Genomics is a highly dynamic field and, as such, represents a moving target for public health. Public health is shifting from a focus on the population towards an emphasis of the individual as a means of supporting the wellbeing of the population. In particular, we are entering the era of predictive, personalised, preemptive and participatory (P4) medicine supported by advanced technological infrastructure. These changes represent a paradigm shift in our approach to healthcare and will go hand-in-hand with a major reclassification of diseases. The challenge now is to understand how all of these changes will impact public health and how to ensure that they are translated effectively into benefits for individual citizens and society as a whole. Thus, there is a need to develop guidelines aiming not to close doors. Instead, the goal is to create a vision that allows for flexibility and adaptability in their implementation in order to have a maximum impact on health, the healthcare infrastructure, health technologies and economic growth in the health sector.

Therefore, the European Commission asked to develop “European Best Practice Guidelines for Quality Assurance, Provision and Use of Genome-based Information and Technologies” to support the Member States (and other relevant stakeholders) to more efficiently and effectively work together at a European level in addressing the challenges deriving from emerging genome-based information and technologies and to prepare for the paradigm shift of personalised healthcare in time. The implementation of the concept of public health genomics being the responsible and effective translation of genome-based knowledge and technologies for the benefit of population health requires modifications of public health and health governance systems on all levels.

The Public Health Genomics European Network (PHGEN II) fulfils this task. It is an EU DG SANCO (European Union Directorate-General for Health and Consumers) funded and European Agency for Health and Consumers (EAHC) issued project (EU Project No. 20081302, 2009–2012), which recently produced the first edition of the “European Best Practice Guidelines for Quality Assurance, Provision and Use of Genome-based Information and Technologies”. The guidelines will assist all EU Member States, Applicant and EFTA-European Economic Area (EEA) countries with evidence-based guidance on the timely and responsible integration of genome-based information and technologies into healthcare systems for the benefit of population health. They build on the extensive work of the Public Health Genomics European Network (PHGEN, www.phgen.eu) being the cornerstone in the development of public health genomics in Europe. Whereas PHGEN I (DG SANCO 2006–2008) identified the need for European best practice guidelines (“mapping exercise”), PHGEN II developed the first edition of these European best practice guidelines using the concept of “genome-based information and technologies” (Bellagio-Model), which PHGEN I established as a scientific benchmark in Europe. In this concept, genome-based information is very holistic and includes not only all “omics” data but also environmental, socioeconomic and lifestyle factors, as well as information on health systems. The process of the development of guidelines was in line with international standards and acknowledges the diversity and cultural differences in Europe. Key experts, such as public health experts, EU lawyers, human geneticists, ethicists, systems biologists, Health Technology Assessment (HTA) experts, representatives from the private sector
and patient groups, as well as policy makers had been involved in PHGEN II.

On 19 and 20 April 2012, experts from across the field of public health genomics representing key European and national organisations and institutions from policy making, academia and private sector came together at the final PHGEN II meeting in Rome – amongst them the European Society for Pharmacogenomics and Theranostics (ESPT) and the European Medicines Agency (EMA) – to discuss the future of public health genomics and to endorse the Declaration of Rome on 19 April 2012, a summary of the “European Best Practice Guidelines for Quality Assurance, Provision and Use of Genome-based Information and Technologies”.

Declaration of Rome

19 April 2012

Preamble

In the past decade, we have witnessed major changes in our approach to public health, not only in terms of research and practice but also the policies that support it. New insights into our individual biological make-up are being obtained from genomics, proteomics, epigenomics, microbiomics and other “omics” technologies. As these data are integrated through the use of information and communication technologies (ICT), we are on the brink of achieving an understanding of the systems biology of human health and disease that also incorporates environmental contributions. In this way, we can begin to envisage new approaches to the promotion and management of human health across the entire life course of an individual. Indeed, we can now consider a future involving truly personalised healthcare in which technological advances are placed at the service of population health. The evidence we now require to demonstrate the benefit of new technologies will need to follow a new paradigm, however. What is required is an assessment of individual benefit rather than overall effects in large populations or even subpopulations of patients. Thus, public health assessment and evaluation tools must now address concepts, such as personal rather than clinical utility.

Information and communication technologies

The increasing role of ICT in healthcare is driven by improved technological options. Combined genomic and phenotypic analysis has become possible owing to advances in technologies to support data analysis and modelling. The complexity of the task when applied to diagnosis and therapy, however, demands algorithms and mathematical models to reduce uncertainties. As a result, efforts are now being made to generate computational models of individual persons (“virtual twins”). Such models can be used to follow individuals throughout their lifetime and enable health professionals to optimise all types of health interventions. In this way, it becomes possible to improve the safety, quality, effectiveness and efficiency of healthcare services. In addition, by following individuals rather than remaining tied to a given healthcare system, it will enable citizens to handle and access personal health-related data whenever needed.

Genome-based information and technologies

PHGEN II builds on the definitions that were developed and agreed in PHGEN I, such as the glossary on public health genomics and the status of genetic information and genetic testing. The definitions provided by PHGEN II take into account the most recent developments in the fields of genomics, systems biology and systems medicine,
which provide the evidence base for the “European Best Practice Guidelines for Quality Assurance, Provision and Use of Genome-based Information and Technologies” (see Figure 1: Research for new insights and innovative solutions to health problems). The terms genome-based information (GBI) and genome-based technologies (GBT) are encompassed by the term genome-based information and technologies (GBIT).

These definitions address the following areas:
- genetics, genomics, functional genomics, systems biology and systems medicine, and the distinctions between them;
- genetic disease, genomic disease and systems biology disease, and the distinctions between them;
- the differences between generic, cohort-based, personalised and truly individualised medicine. Based on these definitions, systems medicine is understood through the integration of genetics, genomics, functional genomics and systems biology.

**Rationale for the European Best Practice Guidelines for Quality Assurance, Provision and Use of Genome-based Information and Technologies**

The ultimate objective of PHGEN II is to enable informed decisions at the macro-, meso- and micro-levels regarding quality assurance, provision and use of emerging GBIT. The means chosen by PHGEN II to achieve this is the preparation of European best practice guidelines to support this decision-making process now and in the future. However, meta-level guidance is also needed. This meta-level guidance can be achieved by ensuring that the ten essential public health tasks, as described within the public health wheel or public health trials (assessment, policy development, assurance) can be adequately fulfilled in each jurisdiction on the basis of a common understanding of best practice guidelines for each task (see Figure 1). Within these best practice guidelines, translational research considerations are combined with system management under the concept of public health genomics.

**European Best Practice Guidelines for Quality Assurance, Provision and Use of Genome-based Information and Technologies**

1. **Research**
   - Keep up with new insights from the basic sciences.
   - Develop transdisciplinary agendas for translational research.
   - Promote sustainable funding for translational research to produce neutral and trustworthy information.
   - Generate evidence to demonstrate when the use of GBIT in public health can improve health outcomes in a safe, effective and cost-effective manner.
   - Engage community members and foster trust by supporting research collaborations and partnerships between academics and the public.

2. **Monitor health**
   - Develop prospective surveillance systems for personal health data that facilitate accurate and ongoing assessment of highly dynamic health information across the life course.
   - Promote the use of personal files that contain comprehensive personal health information including ‘omics’ data and their interaction with all other health determinants.
   - Ensure that data obtained from different sources and for different purposes can be securely linked.
   - Maintain the locus of control for health information with the individual citizen.
   - Support self-monitoring using ICT tools.
   - Develop new strategies for the use of GBIT within the public domain.
   - Maintain an infrastructure for the sharing of GBIT data in public health settings.
   - Increase the use of Health Needs Assessment (HNA), HTA and Health Impact Assessment (HIA) tools for the evaluation of GBIT in public health.
3. Diagnose and investigate
- Move from symptom- and phenotype-based approaches to pathway-based cloud diagnostics for the early identification of health problems in individual patients.
- Move from clinical utility to personal utility.
- Identify which information is relevant to an individual, when, and for what purpose across the life course.
- Use GBIT to identify hazards to population health.
- Identify and assess new GBIT for proactive and timely decision-making.
- Ensure that the assessment of GBIT is comparative, comprehensive and constructive.

4. Inform, educate, empower
- Promote health literacy amongst all stakeholders: enable citizens (including health professionals), individually and cooperatively, to access, understand, appraise and apply information that will facilitate the application of GBIT for the benefit of individual citizens and their communities.
- Promote person-centred healthcare.
- Promote social media to enable proactive consumers (“prosumers”) to manage their own health.
- Establish online platforms dedicated to informing users about validated GBIT as well as available related health services.
- Support participatory and personalised healthcare through the implementation of decision support tools that link the values and preferences of citizens to the best available evidence on GBIT.
- Ensure that potential users receive guidance on when and how to use public health assessment tools (HNA, HTA, HIA) applicable to GBIT.

5. Mobilise community partnerships
- Support the establishment and maintenance of national task forces (NTFs) on public health genomics. NTFs provide a platform for public health practitioners, basic scientists in genomics, HTA officials and policy makers to listen to, learn from and contribute to public health genomics, and to define the policy questions regarding GBIT as well as to assess GBIT at different stages in their life cycle.
- Promote public-private partnerships by establishing mechanisms, tools and models to link the needs of healthcare systems to those of the private sector and to foster the development of individualised technologies (e.g., learning adapting levelling model).
- Reinforce the key role of institutes of public health in community engagement.
- Promote patient- and citizen-oriented social media activities as a new form of community partnership.

6. Develop policies
- Reinforce the collaboration between PHGEN NTFs, national HTA agencies and parliamentary technology assessment groups to develop strategies to inform policy makers on the introduction and iterative assessment of GBIT in an effective, efficient and timely manner.
- Promote policies that cover all phases of the innovation pipeline by combining technology transfer activities with health policy processes: laboratory – enterprise, enterprise – regulation, regulation – reimbursement, reimbursement – disinvestment.
- Improve the implementation of promising GBIT under conditions that safeguard the wellbeing of citizens.
- Support health policies related to GBIT based on good governance and trust.
- Treat GBIT as the most holistic approach to health information when developing health policies.
- Ensure that public health genomics works towards health in all policies.
- Support health policy making that takes into account the best available evidence, real-world context, resources and population characteristics as well as the needs, values and preferences of stakeholders.
- Translate knowledge in a timely manner from basic sciences into healthcare applications.

7. Enforce laws
- Use the dynamics of GBIT as a unique opportunity to frame and enforce laws and regulations proactively.
- Ensure that GBIT and their use in public health meet applicable legal standards. In this regard, the privacy and security of personal health information should be safeguarded in accordance with applicable law.
- Work to correct perceptions of genetic exceptionalism and promote laws and regulations that address personal health information as a whole.
- Use modern ICT to protect personal health data.
- Assess existing legal frameworks applicable to public health genomics on a regular basis and adapt them when necessary to ensure the consistency and visibility of enforceable rules on the use of GBIT in different contexts.
Brand and Liu (PHGEN II): The 2012 Declaration of Rome

- Support implementation of the EU Data Protection Directive amongst European Member States to allow the use of personal health data for personal and public health purposes and to improve the outcome of health interventions.

8. Link to/provide care
- Reduce inequalities in health through sustainable access to and use of GBIT.
- Develop systems that support interoperability between personal and public health management.
- Support the integration of P4 medicine into healthcare provision.

9. Ensure a competent workforce
- Integrate GBIT into the professional training and lifelong learning curricula of health professionals.

10. Evaluate
- Establish and support a holistic and systems-based evaluation of the impact of GBIT, taking into account economic issues and the different European health systems.
- Promote a system in which technology transfer activities and policy-based public health assessment tools (HNA, HTA, HIA) run in parallel for the timely, effective and efficient evaluation of GBIT.
- Help and support the development of methods, information systems, tools and resources to adapt assessment tools to changing requirements.

Concluding remarks

The proposed list of guidelines under the Declaration of Rome is crucial for the implementation of GBIT amongst European Member States in order to improve public and personal health. Future PHGEN activities will continue to build on previous work to provide a platform for the developments indicated in these guidelines. We therefore strongly recommend that PHGEN activities continue to be supported on European, national and regional levels within the applicable healthcare framework.

The next step: implementation of the 2012 Declaration of Rome in the EU Member States

Because health is not just a value in itself but also a driver for growth, only a healthy population can achieve its full economic potential. As mentioned in the Europe 2020 agenda ‘promoting good health is an integral part of the smart and inclusive growth objectives for Europe 2020. Keeping people healthy and active for longer has a positive impact on productivity and competitiveness. Innovation in healthcare helps take up the challenge of sustainability in the sector in the context of demographic change’, and action to reduce inequalities in health is important to achieve ‘inclusive growth’.

Thus, as the next step a Joint Action (JA) “Public Health Genomics and Personalised Healthcare: Implementing the ‘European Best Practice Guidelines for Quality Assurance, Provision and Use of Genome-based Information and Technologies’ in rare diseases and cancer” is planned being a joint financing of a public body or non-governmental organisation by the European Community and one or more Member States. The planned JA fully supports and implements the Innovation Partnership Flagship Action of Active and Healthy Ageing. It covers not only Innovation/Genomics and Health in All Policies (HiAP) in the current programme “Together for Health” (2008–2013) but it also highly prepares for and contributes to the new programme “Health for Growth” (2014–2020) by applying innovative solutions for improving the quality, efficiency and sustainability of health systems, putting the emphasis on human capital and the exchange of European best practices. As such, the planned JA will help Member States, which are under pressure to strike the right balance between providing universal access to high-quality health services and respecting budgetary constraints, to reduce healthcare costs and substantially improve the quality of care to all citizens now and in the future. The European best practice guidelines developed within PHGEN II and summarised in the Declaration of Rome address many areas of the Health for Growth Programme, such as HTA, medical devices, clinical trials and medicinal products, and strengthen the link between technological innovation and its effective and responsible uptake and commercialisation.

Therefore, the planned JA will be a very timely and essential next step by:
- Supporting the Member States to prepare in time for the paradigm shift towards personalised healthcare.
- Bringing together European stakeholders with a common objective and commitment to reduce the burden of common complex and rare disorders, and providing Member States with a framework for sharing information, resources, best practices and expertise in monitoring, surveillance, knowledge integration, prevention and care.

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- Helping in the identification of common action at an EU level that can provide added value to national efforts.
- Helping with the implementation of the HiAP approach and the concepts of HNA, HTA and HIA in supporting action for active and healthy ageing.
- Serving as an umbrella for researchers from the different stages of translational research in the life sciences (“from cell to society”) and market authorisation, as well as fostering this translational process to the policy making and public health level.
- Focusing on two key policy areas of application, rare diseases and cancer.

- Using the well-established 13 NTFs of PHGEN I as the core group and extending it to the maximum of Member States.

In conclusion, building on PHGEN I and II the planned JA will help address the transition to personalised healthcare and personal health from the data integration and modelling perspective points of view in all EU Member States, Applicant and EFTA-EEA countries within the upcoming years.

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