Executive Summary:

EuroGentest2 dealt with the harmonization of genetic testing and the improvement of quality of genetic services throughout Europe. This initiative started in 2005, with the creation of EuroGentest and its funding as an NoE. The coordination action (CA) aimed to continue the activities, by keeping all the stakeholders together, and covering different aspects of quality assurance. New standards were set, more training courses were organised, policy issues in genetic testing were addressed, and information to patients and public was provided. This, in our opinion, has contributed to the quality of the genetic services throughout Europe. The project included new fields and topics such as prenatal testing, next generation sequencing (NGS) and direct-to-consumer services (DTC). Thus, EuroGentest provided up to date information and guidance in a fast moving domain like human genetics.

EuroGentest organised expert meetings to set a quality standards for genetic laboratories and for health professionals, aided in writing guidelines and policy statements and hosted workshops on implementing a quality management system (QMS), laboratory accreditation and diagnostic validation. EuroGentest has, in conjunction with the European Society for Human Genetics, also been providing expertise for policy makers and translating the needs of the health professionals to European guidelines and regulations. EuroGentest has been attending meetings of EUCERD, IRDiRC and other international organisations, and has been interacting with the Joint Research Center of the European Commission, to outline a future for genetic testing in Europe. Members of EuroGentest were actively involved in the revision of the ISO 15189 norm and in the recast of the IVD regulation at a high level, on behalf of the genetic community, but mostly for the sake of the patients and the families.

 Basically, this has been the realm of EuroGentest: improve the quality in laboratory and clinical genetic testing, for the sake of the
patients and their families. At EuroGentest, we have been able to further unite Europe through harmonization and through mutual exchange of ideas and insights. EuroGentest has become a brand name for quality and training in genetics, and for best practice guidelines. It will be sustained by closely collaborating with the European Society for Human Genetics, from 2014 on.

Project Context and Objectives:
EuroGentest2 was a European coordinated action for the harmonization and further improvement of genetic services, especially genetic testing across Europe.

Genetic conditions may arise from multiple genetic abnormalities resulting in different clinical presentations. The current technological innovations in human genetics, e.g. the extremely rapid development of massively parallel sequencing technologies, pave the way for entirely novel strategies in clinical genetics and laboratory diagnostics. The knowledge of the human genome is also steeply increasing. The elucidation of the complete human genetic sequence in the context of The Human Genome Project has been instrumental in this.

Due to these factors, the demand for genetic analysis in the human health care system is drastically increasing. Analysis of the genome currently incorporates three different laboratory disciplines: cytogenetics, molecular genetics and biochemical genetics, so depending on the clinical question, genetic results may be given for a specific gene or at a whole genome level.

Genetic testing, which includes genetic counselling, is an interactive process involving the patient and his/her family, the genetic laboratory and the referring clinician or clinical geneticist. For all genetic tests, accurate results and interpretation are essential as there may only be a single opportunity for testing – for instance in the prenatal setting, where it is obligatory to minimize repeat sampling in order to avoid the hazards and stress of unnecessary invasive procedures. Or, some patients request presymptomatic testing for a severe familial disease, and have no clinical phenotype or symptoms at the time of testing; however, the result has huge consequences for their future. Likewise in newborn screening, in non-invasive prenatal diagnosis (NIPD), prenatal diagnosis (PND) and pre-implantation genetic diagnosis (PGD), a test is undertaken before any clinical phenotype is evident. For prenatal testing, the parents may be presented with very difficult decisions, with profound, lifelong implications.

Consequently, it is essential that a genetic laboratory and a clinical genetic service have in place reliable procedures underpinned by a robust quality management system, to minimize errors and failures and to reassure the patient and the referring clinician that international standards are being met.

Laboratory Quality Management (QM) is a concept that covers diverse aspects of a diagnostic genetic service including such parameters as laboratory accreditation, external quality assessment (EQA), control materials, training, document control, maintenance of equipment, internal audits, transborder specimens, etc. EuroGentest2 has built on the EuroGentest NoE achievements by further harmonizing the genetic disciplines through common/joint Best Practice Guidelines, Training Programmes and EQA schemes. In addition the introduction of new control materials and validation guidelines, has provided a sustainable framework for diagnostic genetic services to implement and integrate, or improve, their quality management systems and help laboratories attain accreditation.

For EuroGentest2, laboratory accreditation (preferably under ISO 15189) was the goal for all genetic testing laboratories in Europe. The project has helped the laboratories that work towards accreditation by organizing interactive training workshops, and tried to keep track of the number of laboratories that effectively reach that goal – although the evaluation and accreditation are mostly a national matter.

EuroGentest has been able to improve the standards, in good standing with the European Association of Accreditation Bodies. Genetics and genomics are constantly progressing and new technologies are introduced at a rapid pace. Hence, individual laboratories cannot easily cope with the cost of development and the requirement of validation. EuroGentest2 wanted to reach out to other EU projects that are focussing on scientific and technological progress, and coordinate the analytical validation of the newest technological platforms prior to their introduction. The latter activity also involves the provision of information and training to the users.

The long-awaited document: “A standardized framework for the validation and verification of clinical molecular genetic tests”, was published, and has been adopted by the laboratories as well as the national audit teams. However, this is not the end of the process: for each individual method, and for the upcoming technologies, interaction and consultation among peers will be required to warrant uniform and effective validations of methods throughout Europe. Hence, new guidelines on ‘next generation sequencing’ for diagnostics are underway. The manufacturers – industries – have been asked to share the burden and responsibilities. EuroGentest2 coordinated the activities, and distributed the information by publishing the validation guidelines.

‘High quality testing’ is not confined to high quality of the laboratory activities only. Instead, high quality genetic testing is a process starting from the correct indication for the test, a fair way to fund testing and the prioritization needed for that, pre-test counselling and consenting to the test, taking and sending the sample with adequate clinical information, a correctly performed test with an adequate interpreting of the result to the referring clinicians, post-test counselling and the other post test actions like informing relatives and organizing possible follow up. Thus, EuroGentest2 strongly aimed at improving the quality of all genetic services associated with genetic testing, across Europe, and at all the stages in this process.

Even if it is generally felt that clinical services are less amenable to quality management, EuroGentest has changed the landscape on that matter as well. Efforts have been made to define the parameters and adapt them to the clinic (e.g. inclusion in the genetic report of
all the relevant information and a proper advice for counselling is already being assessed by some EQA schemes). A clinical genetic service can also be evaluated through quality criteria like uniformity of practice, traceability, turn-around-times, patient satisfaction, etc. EuroGentest has issued several guidelines and organized ‘train-the-trainer’ courses, to assist and improve quality management of the clinical genetic services.

As resources for healthcare provision are limited, it is essential that new and existing healthcare practices are scrutinised to ensure that they bring benefit to patients. This is particularly true where leading-edge technologies are employed and highly-publicised research results create expectations among patient groups and result in a demand for the newest interventions. Here, at the interface between laboratory and clinical service, is the study of the clinical utility of laboratory tests. The project contributed significantly to the development and distribution of ‘clinical utility gene cards’. They are essential for good practice, but they will also allow policy makers and governments to decide about the reimbursement of genetic tests. To cope with circumstances where public resources are not sufficient to provide funding for all beneficial genetics tests, the project additionally addressed the issue of prioritization. Even if quality, clinical utility and technology are at the heart of this project, the network and participants wanted to also commit to the other difficult and upcoming issues in community genetics. With the advent of the whole genome technologies, unsought or unsolicited results are generated during the analysis. It was important and urgent to develop protocols on how to handle such unsolicited findings in clinical practice. Similarly, (neonatal) screening can confront parents, individuals and physicians, with unexpected information. The globalisation of genetic testing raises serious and significant governance challenges. Genetic testing services are provided under widely varying conditions, diverse and heterogeneous quality schemes, differing national regulations and often in the absence of reference measurement systems and accreditation. In a global market the quality of testing and the safety of patients can only be assured if there is some measure of transborder coordination and a minimum quality standard.

In addition, Direct To Consumer (DTC) testing in genetics is increasingly being offered in a most liberal and practically unregulated way. Private genetics companies are creating an international market for susceptibility tests by selling direct to the public over the internet. The providers seem to neglect the impact (or the lack of it) that it may have on the individual, and on health care provision as a whole. Possible future DTC offers of whole genome sequencing will change the view from the rather meaningless risk profiling of today, to finding gene mutations with fundamental impact on individuals and families.

The general public needed to be informed with regard to the possibilities of genetic diagnostics. Ethical issues have been addressed with care and professional expertise. The EuroGentest2 consortium consisted of leading scientists and practitioners, providing cutting edge knowledge with respect to these quality management aspects, ethical and societal issues. This approach warranted the development of diagnostic tools designed to restrict genetic testing to relevant medical factors, and supported the idea that medical genetic testing has to be carefully embedded in clinical genetic counselling.

Patients benefit from a well organised and integrated genetic service based on harmonised guidelines. A further standardisation of procedures and the availability of guidelines through the website will lead to better educated health care providers. Correct information on the utility of genetic tests as well as tools supporting priority setting in genetic testing shall contribute to availability of at least the most important tests also in economically less advanced countries.

The existence of a database for referral of clinical samples, that includes the QAu status of genetic testing laboratories, is of great importance. This has been achieved through a collaboration with Orphanet. Quality information is now highlighted in the diagnostic laboratory database, and the laboratories that have the highest level of quality management, through accreditation and certification, are now listed first. This will allow clinicians to find out where a (rare) genetic diagnosis can most reliably be confirmed.

In conclusion, this project thus aimed to coordinate, at a European level, a number of important aspects of genetic testing which are directly or indirectly relevant to the patient and the public. Eurogentest2 built on the expertise of EuroGentest NoE and SAFE NoE, Further-more, EuroGentest2 has forged ever closer links with the professional organisations in genetics, prenatal diagnosis and reproductive medicine. The coordination action has delivered what has been proposed, and has reached almost all milestones, as planned.

Project Results:

At EuroGentest, we believe that accreditation is the norm. Good, uniform and measurable quality can be reached by implementing a Quality Management System (QMS) in a genetic laboratory in the most comprehensive and effective way, and then subject it to an audit on the basis of the international norm.

To assist genetic testing laboratories prepare for and achieve accreditation, interactive workshops were organised in English and in French. In 2011-2013, a total of 15 workshops were organized, either on behalf of EuroGentest, in collaboration with the Agence de la biomedicine in France, or together with a national human genetic society, and eventually also with the European Society for Human Reproduction and Embryology (ESHRE). Over 300 geneticists and laboratory specialists have participated in these courses. Additionally, 4 E-courses were organised, which also allowed low income countries to participate in training due to lower costs (no travel). Up till now 137 unique participants from 49 different countries participated in the 4 online courses on accreditation and validation. Each course
consisted of a live or recorded presentation, a quiz and a forum discussion. We have noticed that there is a high demand for information on quality management and working towards accreditation and validation. Each year, the calendar of the workshops for the next year was posted on the EuroGentest website well in advance and for each workshop at least one email-invitation was sent. These workshops were also highlighted in the monthly EuroGentest newsletter.

To improve the quality of the database of genetic testing services in Europe, EuroGentest and Orphanet have defined a mechanism to provide validated information on quality management of laboratories. This mechanism has been accepted by the management board of Orphanet and is described in detail in the Orphanet Standard Operation Procedures. To implement this new mechanism, it was necessary to modify the Orphanet database in order to publish the validation stage of the data on the website. It is now fully implemented. On behalf of EuroGentest three training sessions were organised for users of the Orphanet portal. In addition, EuroGentest and Orphanet have organised several expert workshops to agree on common terminology for the description of clinical features (the so-called ontologies). This will increase the interoperability between genotype and phenotype databases.

External quality assessment (EQA) is a tool to increase quality in the laboratory and is required for accreditation. The four European EQA schemes (CF Network, ERNDIM, CEQA and EMQN) continue to work together sharing experience and protocols of the EQA process to improve individual EQA schemes and also to harmonise EQA processes as well as poor performance criteria and poor performance designation. In terms of harmonization, a common template has been designed for the assessment of EQA data and the European EQA providers now use common marking criteria for genotyping and interpretation. A manuscript is in preparation on the improvement of interpretation content of laboratory reports based on the results of an EQA survey. EQA participation data is made available on the Orphanet portal and online registration for EQA schemes is available for CEQA, CF Network and EMQN to promote accessibility. EQA participation data is given in EQA Scheme Annual Reports. All 4 European Schemes submit Annual Management Reports to the European Society of Human Genetics (ESHG) for review using the same content format. The websites of CEQA, EMQN and ERNDIM have been modified to make them more user-friendly. The EQA schemes of CEQA, EMQN and CF network have been accredited and ERNDIM is working towards accreditation. Thirteen new pilot schemes have been developed in 2011-2013, including one for Next Generation Sequencing (NGS), Pre-implantation Genetic Diagnosis (PGD) and Non-Invasive Prenatal Diagnosis (NIPD) and several new full EQA schemes have been made available. Several best practice meetings were held that lead to a number of new published guidelines for best practice in order to improve laboratories to the use of good standardized best practice in genetic testing.

Reference materials are important to provide quality in genetic testing, however their availability is scarce. Presentations and workshops were held at international meetings to raise awareness of this problem. A survey of reference materials needs and uses was collated and published as part of a wider survey of quality indicators in genetic testing laboratories. Clear new needs were identified in several categories and these were disseminated to reference materials producers for inclusion in their plans. Networking and lobbying by EuroGentest brought the SME Horizon Diagnostics in contact with EMQN. They became a supplier of materials for molecular pathology EQA schemes and EMQN will use the newly-launched NIST Standard Reference Material for Huntington disease to calibrate the EQA materials distributed in the 2012 EQA scheme for Huntington disease. This will allow participating laboratories to calibrate their own assays and establish traceability to the NIST standard. Horizon was also introduced to the Association for Molecular Pathology’s email list server CHAMP, which connects lab directors, experts and suppliers. In September 2013 an expert workshop was held to bring together experts in the field and resulted in the development of an updated database that will become available early 2014. In this database, knowledge acquired from the validation and use of cell line-derived DNAs in EMQN EQA schemes over 14 years has leveraged to produce a catalogue of available materials for the most commonly-requested genetic tests. The database contains 471 source materials, including many that have been validated as normal controls for multiple genetic disorders and genes - these are specially important in EQAs for tests that, in common clinical use, rarely yield a positive result.

Providing good quality in genetic testing is not limited to the laboratory testing. It encompassed the complete provision of good quality in clinical genetic service, going from the correct indication for a test, to the adequate counselling for patient and their family. A questionnaire on ‘Principles of good practice’ in clinical genetics was distributed and the results were discussed at an expert meeting. A second meeting was held on informed consent procedures and a third on genetic testing for genetic forms of diabetes (MODY). Two guidelines have been published: one for introducing new genetic services and one on informed consent for NGS in diagnostics.

To improve genetic services, guidelines for genetic counselling for pre-symptomatic testing, for prenatal diagnosis (incl. non-invasive prenatal diagnosis or testing; NIPD or NIPT) and revised guidelines for pre-implantation genetic diagnosis (PGD) have been published. Two new patient leaflets on NIPD were developed and are available on the EuroGentest website. Three review papers have been published on the subject of Direct-To-Consumer (DTC) testing. One addresses users’ perspectives, one the views and experiences of health professionals and one policies pertaining to DTC. An interactive decision tool has been developed to provide guidance for health professionals managing requests that arise from DTC testing and is available on the EuroGentest website. For the development of all these guidelines and tools, several expert meetings were held to bring together the needed expertise. To directly aid the genetic counsellors, seven ‘Training the Trainers’ workshops were held to provide professional guidance on genetic counselling (5 online and 2 face-to-face).
To gather opinions on how genetic tests can be prioritized a pilot study has been completed, and a manuscript reporting the results of a discrete-choice experiment (DCE) among 594 participants has been submitted. A stakeholder workshop was held on prioritization and a consensus document is being finalized. A theoretical framework for prioritizing genetic tests was developed which will also be submitted for publication soon.

Clinical Utility Gene Cards (CUGCs) are documents that assess the clinical utility of a genetic diagnostic test and provide practitioners with good practice information on genetic tests for specific diseases. In 2011-2013, 89 new CUGCs were published in the European Journal of Human Genetics (EJHG) and 11 CUGCs were updated. They are permanently implemented in the Orphanet rare disease portal and new CUGCs are announced in the EuroGentest newsletter. In order to adapt the CUGC format to new technologies like NGS, a diagnostic panel data collection was prepared and made available through EuroGentest.

New technologies are emerging in the field of genetic testing and are finding their way into diagnostics quickly. One general consensus document on diagnostic NGS is in preparation, the final draft was completed at an expert meeting in November 2013, and they will be submitted for publication soon. Two expert workshops on PGD were held, one for Cystic Fibrosis in 2011 and one in 2012 to establish guidelines for triplet disorders. Both resulted in draft guidelines which will be submitted for publication.

A high impact guidance document has recently been published entitled 'Current issues in medically assisted reproduction and genetics in Europe: research, clinical practice, ethics, legal issues and policy. European Society of Human Genetics and European Society of Human Reproduction and Embryology'. This was a close collaboration between ESHRE, ESHG and EuroGentest. EuroGentest is also concerned with providing expertise for policy makers and translating the needs of the health professionals to European guidelines and regulations. Several members were actively involved in the revision of the ISO 15189 norm and in the recast of the IVD regulation. In preparation for the latter, a successful expert workshop was held in 2011.

A new post-graduate master has been set-up in collaboration with a number of the major universities: “Quality Improvement Sciences in Healthcare. Improving clinical practice; an evidence based course”. This will enable professionals to acquire a certificate on the topic of quality in health care.

EuroGentest organised three international Scientific Symposia: Leuven (2011), Nijmegen (2012) and Prague (2013). An average of 250 participants from Europe and beyond was present at these meetings. EuroGentest was also present at the yearly conferences of ESHG with an informational booth where several flyers were available on all the activities of EuroGentest and where people could get in touch with the experts themselves. Additionally, several satellite meetings were organised on behalf of EuroGentest partners during the ESHG conferences.

The EuroGentest website has been created during the EuroGentest NoE project in 2005 and has been updated continuously. It provides easily accessible information on genetic testing for laboratory and health professionals, patients and their family and the general public. More than 3000 people are registered to the website, to receive the monthly newsletter. In this newsletter, general news on genetic testing is provided, as well as specific events or outcomes from the EuroGentest project.

Potential Impact:
In terms of training more than 15 workshops were held on different topics regarding quality management systems and accreditation with a total of 339 participants. Each workshop is evaluated and feedback from participants is collected via questionnaires. Apparent from these responses and from feedback at the EuroGentest booth at the ESHG conference is that these workshops are very popular. They have proved to actively aid laboratories in their process towards accreditation. To increase accessibility of training for low income countries, E-courses have been developed: 4 E-courses on validation and accreditation have been held, with a total of 168 participants. The accreditation of the EQA providers is almost complete, CF network, CEQA and EMQN are accredited and ERNDIM is working towards accreditation. In January 2014, CEQA and UK NEQAS for Clinical Cytogenetics will merge to create an EQA provider with expertise that is both deeper and broader than any other. EMQN and ERNDIM will continue their activities independently. ESHG will continue to support communication between the EQA providers to guarantee continued harmonization.

A comprehensive database for reference material for the most commonly-requested genetic tests has been created and will become available soon. Another important output is a strengthened and expanded network of experts in reference materials for genetic testing. To allow linking between genotype and phenotype databases EuroGentest aims to provide standards to be used for public databases. A survey has been done to collect relevant terminologies used by the community to describe phenomes and a position paper on this is drafted. Orphanet will continue these activities in collaboration with the ESHG and IRDiRC.

EuroGentest has generated numerous policy documents on genetic testing. The work on direct-to-consumer (DTC) testing led to three important reviews and an interactive decision tool for professionals. EuroGentest has also been involved at a high level in the recast of the in vitro diagnostic device regulation and the new ISO15189 norm. The patient leaflets that were developed during the EuroGentest NoE were translated into three additional languages and two new leaflets have been created on non-invasive prenatal testing. A leaflet on DTC is being drafted. The total number of leaflets and languages thus stands at 15 and 32 respectively. This is sufficient to serve all European populations, and to help most patients who have migrated to Europe. It is a resource that is used in the waiting rooms and at consultations in clinical genetic services and other medical centres. A general leaflet on genetic testing was developed in collaboration
with the Council of Europe in 18 languages. The development of CUGCs (Clinical Utility Gene Cards) has been successful: 89 new CUGCs were developed, of which 11 are updated ones. In order to adapt the CUGC format to new technologies like NGS, a diagnostic panel data collection system was prepared. The continuation of the CUGC’s is guaranteed by ESHG. In EuroGentest2 a new field in genetic testing has been explored: prioritization of genetic testing. This work has led to groundbreaking publications that will set the standards. Several guidance documents have been written on new technologies in genetic testing (NIPD, PGD, NGS) and on genetic counselling.

Towards the end of the project, in September 2013, a survey was conducted among directors of molecular, cytogenetic and biochemical genetic services of private and academic labs. The results clearly indicated the need for EuroGentest to continue. This will be done by integrating with the European Society of Human Genetics (ESHG). The website has already been transferred to the ESHG server. All the documents and tools that have been developed by EuroGentest will thus remain available for the public. In addition, we are working together with the ESHG to create an interactive network of genetic labs and to organise a EuroGentest workshop at the annual ESHG conference to remain connected with the genetic community. We are confident that with this integration all the work done by EuroGentest will continue to have a positive impact on the quality of genetic testing in laboratories in Europa and will even further expand in the future.

List of Websites:
www.eurogentest.org
EuroGentest
Center for Human Genetics
University of Leuven
Herestraat 49 Box 602
3000 Leuven
Belgium
Tel +32 16 340321
Fax +32 16 345997
General: admin@eurogentest.org
Website content: webmaster@eurogentest.org

Share this page

© European Union, 2019