

## **EuroGentest workshop on Reference Materials (RMs) for new genetic testing technologies**

The Institute for Reference Materials and Measurements (IRMM) of the Joint Research Centre of the European Commission hosted the workshop on 24<sup>th</sup> April 2008 in Geel, Belgium, as deliverable of the WP1.6 of Unit 1 of the Network of Excellence.

All presentations are posted on the EuroGentest website ([www.eurogentest.org](http://www.eurogentest.org)).

Participants from EuroGentest, RMs producers and technology developers from Europe and USA presented their view on the current situation and the future needs.

The quality control in genetic testing requires the availability of control materials and RMs. RMs can be classified according to their use and IRMM has released a related guidance document (see [www.eurogentest.org](http://www.eurogentest.org), section Lab Quality, reference materials, guidelines) as well as a paper on the certification of RMs for genetic testing (Clin Chem Lab Med 2008, 46:463-469). Of note, the ISO Guide 35 (2006) defines the minimal quality criteria of a RM by contrast with the various legislative requirements (FDA clearance, CE-marking, WHO approval) that do not tackle in detail the quality of a RM.

As the EuroGentest list of the 12 most-wanted RMs for hereditary genetic disorders is nearly fulfilled, RMs for other genetic testing disciplines (haematology, pharmacogenetics, cytogenetics, pre-natal testing, etc) and new technologies development and validation are to be developed. Of note, the individual development of RMs for single gene disorder is preferred by the genetic testing community instead of generic RMs, although it is admitted to be impossible to produce RMs for all genetic alterations.

The new technologies are looking at several genes at a time (array CGH, SNP arrays, whole genome sequencing...) in contrast to "traditional technologies". For these new technologies, no RMs are available. Questions arising are: How do you perform quality control for microarrays? How to validate all features on an array? What is a normal genotype?

Array CGH manufacturers produce chips for diagnostic detection of copy number imbalances. Array CGH is a screening technique for which patient samples are used as controls. The controls should be high molecular weight (> 100 kb) and free of impurities. ATCC, Coriell and Promega provide sources of gDNA, but the ethnicity and a well defined copy number polymorphism should be considered for selection of adequate array controls.

C. Foy (LGC, UK) introduced the next generation of sequencers and arrays used for clinical purpose, their applications and challenges.

The International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) structure and aims, as well as data of the EQUAL project (FP6) were presented by M. Pazzagli. The published data demonstrate that the pre-analytical phase (DNA quantity and purity) constitutes a critical point of the final results. The SPIDIA project (FP7) was presented as well, dealing with the pre-analytical phase for new technologies in *in vitro* diagnostics.

US manufacturers produce FDA-registered human genomic quality controls (HGQCs) as CYP2D6, analyte-specific reagents (CYP2C9 and VKORC1), and *in vitro* diagnostic kits (510k submission for warfarin therapy).

The RMs needed in cytogenetics should cover the whole genome analysis as array CGH is covering a broad spectrum of analyses from a few bp to 100 Mbp. The wished list of RMs was described as consisting of DNA from normal male with known copy number variations (CNVs), DNA with known abnormal duplication, known abnormal deletion, MECP2 duplication or X chromosome anomaly, DNA from normal female with known CNVs and mosaic low level sample. NIBSC will commit to the establishment and banking of cell lines for CGH from abnormal genotypes.