

# Xpert™ BCR-ABL Monitor

*Simplified, rapid testing for  
improved CML patient management.*



CE IVD In Vitro Diagnostic Medical Device

defining *on-demand* molecular diagnostics.

 **Cepheid®**  
Bring answers to life.

# Xpert™ BCR-ABL: Real-time PCR assay for the detection and quantification of the p210 transcript

The Xpert BCR-ABL Monitor™ assay, which detects the BCR-ABL chromosomal translocation, is a quantitative nested real-time reverse-transcription PCR (RT-PCR) assay, intended as an aid in monitoring the p210 (b2a2 and b3a2) transcript in peripheral blood lymphocytes (PBL) of patients with chronic myelogenous leukemia (CML). This revolutionary assay boasts features not available in current testing methods, including: minimal hands-on time while delivering answers in just over two hours, and unprecedented sensitivity, specificity and reproducibility that are achieved by virtue of the world's first nested real-time PCR system.

## quantitative RT-PCR:

Current practice guidelines from Europe Against Cancer and National Comprehensive Cancer Network (NCCN) for management of patients with CML call for use of quantitative Reverse Transcription Polymerase Chain Reaction (RT-PCR) assays during the initial workup of patients with chronic phase CML, to monitor for minimal residual disease, and to identify patients who may

be at a high risk for relapse<sup>1,2</sup>. RT-PCR has been shown to be an accurate and highly sensitive method for detection of the BCR-ABL fusion gene<sup>2-13</sup>, and is more sensitive than Fluorescence In Situ Hybridization (FISH) or cytogenetics<sup>2</sup>.

## sensitive:

An additional advantage of quantitative PCR versus FISH and cytogenetics is the high correlation of PCR results

Xpert:  
in action

obtained from bone marrow and peripheral blood samples<sup>1,2</sup>. Therefore, PCR may potentially reduce the bone marrow aspirations currently required in testing patients with CML.

## integrated:

The GeneXpert® is the only system to combine sample preparation with real time PCR amplification and detection for fully integrated and automated nucleic acid analysis. The system purifies, concentrates, detects, and identifies targeted nucleic acid sequences in about 2.5 hours.

## flexible:

The GeneXpert System's unique random access capability enables users to perform from one to 16 molecular tests concurrently. And because runs can be started at different times, multiple operators can easily use the GeneXpert System simultaneously. With the GeneXpert System, the days of inefficient batch processing are finally over. Specimens can now be processed on demand — 24 hours a day, 365 days a year.

Xpert:  
by design

## easy to use:

The GeneXpert System requires minimal hands-on time. Users simply insert the biological sample for testing in a self-contained cartridge and the GeneXpert System does the rest.



## Reproducible:

Provide the best patient management decisions.

Table 1: Assay Precision

Sample	Avg% BCR-ABL/ABL	% BCR-ABL/ABL Std. Dev.
Negative BCR-ABL	< 0.000157%	-
Low BCR-ABL	0.00430%	0.00477%
Moderate BCR-ABL	0.954%	0.397%
High BCR-ABL	12.24%	5.03%

Precision was evaluated in a three-site, blinded, comparative study using four specimens with varying concentrations of BCR-ABL. A total of 240 specimens were included in the study. Study specimens consisted of four sample levels: negative, and one of each of low, moderate, high BCR-ABL RNA levels. These specimens were prepared using whole blood from healthy donors with different levels of K562 RNA. Each value represents 60 specimens run over five days at three evaluation sites with multiple operators.

## Specific:

Ideal for monitoring in CML patients.

The specificity of the assay was tested using 41 normal citrate and EDTA blood specimens from three sites. All normal specimens were negative for BCR-ABL, yielding a specificity of 100%. The specificity of the assay was also tested at two sites using a collection of 11 blood specimens from patients with other myeloproliferative disorders including acute myelogenous leukemia, acute lymphocytic leukemia, Hodgkin's lymphoma, multiple myeloma and follicular lymphoma. All of these samples were negative for BCR-ABL, yielding a specificity of 100%.

## Sensitive and Qualitative:

Provide the best patient management decisions

Table 2: Assay Performance

Test Results	Number of CML Samples
Negative by both methods	14
Negative by the laboratory-developed method but low positive by the GeneXpert	2
Low positive by both methods	8
High positive by both methods	15

The performance of the assay was tested at two sites using collection of 39 samples from patients with CML. Both sites also ran their laboratory-developed assay for comparison. The data were grouped into three categories:

- Negative (<0.01% BCR-ABL detected)
- Low positive (0.01% to 0.05% BCR-ABL detected)
- Positive (>0.05% BCR-ABL detected)

Figure 1: Limit of Detection and Linearity

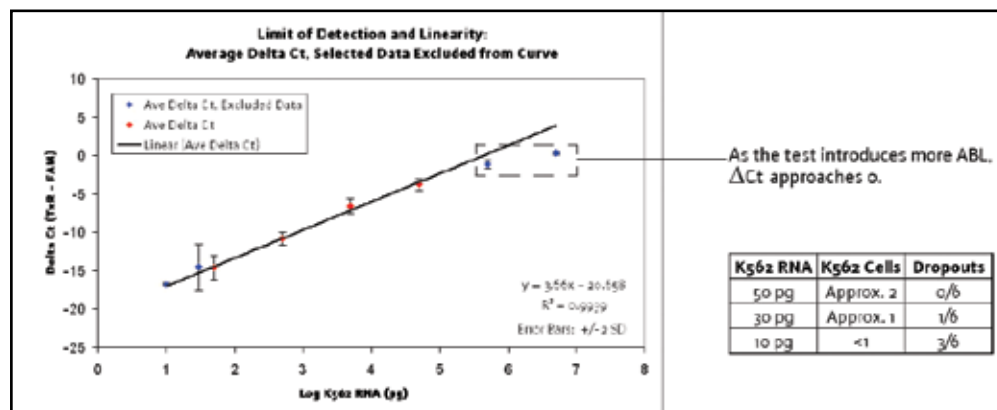


Figure 1 shows the limit of detection and linearity data generated from a single run.

Figure 2: Easy to Interpret Software Output

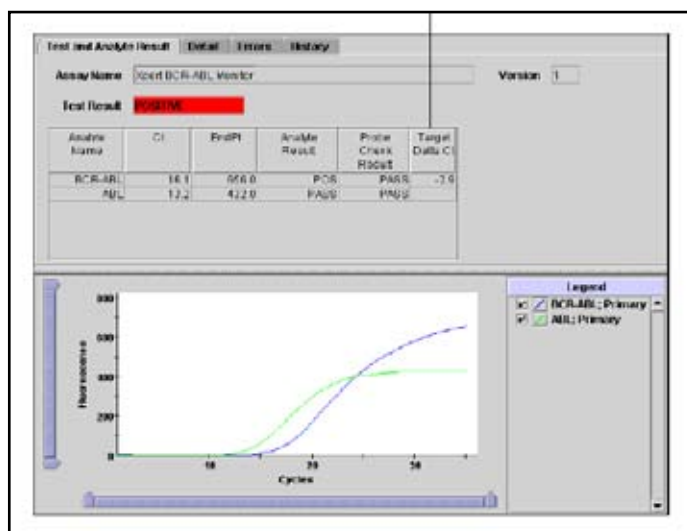


Figure 2: GeneXpert Dx System: View Results window, positive result. The delta Ct value is used in conjunction with a lot-specific PCR efficiency value provided to calculate the percent BCR-ABL/ABL.

## Ordering Information

GeneXpert BCR-ABL Assay ..... Catalog No. RBCR-100N-10  
(10 cartridges with reagents)

### References:

- Gabert J, Beillard E, van der Velden VH, et al. Standardization and quality control studies of 'real-time' quantitative reverse transcriptase polymerase chain reaction of fusion gene transcripts for residual disease detection in leukemia - a Europe Against Cancer Program. *Leukemia*. 2003; 17:2318-2357.
- NCCN. Clinical Practice Guidelines in Oncology: Chronic Myelogenous Leukemia. Version 1. 2006.
- Kantarjian HM, Talpaz M, Cortes J, et al. Quantitative polymerase chain reaction monitoring of BCR-ABL during therapy with imatinib mesylate (STI571;Gleevec) in chronic-phase chronic myelogenous leukemia. *Clin Cancer Res*. 2003; 9(1):160-6.
- Gabert J et al. Standardization and quality control studies of 'real-time' quantitative reverse transcriptase polymerase chain reaction of fusion gene transcripts for residual disease detection in leukemia-A Europe Against Cancer Program. *Leukemia* 2003; 1-40.
- Sawyers C. Chronic Myeloid Leukemia. *NEJM*. 1999;340(17): 1330-40.
- Deininger MW, Goldman JM, Melo JV. The molecular biology of chronic myeloid leukemia. *Blood*. 2000; 96(10):3343-56.
- Goldman JM, Kaeda JS, Cross NC. Clinical decision making in chronic myeloid leukemia based on polymerase chain reaction analysis of minimal residual disease. *Blood*. 1999; 94(4):1484-6.
- Radich JP. The detection and significance of minimal residual disease in chronic myeloid leukemia. *Medicina (B Aires)* 2000; 60 Suppl 2:66-70.
- Hochhaus A, Reiter A, Skladny H, et al. Molecular monitoring of residual disease in chronic myelogenous leukemia patients after therapy. *Recent Results Cancer Res* 1998; 144:36-45.
- Hochhaus A, Reiter A, Saussele S, et al. Molecular heterogeneity in complete cytogenetic responders after interferon-alpha therapy for chronic myelogenous leukemia: low levels of minimal residual disease are associated with continuing remission. German CML Study Group and the UK MRC CML Study Group. *Blood*. 2000; 95(1):62-6.
- Radich JP, Gehly G, Gooley T, et al. Polymerase chain reaction detection of the BCR-ABL fusion transcript after allogeneic marrow transplantation for chronic myeloid leukemia: results and implications in 346 patients. *Blood* 1995; 85(9):2632-8.
- Olavarria E, Kanfer E, Szydlo R, et al. Early detection of BCR-ABL transcripts by quantitative reverse transcriptase-polymerase chain reaction predicts outcome after allogeneic stem cell transplantation for chronic myeloid leukemia. *Blood*. 2001; 97(6):1560-5.
- Deininger M, Buchdunger E, Druker BJ. The development of imatinib as a therapeutic agent for chronic myeloid leukemia. *Blood*. 2005; 105(7):2640-2653.

Practice of the patented polymerase chain reaction (PCR) process requires a license. The GeneXpert® System is an authorized thermal cycler and may be used with PCR licenses available from Applied Biosystems. Its use with authorized reagents also provides a limited PCR license in accordance with the label rights accompanying such reagents. Purchase of this instrument does not convey any right to practice the 5' nuclease assay or any of the other real-time methods covered by patents owned or controlled by Roche or Applied Biosystems. Cepheid's GeneXpert® System is a licensed real-time thermal cycler under Applera's European Patent No. EP 0 872 562, Japanese Patent No. JP 3136129 and patents pending, for all fields including human *in vitro* diagnostics except for diagnosis and monitoring of HIV and HCV infections.

### CORPORATE HEADQUARTERS

904 CARIBBEAN DRIVE  
SUNNYVALE, CA 94089  
USA  
TOLL FREE: 1.888.336.2743  
PHONE: 1.408.541.4191  
FAX: 1.408.734.1346

### EUROPEAN HEADQUARTERS

VIRA SOLELH  
81470 MAURENS-SCOPONT  
FRANCE  
PHONE: 33.563.82.53.00  
FAX: 33.563.82.53.01

