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

Han van Krieken,1,2 Sandi Deans,3 Jacqueline A Hall,4,5 Nicola Normanno,6 Fortunato Ciardiello,7 Jean-Yves Douillard,8 on behalf of IQN Path A.S.B.L

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).1 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
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 im-
portant 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 organi-
sers results in improvement.2 The interaction of test pro-
viders 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
countries and between drugs, no country being gener-
ally 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 the results. There were many similarities and experi-
cences 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 pre-
seated 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 tech-
niques are already available as well as data from small
patient series. It is already quite clear that there is vari-
ation 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 implementa-
tion of liquid biopsy in lung and colorectal carcinoma
were summarised by Jean Wes Douillard and Jesús
García-Foncillas. The plans for an EQA testing on liquid
biopsy under the umbrella of IQN Path were also illu-
strated 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 har-
monisation 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 approach-
ing: 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

Author affiliations
1Department of Pathology, Radboud University Medical Center, Nijmegen, The Netherlands
2Department of Human Genetics, Radboud University Medical Center, Nijmegen, The Netherlands
3Department of Laboratory Medicine, UK NEQAS for Molecular Genetics, Royal Infirmary of Edinburgh, Edinburgh, UK
4IQN Path A.S.B.L, Luxembourg, Luxembourg
5Faculty Medicine, Division of Cancer, Department of Surgery & Cancer, Imperial College London, London, UK
6Cell Biology and Biotherapy Unit, Istituto Nazionale Tumouri “Fondazione Giovanni Pascale” IRCCS, Napoli, Italy
7Division of Medical Oncology Seconda Università di Napoli, Naples, Italy
8Chief Medical Officer, ESMO Lugano, Viganello, Switzerland

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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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