeholders:

- o Policy maker level on different levels ranging from law development and enforcement groups to institutions (also ethical review boards/committees) involved in formulating regulations, guidelines, recommendations and best practices;
- o Professional level that entails professionals as users of genome-based information and technologies including clinicians, counsellors, health care staff and professional organisations; and
- o Lay people or citizens level including patients, consumers, citizens, often represented by non-governmental (patient) organisations but also media personnel delivering messages related to public health genomics (including on the internet).

2.3. Working group members and task allocation

2.3.1. Core WP Group Members

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Allocated tasks

- ✓ Internal coordination
- ✓ Production of deliverables

- ✓ More specific task allocations according to the wheel:
 - SDU: Inform, Educate, Empower / Mobilise Community Partnerships / Assure Competent Workforce / Evaluate
 - INSERM: Monitor Health / Diagnose and Investigate / Develop policies / Enforce law / Link to-Provide Healthcare /

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Allocated tasks

- ✓ Participation in assessments
- ✓ Expertise and input

2.4. Background documentations

2.4.1. General background – Public Health Approach in public health genomics

The main aim of public health is to assure conditions in which people can be healthy and thus improve the health of the population. This is done by using organized efforts of the society. These efforts range from policies in different sectors of the society, to programs and environmental interventions and further to organizing health care and providing guidance for individual patient care (12; 107). Public health genomics has been described *as the responsible and effective translation of genome-based knowledge for the benefit of population health* (11).

The central values of public health as well as of health promotion are *equity*, working in *partnership* with different stakeholders, respecting community *values* and priorities. Public health programs provide information and advice to secure equality of opportunities and access to health enhancing environments (126).

Public health actions are traditionally targeted to populations or subgroups of populations and to communities. Decision making about program provision (*e.g.* screening, vaccinations) happens on policymaker and expert level but in collaboration with representatives of citizens; thus seldom directly with individual citizens (*see e.g.* 5). This poses a challenge in tailoring information and services so that they would fit large, often heterogeneous groups with *e.g.* very different interests, knowledge levels as well as resources.

The traditional biomedical approach on the other hand, has individual (or family) as a target. Consultation takes place in face-to-face clinical encounters within organized health care, and *e.g. informed consent process* of individual. This allows individually tailored advice in decision making about tests and care. There has been a trend towards patient-centered care in the clinical field, which tailors care based on individual preferences and conditions (5).

Finding a balance between population-based and individual strategies is a central and important challenge for the future development of public health genomics. Developments towards personalized medicine/health care in public health genomics call for re-evaluation of both the traditional public health paradigm and the traditional clinical paradigm. A new approach is needed, which builds upon the evidence and know-how of both the public health and clinical fields and does it in partnership and in good *coordination between clinical medicine and public health* (12).

Public health needs to learn to apply a more personalized approach instead of stratification of population into groups. The role of public health in public health genomics is to provide guidance, regulation and organization of health systems and health care, manage priority setting, resources allocation, reimbursement and insurance strategies. The regulatory tasks include *e.g.* protection of privacy, confidentiality, data protection and safeguards against discrimination (18; 10; 14). Policy development is one central area of public health and in the field of public health genomics this could include formulation of standards and guidance which promote the appropriate use of genetic information and the effectiveness, accessibility and quality of genome-based technologies and services and related information.

The clinical field needs to find ways to prepare for less control of the information and services now often more provided outside organized health care. Developments such as genomic profiling of individuals (based on several low susceptibility genes), pharmacogenomics, claims of nutrigenomics and services such as availability and offering direct-to-consumer genome-based technologies, and also biobank possibilities - as well as media coverage of genomic promises and threats - happen *largely outside organized and well controlled clinical settings* with their planned budgets. Sources such as media are used to make decisions instead of the clinical setting, in which clinical professionals can supervise the user in the decision making process (171).

In the public health approach citizens and other groups of *stakeholders in the democratic and social process have an active role in decision making* about their own health and the organisation of health services (*e.g.* priority setting in policy). This requires well developed genomic and general health literacy and resources for informed decision making.

In the era of the public health genomics, there is a need for *new, constantly updated and trustworthy guidance for individual citizens to empower them in navigating through the rapid changes in information and technology*, but also for policy makers and professionals as users of genomic information. Further, the public health system as well as other sectors of societies, including legal, social and educational sectors, needs to be prepared for the challenges and consequences (e.g. spill -over effects of e.g. direct-to-consumer testing) of these developments.

2.4.2 The contribution of the PHGEN II USE pillar

The USE pillar applied the approach and material provided by the coordinating team in Maastricht. The first step was to get an overview of the state-of-the-art of the existing guidance in the area relevant for public health genomics. This was done by literature searches as well as scientific assessment of the compilation of the guidance documents in the USE area (n=42) provided by the coordinating team in Maastricht. These documents included overall legal and ethical documents about health services, information and about research principles and practice. They also included published genomics-related clinical guidelines. The scientific assessment was done by using a modified version of the AGREE instrument (Appraisal of Guidelines Research and Evaluation, www.agreecollaboration.org).

The modifications were targeted towards the public health tasks assessment. A major modification of the AGREE instrument was made to develop an instrument for the different user groups, for the public health approach, and based on the know-how and the state-of the-art in the challenges of genomics, especially from the perspective of the social and behavioural sciences, ethics and law. The instrument was given the working name of 'PHGEN guidance assessment tool', and it was piloted and validated before its use. In addition, a new group of items was developed to measure the extent of use of the evidence-base in formulating the guidelines. Further, the guidance documents were assessed from the perspective of the coverage of the relevant contents to cover the issues at stake in the new public health genomics developments. In the following the lessons learned from the guidance assessment are integrated into the relevant parts. The work is being written into several international research papers, among them a methodological and theoretical paper; all of these

will duly acknowledge the PHGEN II project and the European Commission funding.

2.4.3. Background for assessment – use/user perspective

2.4.3.1. Monitor Health

Identified issue

We are addressing here the following identified issue: How could users influence the health monitoring?

The assessment work brought up the following useful findings

Health monitoring using genome-based information has been considered as a missing issue in the studied texts that necessitates new developments in public health genomics.

Background

The use of genome-based technologies and the profusion of genome-based information in medicine need to be conceived in a way allowing the exercise of health monitoring tasks organised in Member States (MS), at the European Union (EU) level and internationally. Traditional health monitoring systems will be impacted by the venue of a large amount of genome-based information and new activities in the field of health data management such as e-health. The development of new indicators related to new kind of information available through genetic testing and screening should be considered and coordinated internationally. Information and education of users are pre-conditions for going towards a pro-active and responsible health monitoring system involving users and genome-based information.

Thus, the following points will be tackled:

- Traditional and new health monitoring activities involving users in a more “personal health monitoring”: identify the new challenges and new opportunities.

- Users' influence on health monitoring activities: consent, autonomy and health monitoring activities including new developments in e-health and records [electronic medical records (EMRs) / personalised medical records (PMRs). Identification of new challenges.

Underlying principles

a. BENEFIT / RISK BALANCE

As a paramount principle in health sciences and in the use of health technologies to *a priori* protect individuals' interests, health and wellbeing this balance is mainly performed by health professionals, ethics committees, policy-makers and regulations in their respective tasks.

b. SANITARY SAFETY

Health monitoring tasks in public health are intended to gather data about diseases, side-effects or malfunctioning in health systems, to alert responsible authorities about the risks of products, substances, activities used in health services, in order that enable them to set up prevention policies and to spread information towards users.

2.4.3.2. Diagnose and Investigate

Identified issue

We are addressing here the following identified issue: How to protect users from the misuse of their genome-based information?

The assessment work brought up the following useful findings

This domain is qualitatively deficient with regards to users' perspective. Poorly covered aspects include: users' rights in the context of wrong diagnosis; the protection of users from defective or inaccurate diagnosis device; employment, insurance.

Background

Users of health services including specific genetic services should be ensured that their biological material and associated personal data, including test results, will be of quality and responsibly managed by health establishments and professionals. The aim is to assess the implications of the development of genetic services both in the private and public sectors,

in clinical and research settings, in terms of uses and misuses of human samples and health data including genome-based information. The practical issues encountered by health professionals, the new challenges raised by technological developments and online services should be considered in order to consistently adapt ethical standards and laws, reaffirm and ensure users' rights. To clearly frame the possibilities of using genome-based information and technologies in health systems and in the society, national and European policy-makers and stakeholders should envisage in a coordinated approach the means to protect users from misuses of their personal sensitive data and from the wrong diagnosis or prognosis using genome-based tests. More certainty for users involved in genetic testing and screening should be assured. The international dimension of the provision of genetic services, of research projects and the movement of individuals seeking health services should be taken into account with regards to users' interests.

The notion of "other social usage" of genome-based technology and information

With "other social usage" we are targeting several situations which are non-health, non-research and non-medically oriented but are involving genome-based technologies and genome-based information for other purposes. We suggest to use the notion of "other social usage" of genome-based technologies and genome-based information as being wider than the notion developed so far by the World Health Organisation (180) and United Nations Educational, Scientific and Cultural Organisation (167) of "non-medical purpose" which is clinically oriented, and those used by the Council of Europe (30) specifically targeting "employment and insurance purposes". The new actors using genetic services and genome-based information include the tested individual, third physical and moral persons. The point here is to assess other social usage and potential negative effects on health systems and in terms of commodification of genome-based technologies and information that legal systems should prevent.

We propose to distinguish health purposes, whether they fall under clinical practice or research that are outside the realm original context / or consent (designated as "secondary uses") (101) from other uses in society, outside health or health research sector such as use in employment, insurance and personal use in recreative genomics (designated as "other social uses"). Difficulties appear when the new use of genome-based information originally gathered for health purposes leave the health sector to enter

other spheres highly influenced by economical concerns, state interests or other non-health-related, non-research-related or non-medical purposes. For these particular re-uses we also propose using the term “other social usage”.

Employers and insurers are adopting a risk assessment approach in their activities. As observed in United States, insurers (e.g. 121) and employers (e.g. 87) could be interested by detaining genome-based information of predictive value. Such usage of health-related genome-based information is potentially discriminatory and requires legal developments and scientific background to cope with existing public concerns regarding to misuse of genome-based information (71-Rec.10, Expl.Rep.2.1.9).

Whereas some Member States have legal frames regulating or including these issues, there is presently legal uncertainty and a lack of clarity in some national legal frameworks which should be assessed. Several ethical legal and social issues have already been identified but, considering the differences between existing systems, some of them remain unresolved, and the legal state-of-art in European countries varies considerably (93; 90;109;69). The same uncertainty in legal disposals concerning the framing of other social usage of health-related genome-based technologies and information related to individuals is observable in the international area (30-Expl.Rep.; 33). Yet, according to the combined reading of Articles 12 and 26 of the Convention on Human Rights and Biomedicine (31) concerning the use of predictive genetic testing for purposes other than health, we could consider that predictive genome-based information could be used only when prescribed by law and where it is “necessary in a democratic society in the interest of public safety for prevention of crime, protection of public health or protection of rights and freedoms of others”. Thus, potential usage of genome-based information by employers or insurance companies should respect the limitations described above, and such usage should be restricted.

This phenomenon is quite unfamiliar in the EU and more research is needed to understand the extent of such usage and the interest of employers and insurers in the access to genome-based information (143; 86). Although we are supporting strict application of the medical confidentiality as it has been suggested by several organisations such as the World Medical Association (WMA;182-para.18,19), debates on this issue should be promoted across the EU involving social partners, professionals, the public and policy-makers.

It is important to cope with these possible uses and to develop national and international instruments as well as strong political commitments of stakeholders.

The use of predictive genome-based information by employers

While employers have a duty to protect the health and welfare of their employees (*e.g.* 23-art.31), the request for using genome-based technologies and genetic information in occupational health could have significant impact on the social equilibrium of our societies if this practice was generalised. The safeguard of the social justice preventing discriminations and stigmatisations based on biological characteristics of individuals, is presently the main concern policy-makers have to cope with rapidly. According to the round-table debates of the European Group of Ethics (51) on this topic, occupational health policies should be based on equilibrium between the need for health protection and the right to work with the aim of protecting health and allowing employment. Several predictive tests with several purposes and implications could be performed at the request of employers but their use should be justified and they should all be scientifically and medically grounded. Individual rights and autonomy should always be respected. Individuals should not be forced to perform a genetic testing for employment reasons (pre-employment test; adaptation of the workplace; medical/health surveillance). They should have given their informed consent and they right not to know should be respected. The access to independent sufficient information like *e.g.* health counselling or appropriate genetic counselling should be ensured. Any refusal from employees should be stated in a written form and recorded by the employer. The employee refusing to perform a test should not suffer from this refusal but occupational health professionals should make him aware of the incurred risks and that he his acting under his own responsibility. Privacy, confidentiality and data protection of test results must be respected. The health information gathered from the test should not be fully forwarded to the employer but kept secret by the occupational health services. Employers should just know whether a found risk is incompatible with the tasks of a specific work.

The specific situation of the applicant or the employee and the economical and social pressures which could weigh on them should be considered as factors of vulnerability when developing policies on genetic testing in the workplace.

It should not be the role of the employer to decide whether or not to practice a genome-based test for a specific work but a shared decision with competent independent authorities.

Genetic information should not be used to exclude a person from employment except where the results provide with a high-level of certainty or where the genetic disease has already appeared and seriously affects the ability of the person to fill in the tasks of the occupation.

Whatever the test performed, a person presenting positive results should have access to all available health services and where relevant specific genetic services, healthcare and treatments intended to prevent or treat the disease.

The use of predictive genome-based information by insurers

In 2005 European citizens expressed strong opposition to the access and use of their genome-based information by private insurance companies (55-fig.23). The difficulty here is to avoid uninsurability of individuals and to balance contractual legal requirements and the risk of discrimination and favouritism grounded on biological or genetic information. The disclosure of prognostic or predictive information for monogenic or multifactorial diseases put different issues on the agenda. Another concern is the familial validity of the predictive genome-based information gathered from an individual and its impact on insurance regimes of the relatives which have not performed any genome-based test. As it has been stated in literature "family history is also predictive genetic information, although it is recognized that the self-reported family history may be inaccurate"(93). There is a need to resolve inconsistencies in current attitudes and policies on the use of family history in relation to the use of genome-based test results. The duty of applicants to disclose all necessary health information to the insurer in the respect of fair and lawful relationships should be contrasted by the identification and limitation of the validated health predictive information which could be used for insurance purposes. Additionally, insurers and applicants should be empowered and educated on the implications and limits of the genome-based information that could be used or required for insurance purposes particularly concerning common complex diseases (93). The extent of such demand is obscure and should be first clarified at national level. Responsibilities and penalties due to fraud should be clarified in application of national laws.

Whatever the case, there are not existing strong enough arguments which would justify compulsory genetic testing to access an insurance service or regime. Thus, insurance companies should be prohibited from requiring insurance-seekers to undergo genetic testing (151).

Prohibit the unfair relationships between genome-based information holders

In order to protect the confidentiality of the genome-based information and the autonomy of individuals, employers should not be allowed to forward available information they accessed on the genetic status of an employee towards a third party such as insurance companies, and vice versa, without the express authorisation of the individual concerned (cf. Best practices on disclosure). This principle should also apply to other public or private health establishments (129-para.7.F). Such inter-professional disclosure outside the health sector for other social usage of genome-based should be prohibited by principle at national and European level. Nevertheless, laws could plan otherwise in restrictive cases.

Communication and disclosure of test results

The disclosure of genome-based information resulting from an individual genetic testing or population screening puts specific ethical and legal issues in terms of equilibrium between individual rights, professionals' duties and the respect of privacy and confidentiality. Disclosure is different from communication because unplanned results or third persons are potentially concerned by genome-based information. Individuals have the right to know/not to know about relevant information for their health or for the health of their family members (30-art.18), but limited exceptions to these rights and to the medical confidentiality are acknowledged internationally (168-art.14;169-art.9;167-part.IV) and by several member states (e.g. 21;115). Yet, the disclosure of genome-based test results requires clear regulatory frameworks and guidelines; adjustments in medical confidentiality; the role of the individuals and health professionals should be clarified. Justified borders to the individuals' right to know/not to know should be clearly stated and justified.

The disclosure of genome-based test results is intrinsically linked to the development of educational means devoted to health professionals and the public about the range and meaning of possible findings. Under this

condition of education, the disclosure could optimistically be tackled as a process improving the public understanding of genetics.

Other issues to consider as regards to the use-users

Among other issues that should be dealt with regarding the possible misuse of genome-based information and technology we will address the role of ethics committees, the situation in case of transfer of samples and data and issues related to the direct-to-consumer genetic testing activities.

Underlying principles

a. IMPERATIVE OF BENEFICENCE

It is the duty of physicians who participate in medical research to protect the life, health, dignity, physical and mental integrity (23-art.1,3;163-art.2), right to self-determination, privacy, and confidentiality of personal information of patients (157). This imperative is also relevant in the research context (181-para.11).

b. NON-DISCRIMINATION AND NON-STIGMATISATION

Any form of discrimination against a person, a group of persons or a community on grounds of his or their genetic heritage is prohibited. No one shall be subjected to discrimination based on genetic characteristics that is intended to infringe or has the effect of infringing human rights, fundamental freedoms and human dignity (168-art.7;170-art.3;169-art.6;31-art.11).

c. PRIVACY PROTECTION AND CONFIDENTIALITY

Everyone has the right to privacy protection and to be treated respectfully regarding private life matters that entail information about his/her health (31-art.10;77-art.16;23-art.7,8). Clinical and research settings should be organised to ensure the privacy and confidentiality of genome-based information related to an identifiable individual.

d. NECESSITY AND PROPORTIONALITY PRINCIPLES

Any risk related to the use of health-related genome-based technology and information (44-art.6;7) must be unavoidable and envisaged proportionally (30-Expl.Rep.) to the health finality pursued, the needs of the individual

involved and the availability of alternatives. Privacy protection measures must also satisfy this equilibrium.

e. QUALITY OF GENOME-BASED TECHNOLOGIES

A responsible translation of research innovations into health services for the benefit of population health should be based on a quality control system using harmonised quality criteria. The analytical and clinical validity, the clinical utility of the genome-based technologies and the reliability of the results should be part of such evidence-based criteria.

f. LEGAL CERTAINTY

The more the legal framework is clear and consistent at the European and national levels the more genetic services will be developed in a responsible way. European and national laws concerning the quality of the products and the quality of health-related services must create certainty in the regulatory framework covering both public and private genetic services. The establishment of clear procedures, rights, duties and chains of responsibilities in the provision and use of genome-based technologies and information is part of this principle.

g. INVOLVEMENT OF INDEPENDENT RESEARCH ETHICS COMMITTEES AND OTHER ETHICAL ASSESSMENT GROUPS

The role and importance of independent ethical committees and groups should be emphasised in assessments of genetic testing and screening practices. Research ethics committees but also clinical ethics' discussion groups should be considered as key actors in the protection of users of genetic services.

2.4.4. Background for Policy Development – use/user perspective

2.4.4.1. Inform, Educate, Empower

Identified issue

We are addressing here the following identified issue: How could users be informed about genome-based information, technologies and genetic services?

The assessment work brought up the following useful findings

This domain of action is considered as well documented but necessitates adaptation to the public health genomics approach and the different categories of users.

Poorly covered aspects include: how to empower users to act responsibly, the psychosocial issues related to the use or the content of GBI; the media as vectors of information; public involvement in the development of guidance; public debates; surveys and communication on genomics in health; the professionals' point of view; direct-to-consumer information available online; communication and understanding of tests results.

Background

The purpose of public health programs is to provide information and advice and to secure equality of opportunities and access to health enhancing environments (126). What follows now is a discussion on this challenge from the perspective of different user levels/groups.

Informing & educating

Informing and educating in the field of public health genomics is extremely challenging due to rapid growth of genome-based information and technology, development and complexity of the information as well as the wide range of vested interests both in public and private sectors and stakeholders in the field. *E.g.* the three user levels of policy makers, professionals as users and lay people, have differing needs, interests, capacities and roles in their respective contexts.

Public health genomics guidance should help different user groups to make informed decisions. Assessment of the guidance documents provided by the PHGENII coordinators showed essential lacks in differentiating the information for different user groups and their literacy levels, *e.g.* many documents were meant for states or other high level policy makers and only one document (patient leaflet) was on the levels of lay people. This is clearly a drawback since research from the *knowledge transfer in the public health science* indicates that the approaches tailored to the needs and levels of knowledge of the target groups are superior to more generic approaches such as available web resources or approaches using specific mediators such as knowledge brokers (47). There is also *evidence from the clinical field* that guidelines targeted to the user level empower users to make more informed healthcare choices and to consider their personal needs and preferences when selecting the best option (183). *Health literacy* is the degree to which

individuals can obtain, process as well as understand the basic health information and services to make an informed health decision (120). Genetic health literacy is an important element and essential ethical value in public health genomics (154;152). The future guidance information in public health genomics should be tailored to the genomic *health literacy* levels of target audiences (120).

A workshop organized by the National Human Genome Research Institute (119) addressed exactly this literacy issue as it listed the priority research areas in the future health applications of genomics: a) to improve the public's genetic literacy in order to enhance consumer skills, b) to gauge whether genomic information improves risk communication and healthier behaviours more than current approaches c) exploring whether genomic discovery in concert with emerging technologies can elucidate new behavioural intervention targets.

From the genomic health literacy perspective especially challenging is that people need to be educated to deal with the uncertainty connected with probabilistic knowledge often used in the connection of genomic information (e.g. 154). From the behavioural research perspective, personalized health messages, especially about changing lifestyles, pose a big challenge since there is strong evidence that effective and sustainable behaviour changes require also environmental change, including social support and facilitating policies (144). Thus there is a need to refine the existing behaviour change theories and methods in order to find relevant model to guide the new genomic health information and related life style changes. Behavioural change seems to be most likely when motivation is high; providing people with genetic information may not increase their motivation and in some cause may decrease in fact. Further research is needed to evaluate to programmes in which genetic information are given, including evaluation of different ways of delivering the information (116). Improved genomic health literacy might also help users to regard genetic factors in the same way as any other determinants of health instead of either privileging them or unreasonably seeing them *exceptional* or demonizing them. Normalizing the perception of genetics would both enable a more rational approach to the use of genetics to benefit population and it would also enable more balanced public debates. (11).

One of the central challenges in informing and educating different user groups of public health genomics information and technology is how to approach and deal with the hype and high, often unrealistic expectations

related to genomics among the users. The guidance documents assessed in the USE pillar of the PHGEN II very rarely transparently revealed any information which could have been used to evaluate neutrality or how up-to-date the guidance actually was in the light of the new information and technology. There is a need for neutral, preferably accredited information sources so that the quality of the information, updating it, potential conflicts of interest of those providing information can be checked in a transparent process. Institutions enjoying trust of the population such as NGO's, professional or scientific organizations etc could function as the above mentioned accredited information sources.

The media reporting reflecting high expectations but also concerns tends to amplify the attention and the scale of the public and private discussion on genomic promises and on the other hand, threats. The social amplification theory (106) provides a fruitful framework to analyze and understand the process sometimes escalating hype. It also indicates the levels and processes of counteraction needed from the society, cultural context and different stakeholders involved. One possibility would be to train science writers among the media representatives. Another would be to develop science communication curricula for educational institutes and in some societies potentially also so called the Science Olympics might function – in the way Norway has recently shown.

User levels and informing: importance of the evidence base

In terms of the scientific level and complexity of genomic information professionals as users are very probably able to read and benefit from research literature (or references to it) such as meta-analyses and reviews and draw conclusions of those for their practice. Although also on this level the everyday practice makes it not feasible to follow the full length scientific papers; for this reason many acknowledged professional bodies such as European Society of Human Genetics and EuroGentest etc. produce evidence briefs.

When it comes to showing how well the provided information, services and guidance in genomics are based on evidence, all user groups need to know and be able to interpret the evidence-base of the actions. Policy makers and decision makers require evidence about cost-effectiveness of the potential actions to be able to prioritize but they (especially elected politicians) also need to know how well the community accepts the actions. The professionals need evidence information as the basis of their practice

decisions. The citizens on the other hand need to know if the information or services are based on proper research or evaluation to be able to make informed choices as consumers.

The difference in the evidence basis of the public health and health promotion decision making compared to *e.g.* to clinical decision making is that many other kinds of evidence than purely research evidence needs to be taken into account. Public health and health promotion fields prefer to use the term '*evidence-informed*' instead of '*evidence-based*' to show the importance of 'other kinds of evidence' instead of the (published) research evidence: *e.g.* contextual issues such as implicit practitioner know-how and traditions, values and resources of the community and policy makers (5, 47). Please see further discussion on the evidence-informed public health decision making in the paragraph page 34.

The results of the assessment of the existing public health genomics guidance for users showed that the guidance seldom explicitly reported the actual evidence-based it was built on; further, it seldom mentioned any feasibility tests (piloting) of the guidance among different stakeholder groups to test the acceptability. From the perspective of good quality evidence updating the guidance is also very important, since it has been estimated that majority of guidelines are apparently out-of-date in some important respects within three years of publication (125;155).

The policy level as users faces challenges in the development of policy to regulate genomics for the benefit of population health. On the institutional and policy maker level there is a high demand of summarized, digested, short documents to help in decision making and prioritization of issues which often lie outside the specific contents knowledge of the decision makers (108). Decision makers often require comparative information for different services and cost-effectiveness information. Decisions on this level largely also rely on the judgment of experts of the field. Thus referencing the sources happens mostly on the level of expert interview, in which the publications may be mentioned only.

The lay/citizen levels, including NGO's, on the other hand, make best use of short summaries (leaflets, (accredited) web site information) and recommendations, which provide contact information or links to further information. The use of personal stories and experiences enhances understanding and digesting often rather abstract information; and specific guidance is easier to grasp than a generic one.

All in all it has been shown that guidance with more narrow and specific scope is of a higher quality than guidance with a wider focus.

Empowering: informed choice, participation and access

The main issues in the empowerment from the user perspective are health literacy, possibilities informed choice and fair and genuine participation in decision making about genomic services in their respective societies and communities as well as have equitable access to information, technologies and services.

From the user perspective probably the most central empowering issue in dealing with public health genomics information, technology and services, is *informed choice*. Further, the emphasis on individual choice can only be fair if all people have the same abilities and capacities to make decisions (126). In this sense *genomic health literacy* (dealt with in the previous paragraph) *is a pre-requisite for making informed decisions and thus empowering users to act in their health issues*.

Genomic health literacy and informed consent are challenging at least in relation to biobanks and databanks, genetic testing and screening, participating in different research projects and also in collecting and using biological samples in regular health care contacts. The challenges here are: how generic and how specific the consent for certain purpose should be; is new consent needed for re-use of samples; benefit sharing; kind of and right to counselling etc. Studies like the longitudinal collection of gene/environment data in research may challenge traditional approaches to obtaining informed consent (122). If the possibilities within the field should be fulfilled the format of informed consent should maybe be changed *e.g. open consent or informed contract*. Public health genomics needs to develop an ethical framework compatible with rapid changes and opening possibilities of genome-based technology, genetic services and research (107). In similar vein, new possibilities for personalized medicine put further pressures on developing ethical principles (122). These advances however emphasise the immediate need for assuring the protection of individuals included, which would require high level guidance and process for assuring the protection (110).

Research in health psychology has developed an enlightening decisional model to study the process of informed choice of *individuals*, which builds on combining the level of knowledge, attitudes and values and actual decision/behaviour (116). For really informed choice individual who e.g. takes a genome-based test should have good knowledge, positive attitudes towards the test and its implications. On the other hand, taking a test with little knowledge or negative attitude can be considered a less informed choice. This model, originally developed for individual decision making, can in principle be applied also for the meso and macro-level decisions of public health genomics in societies (e.g. decision on providing genetic screening, reimbursement of (further) genome-based tests done on the private sector or via internet) in line with analogy between clinical medicine and health promotion/public health interventions (5). In these situations decision makers are communities (e.g. via politicians), societies (of e.g. experts) or citizens/patients (e.g. NGOs). For a public health decision model (153) - please see Figure 1 and its explanation on page 35. For public health genomics the traditional bioethical framework that focuses on the protection of the individual, falls short. Many interventions – even if they are provided on individual level may have consequences for healthy populations and families related to an individual (126). For this reason the present codes of clinical medical practice often present high priority to individual autonomy, which from the population-based focus is imperfect for the practice of public health (126).

Public health focuses on public care for the health of all people, and in line with that public health genomics has to cope with the justice as the first virtue of social institutions. Due to scarce resources social institutions need to find the right balance between liberty (respect for individual autonomy and self-determination) and equality while implementing procedural fairness and the inviolable human dignity of every human being. This can be described as the norm *social justice*, where the individual rights and welfare on one side have to be balanced against the rights of the population on the other side, also referred to as health maximization. Justice rather than social utility is more compatible with human dignity, which is an important component of public health genomics (154). In this relation it has also been proposed that perhaps it is more ethical to use the model of *informed contract*, which is based on the idea of *benefit sharing* (e.g. see page 34) between the consumer and the provider, instead of informed consent and informed choice in the doctor-patient relationship (Brand 2006).

The assessment of the existing public health genomics guidance indicated that the involvement of stakeholders in the development of guidance was lacking and it was unclear whether the views and preferences of the target users were sought.

However, the prospect that findings from genomic research will soon bear fruit creates a need for a perspective, which still demonstrates a commitment to avoiding harm but also better enables the society to reap the benefits from the expansion in public health genomics. This perspective suggests a formulation of a *social contract between science and other stakeholders* involved in public health genomics. To establish a framework involving reciprocal obligations by science and society certain conditions are needed. The field of science should provide the society with: a) clear formulation of goals and visions of what constitutes benefit, without overstatement of benefit; b) commitment to achieving these goals over the pursuit of individual interest; c) high transparency and involvement of the public in the scientific process. Likewise, the society should provide some conditions: a) trust to the scientific process and the goals; b) support to research by participating in research; c) support for greater academic freedom, free from manipulation by political goals or ideology and sustained reliable funding. The implementation of the framework would require a high level of education of the public (122).

A move away from the emphasis on the rights of an individual to act exclusively in own interest; towards new ethical principles containing ideas of *social altruism*, solidarity and universality is needed in the field of public health genomics. Indications for this have already been reported in several studies describing people's motivation to donor samples and to participate in research beyond their own benefits and interests (see e.g. 95;159;160). Solidarity and social altruism however, flourish in the atmosphere of high level of transparency in information and guidance provided, in the atmosphere of trust. For the realization of this e.g. the guidance documents should reveal conflicts of interest, funding of the guidance, information, or services production. This transparency was not visible in the present public health genomics guidance documents assessed in the PHGEN II project.

Underlying principles

a. THE EMPOWERMENT OF USERS AND THE DEVELOPMENT OF HEALTH AND GENETIC LITERACY

Public health genomics policies should allow the public and users of genome-based technologies and information to develop the necessary knowledge enabling responsible behaviours.

b. TRANSPARENCY AND QUALITY OF INFORMATION

As principles of good governance and fair relationships, objectiveness, reliability and accuracy of the health information provided to individuals must be ensured.

c. ACCESS TO ADEQUATE SUPPORT

Users of genetic services must have access to all adequate available supports and services related to their health status.

d. NO GENETIC DETERMINISM

Public and private policies related to genetic services and genome-based information must ensure that the erroneous idea of genetic determinism will not be spread through our societies. This involves education of the public.

2.4.4.2. Mobilise Community Partnerships

Identified issue

We are addressing here the following identified issue: How users can mobilise and act to improve their position and influence?

The assessment work brought up the following useful findings

The mobilisation of community partnerships and the possibility for users to mobilise and act to improve their position and influence is considered as missing.

Background

Community responsibility and partnerships in public health genomics

Public health and health promotion actions are inherently community actions based on genuine and equal partnership of different stakeholders. Interestingly, there has been a development in the health promotion thinking from the ground breaking Ottawa Charter for Health Promotion in the late 1980's to the Bangkok Charter of 2005. The major change

acknowledges the central role of governments and states in guaranteeing conditions which enhance health and wellbeing of the citizens. This new emphasis does not diminish the role and responsibility of the citizens and their settings in health; instead it highlights the shared partnership and the importance of national and international regulations and support systems as well as guidance. The Bangkok Charter specifies the commitments in the promotion of health as a) central to the global development agenda; b) focus of communities and civil society; and c) the requirements for good corporate practice. This development reflects the changing world in the early 2000 in terms of rapidly growing technology, including genomics, commercialization, new emerging health threats, inequity between genders and other population groups etc. This renewed thinking in public health and health promotion fits very well to the central challenges in the guidance for public health genomics.

To guarantee interdisciplinary and multi-disciplinarity (see 11) in public health genomics different user levels and groups such as policy makers, professionals and citizens/patients representing different backgrounds need to be involved in policy making and practice development. At present this seems not yet to be the case as shown by the analysis of the public health genomics guidance done in the USE WP PHGEN II.

To be able to provide *e.g.* comprehensive and ethical guidance in the field of public health genomics, we need shared transparent partnerships, which can be voluntary agreements between partners *e.g.* public and private sector to work cooperatively towards benefitting from the genomics developments, *e.g.* in the area of pharmacogenomics or nutrigenomics. Another example could be collaborative improvement of health care services and guidance, *e.g.* collaboration between different user levels. Here a good example is the EC funded Rare Diseases Project, in which patients and families, patient organizations and professionals in the Centers of Expertise on Rare Diseases together have contributed to the needs assessment, evaluation of the services and commented on recommendations developed aiming at improving services (Available from: <http://www.eurordis.org/>). This is in line with stewardship model introduced by Nuffield Council on Bioethics in 2007 (126) as the recommended present-day public health ethics framework. This model also reinforces the basic idea of the health promotion in and by communities, since it emphasizes the role of the government and state responsibility to look after the important needs of people both individually and collectively. Stewardship means the obligation of states to seek to provide conditions

that allow people to be healthy, especially in relation to reducing health inequalities (126). Public health genomics, which is largely based on high-technology developments, especially needs to beware the equity in access to its information and services. This is also explicitly described in the founding documents of the public health genomics such as the Bellagio report of 2005 (11).

Community responsibility in public health genomics should also extend to the *research agenda* of the societies. An important reason why genome-based discoveries have not yet realised their public health potential is probably the prioritization of attention and funding more on the scientific discovery in genomics than on the application, implementation and evaluation stages in genomics based information (19). Another challenge of public health genomics research is the balance of funding from multiple sources, often through a combination of support from commercial, public and voluntary (charitable or philanthropic) organisations (144). The involvement of so different stakeholders may create tension about the goal of public health genomics (144). Further, this kind of collaboration needs to be transparent so that it can create and maintain the public trust (95) and enable informed decision making by different user groups. An example of services especially vulnerable in this respect is *e.g.* genetic testing, where private companies offer tests (direct-to-consumer testing). The assessment of the public health guidance documents revealed insufficient reporting of the independence of the recommendations and of the acknowledgement of possible conflicts of interest of the guideline development group.

Equal partnerships have potential to enhance '*public good thinking*' and *social altruism* and also enable fair distribution of the fruits of collaboration in research, and other kinds of partnerships to enable '*benefit sharing*', the concept, which is more and more gaining ground especially in commitments to research such as genomic research with high potential of yielding surplus both in economic and social terms. One example of this kind of benefit sharing could be the experience from a NGO requiring monetary revenues to the NGO from drug companies using genetic samples of their members.

Evidence-informed multidisciplinary PHG

As described above, in public health and health promotion the term 'evidence-informed' instead of 'evidence-based' is commonly used. Public health guidance both for practice and policy making needs to be based on the best available evidence. However, decision-making in public health

policy process happens in *the intersection of best available research evidence, environmental and organizational context, resources including practitioner (and policy maker) expertise and population characteristics, needs, values, and preferences* (Figure 1) (153). Public health recommendations cannot be purely technical because they need to address social, economic and political context (48; 5).



Figure 1. Intersection of public health decision making (Satterfield et al 2009)

The USE pillar applied an up-to-date evidence grading system for public health decision making in line with NICE (125) and Satterfield et al in 2009 (153). The system provides a comprehensive way to combine research evidence, best practice evidence and contextual applicability. The assessment of the existing public health genomics guidance revealed that the evidence background of the guidance formulated was not explicitly documented either in terms of research evidence, practice-based know-how or contextual fit.

Value judgements are inherent part in the development of public health guidance and related decision making (125; 48). Social values may concern aspects such as: balancing benefits and costs, the importance of respecting individual choice, the requirement to reduce health inequalities and the importance of consultation with the community (48; 125). These principles

are compatible with the stewardship of public health interventions proposed in the report of the Nuffield Council on Bioethics on ethical issues in public health (48), and particularly the ethical dimensions concerned with constraints or conditions to limit state action (126). The stewardship model can help to achieve public health goals that are highly relevant.

Underlying principles

a. USERS' REPRESENTATIVENESS

Individuals have a right to be represented by different community partnerships. Access to relevant representative groups acting in the interest of individuals must be ensured. Any representation must have been freely consented by the individual and must not have consequences on the availability of health services.

b. DEVELOP PARTNERSHIPS WITH COMMUNITY PARTNERSHIPS

Active partnerships with the diversity of community partnerships concerned by genetic testing and screening practices are part of the good governance principle. Such partnerships with policy-makers must be developed and used in the frame of public health genomics.

2.4.4.3. Develop Policies

Identified issues

We are addressing here the following identified issues:

How could users be protected by public health genomics policy?

How could users participate in public health genomics policy?

The assessment work brought up the following useful findings

The protection of users in public health policy is considered as qualitatively deficient and need to be developed in public health genomics.

Poorly covered aspects include: monitoring/control authorities; transparency; precautionary principle; direct-to-consumer services and advertising; use of e-health technologies; price-pricing of tests commercialised; benefit sharing in research; role of the EU.

The participation of users in public health policy development is considered as uncovered.

Background

Responsible public health genomics necessitates policy developments ensuring individuals' rights and freedoms in the provision of genetic services. The EU and Member States should work together on the building of a consistent ethical and legal framework and institutional system allowing genetic services to be controlled to the benefit of public health. Developments to be performed in policy should always consider the opinion and the role of the users of genetic services, genome-based technologies and information, in regard to the technological developments, ethical, legal and social dilemma in health services which are going to be more and more computerised, data-driven and influenced by genetics and genomics, P4 or stratified medicine.

Health in all policies – HiAP

There is strong evidence that health is created not only by individual behaviours and choices or not even within health sector but more widely by living conditions, environment, structural aspects of societies, including policies in sectors beyond health sector. Individual choices are not independent of the social practice, values, resources, culture and so on. Public policy should promote health in all policies (147). Smoking and its variation in the course of varying international and national policies, *e.g.* on taxation, environmental precaution as well as group counselling and support and *e.g.* individual drug therapy, functions as a vivid example of the multiplicity of imbedded individual, environmental and policy systems. Similarly, public health genomics needs to differentiate policies on genomic information and potentials in macro, meso and micro-level systems. The social responsibility of public health and public health genomics needs to provide structures, policy decisions and policy programs that promote healthy lifestyles and good health. Further, the importance of social determinants (determinants of determinants; 118) needs to be acknowledged. The four principles of EC health (together for health) strategy are: a) a strategy based on shared values; b) health is the greatest value; c) health in all polices; d) strengthening the EU's voice in global health. The HiAP principles are related to the recent recommendations of the WHO Commission of Social Determinants and Health, led by Sir Michael Marmot. The overarching recommendations are: a) improve daily living conditions; b) tackle the inequitable distribution of power, money and resources; c) measure and understand the problem and assess the impact of action. The principles of HiAP and recommendations of the Marmot

Commission fit very well to the agenda of public health genomics (11). In the area of public health genomics, an additional challenge lays ahead. The knowledge from genomics should be transformed into breakthroughs for public health. If the integration is left to market forces or 'laissez-faire' scientific and technological policies, genomics will increase the division the aspects of health inequalities in public health genomics (123). Three policy approaches play a significant role in avoiding health inequalities; those targeted at a particular disadvantaged group; those targeted at a particular at risk group; and those offered universally, although in practice the distinctions can become unclear. Some people might benefit from all three, and many people who might benefit from strategies aimed at disadvantaged groups might also benefit from those aimed at the risk groups (126).

Underlying principles

a. HEALTH IN ALL POLICIES

A high level of health protection in all policies must be ensured in policy-decision making at international, European, national, regional and local level. Health considerations must be integrated into other policies and sectors beyond the health sector, in a horizontal approach, for the benefit of population health and human rights' protection.

b. A VOLUNTARY APPROACH IN GENETIC SERVICES

Autonomy, self-determination and consent of individuals to any genetic testing or screening process must be ensured by national and European public health genomics policy.

c. EQUITY, SOLIDARITY AND JUSTICE IN THE ACCESS TO HEALTH SERVICES

Every individual, group or sub-group of population, must have access to appropriate health services and where relevant specific genetic services whether they are clinical or research-oriented, and related healthcare, prevention and treatment services through health systems regardless of their social, cultural or economical background. Access to health services must be grounded on the principles of equity (31-art.3;35-Appendix,para.I.4), solidarity (163-art.17) and justice at national, European and international levels (175;176).

d. TRANSPARENCY IN HEALTH SERVICES

Health services including genetic services must be organised in order to ensure transparency in their activities towards users of the services and

towards health authorities. Users of genome-based technologies and information must obtain sufficient relevant information to act responsibly in accordance with enforceable international laws and regulations.

e. PARTICIPATORY DEMOCRACY IN PUBLIC HEALTH GENOMICS POLICY

The EU and Member States must promote citizens' pro-active role in public health genomics policy development, gather and integrate representative public views and expectations about the ethical, legal and social aspects related to the use of genome-based technologies and information in health.

f. LEGAL CERTAINTY

Policy-makers must create more legal certainty concerning genetic testing and screening to the benefit of users of genetic services. Users must be entitled to know their rights, duties and responsibilities in the variety of contexts involving the use of genome-based technologies and information as a condition to ensure their autonomy and justice in genetic services.

g. NO GENETIC EXCEPTIONALISM

Genome-based information is personal sensitive data, partly related to health. Legal frameworks applying to privacy protection in the use and processing of personal sensitive data must systematically apply to genome-based information, under the same high level of quality and confidentiality enforceable in other categories of sensitive data (71-Rec.3).

h. INSTITUTIONAL OVERSIGHT

The EU and the Member States must designate competent authorities to oversee the provision of genome-based technologies, the management and use of human samples and associated data in the public and private health sectors.

i. THE DECOMPARTMENTALISATION OF HEALTH SERVICES

Public health genomics policy must develop partnerships, laws and procedures in order to diminish dichotomies between the public and private health sectors, clinical and research areas and increase interactions for public good in a climate of trust for the individuals involved in genetic testing or screening. Clinical and research infrastructures, including biobanks and databases, are interdependent and must be organised in a collective effort to improve population health, to maximise the use of available resources, communicate and cooperate according to clear procedures.

j. INTERNATIONAL COOPERATION

The public health genomics should sustain solidarity in genomics developments and not increase health inequalities and should be conceived, regulated and developed in an international cooperation involving all relevant stakeholders. This includes the development of partnerships with the developing countries, of health systems capacities and the setting up of international benefit and data sharing policies concerning research.

2.4.5. Background for Assurance – use/user perspective

2.4.5.1. Enforce laws

Identified issues

We are addressing here the following identified issues:

Which laws are protecting users' interests?

How can users be ensured of law enforcement?

The assessment work brought up the following useful findings

This domain is qualitatively deficient.

Poorly covered aspects include: consumer law, intellectual property law, e-contract law.

Background

Users of genetic services have several rights intended to protect their dignity and their integrity in clinical and research applications of genome-based technologies and information, and to empower them and their families in health decision-making.

In line with the Additional Protocol of the Convention on Human Rights and Biomedicine concerning Genetic Testing for Health Purposes of 2008 (30), a wide number of International and European guidelines tackle these rights in the context of healthcare and medical research activities - yet in a fragmented way where an integrated approach would be required in the context of public health genomics. The common ethical and legal principles need to be pooled and adapted, in practice, according to the new paradigm of clinical/research activities in public health settings, the category and the implications of the tests and information at stake for individuals.

The re-affirmation of users' rights in individual genetic testing and population screening should be conceived as balancing the obligations of health professionals in the use of genome-based technologies and related information. Freedom of research and individuals' freedom should find equilibrium in regulations.

Underlying principles

a. MOBILISE AND DEVELOP EXISTING RULES TO CREATE LEGAL CERTAINTY ABOUT ENFORCEABLE LAWS

To ensure the individuals' rights a number of existing European directives and national laws concerning both the quality of the products and the quality of services related to prevention, healthcare and research activities are relevant to develop a consistent regulatory framework covering public and private health services including genomics/genetics and different contexts of their uses. Policy-makers must strive to mobilise and develop existing rules with regards to the protection of users in health services.

b. ENSURE THE QUALITY AND SECURITY OF GENOME-BASED TECHNOLOGIES

A responsible translation of research innovations into public health systems for the benefit of population health should be based on a quality control system using quality criteria ensuring the analytical and clinical validity and clinical utility of the genome-based technologies for the reliability of the results to the benefit of users' health. Such a system needs to be organised both at the European and the national levels.

2.4.5.2. Link to / Provide Care

Identified issues

We are addressing here the following identified issues:

What are the rights of users?

Which kinds of services are offered and access conditions?

The assessment work brought up the following useful findings

The description of users' rights in public health genomics is considered as being qualitatively deficient.

Poorly covered aspects include: users' rights in direct-to-consumer genetic services; responsibilities in genetic services; reimbursement; ownership issue concerning genome-based information.

The kind of services offered and access conditions constitute a gap and are considered as qualitatively deficient in assessed texts.

Poorly covered aspects include: involvement of a medical intermediate, cost assessment and reimbursement.

Background

Public and private health services and in that case specific genetic services should exclusively propose clinically valid and useful genome-based tests in order to provide health services of high quality and reduce the risks for users and professionals to be confronted with errors, false diagnosis or prognosis which could have negative effects on the health and welfare of individuals. On this foundation, users' rights must be identified and protected through the provision of responsible services. The re-organisation of existing health services, and where relevant of specific genetic services, must be envisaged according to the necessary measures to ensure users' rights in the use of genome-based technologies and information.

The issue of the regulation of the direct-to-consumer genetic testing market must be consistently tackled with the enforceable rules to genetic services in health systems and ensure minimum quality criteria in services offered.

Informed consent

An individuals' right to give informed consent to any genetic testing or screening procedure should be respected in all genetic services. This important step could necessitate taking time and reflection from individuals and professionals. Indeed, obtaining the explicit informed consent from the individual before performing any medical genome-based test heralds several issues which vary according to each situation. If there is a need to clarify the ethical issues related to the kind of genome-based technology to be used and the minimal information to be provided to the subjects, there is no need to create new rules for consent in the genetic area. The shared decision-making process, the autonomy of individuals and the safeguard of the confident patient-doctor relationships should be highlighted in good practices guidelines. The universal doctrine of consent is applied to the P4 medicine, medical care, prevention, treatment and research. Yet, practices are varying in Member States. It would be beneficial for users of genetic

services to have assurance of good practices in informed consent for genetic testing at the EU level.

According to national and international laws, consent needs to be given for the procurement and use of human samples and the processing of associated data in the frame of individual genetic testing and population genetic screening. Exceptions to consent are planned by law in the processing of personal data for public health purposes; however public health genomics should aim to direct involvement of participants, through consent procedures or other means. Each case needs to be documented according to individual's situation and enforceable laws.

The scope of the genetic analysis is a particularly important element to make understandable to the individuals as it is conditioning the uses of samples and data and the extent of individuals' rights.

New challenges related to sequencing for research or high throughput technologies being introduced in health practices need to be publicly debated. Individuals and citizens need to be educated about these new technologies being at the centre of the genetic "data storm" (124). The provision of minimal pre-test information is crucial for the autonomy and well-being of the person involved in the testing process and for safeguarding.

Specific ethical issues in consent to genetic testing

Ethical issues related to consent to predictive genetic testing

The predictive value of the test result could have serious implications on the health and the social environment of the individual and his/her family. Emotional and psychological consequences of having predictive information on the occurrence of a disease and the possibility of indirect physical harms due to bad orientation of treatments should be weighed and communicated to individual during informed consent. The interpretation of the test results necessitates explanations provided by competent health professionals. The provision of pre-test and post-test genetic counselling involving medical geneticists but also, if necessary other specialists, is recommended. The right to a second medical opinion should be admitted.

Ethical issues related to consent to pharmacogenetic testing

There is an important question regarding whether voluntary consent to pharmacogenetic testing can truly be obtained in the context of clinical trials or in clinical practice. The Nuffield Council on Bioethics noticed that if

researchers require genotyping as a condition of enrolment in a study, patients might not feel able to refuse, especially if they think it is possible that they may get some personal benefit. Indeed, in some cases, taking part in a clinical trial may be the only way for a patient to have a chance of obtaining a particular medication. While this perceived lack of choice on the part of patients may arise to a similar extent in any trial of a new medication, it may be of particular concern when the research involves taking DNA samples because of public perceptions and concerns (127).

Treatment associated with a result should be equally available to those having the same needs. Otherwise the translation of genomic knowledge into clinical practice would aggravate disparities among people.

An individual's serious side effect or absence of response may have important implications for drug treatment of blood relatives. Indeed, the unit of care with respect to drug treatment may include the individual as well as the family; physicians should be alert to the implications for the relatives of a patient who suffers a serious adverse drug reaction, and should initiate appropriate health or genetic counselling and applicable report activities to health monitoring authorities.

Voluntary sharing of pharmacogenomics information within families should be encouraged (100).

Ethical issues related to consent and cascade testing

In situations where a cascade testing is necessary and justified, the health professional should inform the individual concerned by the initial genetic testing and let him free to decide whether contact directly its relatives or to involve the family doctor as an intermediary. Consent of the persons concerned should be sought. The risk of communicating results to the family without seeking the consent of the persons concerned by the result is to cause psychological harms through unsolicited contact. A genetic counselling should be systematically offered to the persons concerned by the result. This also puts legal issues concerning non-consensual disclosure, breach of confidentiality and the disrespect of the right not to know. Depending on the situation, it would be a good practice to consult an ethics committee on the disclosure issue.

Ethical issues of consent related to genome-wide sequencing

The clinical usefulness of having a total genome sequenced is considered as very weak and the related ethical issues are numerous (145). To date, in many instances genome-wide sequencing lacks clinical utility and should not

be proposed outside of the research context. The ethical, legal and social implications of the entire genome sequencing need to be addressed and debated at the Member States level and in an EU context. The highly familial interest in genome sequencing, the possibilities offered to update associated information of a sequence and the importance of the re-contacting process to consent further uses should be considered with a public participation with regards to informed consent to the whole genome sequencing.

Ethical issues related to the direct-to-consumer genetic testing and home-tests

Apart from the important issues of the regulation need of this growing market and the quality of the information provided, the informed consent process dispensed online should be reinforced by particular measures intended to avoid misleading and to allow consumers to act responsibly in a confident relationship.

Consent and participation of the user in research biobanks or databases

The public health genomics should be conceived as a dynamic virtuous circle in which research is linked to healthcare and healthcare is linked to research. Responsible and organised research activity interacting with clinical services is the source of a real public health genomics. Taking into account this new paradigm, genetic testing and screening should be an opportunity for users to express their solidarity in participating in research activities involving the storage of their materials/data. Thus, when seeking the consent of participants to clinical genetic testing or population screening, this option should be offered and easily identifiable in the consent form, documented and discussed with the health professional. The purpose of the participation should be sufficiently defined to plan this. Users' rights and freedoms in research should be protected including in cross-border activities. We propose to use the Organisation for Economic Co-operation and Development (OECD) guidelines on human biobanks and genetic research databases as a benchmark for developing good practices (129).

Consent to genetic screenings should also be reaffirmed.

Underlying principles

a. INDIVIDUAL FREEDOM, AUTONOMY AND SELF-DETERMINATION

The involvement of individuals in the use of any medical genome-based test must never be imposed. The individual interest should always prevail on the interests of society and there should not be systematic or compulsory programs imposed by society. This fundamental value applies both in the context of healthcare and research involving human being as a matrix from which derived several rights. Individuals must have voluntarily and freely consented to the test after having been duly informed. The autonomy and self-determination includes by principle the individual's right to a comprehensive, reliable, accurate and relevant information (science-based information), to know / not to know about a result, to appropriate counselling, including the consideration of test results, to access their own genetic information and warranted health services including specific genetic services but also to refuse or to withdraw from a genome-based test process. The freedom of persons to make decisions regarding their health, medical care and/or their involvement in research is essential in the modern practice of medicine (71-Rec.6b;181-para.11).

b. NON-DISCRIMINATION AND NON-STIGMATISATION

Genome-based information must never be used to discriminate or stigmatise individuals and their relatives, a group of individuals or a population. The use of health-relevant genome-based information, and particularly predictive test results, generated by public or private genetic services, must only serve the health interest of the individuals.

c. ADEQUATE PROTECTION OF VULNERABLE PEOPLE

Individuals presenting with particular vulnerability in their health status or cultural, economical, environmental and social background must be protected by specific procedures ensuring their rights and freedoms in genetic testing and especially in screening procedures. Vulnerable persons must be considered as individuals disposing of the same rights as others but suffering from specific impediments.

d. PRIVACY PROTECTION AND CONFIDENTIALITY

Genetic information resulting from a genome-based test may represent individual, family or population data. Despite this, individual and populational results of a test should be subject to the same privacy protection and confidentiality rules. The professionals involved in genetic services and the use of biological samples and related data (handling, storage, processing, transfer, retrieval and destruction) must respect the privacy of individuals and the confidentiality of information throughout the testing process and during the entire period of use and storage of the

material. Precaution must be taken to minimise the impact of the genetic investigation on the physical, mental and social integrity of the individuals.

e. ACCESS TO AND CONTROL THE USE OF GENOME-BASED INFORMATION

Individuals involved in genetic testing and/or screening must be able to easily access and control their personal data, including genetics test results, to ask for information about what they are used for and order their modification, such as anonymisation or destruction. Access and use of available genome-based information by third parties must be documented and consented by the individual or approved by an ethics committee or another competent authority respecting national and international laws.

f. CONTROL THE USE OF THE STORED BIOLOGICAL MATERIAL

The use of human biological material stored for research purposes must have been consented by the participant or his legal representative. Refusal must not trigger penalties in terms of access to healthcare or other prevention or therapeutic means. Limitations to the exercise of this right to control must be justified and communicated to the individual concerned.

2.4.5.3. Assure competent workforce

Identified issue

We are addressing here the following identified issue: How can users influence assurance of competent workforces in genetic services?

The assessment work brought up the following useful findings

The issue of the pathways for ensuring good practices in genetic services is considered as missing.

Background

Despite the prevention policy intended to filter genome-based innovations issued from research sector according to quality criteria, cases where users suffered from a prejudice should be considered by policy-makers and adequate means to ensure *a posteriori* the protection of users' rights should be developed. Indeed quality assurance schemes cannot fully comply with claims from users or prevent potential harm completely.

Underlying principles

a. COMPLAINT SYSTEMS WITH PROVIDERS OF GENETIC SERVICES

Users should have the possibility to act with the responsible professionals in order to express their claims related to a genetic service provision. Direct communication with the professional concerned must be made possible as a part of the quality of the service.

b. RIGHT TO EFFECTIVE JUDICIAL PROTECTION

This general principle of law enshrined in the EU (23-art.47; 26; 24) and national laws must apply with regard to genetic services in a consistent way. Users must have access to an independent justice, and legal remedies should be open to them. This includes guarantying a sufficient number of judicial personnel.

2.4.5.4. Evaluate

Identified issue

We are addressing here the following identified issue: How can users influence the evaluation of genetic services?

The assessment work brought up the following useful findings

The influence of users in the evaluation of the genetic services is considered as missing.

Background

This topic is highly related to other WPs.

Underlying principles

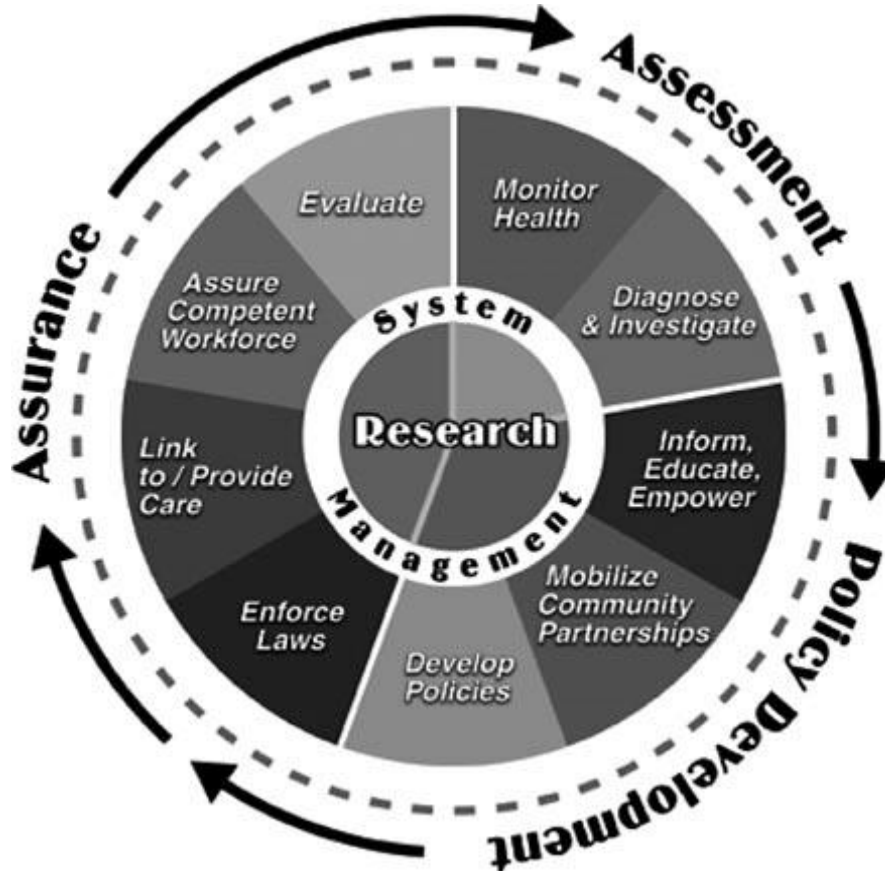
a- USERS AND THE PUBLIC AS EVALUATORS OF HEALTH SERVICES AND SPECIFIC GENETIC SERVICES

In addition to the consultation processes of users of health services including genomics / genetics and citizens in policy development, the empowerment of users and the public to evaluate current health services and the use of genome-based technologies and information must be considered.

b- USERS' DIRECT EXPRESSION

Freedom of expression must be guaranteed, and the means for users to evaluate health services provided or available must be developed both within and outside of the health services and specific genetic services.

3. The Guidelines (following the wheel per section of the wheel)



ACTION PRINCIPLES (10 Essential Public Health Tasks):

Research (Task 10: VU group)

3.10.1 Recommendations

a *(text here)*

b

c...

3.10.2 Best Practices

a *(text here)*

b

c...

Assessment (Tasks 1-2: all three pillars)

3.1 Monitor Health

This function corresponds to the surveillance function in public health which can be viewed as (broad interpretation) applying to two objects:

a) health problems:

- this corresponds to health needs assessment (epidemiology, burden of disease, users' perception of needs...)
- guidance can help define what information should be collected and how...

b) emerging technologies:

- this can be organised as a form of horizon scanning to scan for potential solutions/options to address health needs...
- guidance on how to organise knowledge transfer from basic research and horizon scanning

3.1.1 Recommendations

EU and MS role:

- a. Autonomy of users in institutional health monitoring activities should be reasonably ensured thanks to the provision of sufficient information and consent before performing the test. Health monitoring agencies

should be entitled to act accordingly, excepted where necessary monitoring activities are laid down by laws and dispose otherwise;

b. The Commission and the Member States should assess the effects that would have the computerisation of sensitive information with regard to users' privacy protection, confidentiality and interoperability of the systems used and with regard to capacity buildings of existing health services;

c. The Commission and the Member States should assess the possibilities to record genome-based test results in medical records and to establish electronic medical records (EMRs), such as personal medical records (PMRs), regarding the advantages, risks and effects on the society and national legal frameworks; public consultation on these issues should be implemented both at the European and national levels;

d. The Commission and Member States should ensure that EMRs shall not be accessed by unauthorised person. No genome-based information shall be added to the EMRs without the prior informed consent of the individual concerned. Medical ethics and national data protection laws should be fully ensured;

e. Users' right to access, modify, block or erase recorded data should be clarified in institutional and personal health monitoring activities considering the nature of the records, EMRs and PMRs, registries or repositories storing or using identified or coded data, and applicable law;

f. Bioinformatics and security systems developments should be promoted in order to ensure quality and security in the storage and management of genome-based information. Adequacy of EMRs requires developing and testing understandable and practical tools providing all necessary options for a professional use and in the case of PMRs all necessary options for an autonomous individual management. Standards for such tools could be designed at the European level. National stakeholders could restrict and adapt this standard record according to their own legislation and ethics;

g. The criteria of the clinical utility should be privileged in order to decide, in a communication process with the individual, whether or not to include genome-based information in electronic PMRs.

3.1.2 Best Practices

a. INFORM AND EDUCATE THE INDIVIDUALS ON THE HEALTH MONITORING ACTIVITIES USING THEIR GENOME-BASED INFORMATION

i. Inform and educate about health monitoring performed by national agencies

The individual involved in a genetic testing process or population screening should be informed that the results of the test could be used for health monitoring purposes by certain agencies. The purpose of the monitoring, the nature and characteristics of the data to be used and the existence of a register or other databases containing personal data should be communicated to individuals, as well as the identity of the agencies. The individual or its legal representative should have the possibility to consent to the monitoring activities explained by the physician. In case of refusal, only mandatory monitoring activities laid down in laws should be performed, and the data at stake should be anonymised as far as possible in order to adequately respect the individual's choices.

ii. Inform and educate about health monitoring performed by the individual

When possible the autonomous individual (data subject) could be involved in a certain level of monitoring his/her own health information. This could be achieved by the development of electronic PMRs allowing the data subject and the authorised professionals to access and use relevant health information in clinical or research context. The establishment of such electronic PMRs should be documented and consented by the individual. Among the information to be provided, it would be good practice to inform the individual about his/her rights, the basic functioning of the record, and when relevant the processes to add, erase, modify the information recorded, to authorise/restrict access to information and finally to close the record. It would also be necessary to

develop standards of information, leaflets about existing EMR explaining the above mentioned information in clear terms.

Such information could be developed by competent experts at national or European level (as in the context of the EuroGentest project activity for example) and could include answers to the most frequently asked questions to physicians or on internet. The following questions could also be considered:

- Why should I give authorisation to my physician to register my genome-based test results in my PMR?
- Why should I keep my genetic information in my PMR?
- What can I do with my personal health information?
- Which would be the precautions to consider?
- What are my rights in case of unauthorised access or use?
- Where can I find more information, support? Etc.

Improve health and genetic literacy, educate users in the management of their genome-based health information are also important related topics. A physical contact point should always be provided to individuals concerned by PMRs.

The European Commission should assist Member States in the development of interoperable records allowing the provision of cross-border health services and the establishment of related high quality standards.

b. ASSESS THE CONSEQUENCES OF THE RECORDING OF GENOME-BASED INFORMATION IN ELECTRONIC MEDICAL RECORDS AND PERSONAL MEDICAL RECORDS

The inclusion and proliferation of genome-based information in public health settings call for computing solutions which will foster the storage, the access to and the use of health genome-based information, the exercise of personalised medicine, the monitoring and the research activities using genome-based information.

The conception and use of EMRs including genome-based information is part of these solutions. The computerisation of health data and genome-based information in EMRs is a current dynamic that puts several organisational, ethical, legal and social issues which should be assessed at national and EU level in respect to users' interests. As a part of the EMRs, the idea of creating an electronic PMR different from the professional medical record already existing is and was established in some Member States but they are conceived in different ways and their states of development is varying from a country to another (81; 40). This

kind of record is designed as a tool fostering the coordination, the quality and the continuity in healthcare as well as the empowerment of individuals. The ethical, legal and social issues linked to such electronic records (39) are narrowly related to the ones put by the computerisation of health systems and the challenges in the developments of our information society. The PMRs involve the autonomous individuals in a pro-active approach regarding their health data, including genetic results, and empower them as the first supervisor of their health data in a very “personal health monitoring” approach. As a health informational tool devoted to the patient, the PMR is also intended to be used and shared by health professionals to find relevant information on the patient’s health and could also be of interest for research activities (1). As for other EMRs, coordination at European level on the format the interoperability (63), the management and regulation of such records could also be envisaged due to the increasing demand of cross-border patients’ movement, healthcare provision and research activities.

This is challenging policy-makers in their ability to establish frameworks that allow the pooling and interpretation of several kinds of health data, a pro-active role of users while protecting individuals in the use of their genome-based information and maximising healthcare and research for the common good.

i. Considerations related to the EMRs in general

A number of current Member States’ legislations are not clear concerning the establishment of EMRs, the recording of genome-based test results within medical records and the role of users. Member States should consider the possibilities offered by the computerisation of genome-based information to the benefit of individuals and population health and inscribe them in relevant legal frameworks or create an ad hoc legal frame.

We also recommend that:

- National stakeholders clarify the various existing health records and identify new EMRs in development or of interest. Users should be able to know and differentiate the medical records according to their content and uses as well as their personal role and the functioning of the record;
- Health professionals and individuals should be both informed and educated about the records as a pre-requisite for the responsible use of EMRs and recorded data. Their involvement in the

management and the use of genome-based information should be based on a shared-decision making and fair cooperation;

- Standard formats of EMRs are developed to store and exchange health information including genome-based information ensuring data quality, security, privacy and inter-actions with individuals;
- The use of the “privacy by design” (65-p.17) principle, or of “privacy enhancing technologies (PETs)” (64) for existing EMRs, are supported in order to ensure the development of secured records for users;
- The security of inter-professionals or inter-establishment electronic networks is ensured;
- Systems allowing users to report problems encountered using an EMR or PMR are developed. They should be easily accessible thanks to a dedicated website for example;
- The above mentioned elements should be considered in a European framework involving national stakeholders and public authorities;
- More debates and public consultations on the e-health developments are implemented;

The centralisation of health information could render benefits to health professionals and diminish the burden to consult dispersed records or registries. Yet, points of views are varying on the issue of the centralisation of electronic medical information and attached risks (94;112). Data protectors warn to centralise due to security risks, the storage of sensitive information in several databases allows better security, others (20) are in favour of this centralisation because of the clarification and the better protection this would allow in the access and uses of such personal data (e.g. better access and control of the uses of personal data; prevention of unwanted access and uses). The centralisation of health data should be managed by an independent competent authority.

In any cases, national data protection authorities should be involved in the monitoring of the uses of such records containing sensitive data, in collaboration with the European Data Protection Supervisor.

ii. Genome-based information that could be recorded in EMRs

According to the variety of genome-based technologies and information that can result from a genetic investigation, national stakeholders should decide what kind of genome-based information could be recorded in the EMRs. Diagnostic information? Predictive test results? Incidental findings

(in research or clinical activities)? Information gathered from commercial health services? Such clarifications should consider the finalities of the EMRs concerned. It seems reasonable to focus this reflexion on the clinical utility and validity of the health information at stake and the lawfulness of services used to have the information. Thus, in summary, EMRs are presently inadequate means to store neither whole genomic sequences which should be stored in other contexts such as human biobanks or genetic research databases, nor non-health-related genome-based information. Yet, the medical history of the patient could be usefully integrated.

iii. Advantages, risks and limits of the electronic recording of genome-based test results

Advantages of such records should be evaluated by the Member States in terms of health benefits, cost-effectiveness, empowerment of the patients and coordination in healthcare and research. Whereas the computerisation of the medical record could fit to the present interest in the EU for a cross-border healthcare provision of high-quality the main risk is to infringe the privacy of individuals according to the uncertainties related to the information and communication technologies (ICTs).

The limits of the establishment of such EMRs are also directly related to their costs and the capacity of existing health systems to access and use secured informatics material. There is still a need to develop quantitatively and qualitatively the health systems in terms of informatics' potential.

Considering their particularities, the opportunity to create PMRs should be tackled at the national level involving the public and the national ethics committees in order to decide whether or not to establish such personal records, to include genome-based information or not, to what extent, for which uses, and if the creation of such tools could be efficient according to the cost/advantage balance. Advantages and inconveniences for health professionals' practices and citizens using more and more ICT in the health sector should be assessed and balanced. The great impact of EMRs including genome-based information in public health practice, in society and legal frameworks should also be assessed.

iv. Issues regarding electronic PMRs that should be dealt with considering their particularities

- Should such records be established for the whole population?

- What kind of genome-based information could or should be registered?
- Which are the advantages, the risks and the limits of having genome-based information electronically registered in PMR?
- According to which procedure the personal record could be accessed and used?
- How can genome-based information be efficiently secured?
- What should be the role of the health professionals?
- What are the rights of individuals that should be respected?
- What is the role of the patient? What could be the means to empower the individual to play a more pro-active role in the management of their own personal sensitive information?
- Should PMRs be centralised?

v. The pro-active role of the individual in a potential electronic PMR including genome-based information

As it has been suggested by the French National Ethics Committee the success of an electronic personalised medical record could be based on a voluntary approach in the creation of such record. Thus, it would be desirable to propose to the user to opt for this option (opt-in) and to obtain his/her approval according to a written informed consent process. Thus, there should not be a mandatory creation of such e-records.

PMR means that the individual should be the owner of the dossier and have a pro-active role in its management. Health systems should ensure the individuals' right to control his/her health information according to enforceable data protection laws. The individuals should have the right to decide to include or exclude genome-based tests' results from the record in a communication process with a physician. Furthermore, any health professional intention to use the information contained in this personal record should be authorised by the individual concerned under the conditions defined by laws. Authorisation consented to access the e-record or part of it could be given or retracted autonomously by the individual. Authorising or denying access to this record could have damageable effects, but the responsibility should be bore by the free individual duly informed. In order to facilitate authorisation/refusal processes, it should be possible to proceed with the use of the name of the concerned professionals or with the use of the name of a health or research infrastructure, thus authorising or refusing access to all health staffs of the designated infrastructure. Justified exceptions from the patient's authorisation to access, add to and use the information

recorded could be restrictively planned by the law. However, the individuals should always be informed about who is using the EMR and this information should be available through the record. In certain exemption cases individuals could be entitled to freely oppose to the planned uses in an opt-out system.

The individuals' right to cancel or erase parts of the record, including genome-based information related to health, raises concerns about the empowerment and liability of users on their own sensitive health data which could be of interest for their health and healthcare. Users should be educated to correctly use such PMRs and understand the implications of their activities. As proposed by the Standing Committee of European Doctors (CPME) (38) if such autonomous changes are performed, "it is in the interests of patient safety and the legal protection of both patients and physicians that there is an electronic 'flag' on the record to indicate this. It is also important that patients are fully and comprehensibly informed about the possible risks to their care by suppressing a part of their medical record".

vi. The role of the physicians in the PMRs

Physicians should act both at the time to open the record and all throughout the life-cycle of the PMR, in the ongoing of the patient's information and as a contact to privilege to discuss about health records. Physicians deeming to include genome-based information appropriately within the electronic PMR of the patient should have the possibility to initiate a dialogue with the individual. Individuals should have the possibility to refuse the registering process of genome-based information without having to justify their choice. Their demand to not include information in the PMR should be respected.

Physicians should be able to inform individuals concerned about the functions, the advantages, the guarantees and the individual's rights connected to the record and recorded information.

The physician proposing or who was asked to include genome-based information in the PMR should be one of the contacts for the individual concerned, as a competent medical intermediate. This necessitates them to be competent in genetics.

3.2 Diagnose and Investigate

In line with the above surveillance functions this assessment function can both (broad interpretation):

- a) confirm and document the importance of health problems, and
 - b) evaluate whether the emerging technologies can be effectively/efficiently used and are appropriate to counter/solve health problems.
- The latter (b) thus combines the previous information and relies on (adapted) health technology assessment, including the ELSi (Ethical, Legal, and Social Implications) and organisational components. The ELSi and organisational components should lead to the definition of the optimal conditions of use for the emerging genome-based technologies and information (including safeguards). If projections are made of the likely consequences of use, a kind of *a priori* health impact assessment can be realised.

Guidance on adapted health technology assessment, *a priori* health impact assessment ...

3.2.1 Recommendations

EU and MS role

a. Individuals as users of health services and specific genetic services have the right to be informed about the handling of their samples and genome-based information. This requirement is particularly important where identified or coded samples and data are used. Consent requirements concerning these uses are varying according to the purposes, the storage, the condition and the characteristics of the material and the situation of the individual. Guidelines should be developed at the European and national levels concerning consent to genetic testing in clinical and research areas;

b. According to the possible usage and re-usage of genome-based technologies or genome-based information we suggest employing the term "other social usage" to target the (new) usage of genome-based technologies or information in society, by insurers, employers, state's administrations but also by the individuals for non-health-related, non-medical and non-research purposes. The lawfulness and acceptability of this usage as well as practical issues on information and consent requirements should be assessed;

c. It is desirable to identify and address the misuses of genome-based information according to their different features: diagnostic, predictive, individual, familial and the purposes of their uses. The public and other stakeholders should be consulted on this issue, and their views should be publicly disseminated;

d. The misuses of genome-based information should be envisaged with regards to health professionals, other involved professionals (e.g. genome-based test providers, data controllers and managers) in clinical and research settings and individuals themselves. The misuses of genome-based information could also result from third parties' activities within and outside the health sector;

e. Users' rights, professional duties and misuses as well as the attached responsibilities should be clearly identified;

f. Establish guidelines on a communication framework of genome-based information resulting from a genome-based test. This framework should include the modalities of communication of the results to the tested individual, to a group or a population in a responsible way. The minimal requirements to disclose test results to third parties such as family members of the tested individual or for other social usage could also be developed at the EU level. Such processes should respect the enforceable laws, the given individual consent, the privacy and the cultural specificities of individuals or groups concerned;

g. The role and scope of the medical confidentiality should be re-evaluated with regard to disclosure issues. Where it is necessary to breach confidentiality, the criteria to legitimate such breaching should be clarified and laid down in appropriate regulations.

The health professionals entitled to disclose the results should be clearly identified and the responsibilities of each stakeholder in the disclosure should also be established according to applicable ethical and legal rules;

h. Samples and data transfers, inside and outside of the EU, for clinical and research purposes, should be consented by the individual concerned and should be more clearly framed and coordinated in order to create more legal certainty and increase the number and the quality of such operations. Opt-in or opt-out systems could be used appropriately according to national laws. The transparency, the tracing,

the responsibilities and the control of transfer activities should also be ensured at the national and EU levels. The Commission should promote collaborative initiatives to inform professionals about applicable legal regimes and good practices to apply in an appropriate format. Rules concerning the transfers of human samples and related sensitive data (including genetic material and information) should be consistently articulated;

i. The consequences of communicating genome-based test results directly-to-consumers should be assessed in terms of use and misuse by customers. The risk of misuses of the results by the companies should also be addressed. The attached responsibilities should be defined. Interdisciplinary research and the development of control and legal capacities concerning this particular area should be promoted;

MS role

j. The regulation of the disclosure process of test results should be developed under domestic laws respecting internationally enforceable rules;

k. The management of incidental findings resulting from the analysis of the genetic characteristics of a person (in research or in clinical context) should be framed at the national level. The clinical utility of such findings should be based on best practices, and physicians should be educated to judge whether or not available information is reliable and relevant for the health of the persons concerned, the relatives or third persons. Cooperation between clinicians and researchers on the meaning of the results should be promoted;

l. The fate of irrelevant or uninterpretable incidental findings should also be clarified. We suggest that they can be stored and used in the context of consented purposes when they are coded and for developing genomics knowledge when they have been and will remain anonymised;

m. The re-contacting process of the individual concerned by a new use of identified or coded samples and data, by useful incidental findings or by another necessary disclosure of testing results should be addressed by policy-makers. Good practices should be developed and identify the

appropriate means to use in re-contacting process and the health professionals involved;

n. Efforts to establish and involve independent research ethics committees and other ethics assessment bodies in clinical and research practice should continue. Members of the committees or other assessment bodies should be trained to cope with the new challenges of human genetics, and their activities should continue being coordinated at the national and European levels;

o. The effects of the anonymisation of samples and data on users' rights should be considered by health professionals and communicated to the individuals concerned at the time to consent;

p. The permanent feature of anonymisation in a research project with regard to the use of data and possibility of re-identification should be considered by policy-makers and ethics committees. The practice of a written commitment from professionals involved in the research not to re-identify the samples and data used should be supported and controlled by competent authorities;

q. The applications from employers and insurers to use genome-based technologies or genome-based information should be legally framed, restricted and follow specific procedures ensuring the respect of human rights and medical ethics;

r. The individual right to use genome-based information obtained from outside the health system in order to access healthcare or other health services within the health system should be evaluated and framed.

3.2.2 Best Practices

a. RESPECT THE INDIVIDUAL'S WILL AND INTERESTS

i. Respect the given consent and privacy

Health professionals handling genome-based information have the duty to protect the individual autonomy, privacy and the confidentiality of health information in clinical and research activities (181-para.11) according to national and European laws. They should be trained to do so.

Whatever the planned use of the samples and/or associated personal data the given consent of the individual involved in a testing process should always be respected. In this regard, the consent forms should be sufficiently detailed and concise to claim expressing the unambiguous will of the individual and should include reasonable boundaries. When the information is identifying and has to be stored, privacy and data protection requirement can partially be ensured using security systems and coding steps according to the proportionality principle. This proportionality aims to protect samples and data in a consistent way with the consent content, its scope, and the requirements of the clinical or research aims. This adequacy between the measures ensuring the respect of individual privacy and the research aims should be systematically assessed by a competent committee. Furthermore, the right of the individual to access or to withdraw samples and data must be respected.

ii. Anticipate the consequences of the withdrawal of consent

The respect of the autonomy and self-determination of the person involved in a genetic testing process requires acceptance that identified or coded samples and associated data might be destroyed or anonymised at any time on an explicit request of the individual. Where materials are stored and used for research the possibility and attached consequences of the withdrawal of the participant's consent such as the fate of the samples and data should be planned and explained to the individual during informed consent process in order to ensure the primacy of human rights and minimise negative side-effects for the research purposes.

When the request for a withdrawal of consent does not explicitly target the destruction of the sample or data, researchers should be entitled to retain them under the condition of a permanent anonymisation. In this case, an explanation of the importance of keeping samples in a biobank and the consequences of the anonymisation on the individual's privacy and rights should be provided.

Destruction of the samples and data

The operator of the biobank or the database should destroy the biological material, all information and data held in accordance with the protocol, the participant's informed consent, the enforceable legislation and regulation including those related to the protection of

privacy and confidentiality (129-Annotations82-87) and the opinions of competent committees.

The operators should also have a policy concerning the management of samples and data in case of discontinuation of their activity. This should include as far as possible necessary steps to retrieve and transfer or destroy all the materials gathered.

b. THE NOTION OF “OTHER SOCIAL USAGE” OF GENOME-BASED TECHNOLOGIES AND GENOME-BASED INFORMATION

The following situations and actors are targeted by this notion of “other social usage”:

- The use of genome-based technologies and/or genome-based information by third parties including insurers, employers, state administrations but also the family of the tested individual;
- The use of genome-based technologies and/or genome-based information by the tested individual outside of the health services;
- The re-use of genome-based information obtained from health services including specific genetic services by the tested individual or third parties for other purposes than health.

Such encompassing notion could be adopted by national and European stakeholders in order to prospectively assess and frame those situations, to discuss related ethical, legal and social issues and to communicate with the public and persons involved in genetic testing.

c. ANTICIPATE / MANAGE THE POSSIBILITY FOR FURTHER USES OF HUMAN SAMPLES AND ASSOCIATED DATA AT THE TIME OF CONSENT

i. Anticipate

In order to avoid complications concerning the lawfulness and the ethics of secondary and other social usage it is advisable that health professionals mention such a possibility during the informed consent process. This approach will also foster the long-term confidence of individuals. The scope of the further uses should be limited in order to not constitute a general waiver of consent requirement. It would seem acceptable to limit the consent to an identified project, a program, a research area, a study on a disease or group of diseases studies. Indeed,

a too broad consent would not be sufficiently protective of the individual's rights and autonomy.

Whenever possible, the mention of a re-contacting procedure in case of unplanned uses of materials gathered should be integrated in the original consent form. Its modalities and the related implications should be explained to the individual.

Concerning secondary usage of specimens and data, some problems could arise for example in studies on rare or unidentified diseases, to determine the scope of the uses of the biological sample and related data and the adequacy of the information and consent procedures to be given. In such cases, the re-contacting procedure may be important and approval of an ethics committee should be sought.

Concerning the potential other social usage of genome-based health information, when it is allowed by national law, the possibility to disclose genome-based information to third parties, such as insurers or employers, should also be explicitly mentioned during the informed consent process. Genome-based information must not be disclosed to insurers and employers if the individual has not consented to it.

ii. Manage the unplanned uses

New consent for secondary usage of samples and data

Obtaining new informed consent from the individual to whom the samples and data are related or his legal representative is regularly tackled in existing guidelines and the literature (129-para.4.5, 4.8, Annotation 41). This process involving a re-contacting procedure is often put into question due to the practical difficulties it implies and the cost of such procedures (156). These criticisms are particularly underlined where studies are performed at population level due to the considerable amount of persons involved and the cost that would induce such re-contacts when the research project is evolving. In these cases, it is important to consider the impact of the changes on the health of the individual, on their rights, the benefits and risks at stake, and to balance this with the guarantees ensured in terms of privacy protection and legitimate research interests. Research (80) on the possible burden, the benefits and the feasibility of re-contacting process should be performed at the national and European levels in order to reach a consensus and develop best practices and alternative methods.

In any cases necessitating a new consent, sufficient information should be provided about the purposes and implications of the new use and the

storage conditions of the material according to applicable laws and guidelines. Thus, opt-in or opt-out systems could be planned.

The Member States should clarify the ethical and legal requirements to adequately ensure individuals' protection, autonomy and self-determination in the cases of secondary usage of samples and data. Professional guidelines should be developed.

Exclusive change of storage duration

Modifications of the storage duration without modification of the purpose of the use of samples and data should not trigger a new informed consent process. Yet, the ethical approval of a competent entity and the information of the individual on such a change should be satisfied. Refusal of individuals should be organised as an opt-out system and be recorded; professionals should act consequently.

For research involving identified personal health data including genetics, the use of sunset clauses whereby consent will only be valid during a finite period of time might be considered as a mean to ensure adequate protection of the individuals' interests (178-Rec.8).

Impossibility to satisfy new consent requirements

As an exception of the new consent requirement, when identified human material or genome-based information are to be used in a medical research and it is impossible to re-contact the individual the recourse to an ethical approval should always be sought (181-para.25). The impossibility should be documented by the applicant(s). Where the use is granted, operators must adequately protect confidentiality and privacy.

iii. Ethical issues of the anonymisation of samples and data procured

The practice of anonymisation of samples and data raise several issues related to the scope of informed consent and the limitation of individuals' rights.

First, anonymisation of human samples and related genome-based information is sometimes used as a basis of blanket consent. As it has been noted recently in the literature concerning pharmacogenomic studies (97) the logic willing that "the more 'protected' the data are, the less specific the consent needs to be" is undermined by some limits to the protection that can be ensured. As an example, the practice of the cross-matching of personal information can lead to re-identify a sample or data originally anonymised. The assurance of anonymity requires

political action, auto-limitation from the operators and innovative activities in the field of anonymisation techniques and bioinformatics at the national and international levels.

Secondly, anonymisation decreases the individuals' rights to control their own samples and data involved in a genetic research: incapacity of the individual to trace his/her material, to access them and to withdraw. Additionally, the anonymisation leads to the impossibility of adding new data to the original ones. These elements should be communicated to the individual during the informed consenting procedure when anonymisation is planned.

iv. Data cross-matching *versus* anonymity

In order to protect the privacy of the individual and his/her family, professionals planning to perform research on anonymised data should sign in their protocol a specific commitment mentioning that the research staff shall not try to re-identify the data. Such a clause could be inserted in specific contracts such as material/data transfer agreements. If the re-identification is necessary for the research purpose, it should be previously consented by the individual or at least approved by an ethics committee.

d. THE OTHER SOCIAL USAGE OF GENOME-BASED TECHNOLOGIES AND INFORMATION: EMPLOYMENT AND INSURANCE

Concerning these other social usage we recommend to the EU and MS that:

- The use of predictive genetic testing for other social usage such as for employment or insurance needs should be restricted by European and national laws and should never be justified by economical purposes. Restrictive exceptions should be explicitly recognised by legal texts;

According to existing EU legal framework (44-whereas34, art. 8), and according to the scientific uncertainty of some already available predictive tests, the use of genetic information in the workplace and by insurers should be prohibited by principle at EU level. Limited exceptions could be planned by national laws where a duty of secrecy equivalent to the medical secrecy is applicable (44-art.8.3,8.4). It should be clearly stated by national governments that the insurers and employers should not directly perform genome-based tests by their own means nor use biological samples to extract genome-based information

without being authorised by competent authorities, following a dedicated procedure. States' organisations could benefit from restrictive exceptions concerning forensic uses and criminal investigations.

- Non-discrimination, non-stigmatisation and solidarity should be stressed in the context of employment and insurance. Best practice guidelines in exceptional fields should be developed. Such establishment of legal frameworks should be actively supported by physicians (182-para.19,23) and health professionals;
- Quality criteria and authorisation processes for the use of genome-based technologies in the workplace should be developed according to the validity and utility of the tests to be used, the necessity of the recourse to genetics according to the scientific knowledge state-of-art, the disease sought, others available preventive means or information sources and the particularities of the activities concerned. Such authorisation process should also be developed for insurers requesting performing a test. The availability of prevention means or treatments for the tested person in employment context could be integrated as a criterion to authorise this practice;
- Lawful uses of genome-based technologies and information in the field of employment and insurance should be implemented by competent and independent medical staffs. The competent authorities should monitor these activities;
- Genetic testing in employment and insurance sectors should be framed as medical acts. The sets of ethical and legal rules applying to medical genetic testing and the individual rights such as informed consent, respect of privacy and confidentiality should be respected. Other existing relevant regulations concerning biobanking and databases could apply;
- As a sensitive personal data processing the full application of personal data protection laws should be ensured in legally allowed social uses of genome-based information;
- The establishment of a moratorium across the EU on the use of genome-based technologies and information for employment and insurance purposes should be considered or maintained within Member States having not enacted proper legislation, or having not clarified the situation, or having not ratified the Convention of Oviedo, as a way to allow stakeholders to express their views on these issues;
- Public debates be organised on these issues;

- Issues related to the use of tests results announcing a late-onset disease should be considered and public views should be sought;
- Research on the employers' and insurers' interests in having access to genome-based information should be promoted;
- Member States strive to create interactions between public and private insurers in order to elaborate and coordinate the enforceable rules according to the legitimate claims of the stakeholders in the national insurance system.

e. COMMUNICATION OF TESTS' RESULTS

In line with the disposals of the Council of Europe Additional Protocol of the Convention of Oviedo on Biomedical Research (art. 13.2.v) and the Additional Protocol on Genetic Testing (art. 18), health professionals involved in health-related genetic testing should be able to return relevant information/results to individuals concerned in a way that respects privacy and medical confidentiality.

i. Communication of individual testing results to the tested individual

Whatever the purpose of the test, individuals are allowed to know about their genetic status. Their wish to know / not to know about the test results should be clarified before and after the test; it is to be respected and recorded. The communication should be preferably performed face-to-face, supervised by a competent physician (e.g. in German law: a medical doctor) and the offer of an appropriate post-test counselling should be envisaged case by case. Confidentiality in communication process must be ensured (61). Adequate supports for the tested individual should be recommended as a part of the quality of the service provided.

Informing participants about testing results is impossible after the samples or the data, respectively, have been fully anonymised. The participant in the testing process must be informed about this fact during informed consent process.

ii. Communication of research population genetic screening results

Individuals participating in pilot population genetic screening research should be informed about the general results of the research. Generally, unless the participant has expressed a contrasting will, the aggregated results of a populational study are sent to the participant by mail (in a secure way) at the end of the project. If there is no obligation to

communicate such information, professionals should act according to the given consent, and the participants should be entitled to ask about the general but also their individual results. In a pro-active approach of the role of users of health services including genetic services the interested participants should be offered appropriate means to address the request for the communication of the results directly to the (public spokesman of the) research establishment concerned in the full exercise of their autonomy and their right to know. This could be easily implemented via a website ensuring privacy protection in compliance with applicable quality standards and providing access to the results of the study. A major issue is to deal with the kind of individual results that could be available on this website (cf. below “incidental findings”).

Another aspect to be taken into account in the communication of population testing results are the cultural sensitivities of social, ethnic or religious groups involved. The appropriateness of the communication tools and process should be conceived not to constitute offences to individuals according to the varying conceptions of human genome-based information, traditions and applicable national laws.

f. DISCLOSURE OF GENOME-BASED INFORMATION TO THIRD PARTIES

i. The consensual disclosure as a principle

Patient-doctor relationships are essential in any disclosure process. The disclosure possibility and attached modalities should have been planned, explained and consented by the individual before the test is performed. Before disclosing, the consent to the knowledge of the test result from the third persons concerned should be sought as far as possible. A risk/benefit assessment with regard to the disclosure should be performed. Direct benefits of the disclosure should be considered in regard to the serious nature of the disease, the quality of the risk assessment and the availability of healthcare or prevention measures for the individuals. Where disclosure appears necessary for the sake / health of a third person, the individual should be informed about the pro and cons of this operation in a discussion process.

ii. General best practices recommendations concerning the disclosures

Generally, concerning disclosures, we recommend to the EU and MS that:

- Whatever the disclosure case, the patient-doctor relationship is essential, the information and the respect of the individuals' autonomy should be emphasised;

The right to know / not to know of individuals concerned should be checked after the test and respected. The tested individual should receive information on the relevance of the results for third parties. Any disclosure of genome-based information, as sensitive personal data, should be, by principle, consented by the tested individual according to enforceable law. Vulnerable persons should not be excluded from the requirement of obtaining information about the disclosure and their assenting should always be sought as far as possible. Health professionals should allow sufficient reflexion time to the tested individual to decide whether or not and how to disclose.

Thus, the primary responsibility of the disclosure is for the tested individual. Third persons are free to decide being informed about the results or not, under their own responsibility.

- Decisions to disclose should always be based on a benefits/risks assessment;

The clinical utility of the available post-test genome-based information should be a paramount criterion to deal with the disclosure issue of test results. The result should be assessed according to evidence and the availability of related healthcare, therapy or efficient prevention means. Communication between physicians and researchers on the interpretation of the results should be promoted. It is important that the clinical utility includes criteria related to the epigenetics and evidence-based environmental factors influencing genetic status in order to correctly assess the necessity to disclose.

The variety of tests available and of the implications of possible results can cause practical difficulties to health professionals coping with the disclosure issue of genome-based test results. Where the health professional has doubt on the validity, the utility of the result or the legality of the disclosure, he/she should exert the medical confidentiality and abstain to trigger a disclosure process. Consultation of an ethics committee is to be advised.

- Any disclosure should involve a competent physician as a medical intermediary;

The individual, like health professionals, should have the right to obtain a second medical opinion on the importance and the

scope of the results in order to decide knowingly whether or not to disclose and to whom to disclose.

- Health professionals authorised to disclose genome-based information should be identified. We recommend that only physicians or trained genetic counsellors can disclose genetic information;
- Several modalities could be planned in order to responsibly disclose relevant genome-based information; they should be consented and adapted case-by-case;
- The offer of appropriate counselling, including the consideration of test results, should be envisaged as a support to the individual and his family in order to explain the results, their implications, to avoid misunderstanding and minimise negative psychological impact;
- Restricted exemptions to the disclosure under individual's consent could be justified by the law;
- Consultation of a competent ethics committee on the disclosure issue should be advised in certain cases. This should be a requirement where it is impossible to obtain consent or to re-contact the tested individual;
- The good practices to disclose should be first developed at the national level in respect of laws, ethics and society views, using appropriate means ensuring uniform or at least consistent practices.

Generally, we recommend to policy-makers not to lay down a legal duty to disclose genome-based information to the individual, relatives or other third persons. A moral obligation conceived as a duty to warn people about important findings should not be included in laws but could be part of the professional ethics and thus be developed, case-by-case in code of conducts or professional guidelines. Indeed, situations vary considerably according to the nature and quality of the test, the results and the cultural, social and economical environment of the tested individual. Health professionals should keep their autonomy of judgement in the assessment of the relevance of the results for the health status considered and decide accordingly in a shared decision-making process with the individual and in the respect of the beneficence principle.

In any cases, the criteria to breach confidentiality of testing results should be developed restrictively and legally grounded. Attached responsibilities should be defined.

iii. Disclosure of the test results to the family of the individual concerned

Genomic information may be transmitted in families. Which disclosure modalities of individual genome-based test results should be applied to the relatives of the person concerned?

While this topic needs more guidelines and public debate some interesting elements can be found in doctrine (115). In view of the above described elements, we propose to policy-makers and professional organisations that the following points be considered in order to elaborate proper guidelines:

- The tested person should be informed about the relevance and implications of the results for the family members (30-art.18) before the test is conducted and before its results are disclosed;
- The interest of the relatives should not prevail over the tested individual's interests and privacy. Physicians should respect the individual's wish to not disclose information (21). This principle may be accompanied by a limited number of exceptions;

The refusal of the tested individual to disclose test results of familial importance and the respect of the medical secrecy by the physicians could cause prejudice of the family members of the tested person. This prejudice could be characterised by a loss of chance concerning a health intervention such as early prevention or treatment of a disease detected by the test of another member of the family. Where the expressed wishes are in contradiction with the professional duty of beneficence an information and discussion process intended to clarify important elements in the disclosure should be initiated by the physicians involving appropriate counselling. Concerning the role of the physicians in such a situation, as it has been proposed by the Nuffield Council of Bioethics (128) and enacted in France (81-art.L1131-1-2), where a physician deems that it would be irresponsible that an individual does not disclose important genome-based information to its family members, the physician should provide to this person sufficient information devoted to help the individual acting otherwise, in the best interest of the health of this relatives. Stakeholders should discuss such cases with regards to the possible exceptions to individual consent to the disclosure.

- The individual should have the option to authorise the physician to take the decision about the disclosure according to the necessity to

protect the health of the tested individuals or their family. The entrustment of the physician should be stated in writing;

- The role and responsibility of the legal representatives in decision-making to disclose should be specified. Legal representatives of a vulnerable person could be entitled to decide about the disclosure issue, in collaboration with the physician, but the personal view of the person should be elaborated as far as possible, according to its level of understanding, without any pressure.

The modalities of the familial disclosure of genome-based information need to be established and tested. In practice,

- Either direct disclosure is concerned from the tested individual to his/her family according to the means he/she deems appropriate;
- Or indirect disclosure involving a physician and/or a clinical geneticist and/or a competent public authority, in accordance with the expressed consent of the tested individual and the law. This could be materialised by an exchange of letters between health professionals and between health professionals and members of the family concerned, prior to face to face consultation at the initiative of the individual family members. In this disclosure procedure, the tested individual from whom the familial genome-based information has been extracted should have the possibility to remain anonymous.

Policy-makers should consider the legal issues related to the family members' capacity to use a disclosed familial genome-based test result for other social usage and the issue put by the potential extension of the individual right to control (180-Table11-pts2,3) these sensitive data particularly when they are stored in a database or laid down in medical records.

iv. Disclosure / Communication of individual genome-based test results to other health institutions

In the disclosure or communication of genome-based information to others health professionals such as hospitals or research infrastructures in the respect of the applicable laws and consented uses of the data, a principle of "shared medical secret" should apply to all staffs handling personal genome-based information. Such disclosures / communications could be performed from clinical to research establishments and

conversely from research to clinics in limited cases but always respecting privacy.

v. Disclosure of genetic test results to third parties outside the health sector: other social usage of genome-based information

We sustain strict application of the medical secrecy concerning other social usage involving third parties. Thus, physicians detaining genome-based tests results should not be allowed to disclose the results to third parties out of the health sector unless such disclosure has been consented, is required by law or authorised by a competent authority.

vi. The non-consensual disclosure: Criteria to particularly consider where a breach of confidentiality to the benefit of a third is authorised and necessary

Where such a possibility would be authorised in Member States, specific guidelines and criteria should be developed. These situations must remain exceptional and the search for individuals consent should be privileged. The necessity of breaching confidentiality and disclose test results should be medically justified. The duty to inform the individual should be respected. Non-consensual disclosure from the physicians could target both test results obtained for a consented purpose but also incidental findings.

The following criteria could be used to characterise the necessity to breach confidentiality:

- The high impact of the test result;
- The clinical utility of the result for the health of third parties;
- The criterion of the seriousness of the disease;
- The individual source or its legal representative is briefed about the intention to breach confidentiality;
- Reasonable efforts to elicit disclosure fail after 2–3 meetings with the source individual or its legal representative;
- Alternative means of contacting the relative have been exhausted;
- The positive approval of a competent ethics body has been satisfied.

g. MANAGE INCIDENTAL FINDINGS

Incidental findings are part of the results of a genome-based test but they present specificities that necessitate a particular approach in terms of management. They can occur in research or in clinical situations where large scale testing is providing a range of results. Although the term “incidental research findings” should be defined at the European level it has been defined in the literature as covering “a finding concerning an individual research participant that has potential health or reproductive importance and is discovered in the course of conducting research but [is] beyond the aims of the study”(185). Incidental findings have to be considered with regard to new genome-based technologies and practices such as whole genome sequencing and high throughput technologies producing a large amount of data (184) and in the context of both individual genetic testing and population screening. They are not restricted to research, as the translation of high throughput technologies is already in practice to a certain degree. In the light of the definitions above incidental findings are only concerning findings with potential health significations. Thus, incidental findings should not include not clearly interpretable findings, unknown genetic variations and information which are currently useless for clinical applications. There is no consensus on the best approach how to deal with such genome-based information but some arguments have been already developed by the doctrine supporting either a “restrictive disclosure policy” or a “qualified disclosure policy” (17). The second approach allowing the return of results to individuals if the results meet certain conditions seems to be the more appropriate approach for a public health policy ensuring a responsible translation of research knowledge in public health settings and a balance of interests at stake. Yet, organisational and practical measures should be developed in order to correctly implement this “qualified disclosure policy”. Whereas the disclosure of incidental findings should respect the general best practices recommendations for disclose some specific elements should be highlighted in the context of incidental findings’ management.

i. Ensure proportionality of genome-based technologies

In connection with incidental findings, the proportionality principle should be highlighted for the appropriate choice of options to suggest to individuals according to their health status and the existence of less risky alternative means. To fulfil beneficiary duty health professionals should gather the opinion of the individual on its genome, on health research

and adapt the options proposed to its feelings and to the available tests. Thus determination of the proportionality would be complete; the testing process would not exceed the health needs of a patient and would be adapted to the individual's thoughts and aspirations for the community.

Adequacy between the technology to use and the present finality sought should be privileged. Generating a lot of data in the clinical context seems useless, but this could have importance for future analyses or research. Thus informed consent of individuals and organisational measures guaranteeing access, re-use and updating of the genome-based information are crucial. The scientist's interest must not be placed over that of the individual. The efficiency, the clinical utility, the risks of creating complexities, of jeopardising users' interests and harm the individual concerned regarding the purposes of the testing process are paramount elements to balance when proposing a genome-based technology. Proportionality leads to advise professionals to adopt a precautionous and responsible approach in the provision of tests.

Ethical issues related to the clinical practice using new technologies generating voluminous or even excess data (sequencing, high-throughput technologies) such as the sequencing of genome from adults but also prenatal and neonatal situations, should be publicly debated and considered in policies.

ii. Establish protective policies: Should incidental findings be systematically disclosed?

The management of incidental findings is directly connected to the scientific knowledge about the meaning of these findings, the current capacity of interpretation of such information. Progress in genomics is quick, but many questions remain to be answered in terms of knowledge and medical applications. As it is stated in literature, prior experience demonstrated that "telling everything may not always be the best option and certainly is not universally practiced" (184). The principle of the clinical utility of the unexpected results revealed during genetic analyses should also here be emphasised to condition the disclosure. Incidental should not mean useless. Otherwise, the disclosure of findings of uncertain interpretation could have negative effects on the life of the individual concerned.

Decision to implement an unrestricted disclosure policy of all incidental findings, as it is sustained by the defenders of an absolute individual autonomy, would necessitate appropriate frameworks which could be

time-consuming for health professionals and costly with regard to the usefulness of the data at stake. The risk is to transmit erroneous information about a genetic variant associated with the onset of a disease, thus, knowledge limitations should be explained to the individual tempted to know all incidental findings. An updating procedure of the findings cannot be an obligation for researchers. In the clinical context the possibility of evolution in the interpretation can be explained and patients could take the initiative to come back and ask for a reinterpretation, but no systematic obligation and liability for future interpretation should lie on the professionals.

iii. Who should be involved in the disclosure of incidental findings?

In a research context, direct contact from the researcher to the individual should be avoided. Researchers deeming incidental findings as being potentially useful should have the possibility to contact a physician designed by the individual concerned in order to inform him/her about the existence and the meaning of such findings. Physicians should be the privileged intermediary in the disclosure process of incidental findings because of their close relationships with the person involved. Appropriate counselling, including the consideration of test results, should be available.

iv. Incidental research findings

Regarding specifically incidental research findings, in addition to the general recommendation on the disclosure issues we recommend that

- New technologies involving the production of large amount of data must be adapted to the aims of the research or of the research infrastructure in relation with which they are used; their use should conform with the individual will and positions about genomics and genome-based information as documented during consent process;
- Communication between physicians, researchers, counsellors and individuals should be particularly promoted in the assessment of incidental findings;
- Each individual wishing to know about results or data generated in a research project should be informed about the limits of the current scientific knowledge; no obligation to communicate uninterpretable data should be put on researchers;

- Appropriate counselling, including the consideration of test results, should always be offered to the individuals concerned when appropriate; this should be the responsibility of competent persons in health services, not as a part of the research itself;
- Guidelines on the management of incidental findings should be developed at the national and European levels;
- The fate of uninterpretable data at the moment of their production and, if stored, the possibilities and conditions to update the information according to knowledge evolution should be envisaged and publicly debated.

h. INVOLVE INDEPENDENT RESEARCH ETHICS COMMITTEES AND OTHER ETHICAL ASSESSMENT GROUPS IN GENETIC TESTING

Considering research ethics committees we are targeting the independent bodies assessing research activities of biobanks, genetic databases, hospitals, clinics and universities planning to perform research involving human subjects, biological material or health data (clinical trials or scientific research). Research ethics committees play a central role in assessing the protocols planning to use human biological samples and associated data. Their main role is to grant approval, case by case, to projects or programs submitted by the responsible investigator before the research starts (approval should also be sought in case of doubt on the validity of an operation in the course of an already approved research). Their opinion is based on an interdisciplinary scientific, ethical, technical and often legal independent assessment (29-chap.III). The establishment of these committees ensuring the enforcement of good practices has recently increased across Europe. The activity of ethics committees is particularly important to protect individuals involved in research genetic testing or screening. The European Commission should strive for fostering capacity building in Member States and continue to support their activities, their consultation, the education of their members but also their independence with regard to political or commercial entities. The Member States and the Commission should go forward in harmonising their tasks and enhance their visibility and coordination at international level.

Other ethical bodies (*e.g.* hospital ethics committees) established within health establishments should also play a role in genetic testing and screening in the clinical and health services context. They do not assess

research protocols but may play an important role in the translation part or the implementation of new activities in the health services. They should not be neglected in such processes. Health professionals dealing with ethical, legal or social issues in clinical practices of genome-based tests should have the possibility to apply for a meeting with such a body. Their role should be specified by national legislations or institutional policies and their advices should be more formalised.

i. SAMPLES AND DATA TRANSFER

Human samples and associated sensitive health data transfers, including genetic ones, increase both inside the EU Member States territory and internationally for research or clinical purposes including genetic testing and screening practice.

As a starting point to avoid misuses of samples and data exchanged we are considering important that users of health services and specific genetic services know that their samples and/or personal data could be transferred internationally for a defined limited purpose. This possibility should be expressly communicated to the individual concerned and included in consent forms. Secondly, applicable rules are not easily identifiable, particularly concerning the international exchanges of human samples for research purposes inside and outside the EU, and there is a growing demand for guidelines from the health professionals and researchers. The tracking of samples and data as well as the controls of the activities performed abroad according to the intended uses is also a current concern for professionals and ethics committees (28). There is indeed a lack of transparency in these operations mainly due to a lack of clarity in applicable frames.

We recommend that

- The European Commission operates a focus on the clarification of rules to the exchanges of human samples for scientific research purposes as well as for health services and promote international cooperation in the establishment of informative databases presenting enforceable laws, administrative rules and ethical standards which should be respected by professionals;
- The European Commission should support the development of European guidelines on the exchange of human samples especially for research activities and explore the possibilities of applying standard clauses for a material transfer agreements building on the work done in existing or currently developing

European research infrastructures (ERI), in other relevant EU funded projects and in the expert group on biobanks presently working as a collaboration between the EU Commission and the Council of Europe;

- The European Commission should also support the development of guidelines for data exchanges with research purposes. They would be a practical instrument complementary to the European data protection Directive and existing European standard clauses for international health data transfers for processing abroad and binding corporate rules (BCRs), to avoid the misuses of genome-based information;
- The networking within distributed infrastructures and the organisation of the traceability of exchanges of samples (cf. BBMRI project) and health data including genetic ones could foster responsible exchanges, transparency and control in a cooperative approach between Member States.

j. ISSUES RELATED TO THE DIRECT-TO-CONSUMER HEALTH SERVICES AND SPECIFIC GENETIC SERVICES

i. Misuse of testing results by the service providers of direct-to-consumer genetic testing

As it has been noticed by recent studies of the remote services for genetic testing, ethical, legal and social issues of this growing market are numerous and would necessitate specific measures. Among them, the practice of “direct research” is problematic with regards to the terms of services displayed, international and national legal frameworks and the consent forms to be filled in by the customer. Indeed, there is a lack of clarity on possible further uses of the samples and data handled for the test’s purposes and, *idem*, concerning the involvement of an independent ethics committee monitoring the uses of samples and associated data by the companies. This need of transparency is important to avoid misleading users. Efforts should be allocated to make explicit the ethical and legal rules applicable, to clarify their terms of services and to develop clear consent requirements in order to clarify the legal bases of their activities. National competent control institutions should be designated to assess the conformity of activities of the companies with the laws and ethical standards.

ii. The networking of users and the risk of a “biopolitisation”

The offer of direct-to-consumer genetic testing services is sometimes linked with the offer to share genome-based information with other users on community portals, forums and others genomic social networks (75-para.4.1). If this idea is apparently not risky, we could face to some bypassing of the meaning of genome-based information which could be harmful for the individuals but also for the society, the solidarity and the public vision of genetics. Whereas the freedoms of expression and thinking are not to be questioned, individual representations of genetic variation could rapidly be driven by other considerations than scientific ones such as the ideas of genetic communities, superiority, the quest for the perfect genome etc. and be used for political claims and other purposes endangering the respect of the human diversity and dignity. Genome-based information resulting from genome-based tests should never been used to discriminate or stigmatise individuals, populations or sub-groups of individuals. An appropriate oversight of the evolution of such communication areas should be put in place and ethical, legal and social researches should be promoted in order to assess the risks resulting especially from the use of genome-based information in social networks. Informing and educating the public is essential.

iii. Misuse of test results by the consumer of direct-to-consumer health services and specific genetic services

The use of such genome-based information should be assumed by the customer. However the possibility that these individuals would be led to consult a general practitioner in order to obtain interpretation of the results should be considered. The difficulty for the general practitioners is to cope with genome-based information, invalid results, conflicting information and to recognise or deny the usefulness of a result. Thus, in addition to the necessary education of the practitioners, education of the individuals on the limits of online health services and specific genetic services and the limits of the results for healthcare action is needed. This problem could be minimised by the establishment of mandatory prescriptions.

Policy Development (Tasks 3-5: all three pillars)

3.3 Inform, Educate, Empower

- Knowledge transfer to macro, meso and micro level decision-makers to empower them with respect to decisions based on information regarding health problems and needs, adequacy of emerging technologies as solutions, limitations of technologies, gaps in the knowledge base, ELS issues...
- Guidance on knowledge transfer strategies, on information repositories, on information needs, on optimal presentation of information (on risks for instance), on issues of health literacy....

3.3.1 Recommendations

EU and MS role

- a. The European Commission and Member States should foster and improve genetic literacy and public awareness on health services including specific genetic services and genome-based information by organising or supporting information campaigns and communications from public authorities, health professionals, patients' organisations and media. These campaigns should cover genetic services in health systems and direct-to-consumer offers;
- b. The European Commission and Member States should put in place online platforms dedicated to inform users about the validated genome-based technologies as well as the available related health services in national territories. General information about health genetics, research and clinical aspects of genetic testing and genome-based information should be included or available through such websites. Other means of information than electronic media should also be considered.
- c. The existing theories on behaviour change and corresponding methods should be refined to find relevant models to guide and monitor the use of genomic health information;
- d. A transparency requirement concerning the characteristics and limits of the tests should be ensured by manufacturers and providers of tests.

Such transparency must be ensured throughout the life-cycle of the tests;

e. A duty of fairness in the provision of information related to a genome-based test or service should be highlighted. There is a need for neutral and trustworthy information (sources) so that the quality of the information, its updating, potential conflicts of interest of those providing genomic information or services, can be checked in a transparent process;

f. The future information and guidance in public health genomics should be tailored to the genomic health literacy levels of target audiences;

g. There is a high demand of summarised, digested, short documents on the institutional and policy maker level but also on professional and lay level, to help in decision making and prioritisation of issues which often lie outside the specific content knowledge of the decision makers;

h. Informed consent and choice form a basis for decision making for individuals as well as for communities. Genomic health literacy is a prerequisite for making informed decisions and thus empowering users to act on their health issues. However, being informed is not enough, users need to have realistic resources, access to *e.g.* technology and services but also guidance in navigating *e.g.* through the health system and implications of the risk/disease information and related treatment options and paths;

i. The education and training programs for health professionals should be developed at national level. Networking of health professionals and experts in genetics should be fostered as a mean to protect users' health and welfare in genetic testing;

j. Users should have access to the necessary information concerning the correct use of a genome-based test. This could be performed by putting appropriate information on the package, labelling and the operating instructions of the commercialised test. The creation of electronic public registers listing all validated tests could be appropriate;

k. Informing and listening to individuals take time; capacity building of services is a condition to a patient-doctor relationship of quality;

I. More research is needed on how to ensure the proper understanding of health and genome based information within the general public.

3.3.2 Best Practices

Low health literacy is a worldwide problem. Empowerment of users in a pro-active approach of the decision-making in genetic testing should respect a high level of quality, whatever means are used to inform or educate them, and increase health and genetic literacy of the population.

a. INFORM USERS THROUGH MEDIA OF QUALITY (TV; press; internet)

Users should be able to freely find relevant information about a genome-based test or related services via the media. The development of the health literacy of individuals is closely related to the messages forwarded by the main media which are the TV and internet; the radio and paper press are also to be included. The media should be partners in the information and education process of the wide public concerning health-related genetic testing and incentives to provide high quality information should be developed such as certification mechanisms. Official information and communications should be spread out thanks to independent media and thanks to official means (ministry websites etc.). Actors of information society communicating on genetic testing for health purposes should be competent scientists, trained to appropriately vulgarise genetic knowledge in order to provide understandable messages (58; 56-pt4). Reliability and objectivity of the information provided should be ensured.

European citizens should have access to general information on genetic research concerning genetic testing but efforts should be done in the provision of useful information, information nearer the practical concerns of individuals.

Both Member States and the EU should work with stakeholders of the information society on the provision of adequate information to the wide public on, among others:

- genetic diseases including rare diseases (59),
- genetic health research,
- health genetic technologies utility and benefits (present uses, limits, and reasonable future outcomes),

- the available health services and specific genetic services in health systems,
- the role and rights of the individual in health services and specific genetic services; the pattern of good practices in services' provision,
- the support offered to individuals and families
- the risks, the ethical and social considerations related to the uses of genome-based technologies and genome-based information

In this view, we support the work of EuroGentest on comprehensible leaflets intended to inform and educate individuals and families on the desirable reflections to address before deciding to make a genome-based test and on good practices in genetic testing (*e.g.* 61).

b. INFORM USERS THROUGH HEALTH SERVICES

The user groups of policy makers, professionals as users and citizens/patients or their representatives need information and guidance in the amount, format and style they can best use and benefit from. The formats might vary from brief summaries to meta-analyses and leaflets or websites with practical information.

Production of condensed (evidence) briefs should be initiated and supported; in the light of the research evidence, these briefs are most effective when they are tailored to the context and purpose. The lay/citizen levels, including NGO's, on the other hand, make best use of short summaries (leaflets, (accredited) web site information) and recommendations, which provide contact information or links to further information. Use of personal stories and experiences enhances understanding and digesting often rather abstract information; and specific guidance is easier to grasp than a generic one.

Whatever the modalities used to inform users in health services and specific genetic services (poster, brochure, pamphlets, audio, video), we support the following recommendations from the International Association of Patients' Organisation (IAPO) Policy Statement on Health Literacy (158) concerning the way to proceed and present information.

Information provided should incorporate:

- A clear and understandable message
- A relevant and tailored informative content
- A culturally and linguistically appropriate format of information
- A participative approach of the reader, viewer or listener

Additionally means used necessitate being tested in pilot study on key audiences.

Information on research activities should be neutral, non coercive and should not constitute an improper inducement to participate in a research (e.g. the participation to a research human biobank and/or genetic database should not be remunerated).

European guidelines on specific information processes for particular areas (54) should be supported. The importance of the patient-doctor relationships should be underlined.

i. Consider time factor in the information processes and re-organisation of health services

Information provided via health professionals to individuals involved in genetic testing necessitate discussion and case-by-case analysis of the interests, risks and benefits of the intervention at stake. Allowing health professionals to be more flexible and to spend time in consultations is an important factor to consider for protecting the individual. Such highlights will have consequences in capacity building and remuneration systems of the professionals involved in health and genetic counselling and other consultations related to genetic testing. Member States should consider this in policy development activities and communicate with health professionals in order to build a more “patient-centred” health system.

ii. Inform through informed consent process (oral and written information)

Individuals involved in genetic testing processes must be informed before they give consent to the test. Standards of information should be conceived at the national level involving relevant stakeholders and such standards could also be conceived consistently at the EU level. Individuals should be informed about their role in testing process. For the informed consent/choice at least the following challenges need to be tackled: how generic and how specific the consent for certain purpose should be; is new consent needed for re-use of samples; kind of and right to counselling etc.

For the community and society (but also for e.g. NGOs) orienting towards informed contract might be an option. This is based on the idea of benefit sharing between different stakeholders in public health genomics.

iii. Inform through an appropriate health and genetic counselling (oral and written information)

We know from the behavioural research that personalised health messages, especially about changing lifestyles, are more effective and sustainable when the environment, social support structures and facilitating policies are in place, too.

Pre- and post-test health and genetic counselling are crucial steps in health-related genetic testing. Genetic counselling should be individualised or familial and such services should be appropriately organised and provided case-by-case in health systems. Genetic counselling should be performed in a non-directive way by qualified and multidisciplinary teams including professional counsellors, physicians, geneticists, ethicists, psychologists, jurists and religious where ever it is needed. Networking of competent professionals in genetic counselling should be sufficiently developed to easily constitute such interdisciplinary staffs. Cultural aspects, social background and abilities of the individuals concerned should be taken into account. Options should be assessed according to the health condition of individuals and limits of the available genome-based technologies proposed should be communicated to individual in order to empower them in decision-making process. The explanation of test results in a post-test health and genetic counselling should not be neglected and should be part of the best practices to develop according to new scientific and technological developments. We recommend using existing international guidelines on genetic counselling (62).

iv. Inform through leaflets and documentations freely available in health services and specific genetic services (written information).

The written information provided in health services concerning genetic testing is a practice well developed. Nonetheless, it is necessitating some developments in order to claim sufficiently informed users. According to a recent study performed across seven EU Member States (114) written information should include risks and limitations of testing as well as discussion of the psychological and social aspects of genetic testing. The information displayed by health services and in that case specific genetic services online need to be overseen by public authorities and

must reach high quality criteria to be considered as constitutive of a responsible service.

c. INFORMATION AND ADVERTISING

Advertising genome-based technologies is raising a lot of concerns because of potentially misleading the users. These elements should be understood in a context where the variety of internet users does not fully understand what the tests are for and what is their status in terms of quality standards applying to the medical devices and health related activities.

Advertising concerning genome-based technologies, innovations and commercial services necessitate applying the principles of fair trade, ensure oversight and perform some regulatory developments. Fairness, objectiveness and clarity in the messages should be promoted and controlled by competent authorities in order to ensure trust in the claims provided and interventions offered. Numerous organisations and authors support the idea that the regulation of medicinal products (42) could serve as a basis to ensure quality and regulate advertising concerning genetic testing. Requirements in terms of advertising related to the prescription of the test, the reimbursement and the health-related value of the test could effectively present high interest in the regulation of genetic testing as well as other modalities developed under the advertising of medicinal products.

The European Medicine Agency (EMA) should be consulted on the feasibility to inspire from this regulation to frame advertising of genome-based technologies and the European Commission should consider its empowerment in control and oversight activities in this domain.

The new developments in this sector should target both advertising towards the public and towards health professionals.

Furthermore, the rights of individuals injured by misleading advertising should be efficiently ensured by existing legal systems and penalties for involved professionals should be adequately foreseen.

d. EDUCATION OF PROFESSIONALS AS USERS ABOUT GENOME-BASED TECHNOLOGIES AND INFORMATION

A responsible approach in health services, including specific genetic services, involves the necessity to support activities in education for health professionals. This should include educational programs at schools, universities and specialities influenced by the use of genome-based technologies and genome-based information. Training of active health

professionals is also important to keep them up-to-date in health practices, innovations and research advances, regulatory developments and foster networking of occupations.

e. EDUCATION OF INDIVIDUALS PERTAINING TO REPRESENTATIVE GROUPS

The role of the patients' representative organisations in the education of individuals should be stressed.

Institutions enjoying trust of the population such as NGO's, professional or scientific organisations etc could function as accredited information sources and also alleviate potential concerns and unrealistic expectations. One possibility would be to train science writers among the media representatives. Another would be to develop science communication curricula for educational institutes and in some societies potentially also so called Science Olympics might function – in the way Norway has recently shown.

f. INFORM AND EDUCATE USERS BY ORGANISING PUBLIC DEBATES AND COMMUNICATIONS ON GENETICS IN HEALTH

Another mean to be considered as a part of information and education programs is the organisation of public debates and communication on genetics in general and genetic testing in particular. Such events should be publicly accessible and pool experts from the various fields of health and genetics from the public and private sector. Efforts in vulgarisation should be promoted and valorised. The public should be able to develop its own ideas about innovations and applications of genome-based technologies. Their views should be as far as possible taken into account in respective policy developments.

3.4 Mobilize Community Partnerships

- This task can be viewed as a major role for the National Task Forces (bringing together genetics, public health, policy makers....) and is an extremely important input for policy development
- Guidance on new business models (health technology life cycle etc.) as well as guidance on stakeholder involvement, setting up of sustainable infrastructure for National Task Forces,

3.4.1 Recommendations

EU role

- a. The European Commission should support the involvement of community partnerships in genetic testing and screening developments;
- b. Free access to existing representative and support groups such as patients' organisations should be ensured to the benefit of the users as part of the quality of health services and specific genetic services;
- c. The European Commission should continue consulting international and national patients' organisations and other relevant representative organisations in the process of developing a public health genomics policy;

MS role

- a. The Member States should develop strategies to involve local, regional and national community partnerships in the policy developments concerning genetic testing and organisation of health systems. Consultations results should be visibly spread and referred to;
- b. The networking of the different community partnerships should be developed and concretised by regular meetings;
- c. The public and private partnerships should be developed.

3.4.2 Best Practices

a. HOW COULD USERS MOBILISE AND ACT TO IMPROVE THEIR INFLUENCE

It is important to allow users to mobilise them and express their opinions about the matters related to genetic testing. Representative groups and alliances must play an important role in the development of public health policies, in supporting and advocating for better health services and specific genetic services and individuals' rights protection. Community partnerships such as patients' organisations also provide individuals with supports, information and education.

Existing community partnerships are quite heterogeneous (formal, informal, local, regional and national aspects). The representativeness of the individuals concerned by genome-based technologies and genome-based information in health services should be organised in comprehensive and visible networks. Community partnerships on rare diseases should not be neglected in such networks.

Information should be provided to users of health services about existing support structures according to health status of the individual concerned. Individuals must remain free to accept or refuse to participate in such organisations.

As the offers of health services including genetic services are evolving in the internet, representative organisations of consumers should also play a role in the public participation in the development of genetic testing policies.

The development of online social networks or in internet fora on health topics could also be a matter of community partnerships concerning health genetics. If they are sufficiently organised, should they be taken into account as an expression of the public opinion? Could they represent an appropriate means for individuals to express personal points of view in sincerity and receive support?

b. ORGANISE REGULAR MEETINGS BETWEEN COMMUNITY PARTNERSHIPS

The different relevant community partnerships representing users' interests in health services or citizens should be regularly focussed in meetings, both nationally and internationally, around issues interesting the developments involving genome-based information and technologies.

Stimulation of interactions between these entities could lead to common positioning on health services and specific genetic services in health systems and the use of genome-based information.

Such activities based on consensus could have a great impact on policy decision-making. Individuals, users or not, should have the possibility to be represented and to participate in public events and open meetings in order to express themselves and share their experiences and feelings as an integrate part of the participatory democracy in public health.

Some important topics for users could be dealt with at these occasions:

- The individuals' place in health services, their roles and rights;
- The individuals' understanding about genome-based information and genome-based technologies;

- The individuals' expectations, fears about genetics and policy developments;
- The professionals' views on the usefulness of genome-based technologies and genome-based information for health care, prevention and diagnostic of common complex and rare diseases;
- The professionals' methodological difficulties in genetic testing;
- The coming challenges and needs in policy with regard to users (e.g. the perception of results indicating the late onset of serious disease and the management of the consequences).

c. DEVELOP COMMUNITY PARTNERSHIPS BETWEEN PUBLIC AND PRIVATE HEALTH SECTORS

Community partnerships should be developed both inside the public health sector but also between the public and private sectors in order to develop consistent policies and share experiences to the benefit of users of health services and specific genetic services. The development of networks and communication between these actors of public health should foster to reach high quality standards in health services and genetic services provisions, clinical and research services for the benefit of users. Whereas economical means allocated to these sectors are varying, challenges in practices are often common and should be discussed.

d. WHEN TO MOBILISE COMMUNITY PARTNERSHIPS?

Relevant community partnerships involving or representing users should be mobilised in order to express their position in the following situations:

- New genome-based technologies are to be integrated in health services;
- Public reviews are necessary on genome-based technologies and genome-based information are performed;
- Regulatory developments and policy developments concerning genetic testing are to be planned;
- Law enforcement;
- Assessment steps of policy and legal frameworks have to be placed;
- Controversial topics concerning widespread genetic testing practice must be evaluated;
- Controversial topics concerning the use of genome-based information need to be discussed;

- Organisational changes and capacity building related to health services and specific genetic services appear mandatory.

In addition, the self-referral of community partnerships and representative bodies of the society's interests should be fostered and their activity should not be limited to requests from governments.

3.5 Develop Policies

- A broad interpretation can encompass under policies: laws and regulations, governmental policies, professional guidelines, quality assurance measures, different types of safeguards ...
- Guidance on existing forms of regulation, development and maintenance of specific forms of regulation, harmonisation issues, ...

3.5.1 Recommendations

EU and MS role

- a. The EU and Member States should consider the consequences of the blurred limits between clinical and research fields and the necessity to have a global approach in regulatory and ethics developments;
- b. Public health genomics field needs to work towards health in all policies. Policies in public health occur and interact on different levels from macro (societal) to meso (community) to micro-level (individuals/families). Policy development needs to be enhanced on all levels with relevant stakeholder involvement;
- c. The EU and Member States should consider the quality of the laboratories and services as the key for translating genome-based technologies from research into the health services. Any use of non-validated genome-based technologies and associated results should be prevented;
- d. The EU and Member States should support the works on harmonised definitions to guide policy-makers in their regulatory tasks. The references to definitions in the regulations concerning health services

and specific genetic services should also be supported as a quality aspect ensuring their understanding and readability for users;

e. The effectiveness of available genome-based technologies and tests in development in research should be assessed regarding, among others, their clinical utility and their implications for the individuals and their relatives. Such assessment should also include cost and be coordinated at the European level by the European Medicine Agency which should have conferred competences to act in the area of genome-based technologies;

f. The introduction of genome-based technologies in clinical practice necessitates establishing criteria of reimbursement of the tests provided. This is to respect the solidarity principle shared by health systems across the EU. These criteria need to be developed at national level. Then they could be coordinated at the European level in the frame of the Directive on Patients' Rights in Cross-border Healthcare 2011/24/EU;

g. The European Commission and Member States should ensure transparency in all operations regarding genome-based technologies' life-cycle, manufacturing, distribution, uses, revocations, public information, clinical and research practices and developments as well as on the necessary transparency concerning the uses of genome-based information;

h. The European Commission and Member States should implement participatory democracy in the establishment of public health genomics policy, organise public debates and reviews which will be used and referred to in regulatory processes. Developments and possibilities in public health genomics with their wide implications on society and population call for societal discussion on reciprocal obligations between science and society. The public consultation is one way to ensure legitimacy and trust in public health genomics policy;

i. Public health genomics, which is largely based on high-technology developments, especially needs to establish equity in access to its information and services;

Equity is best enhanced by tailored guidance and information which is sensitive to the social groups and conditions, including literacy, participation, respect of different values and facilitating access to

information and access but also cares and supports structures (e.g. re-imburement) for citizens in different stages of health and health care provision.

j. At present large part of research funding is used for basic science research on genomic discoveries, technologies and clinical applications. Time will come to shift some support towards a public health genomics approach;

k. The EU and Member States should promote auto-regulation of providers of genome-based technologies and associated services. This includes the private companies acting in the internet;

l. The European Commission should clarify EU regulatory competence on genetic testing and identify areas where harmonisation is possible/needed/agreed as well as areas where coordination is sufficient to ensure user protection. The domains of competence penetrated by genetic testing activities need consistent regulation;

m. The European Commission and the Member States should create a consistent oversight system of genetic testing and screening in health systems. For doing so competences of existing authorities in genetic testing should be assessed in order to assign monitoring tasks concerning both the introduction process of genome-based technologies into health services but also ongoing health and research practices using genome-based technologies and information. Such institutions should be consistently coordinated at the EU level and cooperate. Tasks to inform users and the public on genetic testing rules, ethics and state-of-art should also be clearly identified;

n. The European Commission and Member States should develop the European data protection in the health sector and enjoy the opportunity to go forward in the harmonisation process of protective principles and rules applicable to adequately protect European citizens with regards to the rapid development of technologies (e.g. 105);

o. The European Commission and Member States should develop benefit sharing policies in research at national, European and international level in a consistent way respecting ethics and enforceable laws;

p. The European Commission and Member States should develop data sharing policies in clinical and research settings and support initiatives in this domain. Such policies should ensure an active role to the individuals concerned and guidelines should be developed. Recognition of data sharing as best practice and element of excellence in research should be considered and incentives should be developed;

q. The European Commission and Member States should develop e-health policies taking into account the implications for users and the benefit/risk and cost/effectiveness assessments. Practical issues related to the possible remote applications of e-health technologies should be considered with regards to enforceable laws, quality aspects and the necessity to preserve patient-doctor relationships and confidence in health services using genome-based information and technologies;

r. The European Commission and Member States should develop regulation and guidelines concerning the direct-to-consumer health services and genetic services;

s. The European Commission and the Member States should ensure that internet service providers apply international and national laws and regulations concerning genetic testing;

t. The EU and Member States should be more engaged in international activities concerning public health genomics at the regional and global levels. Such efforts should also increase collaborations, promote European patterning, productively exchange views, experiences and develop sustainable policy and partnerships with other countries in the respect of human rights and freedoms. The creation of a common matrix of referrals in terms of legal and ethical texts or guidelines could be part of this activity;

u. Enforceable rules and guidelines concerning the trans-border exchanges of human biological samples should be developed at the EU and national levels in a consistent way in order to clarify ethical, legal and administrative requirements in such operations. Modalities to export and import human samples inside the EU should not constitute a disproportionate burden for professionals but the development of clear legal frameworks are necessary to ensure individuals' rights;

MS role

v. Member States should ratify the Council of Europe Convention on Human Rights and Biomedicine and its Additional Protocol on Genetic Testing for Health purposes as an efficient means to ensure minimal users' protection and work in their own jurisdiction with common benchmarks;

w. Member States should support and encourage activities of the EU in the field of ethics and human rights in genetic testing considering the added value of its activity for the fields concerned. They should strive to create more integrated health policies.

3.5.2. *Best practices*

a. THE NEED TO PRIORISE RESEARCH ACCORDING TO CLINICAL UTILITY

An important reason why genome-based discoveries have not yet realised their public health potential is based on the prioritisation of attention and funding (19). Up until now the attention and funding have been directed towards the scientific discovery in genomics rather than application, implementation and evaluation stages in genome-based information (19). Funding mechanism needs to be balanced towards implementation and research in evaluation instead of continued emphasis on genome-based discoveries. This should happen on EU level, on national levels and on local level.

Identifying areas where the implementation of genetic testing and screening could be more efficient in terms of health benefits and costs for populations is a goal to achieve. In this task, scientific evidence and knowledge should be assessed as well as related ethical, legal and social issues. This identification should not neglect the equity and solidarity principles in modern societies, in health research, in health services and should not undermine fundamental researches (56-pt3.9) or researches on rare diseases. The public must be consulted.

Pharmacogenomics is one of the most promising sectors for PHG in that sense that it could highly influence and improve both the development and the use of medicines. To date, pharmacogenomics is the cornerstone of personalised or stratified medicine. European citizens' are also favourable to the development of pharmacogenetics (57-fig.4).

Pharmacogenetic testing necessitates conducting more fundamental and clinical research intended to identify new evidence-based medicines and to follow the evolution of the drug responses for managing potential

adverse reactions. The EU and Member States decision-makers should promote the appropriate use of pharmacogenetic tests in clinical trials in the respect of existing laws and regulations (127). The outcomes related to the development of new knowledge, new medicines and stratified medicine should be then integrated in public health settings in the respect of equity in access to these services. Pharmacogenetic tests presenting a potentially attractive cost-effectiveness balance should be in the frontline of the establishment of national reimbursement policies. Additionally, the development of pharmacogenomics research and related genetic testing could be of major importance for the understanding and treatments of rare diseases. Rare diseases should not be neglected in medical research. European projects should be promoted and be as far as possible oriented towards clinical usefulness, applications of research knowledge and genetic testing processes. Clinical trials should also be supported in this area. Incentives to develop research in these areas should be planned and implemented both at the national and European levels (100-Rec.19).

Controversial research areas such as nutrigenomics should also be identified and continue developing their scientific evidence-base before envisaging their introduction in health services.

b. THE NEED TO EVALUATE THE COST-EFFECTIVENESS OF GENOME-BASED TESTS AND ORGANISE REIMBURSEMENT POLICIES IN A PUBLIC HEALTH APPROACH

The principles of justice and solidarity should be respected in genetic testing. This urges Member States to conceive an adequate reimbursement system for users, a system that should be then coordinated at the EU level in the frame of the recent Directive on the Reimbursement of Cross-border Healthcare. For doing so, new reimbursement criteria should be developed. Among them, it could be agreed that the clinical utility of the test performed should be a paramount element in the tests' reimbursement system.

c. PRECAUTION IN GENETIC TESTING: FROM A PRECAUTIONARY APPROACH TO THE USE OF THE PRECAUTIONARY PRINCIPLE

It seems adequate that the European Commission and the Member States adopt a precautionary approach in public health genomics tasks with regard to the variety of tests and information generated but also to the usage and spreading of genome-based information outside the health sector. Such an approach allows the establishment of preventive

systems and policies ensuring *a priori* the effective protection of individuals. A majority of European citizens favour precaution where risks related to a health technology are uncertain despite the benefit that could result from this technology. Yet, proportionate risks are accepted (56-pt.3.9). Risk management is thus an important element of genetic testing policy development.

According to a recent public survey in the EU (56-pt3.9), 78% of the questioned persons are considering a scientific discovery as not being in itself “good” or “bad”, only its use is important. Some Member States have developed specific regulations for genetic testing and others have general legal frameworks including the framing of genetic studies involving human biological samples and the practice of genome-based tests for health purposes. Member States, as well as the EU, should assess their legal frameworks with regards to the technological developments in this sector and as regards to the possible other social usage of genome-based information in order to take appropriate disposals creating legal certainty and sufficient protection for the individuals.

The precautionary approach would also diminish the use of the precautionary principle which is regularly criticised as a blocking principle. Yet, it is important to underline that this principle aims not to definitively forbid a product to circulate and be used on a given territory but calls for more developments and scientific evidence on its security. Whatever, decisions based on the precautionary principle in the frame of the modalities developed by the European Commission (66) should clearly refer to the principle and should be spread across the EU.

d. ENSURE THE GENETIC NON-DISCRIMINATION AND NON-STIGMATISATION BY LAWS

In the assessment of existing legal frameworks in Member States and at EU level the non-discrimination and non-stigmatisation principle should be reaffirmed by law with regards to the use of genome-based information and cover all sectors of the society. In this regard, referrals to the Charter of fundamental rights of the EU (23), particularly Article 21, should be supported. The EU and Member States could get inspiration from the countries having developed a legal framework including the American Genetic Information Non-discrimination Act (GINA) (161) adopted in 2008.

e. APPROXIMATE THE RULES ON THE USE OF HUMAN SAMPLES AND ASSOCIATED DATA

The use of human samples, health and genome-based information in genetic testing and medical research is a paramount need. They can be used separately for different purposes but they are more often used or stored together. The development of genetic testing practices and biobank infrastructures across the EU calls for new regulatory approaches creating more interactions between samples and data regulations, in a global approach. Such developments are well represented in international guidelines of the OECD (129) and the Additional Protocol to the Convention on Human Rights and Biomedicine concerning Genetic Testing for Health Purposes adopted by the Council of Europe (30-Expl.Rep.). Member States legislations are varying both in the way to articulate such frameworks and to conceive collections of samples and data. Some specific national legal frameworks include such approximation concerning genetic testing (69) or biobanking for example and this opens new ways of thinking enforceable rules and foster clarity for users. Yet, this approach should be further explored in the development of legal frameworks. In order to foster research activities and maximise the use of available resources we support the approximation of the regulations of samples and data and efforts to clarify and simplify enforceable rules. Such an approximation of legal frameworks is concerning both the EU and national frameworks. At EU level this includes a work on the current Directive 95/46/EC concerning the health sector, the scope of the Directive 2004/23/EC on the general framework for the safety and quality of tissues and cells, the Directive 2006/17/EC concerning certain technical requirements for the donation, procurement and testing of human tissues and cells and the Directive 2006/86/EC concerning traceability requirements, notification of serious adverse reactions and events and certain technical requirements for the coding, processing, preservation, storage and distribution of human tissues and cells.

In line with this idea and the concretisation of the European Research Area (ERA) we are encouraging the networking of human biobanks developed thanks to a distributed dedicated European infrastructure in the domain (BBMRI project). It is also interesting that the same networking and interoperability dynamic is applied to the databases containing genome-based information, together with other kinds of information as started in other European infrastructures and several FP7 projects such as GEN2PHEN. This would allow, in addition to the sharing

of samples, to foster data sharing policies and approximation of the applicable rules. It is noticeable that at the international level P3G (Public population project in genomics) has also added databases to its harmonisation mission.

f. DESIGNATE / INVOLVE / CREATE COMPETENT AUTHORITIES IN GENETIC TESTING OVERSIGHT

Enhancing institutional oversight and governance of health services and where relevant specific genetic services for ensuring users' protection necessitates building a consistent system in Member States and more coordination in the EU.

Member States should clearly designate or create a competent authority to develop public health genomics policy and enforce laws, to manage the provision of genome-based technologies through the national health system and to oversee the market, the uses and the effects of genetic testing practices in clinical and research areas. These authorities should inform, educate and warn users about available tests, their characteristics, their uses and good practices to apply in clinical and research settings. Oversight institutions must have necessary powers to control health institutions providing health services and specific genetic services in a European network ensuring coordination and fair cooperation. Regular reports to governments and to the European Commission on these ongoing should be part of the tasks of such institutions.

The European Commission should also designate or create a competent authority in charge of the oversight and coordination of national activities in the field of genetic testing. This authority should work close to the national authorities, gather documentation, reports and public consultations results, organise meetings and inform the European institutions on the ethical, legal and social evolutions with regards to genome-based technologies. We recommend to the European Commission to assess the capacities of the EMA to manage such tasks considering the achievements of this institution and the necessary capacities to develop in connexion with this domain. Alternatively, in case it seems appropriate to create a new agency, the Commission should plan *ab initio* the cooperation with existing European entities such as the Directorates-General (DG) Sanco, Research, Enterprise, Internal Market, the EMA, the European Data Protection Supervisor (EDPS) and the European Group on Ethics in Science and New technologies (EGE).

The challenges put by the "e-governance" should also be considered in the frame of health services and specific genetic services. The performing

of oversight mechanisms and regular studies of the direct-to-consumer market such as the one performed by the EU Parliament STOA board (75) should be promoted. The role of the European agency in charge of the oversight of the security of networks (ENISA) should also be considered with regards to health services including genetic services.

g. INVOLVE THE NATIONAL, EUROPEAN AND INTERNATIONAL ETHICS COMMITTEES

Internationalisation of medical ethics allows the implementation of international forums of national ethics committees such as the European NEC-FORUM. Such initiatives should be fostered and the ethical, legal and social issues of health services using genome-based information and technologies in health systems should be inserted in the agenda of these meetings.

Co-operation between international bodies should also be supported by the European Commission. This should target:

- The EU Commission services, the EGE and the international bioethics platform,
- The Council of Europe services, Steering Committee on Bioethics (CDBI) and
- United Nations Organisation services, the UNESCO's International Bioethics Committee (IBC), World Commission on the Ethics of Scientific Knowledge and Technology (COMEST) and
- OECD services on scientific and technological innovations.

Other services of the EU Institutions tackling legal, ethical and social issues of new health technologies such as the specialised internal units of the European Commission and the EU Parliament should also be involved in the building of a public health genomics framework.

Interactions with non-governmental stakeholders and other professional or patient organisations, such as the European Society of Human Genetics (ESHG), the CPME, the Human Genome Organisation (HUGO), and more specialised organisations such as the European Nutrigenomic Organisation (NuGO), should also be developed.

h. DEVELOP THE EU FRAMEWORK FOR PRIVACY PROTECTION IN THE HEALTH SECTOR

The principle of “health protection in all policies” should be now consolidated by the setting up of a new principle of “privacy and data protection in all policies”. This is encompassed within the Article 16 of the Treaty on the Functioning of the European Union (TFEU). Sensitive and health data protection is an important matter where the EU has an active role. Existing framework of data protection is currently well developed on a general level but some important aspects of health data protection should be underlined and some new developments could be performed in order to clarify the enforceable rules in this domain and develop right now a real European health policy taking into account national experiences in a bottom-up approach. This aims to enhance effectiveness of European data protection law to the benefit of European citizens’ health and trust. In this optic, implications of the production of health data in genetics, the construction of the ERA and the ERI could foster the movement and the will to elaborate such a shared policy and to go forward in the regulatory framework. The documents produced by the EDPS and the Data Protection Working Party (DPWP) established under the Article 29 of the Directive 95/46/EC are, among others, a good basis for these developments. Several policy and regulatory developments could be envisaged in collaboration with stakeholders to reach this objective (cf. Best practice o.)

Which could be reflexion tracks for the near future of European privacy and data protection in health sector?

- Move towards more harmonisation in health sector?
- Develop individuals’ rights in the health sector with regards to the variety of health data and genome-based information;
- Clarification of actors involved and harmonisation of professions;
- Networking of institutions and executive agencies in data protection;
- Improvement of EU capacities in the assessment and enforcement of ethical, legal and administrative rules in health activities using genetic information.

A broader international cooperation on privacy protection and law enforcement should be part of this action line (132).

i. DEVELOP E-HEALTH POLICIES AT NATIONAL AND EUROPEAN LEVEL

The e-health sector is developing regarding health practices at several levels (70) with a great potential of added value, in terms of quality and cost, in the context of transborder healthcare provision. The protection of users of such technologies should be ensured essentially by quality assurance tools, regulation and ethics. Initiatives of the EU Commission in this domain should continue and be supported by Member States in order to exchange practices and developments and create a European e-health system. The public should be consulted on this new dynamic and e-health best practices guidelines should be developed (67).

Among the issues put by the use of e-health technologies concerning genetic testing we recommend to consider:

- The necessity to inform users about the variety of e-health services (telemedicine, information websites, commercial websites);
- The necessity to ensure acceptability of e-health by the public;
- The effects of the dematerialisation of patient-physician relationships (quality and confidence in health services and specific genetic services);
- The possibility to deliver electronic medical prescription (reliability of the prescription);
- The possibility to provide individuals with remote appropriate counselling, including the consideration of test results, (quality and reliability);
- The transfer of test results directly-to the consumer by electronic means (security and autonomy of individuals);
- The possibilities to include genome-based information within electronic records (security and privacy protection);
- The necessary adaptation of health services (capacity building - infrastructures);
- The necessary training of health professionals in the use of e-health system (for the benefit of users and individuals concerned the use of electronic systems in health services should be simple and practical);
- The provision of health information via internet websites (quality)
- Enforceable regulation at EU and national level (68): Services regulation, e-commerce regulation, needs to create specific regulation? (clarity, consistency and high level of individuals protection).

“E-governance”, “e-learning”, and “e-security” initiatives should be promoted and considered by stakeholders and policy-makers as important elements in the development of a responsible e-health policy. The concepts of “privacy by design” as well as the use of PETs to protect users’ interest could also serve as criteria in the assessment of the adequacy of e-health innovations as in certification processes. The European Commission should explicitly recognise these aspects as important in the e-health sector and envisage placing an obligation on manufacturers to include such principles and technologies in their innovative activities under the Article 17 of the Directive 95/46/EC. The EU potential in ICT developments should be considered as bringing a considerable added value in the development of standards and secured interoperable systems in health sector.

Websites’ creators and hosters having already an amount of obligations concerning their services online should be sensitised about the implications of genetic testing and the enforceable regulation to medical/research activities involving human beings. Incentives to create procedures and technical measures intended to provide ethical services and protect users could be envisaged such as the delivering of a quality label granted at European level and recognised by competent authorities. The EMA, in cooperation with others competent authorities could be involved in the delivering of such a quality label.

j. DEVELOP POLICIES ON BENEFIT AND DATA SHARING

In the frame of the ERA and the goals of the EU Strategy of Lisbon, benefit sharing and data sharing are important principles to put into practice in health services and specific genetic services. Research using genome-based information and technology obliges to find equilibrium between altruism, profit and reciprocity. This equilibrium could be found in the organisation of sharing policies targeting both the practical outcomes of the research performed (benefit sharing) and the optimisation of data gathered from the research to the benefit of other health research (data sharing). In such policies the notions of public good and community resources should be taken into account.

i. Benefit sharing policy development in research

Benefit sharing in health research is internationally accepted and based on the principles of justice, solidarity and common heritage.

As it has been defined by the HUGO, “A benefit is a good that contributes to the well-being of an individual and/or a given community (e.g. by

region, tribe, disease-group...). Benefits transcend avoidance of harm (non-maleficence) in so far as they promote the welfare of an individual and/or of a community. Thus, a benefit is not identical with profit in the monetary or economic sense. Determining a benefit depends on needs, values, priorities and cultural expectations”(99). In a very practical way, benefits resulting from health research discoveries, knowledge and applications could be conceived as the access to quality prevention, diagnostic, treatment means and other health services engaging research innovations. Benefit sharing should be incorporated as a principle in EU law concerning genetic research and practical guidelines should be developed according to the different kind of individuals and groups involved. The participants in a research should not be the only one targeted by the access to the benefits, a benefit-sharing policy must be based on a global level and aim all individuals for whom access to an innovative health service is recommended and justified. However, the communication of research outcomes and associated new health services should be primarily provided to research participants.

ii. Data sharing policy development

Data sharing policies are also a condition to optimise research using available resources and to increase benefits in health research outcomes. This aims both genetic research but also public health research such as health monitoring activities and publications’ related issues. Some activities in the international area have been implemented concerning data sharing policies such as the development of guidelines (133) and statements (173). Such activities deserve being acknowledged even if they include some limitations in their scope. As in the matter of benefit sharing, the data sharing policies should cover public and private sectors and become a norm in health research activities respecting the same ethical line. Individuals should have consented to these operations and be systematically informed about such sharing (kind of information / purpose). Conditions to appropriately inform users should be developed. A related issue to the protection of individual privacy in data sharing is the re-identification of individuals by the use of several information which could be linked (cf. Assessment).

There is a need to go forward (146) in data sharing and to consider internationally operational and technical systems to share data protecting both individual rights and intellectual property. Some domains such as the pharmacogenomics urge to apply data sharing into practice (100-para.2.2,2.3,2.4). Incentives to appropriately share data such as

genome-based information should be developed in order that “usurpation” is prevented and that the work done to generate and open the access to these data be recognised (e.g. 13). The development of commitments from the investigators should be promoted and could be inserted in SOPs. European guidelines involving all stakeholders should be developed.

Ethical, legal and social aspects of benefit sharing and data sharing in health genetics need to be more studied with the purpose to create international guidelines and practical tools in these domains. Benefit sharing and data sharing policies should be sustainably developed both at EU and national level and should be, in fine, systematically planned by health professionals and researchers, included in the protocols of collaborative research and assessed in the ethical review of a project.

k. DEVELOP THE DEMOCRATIC PARTICIPATION IN PUBLIC HEALTH GENOMICS

The public and users of health services and specific genetic services as partners, this is the goal to achieve in order to create trust and conceive legitimated and well accepted policies concerning genomics. The development of science-society dialogue and relationships is a key issue in public health genetics to ensure legitimacy of interventions. This topic is fundamentally related to the ability of the EU and Member States to inform and educate citizens on the pro and cons of genetic testing and screening programs for health purposes and related genome-based information. As it has been noticed several times the practice of the public involvement necessitates being intensified and better reported in policy developments (8). By the “public” we mean all the citizens, patients’ organisations and other representative groups of individuals, and we acknowledge that it corresponds to several “publics”. Public consultations aim is to provide policy-makers with information gathered from various interest groups, publics and stakeholders, which should be integrated in policy-making process. The OECD has developed useful recommendations (131) that could be used in the frame of public health genomics.

Practically, we suggest using existing tools of public participation to tackle issues related to health services including genetic services and the use of genome-based information.

Thus we recommend that

- The European Commission launches a Eurobarometer on public health genomics including services organisation and e-health, the storage, uses and transfers of genome-based information, of human samples;
- Member States organise societal debate, public consultation, surveys or other forms of stakeholder hearings and involvement to formulate a social contract between science and other stakeholders involved in public health genomics.

Other exercises of direct participation or evaluation from users of health services including genetic services could be developed, tested and consistently inserted in the public participation strategies (cf. Evaluate). Studies on the impact and the use of public participations in policy developments should be envisaged.

I. CONSIDER THE IMPLICATIONS OF PUBLIC HEALTH GENOMICS FOR THIRD-COUNTRIES

The regional development of public health genomics policies in the EU could have negative impact on emerging and developing countries. In this regard we support the “global health” approach and the role of the EU in international cooperation. Solidarity and international cooperation for a global public health genomics and comprehensible ethical framework should be part of the agenda of the EU in the next decades. The promotion of benefit sharing, data sharing in the respect of human rights, solidarity, equity, and cultural differences is crucial. Debates and partnerships should be promoted particularly in the frame of the WHO.

m. TOWARDS CLOSER COOPERATION WITH THE COUNCIL OF EUROPE

The Council of Europe is developing high level standards of individuals’ protection in biomedicine and genetic testing. The EU as well is ensuring a high level of health protection in all policies and respects the principles laid down in some fundamental texts such as the Convention for the Protection of Human rights and Fundamental Freedoms (CETS No.005). Together, the EU and the Council of Europe could act together towards a more comprehensive framework of users’ protection in the health sector and go towards a “common space for human rights protection across the continent” (37). We recommend to the EU to consider, in collaboration with the Member States:

- The adherence of the EU to the Council of Europe organisation;
- The EU accession to other key Council of Europe conventions, monitoring mechanisms and bodies to ensure consistency of

standards and of the monitoring of their implementation by the member states (37);

- The production of common documents concerning biomedical ethics and individual rights in genomics;
- The development of neighbourhood policies in genomics medicine ensuring quality in health services and protection of individuals.

n. CONSIDER THE SPECIFICITIES OF THE DIRECT-TO-CONSUMER GENETIC TESTING IN REGULATORY PROCESS

The direct-to-consumer genetic services and related concerns with regards to users' protection are giving importance to the building of a public health genomics policy. The direct-to-consumer activity is covering both the provision of health services including genetic services online but also the direct-advertising of genome-based technologies (98). Whereas such activity online is claiming the complete autonomy of individuals in the access to their genome-based information about several diseases and traits, concerns about the potential misleading of and harms to lay people which could have an impact on health systems and negative effects on the public perception of medical genetics (53) should be considered in policy developments.

Users', citizens', professionals' and industries' point of views, expectations and concerns should be sought on this new market. More cooperation between the EU and the United States on ongoing regulatory activities (85) would surely be constructive.

Communication and education of the citizens on this topic should be developed. Indeed, because it is regularly evolving according to the published opinions and guidelines, an oversight, a risk assessment and further multidisciplinary researches are needed to better understand implications of this market for public health. Considering this movement initiated by the service providers as positive, this is not sufficiently generalised and could sometimes only be "façade changes", some other aspects need to be addressed by policy-makers. We recommend using the work of the STOA, the HGC and relevant literature to organise a policy and legal framework of direct-to-consumer health services and genetic services. We are supporting the work of the European Society of Human Genetics (ESHG) on guidelines intended to ensure the quality of the services and advertising provided online. The "traditional" health services should be based on strong quality criteria and concentrate the essential of health genome-based technologies; thus commercial activities could continue only under the condition of efficient guarantees for individuals.

The following concerns should be considered:

- Concerns about the quality of the commercialised tests and attached services (75-Annex2;98);
- Concerns about the transparency of activities performed by the companies;
- Concerns about the quality of the information provided through the websites and the advertising of genome-based technologies;
We support the application of the HONcode developed by the Commission as a benchmark for creating quality assurance schemes, the eYouGuide development in the health area and the initiatives developed in the frame of the Digital Agenda for Europe.
- Concerns about the governance of health services including genetic services online and capacities in law enforcement and appropriate controls;
- Concerns about the enforceable regulation (cf. enforce laws);
- Concerns about minors' protection, informed consent and theft of samples and protection of privacy;
- Concerns about the consumerist approach of health technologies and initiative offers such as packages or sponsoring of users.

o. REGULATORY CONSEQUENCES AND OPPORTUNITIES FOR THE EU

i. Fund the competences of the EU in public health genomics

According to the number of domains that could be influenced by the use of genome-based technologies and genome-based information in health systems it appears important that the EU takes position on its competences.

Indeed, the more genome-based information will be produced the more they will be used. Even if they have been originally extracted in the health systems, the other social usage of such sensitive data should not be neglected. The EU has today the chance to be in a prospective approach concerning the future uses of genomic information compared to other places where certain abuses have been reported. The Union should take this opportunity to develop health policy at EU level and to prevent potential abuses by being actively involved in regulatory and oversight activities to create a European pattern. For doing so, discussions with Member States should be engaged and the definition of

the competences of the EU should be clearly established according to the EU treaties (Treaty on the Functioning of the European Union [TFEU], Treaty on European Union [TEU]). The opportunity to establish new competences related to health protection and genomics should be considered.

Legal basis for the European activity in public health genomics according to the fields concerned by health-related genome-based technologies and genome-based information:

- Internal Market (Article [Art.] 4 and Art. 26 and following, TFEU);
- Service delivery (Art.56 and following; TFEU; knowing that health services are excluded from the Service Directive 2006/123);
- Data protection (Art.16, TFEU and 39, TEU);
- Health protection and Public Health (Art.6 and Art.168, TFEU);
- Research (ERA, Art.179 and following, TFEU);
- Consumers protection (Art.169 and following, TFEU);
- Employment (Art.145 and following, TFEU);
- Social policy (Art.151 and following, TFEU);
- Justice, Freedom and Security Area (Art.67 and following, TFEU).

ii. Build consistence between existing applicable texts and develop public health ethics

The EU has already enacted directives establishing rules and responsibility regimes at different levels and in different sectors which are affected or could be soon affected by the use of genome-based technologies and information. Indeed activities in the field of genetic testing are blurring the line between several areas of law (cf. Law enforcement).

The European Commission, in collaboration with Member States should strive to find innovative solutions to link existing regulations and guidelines to insert health-related genetic testing activities in relevant legal frameworks going thus toward more legal certainty in the stratified medicine landscape. The creation of specific texts could also be envisaged.

Additionally, the development of public health ethics should not be neglected and should be developed and referred to within regulations that applies or should apply to genetic testing activities at national and European level.

iii. The revision of the IVD Directive 98/79/EC from users perspective

The dialogue between policy-makers, health professionals and manufacturers of genome-based tests should be fostered in order to appropriately classify genome-based technologies. Generally, we support the proposals made by the European Council concerning innovations in medical devices (73). With regards to users' protection we are supporting the recommendations of the ESHG on genetic testing in public health framework (52) on the regulatory developments of the current Directive 98/79/EC (45). The risks for users of genome-based tests should have been assessed and controlled before their introduction in health services or consumption market and the evolution related to their use should be monitored after this introduction. Quality assurance calls for a new categorisation of genome-based technologies according to their risks and their uses conditions. Thus criteria concerning the quality of the services associated to the testing device should be considered in the frame of the EU IVD Directive revision process.

We would like here to make a focus on the tools which should be available to users in order that they can act knowingly. The following elements are concerning all kinds of genome-based tests used in health systems and those commercialised via internet.

The users should have access to:

- The label or certification meaning concerning a particular test or genetic service;
- A link towards a competent health authority and towards an official list gathering authorised quality devices;
- A clear notice explaining the correct use of the device and the rate of reliability of the results and providing general advises in case of positive results.

iv. The revision of the Directive 95/46/EC and issues related to health data including genome-based information

Whatever the context of the genetic service the regulation ensuring the privacy and data protection must apply. Specificities related to the health data, as personal sensitive data, should be developed in the relevant European regulations. New texts creating a specific corpus for health data could be envisaged.

There is no European integrated and harmonised policy for health and health data protection. However, genome-based information is sensitive information as defined in the Directive 95/46/EC even if this is implicitly encompassed by the mention of health data. Such an absence is challenging in the genomics era. Technological developments in genome-based information analyses devices and methods urge to adapt and clarify legal frameworks both at EU and national level. The EU Directive 95/46/EC, currently under revision, is the main matrix of the European data protection policy ensuring the fundamental rights of individuals. However, the health sector is challenging the effectiveness of privacy protection rules due to the rapid developments of this domain, the increasing production of genome-based information both in clinical and research areas, the computerisation and exchanges of health data for several purposes and the particular issues put by these new developments. The following points aim to identify the needs and options which should be considered in the modernisation of the EU law with regards to genome-based technologies implications and genome-based information.

Which are elements to consider in the building of a European health policy including genomics?

a) Towards a general EU Regulation on data protection?

Moving towards greater harmonisation by adopting a Regulation replacing the Directive 95/46/EC and creating a global and unique framework could be a solution to definitively affirm and ensure the commitments of the EU in data protection, including health and genetics ones. As it has been noted by the EDPS, all the elements come together to establish a strong general data protection framework in the EU law. The Charter of Fundamental Rights of the European Union (CFREU) and the Article 16 of the TFUE give an individual right to data protection

and the abolition of the pillar structure of EU policies expand the data protection to all the EU policies (horizontal approach). So, a Regulation seems to be the most appropriate tool to use in order to establish a solid and effective basis (consequences for judicial remedies) for the EU-wide protection of personal data (49-para.16,25, chap.5). A Regulation but not a complete suppression of the flexibility allowing the MS to take more stringent measures, their leeway in the establishment of national law concerning both data protection and health policies should be preserved as far as possible.

- b) Towards a Directive on privacy protection in the storage, processing, management and international transfer of sensitive personal data in the health sector?

In this respect the European Commission could work on the legal basis of the EU action in the protection of health data and genome-based information.

- Explore the possibilities to set up a specific Directive (assess the added value of such a proposal);
- Adopt a sector-wide approach...

It seems appropriate to adopt a sector-wide approach concerning health sector. This approach should include health data and genome-based information in a wide interpretation. The scope of this directive could address both healthcare and research activities using sensitive personal data and both the public and private sector. The Commission should envisage this Directive in a horizontal approach involving several departments and DGs. This approach would also necessitate mentioning the specific health data protection in the future Directive/Regulation replacing the current Directive 95/46/EC.

... including the use of electronic systems;

In its opinion No. 13 on the ethical use of personal health data in the information society, the EGE states that there is still no specific EU legislation in the field of personal health data protection and hopes that a directive will be

put on the study to consider the challenge posed by the computerisation of such data.

- Use the relevant principles set out in the CFREU in connection with the use of genome-based information and reaffirm its binding feature for MS;
 - Refer to the work of the Council of Europe: the Convention of Oviedo (the Art.10 concerns the respect of privacy) and its additional protocols in addition to the reference to the Convention n.108;
 - Develop the data transfer procedures in a consistent corpus, clarify the role and importance of the binding corporate rules (BRCs), of the standard operation procedures (SOPs) and other contractual techniques;
 - Art.29 DPWP: it would be interesting to promote the creation of ad hoc working groups in the health area.
- c) Clarify the actors (*e.g.* 6) of data processing and their respective roles and responsibilities in a clear text. This practical concern is important and need to be dealt at EU level in order to foster consistency in political activities and fair cooperation between Member States. This targets the role and responsibilities of National authorities / Data officer / Data controller / Data processor / Data manager plus in the health sector the Health professionals / Researchers / Promoters.

The protection of fundamental rights at the centre of the revision of the general framework

The revision of the European framework should focus on the protection of fundamental rights and freedoms of individuals giving them the key for a certain control over their health data. Therefore, their rights should be clearly reaffirmed at the EU level and specified for health activities (healthcare / research) in a particular legal instrument as well as organisational measures to enforce them. In this view, talking about "data protection" can be misleading; it is more the protection of people's privacy and rights than merely data protection which is one of the mean to protect privacy. New rights could occur and complete the general framework with regards to national laws developments.

- It is about creating a balance between freedoms (individual/research) and security;
- Promoting the European social pattern based on fundamental rights and common ethical principles;
- Support interdisciplinary research on the ethical, legal and social aspects in the field of health data and genome-based information protection at all levels (EU/MS) and foster bottom-up activities (2).

Assurance (Tasks 6-9: all three pillars)

3.6 Enforce Laws

- A broad interpretation is needed to encompass the application of the range of policies considered (e.g. Health in All Policies, ...).
- Guidance on mechanisms to disseminate and to enforce laws, regulations, policies, quality assurance measures (accreditation, EQA ...), means to protect and involve users (informed consent tools, ...)

3.6.1 Recommendations

EU and MS role

a. The EU legal framework related to health services including specific genetic services should be clarified and further developed on the basis of relevant international regulations and national laws and experiences in the respect of the legal diversity. This task would diminish potential negative effects in the practice of “law shopping” for individuals using cross-border services and foster law enforcement;

b. The European Commission and Member States should initiate the articulation of existing legal frameworks which should apply both to health services including genetic services provided through health systems and services provided by commercial companies. This is targeting regulatory texts of consumption law and medical law as well as the ethical regulation of the use of human samples and genetic data including genome-based health information developed at European and National level;

Such a task should take into account the necessity to enhance interconnections between clinical and research activities and to insert medical ethics and best practices in commercial activities related to health and genetic services.

The establishment of clear legal frameworks concerning health services including genetic services is a pre-condition to assure effective law enforcement. This theoretical work is a necessary step to achieve in order to foresee other specific measures protecting the rights and freedoms of individuals involved, for example in direct-to-consumer services. The creation of specific European guidelines should be part of this agenda.

c. The European Commission and Member States should assess and use existing responsibilities chain created at EU level to cover the responsibility of the manufacturer, of the provider or of the individual user in the damageable use of a genome-based technology (*e.g.* bad quality test) or genome-based information (*e.g.* erroneous result);

d. The Member States and the Commission should strive to rapidly ensure an effective oversight of the direct-to-consumer health and genetic services activity by executive agencies;

Then, the competent national authorities and the European Commission should regularly evaluate the respect of human rights and good practices by online providers of direct-to-consumer services and organise a system allowing national authorities to inform European citizens and other authorities about important events as, for example, the evolution of national laws concerning such services. Appropriate means to spread this information across the EU and Member States should be considered.

e. The Member States should strive to take clear position and adopt legal texts on individual genetic testing and the use genome-based information for other social usage. As a part of this task, the establishment of voluntary moratorium by insurers and employers should be welcome and serve to initiate debates which could lead to a positioning of policy-makers and, then, to a European consensus;

f. Reflections and public consultations about the ethical, legal and social issues related to the genome sequencing and the use of high-throughput technologies in clinical or research practices and their

implications for users should be promoted and taken into account in the regulatory developments of genetic testing practices;

g. The European Commission and Member States should take into account that the risks of harms in the use of wrong genome-based information, diagnosis or prognostic ones, could either result from the provision of a bad quality genome-based test or from the misinterpretation of the test results or by negligence in the organisation of the service. This has consequences in law enforcement;

h. We support the creation of incentives and European code of practice for genome-based tests' manufacturers fostering the development of products of best quality and allowing users to be sure to use a testing device guarantying accuracy and reliability of their results. These elements should be components of the European quality assurance system;

i. The characterisation of the medical act is crucial to determine enforceable laws and responsibilities attached to the prescription and the use of a non-validated test or to the misinterpretation of results. The new challenges put by the remote health services including genetic services in terms of applicable law and responsibilities should be dealt with, national legal frameworks should be developed and articulated in European collaboration;

j. Due to the complexity of certain situations efforts should be allocated to the traceability of the tests from their production, their distribution, to their provision and final use in order to foster the establishment of applicable laws and liabilities;

k. The European Commission and Member states should establish guidelines for the transfer of human biological samples for genetic testing and for interventional and non-interventional research purposes including clear disposals on the rights of individuals and obligations of professionals involved;

There is a lack of European guidelines on exchanges for scientific research purposes. A clarification would benefit all the stakeholders and foster networking of scientific collaborations. This would necessitate more coordination between competent authorities in Member States and such guidelines should include information on the prerequisites for exporting or importing samples and data,

documentation to be recorded, exchanged or transmitted by each part and other practical information to comply with for respecting good practices. It is also desirable to foster controls of these operations within Member States and ensure transparency.

l. Providers, health professionals and individuals as users should be entitled to know their rights, duties and attached responsibilities in the use of genome-based technologies, in the provision of genome-based information and with regard to the interpretation of results;

m. Health services including genetic services should be organised in such a way that the rights and freedoms of users are respected. The accessibility, the transparency and the relevance of the given information should allow users to know the available health services, their appropriateness with regard to a considered health status, their role and their rights in order that to enable them acting autonomously, freely and knowingly. Based on the products of European organisations such as the tools developed by EuroGentest, the means to inform the public, patients, vulnerable peoples and their relatives should be developed at national level;

EU role

n. The EU and the Council of Europe should clarify the system of remedies between the Court of Justice of the European Union and the European Court of Human Rights (46) with regard to the protection of users of health services including genetic services;

o. The European Commission should support the moratorium established in several Member States over the uses of genome-based tests and tests' results in the insurance and employment areas. To date, the Commission should consider the disparities within national frameworks and forbid by principle the transnational use and disclosure of genome-based information to employers and insurers due to the potential discrimination that their use could entail for individuals and their families until Member States establish their positions and/or decide to reach a European consensus. Initiatives to discuss this issue at EU level should also be considered. National legislators authorising the use of genome-based information including health data by insurers and employers should plan this possibility restrictively and justify it by legitimate purposes and guarantees;

p. Issues surrounding the protection of individual privacy and autonomy following the publications of their genome-based information should be discussed and framed at EU-level. More transparency and resources traceability should be promoted;

q. The Member States should be entitled to legitimately restrict the movement of certain tests or services on their national territory for an overriding public interest protection such as the protection of users' health, as patients or consumers, according to the rules laid down by the Treaty of Lisbon concerning the free movement of goods and services in the EU and the jurisprudence of the Court of Justice of the European Union;

MS role

r. The direct-to-consumer genome-based tests offered online should be framed and guided by the general rule "non-risk test, more freedom";

This means that the EU risk-classification of the tests, as well as their classification in terms of clinical utility, could deeply influence the national policies on the access and the use of direct-to-consumer health services including genetic services and tests results. Where a test is commonly deemed as not generating serious consequences for the individual and its family, consumers should be free to access these products under their own responsibility. Member States should develop a legal framework ensuring individuals' rights and limitations for this new market.

s. Member States should search for and consider public opinion concerning the ownership of genome-based information and property rights balancing human rights' protection and economical necessities;

Member States should consider the importance of the individual right to control the uses of their samples and personal data and envisage to develop the notions of "co-custodianship" of identified and coded samples and data, as far as they are related to the individual, and of "common resource", "public good" for the other categories of samples and data provided for research.

This could be a basis to deeper regulate the rights of the stakeholders in biotechnological research and innovation using human samples and data, increase the trust of citizens in research and improve their relationships with industry. This also puts the issues of benefit sharing and reinvestment of financial gains to the benefit of population health.

3.6.2 Best Practices

a. THE DEFINITION AND CHARACTERISATION OF THE MEDICAL ACT

As an important element to enforce laws, to establish reimbursement possibilities and to avoid conflicts of laws and jurisdictions, the definition of what is considered as being a medical act is crucial. Some areas such as e-health activities are particularly concerned.

We recommend to the EU considering and integrating the definition (76) given by the UEMS in 2009 in relevant texts.

b. CONSIDER THE WRONG DIAGNOSIS/PROGNOSIS RESULTING FROM THE USE OF A BAD QUALITY TEST

Where a quality control system will ensure the validity and utility of genome-based tests to be introduced in public health settings the probability of being confronted with wrong diagnosis or prognosis will hopefully diminish. However, the enforceable texts ensuring the rights of the individuals concerned by a prejudice in relation with the use of a bad quality or non-validated testing device offered either by public health services or by other providers such as online companies should be clarified.

The fact that users' could have the onus to prove that they have been endangered by the use of a test and the link between the damage suffered and the use of a testing device (e.g. 43 - in the frame of defective products) seems to be disproportionate due to the poor genetic literacy of ordinary people. Such onus would be, in practice, very complex and insufficiently protective of lay people. Providers having the obligation to only provide users with validated and secured products, should also have the onus to demonstrate the respect of such obligation according to national laws.

The information of users on validated genome-based technologies is thus important to allow them to make their choice and to agree to the use of a test. In such undertaking the connection of several legal frameworks appears feasible and important for such purpose.

c. CONSIDER THE WRONG DIAGNOSIS/PROGNOSIS DUE TO A MISINTERPRETATION OF TEST RESULTS

Users could be harmed by the use of misinterpreted test results which have triggered the provision of inappropriate healthcare, drugs or behavioural changes.

Whereas the misinterpretation of genetic screening results can only be supported by health professionals due to the specificities of the implementation context of such process, the misinterpretation of individual genetic testing results could not only be envisaged by the health professionals but also by the individual user. This last situation could be more and more encountered due to the offer of direct-to-consumer genetic testing and the direct provision of genome-based information. Each situation should be anticipated. Whatever the case, information and education of the public and professionals is crucial. It will increase genetic literacy and quality of health and genetic counselling; the right to a second medical opinion would reduce risks of harms related to the interpretation of test results. The laws applying to medical liability are directly concerned by the hypothesis of harms due to a misinterpretation of the results.

A last hypothesis concerning the misinterpretation of test results is the default of the genetic service. Where the genetic service has not totally provided customers with all necessary quality services responsibilities could be differently established.

d. TO CLARIFY ENFORCEABLE LAWS TO AND RESPONSIBILITIES IN HEALTH SERVICES AND SPECIFIC GENETIC SERVICES

The rights and duties of users as individuals involved in individual genetic testing or population screening should be reaffirmed by national and European laws and good practices effectively respected in health systems. This would increase trust in the use of health services using genome-based information and technologies including specific genetic services. The development of the Public Health Europe and the ERA necessitates to perform such a work and to increase the linkage with the relevant frames to claim ensuring a responsible area for individual rights in the health services.

The actual state-of-art in European and national policies and legal frameworks impacted by the possible uses of genome-based technologies and information needs to be clarified to ensure visibility of enforceable rules to the benefit of individuals' protection. The developments of genetic testing practices are evolving both within and

outside health systems, in clinics, research and on the internet, each areas being regulated by specific rules. The purpose here is to disentangle complexities due to the rapid evolution of the genomics innovations' spreading and to consistently apply health in all policies principle.

The European charter of fundamental rights and relevant existing EU directives should serve as a basis to protect users' interests in public health genomics. The European Charter of Patients' Rights could also be used in relation to genetic services. Additionally, the relevant works of other international bodies such as the Council of Europe but also the work of the WHO, the UNESCO and the OECD should be integrated in the development of the EU legal framework.

There is no European directive on the medical liability, somain which is so far exclusively regulated by national law. The following legal texts are of interest to frame health services and testing practices in several contexts and to find relevant rules concerning rights and responsibilities, particularly where users are involved in e-health activities or have been confronted to misleading services, erroneous genome-based information or to the use of a bad quality test. These texts are providing general legal provisions concerning quality aspects in the medical area but also in the consumption domain. They could be used and adapted to frame or build a new adequate framework for the variety of genetic testing activities.

i. Establish responsibilities

Responsibility of the manufacturers about the quality of the products

- The Directive 98/79/EC covering the placing on the market and the putting into service conditions for in vitro diagnosis medical devices, as the specific regulation applying to genome-based tests commercialised within the EU (141), requires some developments in order to include new state of the art in genomics, new quality criteria intended to protect the health of end users and attached responsibility of the manufacturer of genome-based test.
- The Directive 2001/95/EC on general quality of the products commercialised (134) and the Directive 85/374/EC on the approximation of the laws, regulations and administrative provisions of the Member States concerning liability for defective products (140) as amended by the Directive 1999/34/EC (135). Whereas these Directives are conceived in the consumption area

and are unspecific to medical devices, nothing excludes them from their scope. The protection of consumers' health and interests coping with defective products provided by online companies is part of the concerns raised by the development of direct-to-consumer genetic testing. Such directives could be referred to in the regulation of this domain.

Responsibility of professionals involved in health services including genetic services

The use of genome-based technologies or genome-based information without being qualified according to existing laws, not providing the relevant information or services for users' empowerment or providing inaccurate, unreliable or erroneous information should constitute professional faults with regard to national and European law. Such general requirements could be re-affirmed in EU law concerning health and genetic services. Attached responsibilities and sanctions should be clearly established by national laws and ensured by jurisdictions. In line with this concern we recommend to the EU to continue harmonising mutual recognition of competences (149) of the professionals involved in genetic testing services as an effective mean to provide cross-border quality health services and to acknowledge efforts of the Member States in education programs.

Responsibility of the individual with regards to genome-based information

Autonomy of individuals and new offers of direct-to-consumer health services and specific genetic services are triggering concerns about the individual responsibility in the use of genome-based information both within and outside of health systems. More autonomy calls for more responsibility. Individual responsibilities should be clarified and should not constitute a total disengaging of health professionals. Thus, shared responsibilities regimes should be developed.

ii. The adequacy of the EU legal frameworks for e-health activities

The adequacy of the EU legal framework on service delivering with regards to genetic e-health services

E-health is a general term encompassing both commercial (as direct-to-consumer genetic testing and advertising) and non-commercial (as

telemedicine, health information websites) computerised activities related to health. The goal here is to target which legal frameworks could be used to frame these challenging activities. Concerning commercial e-health services it seems that the European regulation of services and the free movement and delivering are relevant to build a consistent frame under the Article 57 of the TFEU, and according to existing reports (68) and the few related jurisprudence of the Court of Justice concerning medical services (27).

The adequacy of consumer law with regards to the direct-to-consumer health services including genetic services

It is important to clarify and develop (4) the regulatory framework of direct-to-consumer services in a consistent way at European and national levels in order to diminish uncertainties and ensure users' health and welfare in the respect of fundamental rights, ethics and laws.

This could be done by applying existing well known legal rules protecting consumers in the e-commerce and e-contract law.

Therefore, we recommend to the European Commission using the following Directives to assess their relevance and refer to them or eventually adapt them according to the issues raised by this particular domain:

- The Directive 2000/31/EC on certain legal aspects of information society services, in particular electronic commerce, in the internal market (Directive on e-commerce") (139);
- The Directive 2005/18/EC concerning unfair business-to-consumer commercial practices in the internal market ("Unfair Commercial Practices Directive") (138);
- The Directive 2002/58/EC concerning the processing of personal data and the protection of privacy in the electronic communications sector ("Directive on Privacy and Electronic Communications") (139), can be a useful text for the use of certain e-health devices;
- The Directive 97/7/EC on the protection of consumers in respect of distance contracts (136);
- The Directive 93/13/EC on unfair terms in consumer contracts (142).

We fully support the policy options proposed by the EU Parliament STOA concerning regulatory needs for online genetic services, particularly those concerning the EU role, the regulatory developments proposed,

the empowerment of the EMA as a supervisory authority and the proposal to create a European Code of Practice.

The recent proposal from the European Commission (72) on a Regulation for an optional European contract law to foster cross-border trade and protection of consumers could have a certain added value for e-contracts in direct-to-consumer genetic testing. Considering certain limitations (72-Para.28), this text could also be envisaged with regard to cross-border contracts of health-related services.

iv. Other European regulations, e-health and direct-to-consumer health services including genetic services

We support the clarification of the applicability of the Additional Protocol to the Council of Europe Convention on Human Rights and Biomedicine concerning Genetic Testing for Health Purposes to the e-health sector and the direct-to-consumer health services. Additionally, the direct-to-consumer genetic testing market should respect the OECD Guidelines on Human Biobanks and genetic Research Databases, the OECD Recommendations on Quality Assurance in Molecular Genetic testing as requisites to protect customers and secure online offers.

3.7 Link to / Provide Care

Two aspects can be envisioned (broad interpretation) relating respectively to the practice and to the organisation of care:

- a) Knowledge transfer to clinicians and application of practice guidelines
- b) "Translation" of new practices into the required organisational changes (e.g. redefining roles and responsibilities of various professionals...) and implementation of these changes (e.g. planning adequate resources, negotiations...)

3.7.1 Recommendations

EU and MS role

a. Policy-makers have the responsibility to ensure the integration of only "proof-tested" genetic testing devices into public health systems. The analytical and clinical validity and utility should be assessed in new quality schemes before introducing any health-related genome-based technology inside the internal market and health systems;

The establishment of a quality assurance and quality control system adapted to the risks of research innovations and their uses conditions is an urgent need to ensure their free movement, to avoid the premature marketing of genome-based tests in the internal market and to ensure *a priori*-protection of individuals.

This would help member states to organise national quality systems in a coordinated approach and finally benefit to the science-society confident relationship enhancing the trust of users in health services and genetic services. Such European quality framework would also diminish the use by the Member States of their legitimate right to restrict the free movement, on their national territory, of products endangering population health.

b. The creation of specific practical tools such as a European label, or quality certification of the testing devices according to accepted norms should be considered. The creation of a publicly available online registry that would compile authorised genome-based technologies introduced, distributed and used for health purposes within the EU should be envisaged as a tool to inform users;

c. The European Commission and the Member States should also envisage creating a licence for the providers of genome-based information and technologies. This should particularly aim the online providers of health services including genetic services;

d. It is necessary to condition the use of clinical useful genome-based technologies to a medical supervision requiring a medical prescription, offering health counselling including appropriate genetic counselling and other efficient supports to the benefit of the individuals and their relatives;

e. The fundamental rights and freedom of individuals involved in individual genetic testing or population genetic screening for health purposes should be clarified and reaffirmed at the EU level in a consistent way using existing relevant texts. The European Commission should create an integrated matrix of relevant international texts protecting users' rights engaged in health services including genetic services, in testing or screening, for clinical and research purposes including online health services including genetic services. Cooperation with national authorities and relevant international bodies to create an integrated corpus of rules should be intensified;

f. Pre-test and post-test health counselling, including genetic counselling should be recognised as a right at EU level;

g. The EU should explore the possibility of creating a European guide for consent to individual genetic testing and population genetic screening. Such a guide would have added value for national policy-makers, health professionals, law enforcement and could be conceived as an incentive for further regulations;

This guide should include parts dedicated to international clinical and scientific research, health and genetic counselling practice, international transfers of samples and/or data for testing abroad as well as the management of incidental findings, the re-contacting process and the return of results, the information about attached risks and implications of getting genome-based information. This guide should be designed as providing minimal information about agreed good practices in the consent process to a genome-based test. It should be developed in cooperation with all stakeholders and should be flexible enough to be widely voluntarily used and adapted to national and individual contexts by health professionals.

h. The right to know/not to know the test results, whether individual or populational, should be respected and embodied within the legal frameworks related to clinical and research practices. The exercise of the right not to know should not be penalised in terms of access to relevant available healthcare, treatment, diagnosis or prevention means; limits of these rights should be clearly stated;

i. Health professionals should be trained to use genome-based tests in an appropriate way; respecting proportionality. High-throughput technologies should only be used where there are clues to get important findings for the health of the individual. Sequencing technologies, particularly concerning vulnerable people such as children or ethnics groups should be medically and ethically justified;

j. The possible involvement of the users of genetic services in research projects using their sample and/or their personal health data should be part of the informed consent process and respect the relevant ethical and legal applicable rules;

Generally, we advise to use the OECD Guidelines on human biobanks and genetic research databases as a benchmark for protecting individuals' interests and implement good practices. However,

Member States should be encouraged to adopt specific legal texts on biobanks and genetic research databases including the protection of individuals' rights.

A particular attention should be paid to the consent given online to commercial entities due to the inadequacy of consent processes. The fact that the consent forms are not explicit concerning the storage and the uses of biological samples and data gathered at the occasion of a test, for research and/or other purposes such as massive sharing, commercialisation, constitute a real risk of misleading consumers. The forms of consent and attached terms of services should be assessed by the national authorities from the States where the provider is established.

k. Before performing the test, users and their family should be informed about the possibility and modalities of a re-contact. National policy-makers should identify the actors and establish clear procedures for doing so;

m. The disclosure of the results to the family members, to other researchers or health institutions or other third parties, should be discussed during informed consent and individuals should be free, according to national laws, to accept and/or refuse certain disclosures. The means to be used in this particular communication process should also be subject to the consent of the individual. The individual should have the possibility to entitle his physician to take an appropriate decision about the disclosure. The decision of the physician should be explained and agreed by the individual. The development of guidelines on the disclosure issues should be promoted;

l. The development of clear guidelines on the protection of vulnerable people involved in genetic testing or screening process should be promoted;

Particular focus should be put on the clarification of the appropriateness of consent process including the modalities to provide adequate information, on the effects of children's assent and dissent, as well as on the follow-up of the child. The evolution of the rights of the child and the possibility and modalities of a re-contacting process once he/she will reach the age of majority should be explained to his/her legal representatives.

3.7.2 Best Practices

a. CREATE AN INTEGRATED QUALITY ASSURANCE SYSTEM FOR HEALTH-RELATED GENOME-BASED TECHNOLOGIES: VISIBLE PREVENTIVE MEASURES FOR USERS

This quality filter shall be the basis of the introduction and the free movement of genome-based technologies to be used within health systems in the EU. Diagnostic tests but also predictive tests and tests used in population screenings should have satisfied high quality level criteria before entering routine practices. Other health genome-based technologies should be developed and maintained in the research area. Identification and classification of health technologies (and those claimed to be) is part of this task. The participation of the public is desirable, particularly on the introduction of new technologies in health practices (high-throughput technologies; genome-wide sequencing). The reassessment of genetic technologies already used and their withdrawal with regards to the gathering of certain clues questioning their reliability or their use should also be envisaged. Reflexions about the possibilities to create EU labels for the tests should continue and could be inspired by the activity of the FDA. Users should be empowered to recognise labels and other “trust marks”.

b. ENSURE EQUITY IN THE ACCESS TO HEALTH SERVICES

Individuals should have the right to access to all available health services including specific genetic services in the public health framework in the respect of equity, autonomy, non-discrimination principle and justice. In line with the national and international recommendations, literature (91) and the spirit of the OMS Tallin Charter (175) of 2008, the development of public health genomic services should be organised in such a way that individuals placed in the same health situation can benefit from the same optimal health genome-based technology and related services, prevention means, treatments and healthcare. This would necessitate developing health and research infrastructures in an organised and dynamic network that would provide high quality services and reduce health inequalities such as geographical barriers. E-health added value for diminishing health inequalities must be taken into account. The reimbursement issue is also important for equity. Availability in access to health services and specific genetic services should be ensured at

national level and coordinated by national and European authorities in a collaborative approach. Adaptation of health services and capacity building in terms of genetic service should be part of the agenda of policy-makers. The cost of such adaptation should be assessed.

The access to direct-to-consumer genome-based tests and home-tests

The issue debated here is the control of the free access to genome-based technologies and genome-based information via commercial websites in order to protect users' interests against irresponsible or endangering services and to defend the image of modern medicine. According to the recognised lack of regulation, the lack of quality of certain websites and the potential harms which could result from these services, the scope of the autonomy principle and the role of public authorities have been put into question. For example France has forbidden (81-art.6, 84-art.L1133-4-1; 84-art.226-28-1) the access to genome-based information outside established health system and thus access to direct-to-consumer genetic services. Considering the possibilities associated to internet, it seems hard to forbid access to these services. It seems to be more feasible to regulate the quality and the use of the genome-based information gathered by using direct-to-consumer genetic services than only acting on the access itself restricting users' freedoms. Work on access conditions is important but this should be balanced by the regulation of the uses of genome-based technologies and information. Whatever the regulation, the empowerment of users and the promotion of professional standards for direct-to-consumer health services including genetic services (e.g. 96) should be part of policy development agenda. The systematic consultation and prescription of health-related tests by a physician and the availability of health counselling including genetic counselling should be considered as highly recommendable for assisting users according to national law and good practices.

c. THE NECESSARY INDIVIDUALISED MEDICAL SUPERVISION

The access to genome-based technologies available for several purposes should be framed and supervised by competent physicians. Communication and a shared decision-making process intended to respond to the health needs of an individual, a family or a population and to involve individuals in health activities using genome-based technologies and information are essential for these categories of test. Qualified health professionals should be involved and represent the

keystone of the testing or screening process. Everybody should have the right to an individual consultation. The medical supervision should be materialised by the provision of a medical prescription allowing users to know that the use of a genome-based test is medically and scientifically grounded and that it could be beneficent for them. A prescription should be consented and granted after the provision of sufficient information about the options, the testing process and the implications of the tests for the individual, his relatives and his social environment. Where necessary the medical supervision of the testing process should continue after performing the test, in a tailored on-going program.

Therefore, we urge policy-makers

- to highlight the necessary medical supervision of genetic testing and screening processes;
- to fix the rules of the mandatory medical prescriptions according to the risks attached to a test and consider the impact of the computerisation of the prescriptions.

d. PRIOR INFORMED CONSENT TO GENETIC TESTING AND SCREENING

i. Towards more EU coordination: A European guide for the practice of consent to the use of health genome-based technologies and information?

The principle of informed consent to individual genetic testing and population screening is embodied in the Member States' national laws in several ways. Due to the international nature of healthcare provision and research activities, there is a need to find an appropriate procedure for informed consent in both clinical and research areas (11-p.9), which would ensure individual's autonomy and privacy protection in genetic testing and screening. This initiative could be envisaged at EU level. The development of guidelines and the development of common tools fostering the coordination between health systems in the EU with regards to genetic testing and screening would create more transparency between stakeholders and more certainty for users.

We suggest that the stakeholders in public health genomics jointly work, at the EU level, on the kind of tests that would necessitate a specific consent in order to initiate the establishment of a European guide ensuring best practices in the provision of accurate and transparent information to users and a minimal protection of their fundamental rights. This would include an integrated view of clinical and research

activities, of samples and data, and would foster the excellence of research in Europe and the provision of responsible transnational health services including specific genetic services.

The use of such a guide should be encouraged in the provision of cross-border health services and researches funded by the EU. This European guide on consent should be consensual, available in all EU official languages, sufficiently concise and flexible according to the different purposes of tests and designed as not restricting the competence of national authorities to embody specific mentions according to their proper ethical tradition and national laws. A European standard of consent form could be put under study in collaboration with representatives of national authorities and experts groups in an interdisciplinary way. In such perspectives, we recommend using the informed consent templates developed by the DG Research of the Commission, those developed by the WHO (179) and the common criteria used in national regulations.

ii. Consent to genetic testing or screening and minimal pre-test information to be provided

There is a wide range of individual genetic testing for health-related purposes. Some tests are in development and others are already used in healthcare routine. Whatever the test, the informed consent process should be designed as a participative process in which individuals can discuss with the health professional, put questions, explain their expectations, their concerns and be informed. The purpose of providing information is to assist individuals in the understanding of the process, the benefits, limitations and the implications of each available relevant genome-based test and possible outcomes. Clarity and quality of information is crucial. The information provided should not be too technical. It is important to use adequate formats to inform individuals, to ensure their understanding and to let them free to express their will to obtain complementary information before making a choice. In order to initiate the coordination of national rules and practices at EU level and the establishment of minimal standards for informed consent in genetic testing we suggest that the following information is taken into account in the respect of human rights, national laws and other ethical standards.

Therefore, before obtaining consent, the individual should be appropriately informed in clear and simple terms about:

- the background and effect of the condition:
 - the personal or familial background necessitating the recourse to a genome-based test;
 - the health condition of the subject and distinction between being a carrier and having the condition;
 - in case of diagnostic testing, the nature of the disease, its possible hereditary feature and implications for relatives;
- the opportunity to have a genome-based test;
- the access to health counselling, including genetic counselling;
- the type of genome-based test and its accuracy:
 - the purpose of the test, test for diagnostic purpose, for prognostic or prevention purposes, for pharmacogenomics, nutrigenomics, for research etc.;
 - the existence of a test's approval by competent authority in terms of clinical and analytical validity, clinical utility;
 - testing limitations due to human biological factors or laboratory errors;
 - the possibility to perform another test and the justification of such possibility;
- the benefits and risks of the testing process:
 - the existence of prevention means or of an available treatment;
 - explanation of possible results including false positive and false negative results, the physical and emotional risks of the procedure as well as psychosocial implications of having test and the potential implications for the relatives;
- the test procedure:
 - the kind of sample to be provided;
 - the kind of health data or other records to be collected and used;
 - the uses of samples and data in the clinical and/or research context including the possible participation in clinical trials, in a biobank or a database;
 - the storage of sample, health data and other genome-based information records and its duration;
 - the name and address of the laboratory performing the test and information about a contact point;

- information about the persons entitled to potentially access the sample and information.
- the foreseeable secondary usage of biological material and data;
 - from clinics to research
 - from research to clinics
 - in research
- the rights of individual and the importance of a shared decision-making process:
 - autonomy and self-determination;
 - the right to withdraw consent and to refuse the entire procedure or other treatments;
 - the right to oppose to any personal health data processing;
 - the right to access to samples and data and related possibilities;
 - the right to know/not to know about the results and possible consequences;
- the protection of privacy and confidentiality:
 - security measures;
 - condition of the samples and data to be used according to ICH definitions (104) of identified, coded, anonymised and anonymous samples and data;
 - possibilities and context of re-contacting the person when the data are coded or identified as well as modalities to renew consent;
- the cost of testing and reimbursement possibilities;
- the post-test situation:
 - the waiting time for the results and the procedure to get test results;
 - access to health counselling, including genetic counselling for individuals and their families and additional support like experts, patient associations or other representative groups;
 - the fate of the sample and associated data;
- the possibilities to disclose tests results to the relatives, other researchers nationally or abroad, the administration, insurers and employers, according to the will of the individual and national law;
- other sources of information about genetic testing, genetics, genomics and health.

More details concerning consent can be found on specific guidelines such as those adopted by the European NuGO concerning studies in the field of nutrigenomics testing (74) and in other documents tackling more

specific issues such as those developed by UNESCO (e.g. 164) or other publications (e.g. 113; 92; 3).

Whatever the content and the scope of informed consent is, it should be recorded at least during the duration of the storage of samples and data so that the health professionals can comply with the ethical and legal rules requiring the provision of consent forms, as at the occasion of national authorities' controls or in ethical approval procedures. In the same way, objections of individuals should also have been recorded. This condition should be clearly reinforced at the EU level.

Concerning the consent process in the particular context of online activities we recommend that the direct-to-consumer genetic testing services

- shall not reduce informed consent process to the simple signature of a consent form;
- respect the minimal standards of information to provide according to the present recommendations or applicable national laws and guidelines;
- offer independent pre-test and post-test health counselling, including genetic counselling in an appropriated format respecting individual's needs in terms of language for example. Among others, the counselling should be performed face-to-face and should allow actual interaction between counsellors and counselees. This offer should be clearly mentioned on the websites;
- design clear consent forms including all activities of storage and use of provided biological material and data and particularly research activities. The opt-out methods does not appear to be adequate in the direct-to-consumer genetic testing context;
- establish procedures easily understandable and available to allow users to exercise their right to withdraw their consent at any time and free of charge, to manage the fate of their sample and data and eventually ask for their destruction when they are identifiable;
- establish procedures intended to guaranty the adulthood of the consumers in the respect of confidentiality and without prejudice to their right to privacy;
- use a specific clause in their informed consent form stipulating that the individual confirms to have fully read and understood terms of services and information;
- record and report errors and adverse events related to their services to competent authorities according to applicable national law.

iii. Consent to population genetic screening

Population genetic screening as a part of healthcare routine

Some population genetic screenings are already systematically used in clinical practice. Whatever the situation, individual informed consent to screening is required. Refusals from individuals should be seen as a part of their autonomy and self-determination right and considered under their own responsibility. The general public should be informed on the rationale of screening programs and their views on controversial genetic screenings should be sought and respected.

Population genetic screening for research purposes

This targets genomic and genetic studies on identifiable population and small groups of persons as families. Population genetic screening may include research based around cohorts, biobanks or disease conditions. Informed consent to these studies should be given individually. Yet, it could also be planned to complement these individual consents with community consent. This proposal issued recently (15) requires community consultation of the target population and finally a community consent which could address issues which are not addressed during individual informed consent process, foster communication about genetics within groups and families. Yet, the feasibility and the new ethical, legal and social aspects of this practice necessitate further studies.

iv. Consent and participation in a human biobanks or genetic research databases and the minimal pre-test information to be provided

Depending on the nature of the research biobank or database and the characteristics of the material, in addition to the above described information to provide to individuals involved in a genetic testing process, they should be specifically informed (129) about

- the purpose of the human biobank and genetic research databases and the importance of the research for the condition of the participant;
- the foreseeable implications, benefits and risks of the participation;
- the unforeseeable implications, risks and benefits (e.g. possibility of incidental findings);

- the identification and location of the biobank or the database as well as a permanent contact point that could be used to exercise participant's rights;
- the policy with respect to benefit sharing;
- the policy and means for ongoing communication with participants;
- the policy of access to human biological materials and data;
- the policy with regards to the feedback of results to the participants;
- the policy with respect to re-contact and the facts and purposes for which such re-contact will be undertaken;
- the policy applicable to the storage and use of samples and data of participants in the event they become incapacitated or die;
- the participant right to withdraw, its modalities, consequences and how exercising this right;
- the policy with regards to intellectual property and the commercialisation of the stored resources.

v. The right not to know

The recognition of the right not to know by national and European legislators should be considered. The right not to know is the hidden face of the right to know; these two rights are inseparable and are both part of the individual autonomy and the respect of privacy. The existence of this right should be communicated to individuals during informed consent process, before performing the test. The provision of adequate and comprehensive information on the meaning and consequences of potential results for their health and for third parties is essential to allow them to use their right not to know. After the test and before the communication of the results, the will of the individual with regard to the exercise of its right not to know should be checked again in order to consider possible changes of mind of the individual concerned. This right not to know should be recognised for all the persons concerned by a result of a genome-based test and conceived in an opt-out approach (130-para. 4.14 and annotation 46). According to several practical difficulties encountered by clinicians and physicians, Member States should develop the practical modalities attached to the exercise of this right.

vi. Conflicting situations: balancing autonomy and beneficence

There are situations where the user's autonomous decision conflicts with the physician's duty of beneficence and raises an important ethical issue. This could be the case at the time to choose a test or to communicate or disclose (72-Expl.Rep.para.7.1.6) certain health information, where the individual insists against the advices of the physician. Generally, the physician should respect the patient's decisions even while trying to convince the patient otherwise.

Limited restrictions (31-art.10.3; 30-art.16.4) to the right to know and not to know the results of the test could be foreseen by national legislations in the respect of the health benefit (*e.g.* clinical utility) and proportionality. There is no international consensus (166-para.43) on exceptional cases, but efforts should be undertaken in that sense. Advice from relevant ethical bodies should be opened to physicians. Member States should develop their proper positions consulting the stakeholders and the public.

e. THE RIGHT TO AMEND AND TO WITHDRAW CONSENT

Individuals or their legal representatives should have the right to amend or withdraw the given consent concerning genetic testing, population screening and participation in a human biobank and genetic research database at any time and without any penalty. This also covers situations where the samples and/or data have been transferred abroad. Therefore, procedures should be in place to manage these changes and to make sure that potential external partner (*e.g.* international research projects) can be contacted, and that they fully comply with the wish to withdraw (since it may be out of the initial jurisdiction).

The right to amend a given consent is in favour of the individual's autonomy. Before performing the test, researchers and physicians should respect the individual's will to restrict the use of their samples and data.

The right to withdraw consent only aims the case where identified samples and data are at stake. The individual should have the right to unlink, anonymise or obliterate their samples or data from any record or repository. The modalities for exercising these rights should be clearly explained to individuals during informed consent process. If the individual does not expressly require the destruction of its samples and data, the professional should be authorised to retain the materials unlinked, anonymously. Exercising this right, the professional should explain the permanent feature of certain modifications such as anonymisation, the alternatives of obliteration as well as the importance

of keeping samples and data anonymised within a research biobank or database.

f. DEPARTING FROM INFORMED CONSENT TO PERFORM A GENOME-BASED TEST

Exceptions to the informed consent principle to use or re-use samples and/or data extracted from a medical genome-based test should be clarified at the national and European levels. In order to protect human rights and fundamental freedoms, limitations to the principle of consent and confidentiality may only be prescribed by law, for compelling reasons within the bounds of public international law and the international law of human rights (166-para.43). The role of ethics committees is important. Users should know about these exceptional situations.

g. THE RIGHT TO ADEQUATE PRE- AND POST-TEST GENETIC COUNSELLING

The increasing number of available options in the use of medical genome-based technologies underlines the importance of genetic counselling and personalised procedures. Such a right should be integrated in relevant national and European texts.

We recommend that:

- the adequacy of genetic counselling is assessed case-by-case;
- genetic counselling must be tailored to the needs of the individual and the family;
- pre-test and overall post-test genetic counselling are emphasised in the relevant regulatory and guidelines development;
- practical tools to provide relevant information to counselees are developed;
- physicians and specialists as well as genetic counsellors should be educated and entitled to provide pre-test and post-test counselling to individuals and their families;
- face-to-face counselling is mandatory;
- cultural specificities are respected (e.g. involvement of a religious advisor);
- national and European guidelines (e.g. 60;62) on genetic counselling in genetic testing and screening should be supported.

It is important that the individual having performed a health-related genome-based test or screening has access to post-test counselling

which explains the results. This represents medical supervision of testing and screening processes.

The organisation of health services should include genetic counselling services which should be easily available. Such services are not yet available everywhere. Identification of the health technologies necessitating genetic counselling should be achieved.

h. THE PROTECTION OF VULNERABLE PEOPLE INVOLVED IN INDIVIDUAL GENETIC TESTING OR POPULATION SCREENING

The limited autonomy and self-determination of the vulnerable people urge to consider the benefits, risks and alternatives of participating in genetic testing in order to act proportionally, in the best interest of the individual. The practice of genetic testing must not be substituted to other efficient prevention or diagnosis methods.

i. Appreciating the opportunity of performing a genome-based test on children

Providers/prescribers of genetic testing involving children should follow the relevant international texts such as the Convention of Ottawa on child health, the Convention of Oviedo and its additional protocols (31;29;30), and the national laws. They should also respect the national, international laws and ethical guidelines concerning research on human beings and, when applicable, good practices in clinical trials such as the Council of Europe European Convention on the Exercise of Children's Rights (36), the EU Directive 2001/20/EC and related good practices including some involvement of genetics (148).

However, there is a need to create specific guidelines on the involvement of children in genetic testing and screening for research purposes and strive to coordinate rules and good practices at EU level according to available tests. A public health approach should be integrated. National and EU decision-makers could inspire from experiences reported by European stakeholders (patient associations, professional organisations) but also from outside the EU (*e.g.* 22) to develop proper guidelines clarifying children's rights and their involvement modalities.

In this task, the following elements should be considered:

- (1) Alternatives to genome-based tests and the best interest of the child;
- (2) Kinds of genome-based tests available and implications for the child;
- (3) Existence of preventive or other therapeutic measures are available;
- (4) Risk management and role of the legal representatives or trusty relative (genetic condition with paediatric onset / adult onset);
- (5) Expression means for the child and value of their expressed will;
- (6) The balance between the best interest of the child and health interests of third persons or parties;
- (7) Incidental findings;
- (8) Recording of genome-based information;
- (9) Ongoing and involvement of the child once he reaches maturity or majority age.

ii. Consent and individuals as vulnerable persons

Generally, the consent of vulnerable individual to the testing process should be expressed, on its behalf, by their legal representatives.

Concerning certain vulnerable individuals and particularly the children, it should also be possible to obtain their assent but the modalities and effects of such assent are unclear.

The EU and Member States should fix a common definition of “vulnerable people” and work on best practices to involve them, and particularly children, in health services and specific genetic services. In this respect, the issue of responsibilities should also be tackled.

iii. Consent and groups as vulnerable communities

The main concern here is to respect the culture and beliefs of the minorities involved in clinical genetics and research with regards to the uses of genome-based information. Specific attention should be paid to not force them to undertake a test. After the test, these populations should be protected from any discrimination and stigmatisation based on testing results. New tools and community approaches could be envisaged.

iv. A specific protection requiring specific means in informed consent process

Particular attention should be paid to the methodology used to provide information and to obtain consent. Various difficulties could appear according to population or individual needs of participants. For example, to provide necessary information to illiterate or quasi-illiterate

individuals, adequate supports to provide the best available information as written documents or videos could be of high interest to assist professionals (180). Member States should provide sufficient resources to take in charge these particular needs in the respect of ethics and human rights. Specific support for the parents of a child diagnosed as affected by a serious disease should also be planned in order to provide them with a tailored procedural and social assistance to face consequences of having a positive test result engaging the health of their children.

i. THE PRIVACY PROTECTION

Privacy should be ensured throughout the testing processes and the existence of the collection of samples and data. There are mainly two elements of privacy protection, the health data protection and the professionals' duty of confidentiality in public and private health services. Both are jeopardised by new challenges in genomics.

Concerning data protection, health and research infrastructures must have physical and technical security mechanisms preventing unauthorised access, unwanted loss or alteration of data. These mechanisms should be regularly tested by the operators and by national authorities in order to update systems. Cloud computing techniques as well as data sharing activities are also developing areas in which security systems should be developed (e.g. PETs etc.) in order to ensure privacy and data protection in data transfer and processing inside and outside the EU. Access to biobanks or genetic databases by researchers should be ruled by an agreement on the protection of privacy and confidentiality signed by the partners. The respect of this agreement should be ensured by appropriate internal or external oversight.

Health professionals and researchers are free to decide about the coding of materials in respect of national laws and ethical approval. This flexibility is essential for clinical and research needs. Users should know the inherent limits to the use of identified and anonymous samples and data. We support the coding of samples and data for clinical and research operations as well as the development of interoperability systems and practical tools ensuring a high level of privacy protection.

As an ethical and legal issue related to the privacy and rights over genome-based information it has been argued that the "data subject" concept could be put into question due to the hereditary feature of certain information which is of shared value for a family. Should the data subject only be the individual from which sample and data have been processed or should it be extended to family? Considering the rights

attached to the data subject and the complexity that would trigger such extension, it is desirable to not modify this notion and to keep the individual definition of “data subject”.

3.8 Assure Competent Workforce

- Training of a range of professionals (as presented at the meeting)
- Guidance regarding core competencies and communication skills (link with users’ information needs...)

3.8.1 Recommendations

EU and MS role

- a. Providers of health services involving genomics/genetics and operators of biobanks and genetic databases should plan accessible and visible complaint systems intended to gather, record and process claims from individuals;
- b. Non-judicial methods of dispute resolution should be privileged and discussion with responsible professionals involved should always be fostered;
- c. Access to justice and legal remedies should be opened to individuals but also to groups of individuals. Member States should consider the possibility to open class actions in health and genetics areas;
- d. The European courts and national jurisdictions should be empowered to deal with relevant requests from users of health services including genetic services. A clarification of conferred competences and coordination between the Court of Justice of the EU and the European Court of Human rights should be considered.

3.8.2 Best Practices

a. OPEN THE PATHWAYS FOR ENSURING USERS' RIGHTS

i. Health services' internal means

As a part of the quality aspects in the reorganisation of health services, users should be aware that several means exist for them to express their claims and to assure the respect of their rights and freedoms, that are available and easily accessible. The development of single contact points for legal affairs could be envisaged as an efficient mean to ensure clarity in the organisation of such *a posteriori* individuals' protection means. A unique contact point could be particularly interesting.

Independent legal advisors should be available for individuals to inform and assist individuals in their démarche.

Internal legal services devoted to the gathering, processing and recording of claims related to the provided services should be developed. Their independence should be guaranteed.

For capacity building in terms of remedy, policy-makers should consider the health services provided by public and private actors including specific genetic services, the biobanks infrastructures and the genetic databases.

ii. Health services' external means

Other existing means which could be used by individuals to stand for their rights should be identified and opened.

b. TO PRIVILEGE NON-JUDICIAL METHODS OF DISPUTE RESOLUTION

Lawsuits are often costly and long. Most of the claims from individuals could be dealt first inside of the services concerned by discussing and searching for compromise. This should also apply to insurers and employers. Where no reasonable compromise can be found, the recourse to a legal remedy could be planned as a second attempt.

3.9 Evaluate

Again, two types of evaluation can be thought of here (broad interpretation):

- a) Evaluation of the implementation and use of the emerging genome-based technologies and information (and ensuing interventions) :
 - Guidance on a posterior health impact assessment

b) Evaluation of the implementation of different types of policies :

- Guidance on policy evaluation

3.9.1 Recommendations

- a. An evaluation schemes for the genetic service by the users should be developed; practical tools of direct expression from individuals should be used;
- b. The evolution of the demand for genetic services with regards to the evolution of the production of innovative devices should be evaluated;
- c. The evolution of the health literacy of the European citizens in genetics and genomics should be evaluated;
- d. The evolution of the impact of genetic technologies and information in health services quality should be evaluated;
- e. The evolution of the impact of genome-based technologies and genome-based information on medical practices should be evaluated;
- f. The participation of users and the public in the building of public health genomics and its impact should be evaluated;
- g. The provision of cross-border health services and specific genetic services should be evaluated;
- h. Regulatory impact on health services, including on direct-to-consumer genetic services should be evaluated considering both legal evolutions and the implementation of good practices recommendations.

3.9.2 Best Practices

Establishing public health policy heralds intense work in long-term. The evaluation of the developments related to this quest should incorporate individuals' views on their experiences, needs, concerns, hopes and solutions they would propose. These *a posteriori* evaluations oriented towards individuals, users or not of health services, should be the

necessary complement of the participation processes in policy developments. They could be achieved alternatively by independent institutional organisations but also by the users themselves and the general public.

a. DEVELOP INTERNAL PRACTICES OF USERS' DIRECT CONSULTATION

Individuals using health services involving genome-based information should be solicited by professionals to express their views on the quality, utility and possible improvements of the services they asked for or are participating in.

Their participation should be used internally and reported to competent authorities.

The practice of satisfaction questionnaires could be envisaged in such contexts.

b. DEVELOP EXTERNAL MEANS OF DIRECT EXPRESSION FOR USERS AND CITIZENS

This is particularly targeting the possibility to develop recognised e-participation tools related to health services including genetic services, e-health services and online genome-based services.

Additionally to the practice of satisfaction questionnaires which should also apply to direct-to-consumer activities, other means to gather and share users and public questioning and remarks could be put in place, either on independent websites or on the websites of the service providers, such as part of a website dedicated to frequent asked questions (FAQ).

The use and interest of internet forum should be evaluated.

Innovative means to record the various experiences of health services could be developed in the internet area.

The respect of privacy in the gathering of users' expressions shall be ensured.

Professionals should consider such activity as a part of the transparency requirement.

4. Technical Progress

4.1. Overview of activities during the period covered in the interim report (November 2010 – November 2011)

4.1.1. Internal WP Skype meeting

Date: 12 January 2011

Participants: Inserm / SDU Teams

Agenda and decisions:

- Modifications of the manual for the prototype of “PHGEN Guidance Assessment Tool”
- Dates for finalising the manual and send it around
- Definition of users: Ethics committees →policy level
- INSERM /SDU to evaluate 16 guidelines
- Number of assessors INSERM/SDU
- Partners’ involvement - Tasks – To scan the remaining user guidelines
- Agreement in Sevilla about the two WP members, who wanted to participate and suggested something?
- Collection of guidelines and other work: EU products versus scientific articles
- Genetic testing versus genetic screening - definition part
- Quantitative / qualitative rating

Date: 21 February 2011

Participants:

- Anne Cambon-Thomsen
- Arja R. Aro
- Arndt Bialobrzeski
- Christina Mischorr-Boch
- Gauthier Chassang
- Ilona Koupil
- Joerg T. Epplen

Apologies from:

- Alastair Kent
- Alexander Haselberger
- Peter Dabrock
- Tobias Schulte in den Baeumen

Agenda and decisions:

- Sharing of the work in the WP for scans
- Mid-time feedback on the manual (including the remarks of assessors on difficulties they met so far, possible enhancement not on the structure

but on explanation of items etc.; the aim could be to enhance the presentation according to reactions without touching the tool)

- Partners views on the form/structure of PHGEN Guidelines

- Sharing of the work for overview of compiled texts

- The sharing itself: The group agreed the task division for covering all relevant compiled texts. Some compiled texts have been left aside due to their poor value for identifying gaps from the WP Use point of view. Some suggestions for the absent members have been established and will be communicated to them for approval. An updated table of the distribution of tasks will also be sent to each member.
- Precisions on the work to be done: The purpose of the distribution of tasks is to point out the gaps within existing texts from users of genome-based information and technologies point of view in order to extract clear items to work on and make guidelines. The members of the WP received a list of general issues (not limitative) that could be used to assess the texts for having a consistent approach within the WP Use group (attached reminder).

In this context users have been defined previously at different levels:

- Policy maker level, incl. institutional level, ethics committees
- Professional level (Professionals as users – both individual professionals and their organisations)
- Lay level, incl. non government organisations (incl. patients, citizen organisations), (daily) media, incl. internet.

By assessing the texts the definition of users should be contextualised with the content of the texts.

- Feedback date of the results: The group suggested to share results on the March 10 2011 and, for those who have impossibility to meet that date, on March 20 2011. The aim is to have a common view on the identified gaps before the Budapest meeting.

- Listing of the difficulties met so far during assessments performed with the WP Use Guideline Assessment Tool and linked Manual (SDU and Inserm):

- Concerning the list of texts shared between Inserm and SDU for the assessments, the EC 25 Recommendations and the Independent Expert Group Report of 2004 are part of the same work, so they have to be merged in one assessment. So the list is now of 16 texts.
- Members of the group involved in the use of this tool agreed to establish the following list in order to make future improvements on the

assessment's materials. Christina and Gauthier will discuss more deeply these issues. The participation of the members is open.

- General issues: the use of background documents from the listed texts should be clarified.
- Concerning particularly the Part.1 of the manual, the assessors:
 - Have met problems for understanding the definitions and differences between the "target users" (cf. Manual, item B.c) and the "target group" (cf. Manual, item A.c, B.b) *Proposal*: Clarify introductive paragraphs of these items.
 - Have felt difficulties to make the difference between "users" as defined in Part.1 and "users" as defined in Part.2 that appear differently. *Proposal*: Clarify the difference in the general introduction of the manual or change word in one of the parts.
- Concerning particularly the Part.2 of the manual, the assessors:
 - Have difficulties for understanding the item concerning the users involvement in law enforcement (cf. Manual, item J.a) and the item concerning health monitoring (cf. item H.a). *Proposal*: Clarify introductions paragraphs of these items but keep them for ongoing assessments of the 16 texts.
 - Have difficulties for assessing general texts in the context of items mentioning specifically the realm of genomics and genetics; *Proposal*: Deal with this issue in the general introduction of the Manual and make modifications whenever necessary.
- Modifications that would have consequences on the structure of the tool and manual should be implemented after the ending of the assessments performed on the 16 texts. All the modifications will be communicated to the whole WP members.
- Other difficulties emerged from the nature of the texts, some are reports, others are statements and there are also guidelines.
- Partners other than SDU and Inserm are welcome to give their views on the above points.

- First views on the form/structure of the final PHGEN II Guidelines

- The group proposed to contact the coordination team for guidance on:
 - The form/structure of the work they are expecting from our WP, we would need more guidance on how to address and present items and guidelines

- Case studies: how to use them in the context of WPs and particularly in the Use one? Is there a specific format for documenting the case studies from the WP Use point of view?
- The above issues could also be discussed in Budapest.

- Other points:

- ✓ The group decided to establish a table with the arriving dates and departs from Budapest in order to plan one hour for a WP Use Workshop.
- ✓ The documents concerning our WP in the Interim Report sent to the Maastricht group for being included in the project interim report to the European Commission will be sent to everybody in the WP.
- ✓ Anne C-T will ask the coordinating team about the date when they will show the project interim report with partners.

Date: 9 June 2011

Participants: Inserm / SDU Teams

Agenda and decisions:

- Work plan for the USE WP. Christina is making a draft (separate document).
- Holiday plan for USE WP
- Current and ongoing work during June and July work: The structure and content of the gaps and aspects in the inventory tables.
- Publication plan (Skype meeting in the beginning of September)
 - Articles (2)
 - Method /ethics (individual ethics vs. ph ethics)
- Additional items discussed
 - Participation in steering committee meeting
 - Participation in 4th Consortium Meeting
 - Participation in EUPHA
- Deliverables to project:
 - Direct-to-consumer chapter (Anne + Gauthier)
 - Master thesis (Arja + Christina): "Quality and Content Assessment of Public Health Genomics Guidelines and Informed Consent"

Date: 21 July 2011

Participants: Inserm / SDU Teams

Agenda and decisions:

- The tables and their role inside the WP
 - Tables are internal documents; they are evolutionary according to the writing process.

- They are not intended to be uploaded on the wiki but they can be sent to others members of the WP use.
- User categories: OK for now, they could also evolve
- Editorial Independence and relevant domain (s): relevant quality item for the assessment domain and policy development domain. Tables will be updated with these elements.
- Input from other WP members
 - How to involve them: ask them to contribute via the wiki. Anne will mail the partners for an update.
- Strategy for the Wiki:
 - Upload something preferably before Gauthier and Anne holidays (August).
 - Connect identified quality gaps and content gaps in our WP and prepare a document to upload.
 - Make comments on existing contributions on the Wiki relating them to the use/users concerns. Suggest to the Maastricht team to create a sort of regular newsletter to warn the members of the project about relevant news on the Wiki.
- Work plan: OK, possible evolutions
- Publication plan
 - Plan for 2 articles
 - Methodological one (SDU pilot)
 - Ethical one (Inserm pilot)
 - To target journal(s)
 - Draft structures (title/bullet points)
 - Present it in Luxembourg
- Writing process
 - Ex. Rigour of Development
- 4th Consortium meeting
 - What to have ready for the meeting
 - Activities of the WP on the Wiki
 - Publication plan
 - Recommendations

Date: 29 August 2011

Participants: Christina and Gauthier

Agenda and decisions:

- Plan activities on Skype / Schedule
- Structure of the content to upload (inspire from WP Provision input)
- Structure of the Guidance (OECD model / Specification of addressees)

- Content to upload

Date: 12 September 2011

Participants: Inserm / SDU

Agenda and decisions:

- Focus point and task division Inserm/SDU (SDU: Policy development: Mobilize community partnerships/Develop Policies/Inform Educate Empower?)
- 4th Consortium Meeting in Leuven (Discussion on the suggested draft for common presentation - Who's going to present what? Who will prepare the slides? Template for Best Practices Guidance and comments from the group members? Workshop? Deadline for sending presentations to Lena: 14 September)
- Wiki (updates before the deadline: 9 September / work ahead)

Date: 19 September 2011

Participants: Inserm / SDU Teams

Agenda and decisions:

- Minutes following the 3rd Consortium Meeting in Budapest

Date: 14 October 2011

Participants: Inserm / SDU Teams

Agenda and decisions:

- Writing process and comments on the first drafts
- Division of the work (the two groups will work on the whole parts of the reports but a more specific sharing of tasks has been necessary:
 - Inserm: Monitor health / Diagnose and Investigate / Enforce laws / Link to-Provide Healthcare / Develop Policies; point 2 of the report.
 - SDU: Inform, Educate, Empower / Mobilise community Partnerships / Assure Competent Workforce / Evaluate; point 4 of the report.
- Length of the report (unlimited)
- References / Annexes and other methodological issues in writing process
- Assessments' results summary to put inside the report
- Schedule to involve partners before submitting report (can vary)
- Integration of the work of Inserm/SDU

Date: 20 October 2011

Participants: Inserm Team / SDU (Arja R. Aro)

Agenda and decisions:

- Writing process and comments on the drafts and new productions
- Length of the report (limited to around 80 pages for the recommendations and best practices without annexes)
- Fix dates for involving partners and prevent them in order that they can book some days to read and send back to us feedbacks
- Mail concerning specific definitions interesting particularly the WP to send to the coordination team in order that they can be worked out and integrated in the VU group's document on definitions.
- Documents to achieve and share

Date: 27 October 2011 (1)

Participants: Inserm / SDU Teams

Agenda and decisions:

- Final dates to send the docs for the interim report according to achievements and work ahead (sending to partners 2 November; reception of feedbacks desirable for the 9 or 10 November)
- Points 2 and 4 of the Report (structure and background documents for the point 2; collect work performed and ask to partners about their last activities)
- Mail for the definitions (proposals from Inserm accepted by SDU; 3 more will be integrated by SDU; mail to send latest Monday 31 October)
- Discussion about the comments on the drafts, difficulties etc.
- Adoption of the Vancouver referencing style

Date: 27 October 2011 (2)

Participants: Christina and Gauthier

Agenda and decisions:

- Organisation of the work; finalising the draft report; continue exchanging and working on the report while waiting for inputs from the partners
- Points 2 and 4 of the Report (structure and background documents for the point 2; collect work performed and ask to partners about their last activities)
- Backgrounds documentation, content and moving of some parts, underlying principles subparts and numbering
- Reference to assessments' results, where, how, title of the tool: "PHGEN Guidance Assessment Tool" is suggested to refer to the prototype
- Overlaps
- Modification of the tool as a new point for the work plan / after the interim report

Date: 14 November 2011

Participants: Anne, Arja, Christina and Gauthier

Agenda and decisions:

- State of the interim report regarding inclusion of comments from partners
- Division of tasks
- Report on discussions, input from other partners during the Copenhagen European public health Conference

Numerous other interactions occurred by mail and opportunity meetings between partners at other meetings.

4.1.2. Other activities related to public health genomics

At SDU

Developing and dissemination lectures to:

- Master of Science students (n=65, international program) 2 x 12 hours (theme: Public health genomics)
- Bachelor of Science students 4 hours (themes: Genetic epidemiology and ethics/ Genetics as health determinant)
- University Colleges students 16 hours (theme: Public health genomics)

Supervision and competence building: BSc in Public Health thesis: using AGREE instrument evaluating Danish screening guidelines.

At Inserm and SDU

Assessment of the compilation of guidelines provided by Maastricht from user perspective (parallel by 5 staff members and students assistants, Unit for Health Promotion, University of Southern Denmark and 5 members of the Inserm U1027 Team 4 composed by geneticists, lawyers and a philosopher)

At Inserm

Developing and dissemination lectures to:

- M2 Bioengineering : 4h (Public health genomics, ethics)
- M2 Immunology and infectious diseases : 4h (ethics)
- M1 Genetics : multifactorial diseases genetics, ethics and genomics (6h)

- Doctoral students on ethics and genetics: ethics and genetics and biobanks (4h)
- Workshop (30/6 – 1/7, 2011, Toulouse) on direct to consumer genetic testing
- European summer school of bioethics and medical law, Toulouse July 4-7 2011 (topic in 2011 : Genetics, with specific sessions on regulation, DTC, consequences with High throughput technologies on public health genomics)

4.2. Involvement in the pilots

Reading of the documents circulated and comments. Exploration planned of the status of user's involvement in the examples chosen.

Involvement in proposing definitions to the coordinator group after discussions with partners.

The group composed by Brettfeld C., Verhaagen M., Englert S. and Haslberger A.G. prepared a preliminary case study report independently from a specific WP, Public health genomics and nutri(epi)genetics: Exploring the wheel.

4.3. Scientific publications

Two kinds of publications are listed below.

4.3.1. Those considered as a direct output of work developed in the project, several of them being still in preparation

- The production process of European guidelines for a public health genomics policy regarding user's perspective - Gauthier Chassang, Christina Mischorr-Boch, Arja R Aro, Anne Cambon-Thomsen (+ others from USE group). (in process)
- The balance between legally binding instruments and soft law in regulating the use of genome based health information in Europe ('legal paper') - Gauthier Chassang, Christina Mischorr-Boch, Arja R Aro, Anne Cambon-Thomsen. (in planning)
- Validation of the clinical agree instrument for public health genomics guidance (methodological paper) - Christina Mischorr-Boch, Gauthier Chassang, Anne Cambon-Thomsen, Arja R Aro (+ others). (in process)

- Challenges in addressing different user levels in public health genomics guidance - Christina Mischorr-Boch, Gauthier Chassang, Anne Cambon-Thomsen, Arja R Aro. (in process)
- Applicability of bioethics principles to public health genomics (Theory/status paper) - Anne Cambon-Thomsen, Arja R Aro Christina Mischorr-Boch, Gauthier Chassang (+ others). (in process)

4.3.2. Those in relations with the topic of the project and that allow showing continuous involvement and recognised expertise in the domains addressed by the project

- A. Cambon-Thomsen. Expert consultation by CCNE (national advisory ethics committee), July 2 2011, Paris, on « Questions éthiques posées par le profilage génétique, la médecine prédictive et la médecine dite personnalisée ».
- A. Cambon-Thomsen. Expert consultation on June 7 2011, Paris at a public hearing of the OPECST (Office parlementaire d'évaluation des choix scientifiques et technologiques) on « LES MALADIES MONOGÉNIQUES : ÉTAT DES LIEUX » session "Les liens entre recherche, praticiens et associations : questions juridiques et éthiques" on « Dimension européenne. Les structures et initiatives de différents acteurs ».
- A. Cambon-Thomsen. Invited expert presentation on Privacy in the context of high throughput technologies in genetics. *UNESCO Tenth Meeting of the UN Interagency Committee on Bioethics*. « Genetic privacy and non discrimination", Paris, 4/3/2011.
- A. Pigeon, G. Chassang, A. Cambon-Thomsen. Are published genomic data free for further uses? Legal and ethical issues in a context of data sharing. European Human Genetics Conference 2011. Amsterdam May 28-31, 2011 (Poster).
- Bialobrzewski A, Ried J, Dabrock P, Privacy revisited? Old ideals, new realities, and their impact on biobank regimes. *Poiesis & Praxis* 8. (DOI 10.1007/s10202-011-0094-x).

- Christina Mischorr-Boch, Master of Science in Public Health thesis "Quality and Content Assessment of Public Health Genomics Guidelines and Informed Consent", 2011.
- Dabrock P, Alt werden in einer Zeit des gesellschaftlichen Wandels, in: Frankfurter Forum, Versorgungskonzepte für eine alternde Gesellschaft, 2010; 2:14-25.
- Dabrock P, Die konstruierte Realität der sog. individualisierten Medizin – sozialethische und theologische Anmerkungen, in: Schumpelick V, Vogel B (eds.), Medizin nach Mass: Individualisierte Medizin - Wunsch und Wirklichkeit 2011; 285-313.
- Dabrock P, Drawing distinctions responsibly and concretely. A European Protestant perspective on foundational theological bioethics, in: Christian Bioethics 2010; 16: 128-57 (doi:10.1093/cb/cbq015).
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- Dabrock P, Leben um jeden Preis? Theologische und ethische Anmerkungen zur These der Rationalisierung notwendiger Gesundheitsleistungen aus Altersgründen, in: Evangelische Arbeitsgemeinschaft für Altenarbeit in der EKD (Hg.), Solidarisch oder gerecht? Gesundheitschancen und Gesundheitspolitik in der alternden Gesellschaft. Hannover 2011; 11-21.
- Dabrock P, Taupitz J, Ried J (eds.), Trust in Biobanking. Dealing with Ethical, Legal and Social Issues in an Emerging Field of Biotechnology 2011.
- Dabrock P, Which duty first? An ethical scheme on the conflict between respect for autonomy and common welfare, in: Dabrock P, Ried J, Taupitz J (eds.), Trust in Biobanking, Dealing with Ethical, Legal and Social Issues in an Emerging Field of Biotechnology 2011; 75-88.

- Gauthier Chassang, Emmanuelle Rial-Sebbag, Anne Cambon-Thomsen, Les aspects éthiques légaux et sociaux des tests génétiques en accès libre, in Séminaire d'Actualité de Droit Médical, Droits des patients, mobilité et accès aux soins, Ve Forum des jeunes chercheurs, ed. Les Etudes Hospitalières, ISBN : 978-2-84874-250-2, Bordeaux 2011, 197-208.
- Kirchenamt der Evangelischen Kirche in Deutschland (EKD) (ed.), Das Prinzip der Solidarität steht auf dem Spiel (EKD-Texte 110) 2010.
- S. Julia, A. Soulier, A. Cambon-Thomsen. Are genetic testing technologies driving clinical practice? European Human Genetics Conference 2011. Amsterdam May 28-31, 2011 (Poster).
- Stellungnahme der Zentralen Kommission zur Wahrung ethischer Grundsätze in der Medizin und ihren Grenzgebieten (Zentrale Ethikkommission) bei der Bundesärztekammer „Die neue UN-Konvention für die Rechte von Menschen mit Behinderung als Herausforderung für das ärztliche Handeln und das Gesundheitswesen“, in: Deutsches Ärzteblatt 2010; 107: A297-A300.
- Tupasela A, Sihvo S, Snell K, Jallinoja P, Aro AR, Hemminki E. Attitudes towards biomedical use of tissue sample collections, consent and biobanks among Finns. Scandinavian Journal of Public Health 2010;38:46-52.

4.3.3. Products

Assessment instrument: “PHGEN guidance assessment tool” and its related manual.

4.4. *Presentations*

- Gauthier Chassang, Christina Mischorr-Bosh, Arja R. Aro, Anne Cambon-Thomsen, “The production process of EU Guidelines for a Public Health Genomics Policy”, European Summer School of Health Law and Biomedical Ethics, Poster presentation, July 2011.
- Gauthier Chassang, “Towards a Public Health Genomics?”, 4th International Conference on the Pharmaceutical Life Cycle – Developments, Uses and Environment,

Oral communication in the Parallel Thematic Session: Round table on genetic tests, rights and users' protection, University Paris VIII, 2 September 2011.

- Peter Dabrock: Ethical opinion on human biobanking law drafts for a public hearing of the Committee on Education, Research, and Technology Assessment at the German Parliament, 25th May 2011

Written Opinion:

http://www.bundestag.de/bundestag/ausschuesse17/a18/anhoerungen/Humanbiobanken/ADrs_17-154_d.pdf

Oral presentation (video):

http://www.bundestag.de/dokumente/textarchiv/2011/34484471_kw21_pa_bildung/index.html

Oral presentation (protocol/meeting minutes):

<http://www.bundestag.de/bundestag/ausschuesse17/a18/anhoerungen/Humanbiobanken/39-110525.pdf>

- Peter Dabrock: Presentation on the role of ethics committees and data protection authorities in the context of biobanking, 7th April 2011, at the German Ethics Council

Slides:

<http://www.ethikrat.org/dateien/pdf/expertengespraech-biobanken-praesentation-dabrock.pdf>

Audio:

http://www.ethikrat.org/dateien/audio/expertengespraech_11-04-07_dabrock.mp3

- Peter Dabrock: Presentation on the importance of the dialogue between science and society using the example of the ethical challenges of individualised medicine, 19th October 2011, EU Office of the Protestant Church in Germany (EKD), Brussels

- Peter Dabrock: Presentation on the ethical and societal aspects of personalised medicine at a conference on ethics of personalised medicine, Institute of Technics, Theology, and Sciences, 6th June 2011.

Conference report:

<http://www.ttn-institut.de/node/1378>

4.5. Wiki-PHGEN contributions

Documents (part of those produced by the WP) were uploaded in the summer 2011; following the consortium meeting in Leuven we only worked on the word documents

according to the structure provided by the coordinating team. Further contributions to wiki will be done after the interim report.

5. Concluding Remarks

The USE work package produced a coordinated document to which all partners of the WP could contribute/add comments. The main points to underline are 1) the deep necessity to take more into account the lay user's perspective in guidelines as this is a strong gap and little of existing guidelines can be used; 2) the usefulness of the definition of the three levels of users utilised throughout the report (Policy maker level, professional level, lay people and citizen level); 3) the interest of anchoring recommendations and best practices in explicit principles.

Some more detailed part of the original report have been shortened for the interim report but all recommendations and best practices are based on an in depth work. The assessment of existing guidelines prior to redact this recommendation/best practice part was done in depth.

A very good collaborating spirit has been at the heart of the work of this WP and the work of the two young investigators at Inserm and SDU (Gauthier Chassang and Christina Mischorr-Boch) under the guidance of their supervisors has been acknowledged by all. The complementarity of the two leading teams (Inserm and SDU) was also felt as a very positive advantage. The WP hopes its coordinated work will make a substantial contribution to the overall report and is ready for next steps.

6. Annexes

6.1. List of abbreviations

We are listing below two sets of abbreviations.

6.1.1. Abbreviations used through the report

Art./art.: article

CDBI: Steering Committee on Bioethics (Council of Europe)

COMEST: World Commission on the Ethics of Scientific Knowledge and Technology

CPME: Standing Committee of European Doctors

DPWP: Data Protection Working Party, or Article 29 Working Group (cf. Article 29 of the Data Protection Directive 95/46/EC)

EDPS: European Data Protection Supervisor

EGE: European Group on Ethics in Science and New technologies

EMA: European Medicine Agency;

EMR(s): Electronic medical record(s);

ERA: European research area

ERI: European research infrastructure

ESHG: European Society of Human Genetics

EU: European Union;

HiAP: Health in all policies;

HUGO: Human Genome Organisation

IAPO: International Association of Patients' Organisation

IBC: International Bioethics Committee (UNESCO)

ICTs: Information and communication technologies;

MS: Member States;

NGO(s): Non governmental organisation(s)

NuGO: European Nutrigenomics Organisation

OECD: Organisation for Economic Co-operation and Development

PETs: Privacy enhancing technologies

PMR(s): Personal medical record(s);

TFEU: Treaty on the functioning of the European Union

UNESCO: United Nations Educational, Scientific and Cultural Organisation

WMA: World Medical Association

WP(s): Work Package(s)

6.1.2. Abbreviations suggested

PH: Public Health

PHG: Public Health Genomics

EC: European Commission

6.1.3. Abbreviations used within the references

Rec.: Recommendation(s)

Expl.Rep.: Explanatory report

Para.: paragraph(s)

p.: page(s)

fig.: figure

part.: part

art.: article

pt(s): point(s)

chap.: chapter

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