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Content

QIAGEN®

Sample & Assay Technologies

Dear valued customer,

Welcome to Issue No. 6 of the MDXpress newsletter, providing you with molecular diagnostics information from all over Europe. In this issue's Spotlight, we focus on diagnostic trends presented at the ECCMID, the key conference for infectious diseases, and we report on recent publications about cervical cancer prevention through HPV primary screening — which assay is best?

Also in this issue is our overview of new developments and discussions in personalized healthcare. We'll also introduce new IT solutions designed to help make you more efficient in the lab, and we share conclusions from a comparative performance study of QIAGEN's HIV diagnostic solution.

We hope you enjoy reading this issue of MDXpress and kindly encourage you to provide feedback about the content of this issue and submit suggestions for future issues. Contact us anytime at MDXpress@qiagen.com.

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Yours sincerely,

Dr. Tobias Ruckes
Vice President
Head of Marketing EMEA

News from the 23rd Annual European Congress of Clinical Microbiology and Infectious Diseases (ECCMID) Conference in Berlin, Germany

The dominant topics at the 23rd Annual Meeting of the European Society of Clinical Microbiology and Infectious Diseases this past April included the importance of accurate diagnosis of healthcare-associated infections (HAI), upcoming new strategies in managing HCV infections, and tuberculosis detection. Over 8,000 attendees from across the globe assembled to share the latest discoveries and newest developments in the areas of microbiology and infectious diseases, and 125 exhibitors presented state-of-the-art solutions for diagnosis and treatment.

Hartmut Goette, Associate Director Marketing, Local Marketing Management; Antje Plaschke-Schluetter, Senior Marketing Manager Central Europe; and Gavin Wall, Senior Scientific Affairs Manager, Regional Marketing EMEA

Healthcare-associated infections (HAI)

Perspectives on gender- and age-specific risks for HAI were presented in a session chaired by Professors Mario Poljak, Slovenia, and Birgitta Evengard, Sweden. Prof. Hilary Humphreys, Dublin, Ireland, discussed data from various studies and concluded that the risk for bloodstream infections with methicillin-resistant *Staphylococcus aureus* (MRSA) is generally higher in men, probably due to higher skin colonization risk, as well as innate immune and endocrinological factors. Prof. Pierluigi Viale, Bologna, Italy, showed that women face a significantly higher risk of developing healthcare-associated urinary tract infections (UTI), which are mainly caused by extended spectrum beta-lactamase (ESBL)-producing and multidrug-resistant Enterobacteriaceae.

The face of HAI in Europe has changed over the past decade, due to multinational, national, and regional strategies for infection control and surveillance, antibiotic

policy, and education. The primary challenges with HAI today are *Clostridium difficile* (*C. diff*) infections, increasing genetic complexity in MRSA infections (e.g., MRSA mecC), multidrug-resistant Gram-negative bacteria, and ESBL-producing bacteria with carbapenem resistance; all of which require fast and cost-effective diagnostic solutions, such as QIAGEN´s reliable real-time PCR tests that will soon be available for use on the QIAsymphony® RGQ platform.

HCV infection management

New hepatitis C virus (HCV) treatment options with second-generation direct-acting antiviral agents (DAAs) will likely reshape the current interferon/ribavirin therapy landscape and redefine HCV diagnosis and treatment practices. Prof. Heiner Wedemeyer, Hannover, Germany, presented the most recent developments in clinical HCV research and provided an outlook for the future. While drug resistance to first-generation DAAs remains a near-term hurdle, requirements for accurate

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1. Kutsyna, G.A. and van Ingen, J. (chairpersons) (2013) Interferon gamma release assay for tuberculosis. In: Final Programme: European Congress of Clinical Microbiology and Infectious Diseases, Berlin, Germany, April 27–30. 60.

viral load testing and treatment monitoring algorithms will be challenges for the next decade, as the clinical implications of test results have to be determined individually for every HCV viral load test.

In addition to the QIAGEN exhibit at the conference, several poster presentations displayed the excellent performance of the *artus*® HCV QS-RGQ Kit on the automated QIAsymphony RGQ for quantitation of viral load in routine diagnostic laboratories across Europe. Results demonstrated that the *artus* HCV QS-RGQ Kit on the QIAsymphony RGQ provides an efficient automated solution for the increasing demand for HCV viral load monitoring, while also meeting EASL Clinical Practice Guidelines requirements.

Tuberculosis (TB) detection

A number of lectures focused on tuberculosis infections, with particular interest in patients with comorbidities such as HIV infection or transplantation with subsequent immunosuppressive treatment. These patients, when harboring a latent infection with *Mycobacterium tuberculosis*, face a significant risk for developing active TB disease and require strict monitoring. Dr. Martina Sester, Hamburg, Germany, presented the results of a large multicenter study designed by the Tuberculosis Network European Trialsgroup (TBNET), which conducts clinically-oriented TB research in Europe. The study clearly demonstrated the superiority of interferon-gamma release assays (IGRAs), for example, QIAGEN´s QuantiFERON®-TB Gold Test, over traditional skin testing for detecting and monitoring high risk patients with latent TB infections (1). Consequently, the speaker recommended the routine use of IGRA testing in immunocompromised patients.

Results of the HORIZON Study — Primary HPV Screening for Cervical Cancer: Which Assay?

The results of the largest independent performance evaluation of commercially available HPV tests, within a primary screening population, have recently been reported (1–5). The HORIZON study evaluated the performance of various commercially available assays, including QIAGEN's *digene*® HC2 High-Risk HPV DNA Test®, within the Danish cervical screening population. The study showed QIAGEN's Hybrid Capture® 2 (HC2) technology demonstrated consistently high performance.

Adrian Smith, Senior Manager Market Development, Regional Marketing EMEA

1. Preisler, S. et al. (2013) Prevalence of human papillomavirus in 5,072 consecutive cervical SurePath samples evaluated with the Roche *cobas* HPV real-time PCR assay. PLoS ONE **8** (3), e59765.
2. Bonde, J. (2012) Cross reactivity of Roche *cobas* HPV Test, QIAGEN Hybrid Capture 2, and Gen-Probe APTIMA with non-oncogenic human papillomavirus types; implications for molecular cervical cancer screening. In: Abstracts Book: Clinical Sciences 28th International Papillomavirus Conference & Clinical Health Workshops, November 30–December 6, 2012, 113.

Reproducibility and positivity rates

HORIZON evaluated unselected, consecutive primary cervical BD SurePath® samples using QIAGEN's *digene* HC2 High-Risk HPV DNA Test, *cobas*® HPV Test, Gen-Probe APTIMA® HPV assay, and CLART® HPV2 microarray. The *digene* HC2 High-Risk HPV DNA Test, using Hybrid Capture 2 (HC2) technology, demonstrated the highest overall positive and negative reproducibility (4). Low negative reproducibility is indicative of false negatives, which reduces the negative predictive value of HPV screening, and low positive reproducibility is correlated to false positives that can compromise the clinical efficacy of a screening program.

▶

The HORIZON study also shows higher than expected positivity rates for PCR assays in a primary screening population. This has implications for the costs and efficiency of a PCR-based HPV screening program, particularly if the evidence to implement HPV testing is based on data generated using QIAGEN's Hybrid Capture 2 technology.

HORIZON study vs. ATHENA trial

In addition to the above group analysis, when specifically comparing the *cobas* HPV Test to the *digene* HC2 High-Risk HPV DNA Test, the authors found that the proportion of positive *cobas* HPV samples was higher than the proportion stated in the Roche®-sponsored ATHENA trial: the age-standardized *cobas* positivity vs. cytology abnormality was 3.9 and 1.7 in HORIZON and ATHENA, respectively. The authors concluded that if the presently-used cytology was replaced by *cobas* HPV in Copenhagen, an extra 11% of women aged 30 and older would (based on historical data) be expected to have a positive *cobas* test without an underlying cervical intraepithelial lesion grade 3 or worse (≥CIN 3).

QIAGEN's Hybrid Capture 2 technology as the gold standard

In addition to having the highest overall reproducibility, the *digene* HC2 High-Risk HPV DNA Test also demonstrated the lowest overall positivity rate of the evaluated commercially available DNA tests. Furthermore, QIAGEN's HC2 technology also showed the highest overall concordance with baseline cytology (1–5). This new data, combined with HC2's proven high sensitivity for detecting CIN 2+, confirms why the *digene* HC2 High-Risk HPV DNA Test, remains the global gold-standard for HPV testing in cervical cancer diagnosis and screening.

3. Bonde, J. (2012) Genotype-specific prevalence of HPV infection in Denmark. In: Abstracts Book: Clinical Sciences 28th International Papillomavirus Conference & Clinical Health Workshops, November 30–December 6, 2012, 114.
4. Ejegod, D. (2012) Reproducibility of HPV detection using the Roche *cobas* HPV Test, QIAGEN Hybrid Capture 2, Gen-Probe APTIMA, and Genomica CLART Assays; implications for molecular cervical screening. In: Abstracts Book: Clinical Sciences 28th International Papillomavirus Conference & Clinical Health Workshops, November 30–December 6, 2012, 115.
5. Bonde, J. (2012) Roche *cobas* HPV and real-time PCR assay using SurePath samples in a screened population with a high background risk of cervical cancer. In: Abstracts Book: Clinical Sciences 28th International Papillomavirus Conference & Clinical Health Workshops, November 30–December 6, 2012, 116.

Personalized Cancer Treatment: the Role of Next-Generation Sequencing (NGS)

Today, doctors and researchers are shifting towards a new approach of cancer treatment. Chemotherapy has long been associated with devastating side effects that outweigh treatment success. By identifying specific cancers and understanding them at the DNA level, we can develop targeted treatments with fewer side effects. Personalized treatments are already showing promise in breast and lung cancers, and melanomas (1).

Joerg Teubner, Senior Marketing Manager PHC/Oncology

1. Taylor, W. (2012) Cancer care: a personal touch. Personalized health: an independent media supplement by Mediaplanet to USA Today, September 2012, 8.

Personalizing medicine

Research is already resulting in drugs that inhibit molecules (EGFR and BRAF) in tumors containing mutations in the corresponding genes. Such mutations contribute to uncontrolled growth. Regulated assays (CE-IVD) for real-time PCR (on Rotor-Gene® Q) and Pyrosequencing® (using PyroMark® Q24) have been developed to complement the effectiveness of such drugs. These regulated assays provide reliable results for determining the mutation status of the patient's tumor, and make it easier to establish an appropriate

test matrix after drug launch. However, personalizing treatment for cancer requires more and more data, and corresponding analyses — the fulcrum of the paradigm shift.

"This breakthrough technology will be highly complementary to established molecular testing with real-time PCR, and it will allow us to generate massive amounts of information on a patient. However, more data is not always better, since it will be critical to understand the clinical relevance in terms of treatment options," says Richard Watts, Vice President Business Development Companion Diagnostic Partnerships, QIAGEN Ltd.

Will next-generation sequencing, or multiplex testing, become the only way of the future? Consultant histopathologist Dr. Philippe Taniere from Birmingham says, "I don't believe one technique will replace everything — we need to cover all the patients, every type of tumor, every alteration, which makes it more exciting. But we need to have some companies with these wide panels of kits and techniques working, and upgrading, to follow the needs."

Next-generation sequencing: the next big breakthrough

Today, our increasing ability to analyze more and more biomarkers in the same tumor has highlighted the value of next-generation sequencing (NGS). Some researchers predict we will soon be analyzing every patient tumor at the DNA level to maximize targets and, as a result, enable a battery of drugs to use in a personalized treatment plan (1).

QIAGEN is preparing to introduce the comprehensive sample-to-insight NGS workflow, that includes meaningful analysis of the massive amounts of information that is generated, to provide solutions for biomedical and clinical applications.

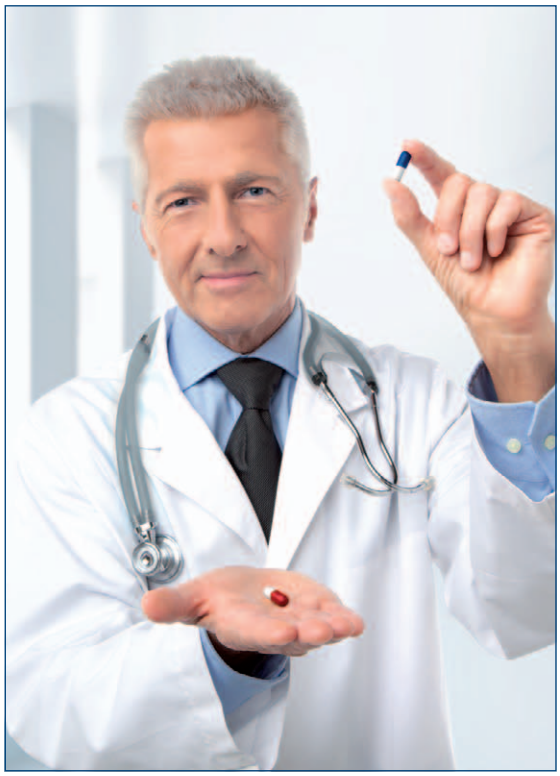
QIAGEN's Companion Diagnostic Partnerships

Personalized medicine is a major trend today, with genetic information enabling the development of customized treatments for each patient. As a result, companion diagnostics that predict which patients are most likely to benefit from a particular therapy, or how a therapy would best be administered to an individual, are becoming increasingly significant. Together, personalized medicine and companion diagnostics allow us to treat the right patients with the right drugs, and increase treatment efficacy, minimize side effects, and improve cost efficiency.

Joerg Teubner, Senior Marketing Manager PHC/Oncology

Making medicine personal

The traditional approach of using blockbuster drugs for all patients suffering from a disease is shifting towards the stratification of patients based on biomarkers. Drugs can elicit a multitude of patient responses and results, creating the need for understanding disease mechanism and drug function at the individual patient level — a more personalized approach. The summary report, *Stratification biomarkers in personalized medicine*, from the Biomarkers for Patient Stratification workshop in Brussels, defines personalized medicine as "a medical model using molecular profiling technologies for fitting the right therapeutic strategy to the right person at the right time, and determine the predisposition to disease at the population level, and to deliver timely and stratified prevention" (1). Companion diagnostics are a key component of this personalized treatment method.



From biomarker to assay

Developing sensitive and specific companion diagnostics is a long and complicated process that involves identification of suitable biomarkers, assay development, and clinical trial evaluations to confirm that the assay is acceptable for use in drug development. As such, it is critical to include diagnostics professionals in the process. This is especially important in commercial environments, where timing is crucial for maximizing success in drug–diagnostic development. In addition, beginning the process early with consultancy from diagnostics professionals can help minimize the risk of failure, preferably beginning during the preclinical phase or Phase I of clinical development. FDA approval, in particular, requires prospective clinical data. Therefore, access to an appropriate diagnostic before beginning clinical trials can be imperative. The companion diagnostic development workflow to achieve a specified goal greatly benefits from expert consideration. ▶

1. European Commission, Health Research Directorate (2010) Stratification biomarkers in personalised medicine. Biomarkers for Patient Stratification workshop, June 10–11, Brussels, 5.

Several tools are crucial for identifying suitable biomarkers during Phase I and II on preclinical and clinical samples:

- Assay design, development, and manufacture
- Range of pre-analytical products and platforms
- Investigational Use Only kits to support clinical trials during client collaborations
- Biomarker and genetic content IP

After the approval of a drug and a companion diagnostic test, the test has to be readily available. A professional in diagnostics should be consulted for assistance, and provide support in the following areas:

- Medical education and advocacy development programs
- Global sales, marketing, and distribution network
- Consultancy and lobbyist for reimbursement support
- Scientific advisory board and KOL management
- Medical education and communication
- Joint symposia at conferences
- Patient advocacy

Molecular Diagnostics Solutions for Classification of Gliomas

Gliomas are the most frequent (70%) primary malignant brain tumors and the Central Brain Tumor Registry of the United States reports an annual incidence rate of 7.3 cases per 100,000 (1, 2). Glioblastomas represent 65% of all gliomas and, despite advances in neurosurgery and treatment, little progress has been made over the last decade for the treatment of this tumor type (1, 3).

Veronique Laloux, Marketing Manager PHC/Oncology, and Joerg Teubner, Senior Marketing Manager PHC/Oncology, QIAGEN GmbH, Hilden, Germany

Diagnosis and therapy

Current diagnosis relies on imaging techniques and WHO classification based on histopathological evaluation. However, this classification relies on microscopic appearance and is limited by high interobserver discrepancies and by imperfect prediction of individual outcomes due to clinical heterogeneity among each histological subgroup (4).

Glioma treatment is based on a combination of surgery, radiotherapy, and chemotherapy. Maximal safe resection, whenever feasible, represents the first treatment option. Since treatment is guided by clinical factors and histological diagnosis, an incorrect histological classification could result in over- or under-treatment (4). Therefore, clinicians are looking for new molecular tools that improve diagnosis and enable more personalized therapies for this heterogeneous disease.

Biomarkers

Several recently identified biomarkers, such as 1p/19q co-deletion, MGMT promoter methylation, and isocitrate dehydrogenase (*IDH*)1/2 mutations, may be useful for refining glioma classification (5). In addition, these biomarkers could provide information for more reproducible and accurate histomolecular diagnosis, and improve prediction of prognosis. These biomarkers also have the potential to guide therapy in the challenging clinical management of gliomas (6). ▶

1. Ohgaki, H. and Kleihues, P. (2005) Epidemiology and etiology of gliomas. Acta Neuropathol **109**, 93.
2. Central Brain Tumor Registry of the United States, CBTRUS fact sheet, www.cbtrus.org/factsheet/factsheet.html (accessed July 17, 2013).
3. Louis, D.N. et al. (2007) The 2007 WHO classification of tumours of the central nervous system. Acta Neuropathol **114**, 97.
4. Van den Bent, M.J. (2010) Interobserver variation of the histopathological diagnosis in clinical trials on glioma: a clinician's perspective. Acta Neuropathol **120**, 297.
5. Riemenschneider, M.J., Jeuken, J.W.M, Wesseling, P., and Reifenberger, G. (2010) Molecular diagnostics of gliomas: state of the art. Acta Neuropathol **120**, 567.
6. Febbo, P.G. et al. (2011) NCCN Task Force Report: Evaluating the clinical utility of tumor markers in oncology. JNCCN **9**, (Supp. 5), S-1.

MGMT promoter methylation

MGMT promoter methylation has been correlated with outcome of glioblastoma patients treated with alkylating agent chemotherapy (7). QIAGEN's CE-IVD marked *therascreen*® MGMT Pyro Kit (cat. no. 971061) provides real-time quantitative measurements of methylation status in exon 1 of the human MGMT gene using Pyrosequencing technology on the PyroMark Q24 system. This molecular assay is intended for use as an adjunct to other prognostic factors, and to provide clinicians with information to assist in the selection of cancer patients who are more likely to benefit from chemotherapies.

*IDH*1 and *IDH*2 mutations

The high frequency and distribution of *IDH*1/2 mutations among specific brain tumors make *IDH*1/2 mutation status a diagnostic hallmark of gliomas, and a strong positive prognostic marker. *IDH*1/2 mutations are found in up to 80% of WHO grade II and III gliomas, and in around 15% of secondary glioblastoma (GBM), but are rarely identified in primary GBM (8). *IDH*1 mutations have been associated with longer survival in glioma patients, highlighting the clinical relevance of mutation status (9, 10).

QIAGEN is excited to announce the new CE-IVD labeled *therascreen IDH*1/2 RGQ PCR Kit CE (cat. no. 873011) for rapid, sensitive, and reliable detection of 12 *IDH*1 and *IDH*2 mutations in DNA from FFPE brain tumor tissue specimens using real-time PCR on the Rotor-Gene Q MDx instrument.

The assay provides, simultaneously, in one step:

- Accurate detection of 7 *IDH*1 (in codons 132 and 100) and 5 *IDH*2 (in codon 172) mutations
- Sensitive identification of 3 main mutations *IDH*1 R132H, *IDH*1 R132C, and *IDH*2 R172K

This molecular assay, which supplements surgical resection, aids in the classification of gliomas, as well as the identification of patients with favorable prognosis.

7. Hegi, M.E. et al. (2005) MGMT gene silencing and benefit from temozolomide in glioblastoma. N Engl J Med **352**, 997.
8. Yan, H. et al. (2009) *IDH*1 and *IDH*2 mutations in gliomas. N Engl J Med **352** (8), 765.
9. Parsons, D.W. et al. (2008) An integrated genomic analysis of human glioblastoma multiforme. Science **321**, 1807.
10. Kloosterhof, N.K., Bralten, L.B.C., Dubbink, H.J., French, P.J., and van den Bent, M.J. (2011) Isocitrate dehydrogenase-1 mutations: a fundamentally new understanding of diffuse glioma? Lancet Oncol **12**, 83.

New CE-IVD *artus* CT/NG Assay for QIAsymphony RGQ

The new *artus* CT/NG QS-RGQ Kit for automated qualitative detection of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* using the QIAsymphony RGQ system is now available.

Adrian Smith, Senior Manager Market Development, Regional Marketing EMEA

New CE-IVD *artus* CT/NG QS-RGQ Kit

The *artus* CT/NG QS-RGQ Kit is a quadruplex assay that includes an internal control. The assay is designed to target an 86 bp region of the *C. trachomatis* cryptic plasmid, a 66 bp region of the *C. trachomatis* genome, and a 74 bp region of the *N. gonorrhoeae* genome. A fourth heterologous amplification system for identifying possible PCR inhibition serves as an internal control.

Dual target-PCR for detecting *C. trachomatis* also ensures robust detection of a new genetic variant (nvCT) that was discovered in Sweden in 2006 and is not detectable with the most commonly used diagnostic tests.

The *artus* CT/NG QS-RGQ Kit is intended for use as a diagnostic test for *C. trachomatis* and/or *N. gonorrhoeae* in symptomatic or asymptomatic patients. The test can be performed on urine or physician-collected urogenital, cervical, and vaginal samples, as well as male urethral swab specimens.

QIAsymphony RGQ assays

The *artus* CT/NG QS-RGQ Kit is QIAGEN's most recent addition to the substantial assay menu available on the QIAsymphony RGQ platform, which has the most comprehensive assay menu of all automated PCR platforms. The release of this new assay underscores QIAGEN's commitment to providing the most complete and automated diagnostic solutions for women's health and sexually-transmitted infections (STI) available on the market today, and is only the first of many assays that will be launched for the QIAsymphony RGQ platform in the coming months.

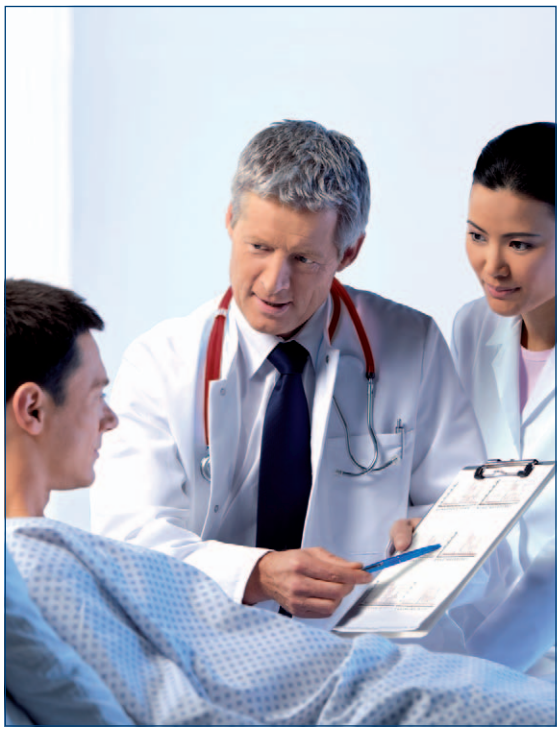
Upcoming Molecular Assays for Healthcare-Associated Infections (HAI)

The United States Centers for Disease Control and Prevention defines healthcare-associated infections (HAI), also known as nosocomial infections, as "infections that patients acquire during the course of receiving healthcare treatment for other conditions" (1). HAI affect hundreds of millions of patients globally, and are responsible for 5.8 million infected patients and 246,000 deaths in the US and Europe each year (2, 3).

Silke Garcés, Marketing Manager Infectious Diseases, QIAGEN GmbH, Hilden, Germany

Healthcare-associated infections

The most common microbial agents involved in HAI are methicillin-resistant *Staphylococcus aureus* (MRSA), *Clostridium difficile* (*C. diff*), extended-spectrum beta-lactamase–producing Enterobacteriaceae (ESBL), carbapenem-resistant Enterobacteriaceae (CRE), and vancomycin-resistant enterococci (VRE). Uncontrolled spread of infection leads to prolonged hospital stays, lengthy antibiotic treatments, and serious financial burden for public healthcare systems. Molecular tests address the urgent need for fast turnaround time and can therefore help reduce patient cross-infection. Rapid diagnosis of affected patients also has the potential to prevent thousands of deaths.



New assays for *C. diff*, MRSA, VRE, CRE, and ESBL

QIAGEN is launching molecular assays for detection of *C. diff*, MRSA, and VRE on the QIAsymphony RGQ platform by the end of 2013, with ESBL and CRE to follow later. All assay workflows are CE-IVD–validated and include Rotor-Gene AssayManager® profiles. Dual-target detection provides superior performance and minimizes false negative results. QIAGEN's product portfolio for HAI testing is the next phase in menu expansion for our flagship platform, the QIAsymphony RGQ, and will allow greater utilization of this innovative workflow solution, which is already well established in blood-borne virus and transplant panel testing.

1. United States CDC homepage for HAI www.cdc.gov/hai/index.html (accessed June 13, 2013).
2. WHO webpage for The global burden of health care-associated infections webinar www.who.int/gpsc/5may/media/infection_control_webinar_19012010.pdf (accessed June 17, 2013).
3. WHO webpage for Health care-associated infections FACT SHEET document www.who.int/gpsc/country_work/gpsc_ccisc_fact_sheet_en.pdf (accessed June 17, 2013).

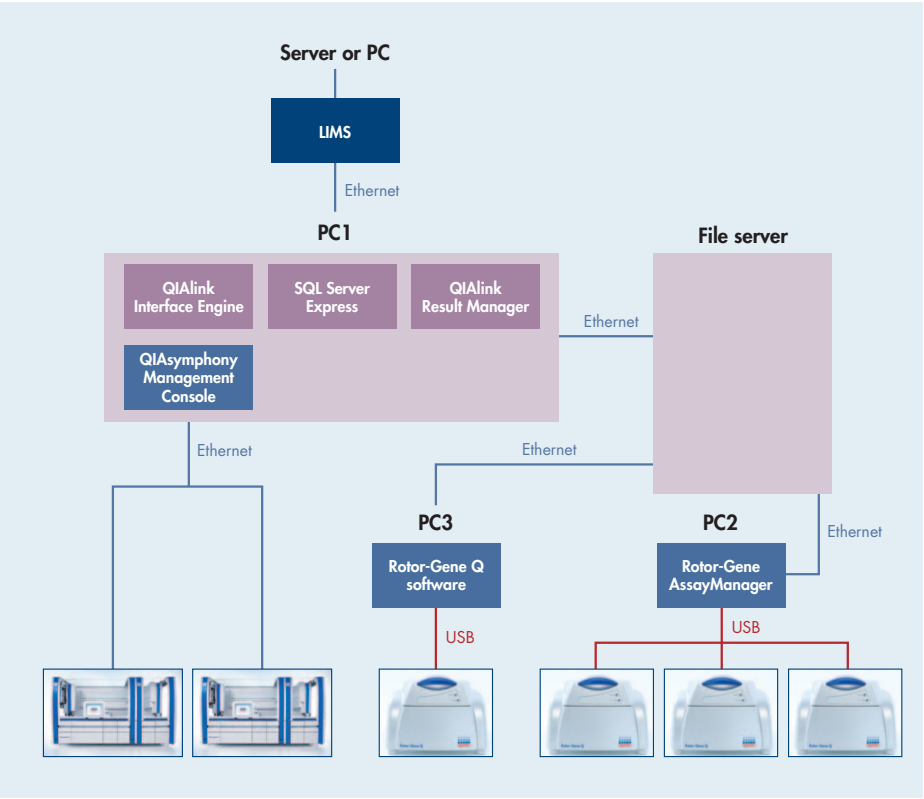
Seamless Integration of QIAsymphony RGQ Workflow into LIMS

Molecular testing laboratories are under constant pressure to provide faster results. Using Laboratory Information Management Systems (LIMS) to handle patient data and store laboratory information increases the workflow speeds and saves valuable staff time. However, a molecular testing workflow may include many steps that are often performed by different instruments. If data flow between instruments and LIMS is not fully integrated, data has to be manually transferred, which can be time-consuming, error-prone, and costly.

Silke Garcés, Marketing Manager Infectious Diseases, QIAGEN GmbH, Hilden, Germany

QIAlink™ to your LIMS

QIAlink software comprises two modules that function in parallel, providing the data handling functionality your laboratory needs. QIAlink Interface Engine automates data transfer between QIAsymphony SP/AS instruments, Rotor-Gene Q, and LIMS, improving the efficiency and productivity of your laboratory workflow. QIAlink Result Manager facilitates quality control by managing all process data from the workflow. Seamless integration of QIAlink middleware into your LIMS and QIAsymphony RGQ workflow is assured by the fast and professional installation service included with the software.



Features include:

- Automated order transfer from LIMS to QIAsymphony RGQ
- Automated transfer of results from Rotor-Gene Q to LIMS
- Verification of results in less time and with less effort
- Complete traceability of all sample-related data
- Fast startup with full installation service

Contact QIAGEN

QIAGEN's specialist team is highly trained and experienced in LIMS integration, and is ready to address your individual integration requests. QIAGEN's LIMS integration service offering is also scalable, so you can choose the level of training and support you need according to your own business requirements. For more information regarding QIAlink software, contact your local sales specialists or send us an email at service_sales_eu@qiagen.com.

HORIZON Study — QIAGEN´s Hybrid Capture 2 Technology Remains Gold-Standard

For this study, 6,258 consecutive cervical samples were collected from the largest cervical screening laboratory in Denmark, which serves all of Copenhagen. In total, 5,072 samples, which are considered highly representative of the Danish screening population, were tested with QIAGEN's *digene* HC2 High-Risk HPV DNA Test, the *cobas* HPV Test, and liquid-based cytology.

Review by Adrian Smith, Senior Manager Market Development, Regional Marketing EMEA, of Preisler, S. et al. (2013) Prevalence of human papillomavirus in 5,072 consecutive cervical SurePath samples evaluated with the Roche *cobas* HPV real-time PCR assay in PLoS ONE (the HORIZON study) (1).

Introduction

Both the *digene* HC2 High-Risk HPV DNA Test and the *digene* HC2 HPV DNA Test (i.e., the *digene* HPV Tests), with Hybrid Capture 2 (HC2) technology, have been thoroughly studied worldwide. As a result, the *digene* HPV Tests are regarded as the gold-standard HPV DNA assay, and most of the data used to support HPV testing in screening programs is based on Hybrid Capture 2 technology.

Although new HPV assays have recently entered the market, these assays differ from QIAGEN's in terms of chemistry and number of viral gene targets, and may also differ in clinical characteristics. Therefore, new assays need to be independently evaluated within the relevant settings to show that they have acceptable performance characteristics before they can be considered suitable for use within a screening program. The HORIZON study independently assessed the performance of the *cobas* HPV test in comparison with the *digene* HC2 High-Risk HPV DNA Test in a primary screening population in Copenhagen.

Prevalence

The authors report that 27% of 5,072 samples tested positive on the *cobas* assay, 20% tested positive with the *digene* HC2 High-Risk HPV DNA Test, and cytology was abnormal in 7% . Among women with normal cytology, 22.9% tested positive on *cobas* and 15.6% tested positive with QIAGEN's *digene* HC2 HPV assay. Among women with ASCUS, the results were 63.4% positive on *cobas* and 64.2% positive on *digene* HC2. For LSIL, the proportions were 79.7% and 89.5%, and for HSIL, they were 88.8% and 90.7%, for *cobas* and the *digene* HC2 High-Risk HPV DNA Test, respectively. In addition, the authors found that 11% of samples with >HSIL on cytology tested negative on the *cobas* assay. The authors note: "In the Danish screening program, women with >HSIL are currently referred for colposcopy without HPV DNA triage" (1). ▶

1. Preisler, S. et al. (2013) Prevalence of human papillomavirus in 5,072 consecutive cervical SurePath samples evaluated with the Roche *cobas* HPV real-time PCR assay. PLoS ONE **8** (3), e59765.

Intra-laboratory assay reproducibility

The study showed that 272/300 (90.7%) samples that tested positive on the initial *cobas* run also tested positive in the second run. The authors conclude that 90.7% positive reproducibility for the *cobas* HPV Test "suggests that the calibration of the *cobas* HPV probe for ''other high-risk genotypes'' was not highly robust" (1). In comparison, data presented at IPV 2012 showed that HPV testing with QIAGEN's Hybrid Capture 2 technology demonstrated positive reproducibility of 99.3% (2).

Comparison with ATHENA study

In this study, the difference between the proportion of positive *cobas* samples and the proportion of abnormal cytology (3.9) was more than double the Roche®-sponsored ATHENA study (1.7). The authors conclude that this finding underscores the need for local trial data before decisions on future screening tests are expanded to regional or national levels.

Summary:

- This is the first study to evaluate commercially available assays in a primary screening population
- Authors show the performance of *cobas* HPV is very different from QIAGEN's *digene* HC2 High-Risk HPV DNA Test
- *cobas* HPV was positive more often than *digene* HC2 HPV in a primary screening population (24% vs. 19%)
- The *digene* HC2 HPV assay showed superior reproducibility compared to *cobas* HPV in a primary screening population
- The *digene* HC2 HPV assay demonstrates better concordance with cytology than *cobas* HPV.
- 11% of women in the study with ≥HSIL had a negative *cobas* HPV result
- Recently introduced assays may not have the same performance characteristics as the *digene* HC2 HPV assay
- Substituting the *digene* HC2 High-Risk HPV DNA Test with the *cobas* HPV assay in a screening program could have significant implications

2. Ejegod, D. (2012) Reproducibility of HPV detection using the Roche *cobas* HPV Test, QIAGEN Hybrid Capture 2, Gen-Probe APTIMA, and Genomica CLART Assays; implications for molecular cervical screening. In: Abstracts Book: Clinical Sciences 28th International Papillomavirus Conference & Clinical Health Workshops, November 30–December 6, 2012, 115.

artus HI Virus-1 QS-RGQ Kit — Suitable for Viral Load Monitoring in Clinical Practice

The primary goal of highly active antiretroviral treatment (HAART) is to reduce the replication of HIV-1 to a minimal level, thus preventing infection of new CD4 cells and slowing the progression to AIDS. Since the first quantitative assays became available in the 1990s, viral load testing and regular CD4 cell quantitation have become the standard of care for HIV-infected individuals, aiming to reduce the HIV-1 titer to <50 copies/ml. This study evaluated the performance of the *artus* HI Virus-1 QS-RGQ Kit for viral load quantitation in a direct comparison with another commercially-available assay.

Review by Gavin Wall, Senior Scientific Affairs Manager, Regional Marketing EMEA, QIAGEN, of Garcia-Diaz, A. et al. (2013). Comparative evaluation of the *artus* HIV-1 QS-RGQ assay and the Abbott RealTime HIV-1 assay for the quantification of HIV-1 RNA in plasma in Journal of Clinical Virology (1).

Assays

Various CE-IVD approved assays are available in Europe, including the ABBOTT REALTIME® system and Siemens' kPCR assay, which is the most recent assay to receive CE-IVD approval. The *artus* HI Virus-1 QS-RGQ Kit has been available in Europe since 2010. It is important to thoroughly compare all assays to established procedures to develop clinical references and validate the assays prior to any change in routine laboratory practice. In addition, because HIV-1 is a very genetically diverse virus, it is important to evaluate the performance of quantitative assays on HIV-1 non-B subtypes.

Statistics

Anna Maria Geretti's group tested the performance of the *artus* HI Virus-1 QS-RGQ Kit compared to the Abbott RealTime assay with 211 HIV-1 positive plasma samples. Emphasis was placed on assay performance with diverse subtypes, including those not included in the CE-IVD claims, and generation of manufacturer-independent performance data. Serial dilutions of the 2nd WHO International Standard were also tested. As the Royal Free Hospital serves a diverse population in northwest London, 55% of the samples were subtype B and 45% non-subtype B, providing a good range of HIV-1 subtypes to test the agreement of both assays. Correlation analysis of results (R^2 = 0.94 for all samples and 0.90 for non-B subtypes) highlight a good comparison of viral loads in multiple non-B subtypes. Five samples were outside the 2SD limits of the Bland-Altman plot (3 quantified higher by Abbott, 2 higher by QIAGEN) but it is important to note that these samples were not subtype-specific. In addition, inter-assay reproducibility of 24 samples tested with the *artus* HI Virus-1 QS-RGQ assay resulted in a mean difference of 0.13 $\log_{10}$ copies/ml.

Summary

In conclusion, the study group showed that HIV-1 measurements obtained with both systems were linearly associated and strongly correlated, with a mean log difference of 0.24 $\log_{10}$ copies/ml. Excellent performance was demonstrated with a highly diverse panel of samples, including 8 samples with complex recombinant sequences, and the paper endorses the *artus* HI Virus-1 QS-RGQ Kit as a valid option for viral load monitoring in clinical practice.

1. Garcia-Diaz, A., Labbett, W., Clewley, G.S., Guerrero-Ramos, A., and Geretti, A.M. (2013) Comparative evaluation of the *artus* HIV-1 QS-RGQ assay and the Abbott RealTime HIV-1 assay for the quantification of HIV-1 RNA in plasma. J Clin Virol **57**, 66.

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