

# Quality to rely on: meeting report of the 5th Meeting of External Quality Assessment, Naples 2016

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Improvement in the clinical outcome of patients with cancer comes in small steps. These steps are being taken by different professionals in different aspects of care: improved diagnosis, better surgery, new drugs, more complete ancillary care and, last but not least, a greater involvement of patients in decision-making. Many small steps will result in a big move forward, provided that the steps are in the right direction. When a diagnostic test fails to identify the correct patients for a certain drug the outcome may be negatively affected. This calls for quality across the whole clinical team and the activities that support the patient.

In April this year, for the fifth consecutive year, representatives of all stakeholders involved in promoting accurate diagnostic testing for anticancer drug selection gathered in Naples in order to optimise the chance that patients will have an appropriate test which forms the basis for the decision of administering targeted treatment. These stakeholders include pathologists, molecular biologists, quality managers, medical oncologists, representatives of the pharmaceutical companies, vendors of synthetic controls for diagnostic methods and equipment, patients and representatives of the European Medicines Agency (EMA). This focused meeting, with no more than 50–70 participants, has already proven to be effective by creating guidelines on a key aspect of quality in the chain: external quality assessment (EQA).<sup>1</sup> The Naples meeting is organised by the Italian Association of Medical Oncology (AIOM) together with the European Society of Pathology (ESP) and the Italian Association of Surgical Pathology (SIAPEC-IAP), with the endorsement of the European Society of Medical Oncology (ESMO). The 2016 meeting celebrated its fifth anniversary, and the start of IQN Path ASBL, a new

organisation that brings all stakeholders together who are involved with EQA.

EQA is one of the activities that measures and evaluates test performance in laboratories. It is usually performed by circulating samples with known characteristics, for example, KRAS mutation or strong HER2 expression, which are tested in the participating laboratories so that they can be evaluated on the quality of testing. This evaluation includes the actual test result, and also the turn-around time and reporting of results. It has been shown repeatedly that EQA leads to improved quality of testing. This sounds simple enough, but there are many challenges: testing methods change rapidly such as, the recent introduction of next generation sequencing; the types of material that need testing now include blood (the so-called ‘liquid biopsy’); the number of targets for testing are increasing (like the evolution of KRAS testing into RAS). These developments call for coordination and harmonisation. EQA provides a quality mark to laboratories that perform testing; therefore it is quite important that this quality mark is reliable. We need to prevent a movement of laboratories towards an ‘easy’ EQA provider, like one director of a programme remarked: “I received a letter from a participant complaining about not passing the bar and threatening to go to another scheme”. Interestingly enough the director of that other scheme was present too and remarked that he received similar letters.....

Fortunato Ciardiello, medical oncologist, gave an overview on the progress made in the treatment of colorectal cancer, including the introduction of targeted therapies, specifically epidermal growth factor receptor-targeted agents. He pointed out that these agents do have some effect when the whole group of patients with colorectal cancer is being treated, but with limited effect. Based

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on the biology of the tumour and treatment, at first patients with a *KRAS*-mutated tumour were excluded from the therapy and later also those who have a *NRAS* mutation. This was achieved thanks to several well-designed retrospective studies and using tissues saved for testing. With proper selection, the drugs have a much better cost-benefit profile and are thus a really important contributor to the better survival of patients with colorectal cancer. This calls for correct testing which was shown to be possible but should not be taken for granted. Results from EQA schemes indicated that there is a learning curve and that feedback from the organisers results in improvement.<sup>2</sup> The interaction of test providers and oncologists is quite important and chief medical officer, Jean-Yves Douillard proposed to come to a mutual agreement between IQN Path and ESMO to take this further.

Concern has arisen about the cost of the new drugs, even after optimal selection by correct testing. Francesco Perrone provided an impressive overview to what the effects of these costly medicines can be. In the USA, a debate has already started on cancer bankruptcy and the effects of financial strain on quality of life and even survival. Although these issues are nowadays not present in most European countries, there is certainly concern regarding the increasing costs of cancer drugs. So why are these drugs so costly? The answer is not so straightforward. Perrone showed that neither the costs of development or high efficacy are the drivers for high pricing. Without pointing too strongly towards the pharmaceutical industry (they do provide important breakthroughs) he did indicate that Europe needs to rethink its policy that health is an issue of member states rather than an issue of the Union: this makes the negotiation power weak, as is exemplified in an elegant study from van Harten *et al*<sup>3</sup> which showed the prices of cancer drugs varies enormously between European countries and between drugs, no country being generally better or worse off. Clearly better deals are possible.

Jola Gore-Booth, representing Europa-colon, provided a sharp insight in the wishes and stakes of patients: they want to trust the healthcare system and indeed want testing to be reliable. She feels that it should not be the responsibility of patients to look for the laboratory that provides good testing although she welcomes openness and transparency. In fact, Jola indicated that she was not even aware of the variation that exist in quality of testing and offered to seek projects in which patients, clinicians and testing facilities can jointly promote improvement.

It was interesting to have a deep insight into how the EMA, represented by Rosa Giuliani, decides that a new drug may be allowed in Europe: it needs to have more benefit than risk, nothing more nothing less. The EMA does not deal with costs or clinical relevance; indeed the healthcare system is not part of the responsibilities of the agency or the European Union for that matter (see above!). It was very much welcomed that the EMA is

open-minded towards diagnostic tests that accompany new (and old) drugs; even when there is already a test available, it is clear that based on experiences from practice better tests can be developed, leading to better patient selection.

EQA providers from Italy, France, Spain, the UK, Germany, Sweden and the European Society for Pathology provided insights into their way of working and the results. There were many similarities and experiences but also important differences. How is sample selection performed, how many difficult samples need to be chosen and what to do with laboratories to perform consistently below an acceptable level? The group decided to create a task force that will come up with a document that addresses these items, to be presented at the 2017 meeting and will be steered by Els Dequeker.

Quite some hours were spent on the challenging topic of blood-based testing. It is clear that this is a promising field that may result in earlier termination of treatment that is not effective and that this type of testing can replace invasive procedures to obtain tissue. Several techniques are already available as well as data from small patient series. It is already quite clear that there is variation between techniques and that the logistics of blood samples, storage and transportation are critical. This obviously calls for a clever approach to EQA, a task that also was assigned to a small working group. Based on experiences from QUIP, the German EQA provider, and UK NEQAS, and inputs from ESP EQA, GenTiss, AIOM and EMQN, a guideline on this topic will be written, coordinated by Manfred Dietel and Sandi Deans.

The most recent progress in the clinical implementation of liquid biopsy in lung and colorectal carcinoma were summarised by Jean Yves Douillard and Jesús García-Foncillas. The plans for an EQA testing on liquid biopsy under the umbrella of IQN Path were also illustrated by Sandi Deans. Results of the pilot phase are expected in the third-quarter of 2016, and it was decided to follow-up the EQA with the preparation of guidelines for liquid biopsy testing. This task was assigned to a working group lead by Sandi Deans, Jose Costa and Nicola Normanno.

The first four meetings on EQA had focused on DNA-based techniques, but it is clear that other tissue-based techniques are relevant as well: presentations from NordiQC and UK NEQAS on the results from EQA in immunohistochemistry indicated that more harmonisation is urgently needed. Although this technology is quite a bit older than DNA analyses, there are recent developments in the technology and the possibility for computer-aided evaluation that a new era is approaching: reliable quantification of protein in tissue context. Experiences with the more traditional approaches, however, show the need for stringent EQA. A working group for EQA for immunohistochemistry within the IQN Path was formed, led by Mogens Vyberg and Keith Miller.

Next generation sequencing techniques are rapidly replacing more traditional methods of determining DNA alterations that indicate eligibility for certain therapies. In fact, the methodology is now so mature that a manuscript could be discussed and that, with a few alterations, will be submitted for publication. This is quite a success from the 2015 meeting, when the task to create this was assigned to a group led by Sandi Deans. It is to be expected that this expert opinion document will serve the community well so that soon reliable targeted testing will become available for the majority of patients with cancer in Europe.

The presence of the industry was a great asset to the success of the meeting, since they were given the floor to show their solutions, which were often very promising and at the same time very practical. Although, or maybe thanks to, this is a very competitive field there was a clear mission for the whole group: to obtain a correct diagnosis for every patient at a very high possible quality at a very low possible price. All had agreed that EQA is an integral part of the whole process, a challenge for all scheme providers and for the IQN Path.

It was a fruitful meeting, not in the least because all participants were dedicated experts and know one another better and better. We believe a critical factor to the success of the meeting is that it is not too large allowing for personal interaction and plenty of discussion. The main risk for the meeting was the fine weather in beautiful Naples; nevertheless, the content of the session was such that these were even more tempting and all remained inside. Without discussion it was agreed that in 2017 there will be a follow-up meeting.

IQN Path ASBL is a not for profit association registered in Luxembourg.

The mission of IQN Path is to provide a coordination platform for EQA providers, testing laboratories, diagnostics companies and the pharmaceutical industry to address common challenges collaboratively and establish harmonisation and increased uptake of EQA in biomarker testing in tissue-based pathology. IQN Path would like to thank its members and corporate sponsors for making the platform such as success and particular thanks to Professor Han van Krieken the president of IQN Path, the Board and Dr Jacqueline Hall the

Executive Director. For more information please visit the IQN Path ASBL website: <http://www.iqnpath.org>

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**Ethics approval** This guideline does not contain any studies with human participants or animals performed by any of the authors. For this type of work human participants were not used and formal consent is not required.

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