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NEWS AND COMMENTARY

Quality issues in genetic testing

Can (should) molecular diagnostic labs improve the quality of their services?

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Diagnostic genetic testing is moving into a new era. What once could be done with a small cell culture lab, a photo-microscope, scissors and some glue is gradually being replaced by big or small boxes attached to computers capable of managing terabytes of information. Bioinformaticians have entered the labs. They are essential in helping the geneticists understand what the machines have done with the DNA that was entered on one side and which generated all these data in the form of numbers or figures after being processed. There is nothing wrong with this new approach and this new technology. It allows us to do what was considered science fiction less than 20 years ago and will finally make a correct diagnosis for the more than 7000 inherited diseases possible, while contributing to a more accurate risk calculation and diagnosis for many common diseases. Nevertheless, we will have to keep our enthusiasm under control and make sure that these new possibilities are implemented correctly and timely, as suggested, for example, in the recommendations of the ESHG, published in this journal in 2011.

The potential problems with the quality of these new services should be a major concern. One way of identifying some of these problems is to examine what is in place or lacking in the diagnostic labs to guarantee good performance. This is essentially what Sarah Berwouts *et al*[1] have done in their paper on Quality assurance, published in this issue of the journal.

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Not all molecular diagnostic labs of the EU could be included in this survey. One reason for this is that, with the exception of the voluntary registration in Orphanet, there is no EU register where all labs can be found. In addition, not all labs contacted would accept to participate in a survey, which may unveil some of their shortcomings. A 33% response rate is therefore a nice result, which also illustrates how European labs have evolved in becoming aware of the importance and the need of quality assurance. Moreover, the laboratory personnel, together with the European Society of Human Genetics, have become a driving force toward improved quality in all aspects of the services. From the survey, it also appears that, if the estimated number of molecular diagnostic labs in the EU is 1055 then more than 2.7 million samples, or a mean of 2560 samples per lab, were processed in 2010. For the EU population of 500 million this means that up to 1 in 2000 Europeans might have used these services in 1 year, a twofold increase over estimates for 2006. In the US, this activity represented a market of $ 5 billion in 2010, which could grow to 15–20 billion in 2021. Addition of the users of the DTC internet services in recent years may even increase this number. In view of these numbers and the launch of disposable sequencers for less than $900 it is no wonder that this market is attracting a lot of interest from geneticists and private businesses in public and private quarters; this gives all the more reasons to monitor the quality.

As the number of diseases for which tests became available increased, the number of samples crossing borders also increased. About 50% of the laboratories sent samples to, or received samples from foreign laboratories within or outside the EU. An excellent incentive for the member states to approve the cross-border directive by 2013, because this trend will only increase, and patients will follow. The activities of EUCERD, the European Committee of Experts on Rare Diseases, which includes the identification of European Expert Centers for diagnosis and therapy, will also stimulate this cross-border collaboration.

An interesting finding is that many labs overestimate their quality status. Terms such as accreditation, certification and licensing are still not correctly understood and give labs sometimes the wrong conviction that they are complying with the highest quality standards.

Initiatives such as EMQN (the European Molecular Quality Network) and the CF Network, which provide external quality assessments for DNA tests, ERNDIM, for enzymatic tests in metabolic diseases, and CEQA (Cytogenetic EQA, set up under the EuroGentest NoE), are initiatives that were initially supported by DG Research and a lot of good will, sweat and energy of volunteers. They had to find a way of becoming sustainable after the European support ceased. Their disappearance would otherwise have left European labs without a well-organized and operational quality EQA provision. The results of these different EQAs still show the need for improved quality in the lab services. Too many labs make significant errors – in some cases 1–5% – even in a particular EQA scheme;[2,3] so one wonders what this would be under routine conditions. Some are even persistent poor performers, but for the time being the EQA providers have opted for offering training, as they have no authority to punish or ban these 'sinners'.

EuroGentest NoE (www.EuroGentest.org), which became a Coordination Action after the end of the 5-year support form DG Research, is trying to continue its efforts to improve the quality of both the labs and of the clinical services. For understandable reasons the latter is even more difficult than the first. A large series of training session all over Europe on quality assurance for labs substantially increased the awareness for quality. The French government, as a result, made it compulsory for all labs to become accredited under ISO 15189.[4]

In collaboration with Orphanet, EuroGentest NoE started a process of validating information on quality assurance aspects for the labs registered in Orphanet. Visitors can now see whether these labs are accredited, certified or licensed, whether they participate in EQAs and for what tests. Regrettably, lack

of financial support at the end of the NoE resulted in a scaling down of this effort.

It is clear that Europe is in need of a competent body responsible for quality assurance of the genetic services. The revision process of the IVD directive, in which EuroGentest together with the ESHG was very active, will probably lead to the recognition of the importance of accreditation for the labs, but also for not considering genetic tests as being simple and of low risk. Nevertheless, we need more. The OECD guidelines for quality assurance in molecular genetic testing, approved by all member states, but for the rest greatly ignored by them, the Clinical Utility Gene Cards developed under EuroGentest, the Best Practice Guidelines developed by the EQA scheme organizers, the self-assessment tool for clinical genetic facilities developed under EuroGentest are all examples of what motivated volunteers have already done. Some member states have already taken initiatives to require quality assurance in certified genetic services. Switzerland, to take an example of a country that is not part of the EU, has already a good legal system in place without too much administrative burden for the labs, to insure that the services are of high quality.[5] Europe should not stay behind. The implementation of the cross-border directive and the directive on Rare Diseases could create an even greater risk for erroneous diagnoses if no initiative is taken to improve the quality of the clinical and laboratory services in the EU. The data provided by Berwouts *et al* in this paper should be used by all geneticists to convince their authorities that an European initiative for genetic quality services would in the first place benefit the patients and their families. ■

CONFLICT OF INTEREST

The author declares no conflict of interest

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2 Patton SJ, Wallace AJ, Elles R: Benchmark for evaluating the quality of DNA sequencing: proposal from an international external quality assessment scheme. *Clin Chem* 2006; **52**: 728–736.

3 Touitou I, Rittore C, Philibert L *et al*: An international external quality assessment for molecular diagnosis of hereditary recurrent fevers: a 3-year scheme demonstrates the need for improvement. *Eur J Hum Genet* 2009; **17**: 890–896.

4 La loi Hôpital, Patients, Santé et Territoires (HPST). http://www.sante.gouv.fr/la-loi-hopital-patients-sante-et-territoires.html, 2011.

5 Office fédéral de la santé publique (OFSP). http://www.bag.admin.ch/themen/medizin/00683/02724/03677/11167/index.html?lang=fr, 2011.