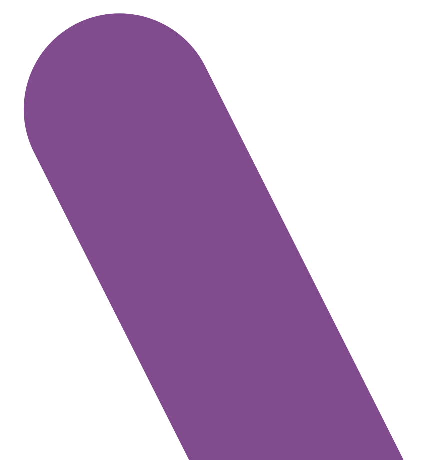
DNA
DIAGNOSTIC

Instruction For Use

HemaVision®-Screen

Screening test for 28 chromosome translocations and more than 145 breakpoints associated with leukemia



Instruction For Use
Cat No. HV01-Screen
DNA Diagnostic A/S
www.dna-diagnostic.com
Revision 2021.04.23

HemaVision®-Screen

Multiplex RT-PCR test
Screens for 28 leukemia causing translocations

del1(p32) (STIL-TAL1)
t(1;11) (p32;q23) (KMT2A-EPS15)
t(1;11) (q21;q23) (KMT2A-MLLT11)
t(1;19) (q23;p13) (TCF3-PBX1)
t(3;5) (q25;q34) (NPM1-MLF1)
t(3;21) (q26;q22) (RUNX1-MECOM)
t(4;11) (q21;q23) (KMT2A-AFF1)
t(5;12) (q33;p13) (ETV6-PDGFRB)
t(5;17) (q35;q21) (NPM1-RARA)
t(6;9) (p23;q34) (DEK-NUP214)
t(6;11) (q27;q23) (KMT2A-AFDN)
t(8;21) (q22;q22) (RUNX1-RUNX1T1)
t(9;9) (q34;q34) (SET-NUP214)
t(9;11) (p22;q23) (KMT2A-MLLT3)
t(9;12) (q34;p13) (ETV6-ABL1)
t(9,22) (q34;q11) (BCR-ABL1)
t(10;11) (p12;q23) (KMT2A-MLLT10)
t(11;17) (q23;q21) (KMT2A-MLLT6)
t(11;17) (q23;q21) (ZBTB16-RARA)
t(11;19) (q23;p13.1) (KMT2A-ELL)
t(11;19) (q23;p13.3) (KMT2A-MLLT1)
t(12;21) (p13;q22) (ETV6-RUNX1)
t(12;22) (p13;q11) (ETV6-MN1)
t(15;17) (q24;q21) (PML-RARA)
inv(16) (p13;q22) (CBFB-MYH11)
t(16;21) (p11;q22) (FUS-ERG)
t(17;19) (q22;p13) (TCF3-HLF)
t(X;11) (q13;q23) (KMT2A-FOXO4)

Instruction For Use for HemaVision®-Screen
Cat. No. HV01-Screen
25 tests per kit

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1. PURPOSE OF THE TEST - SCREENING FOR 28 TRANSLOCATIONS (INTENDED USE)

HemaVision®-Screen is a CE-marked *in vitro* diagnostic test for 28 leukemia causing chromosomal translocations including more than 145 breakpoints plus associated mRNA splice variants. Furthermore, it detects new breakpoints and mRNA splice variants for the 28 translocations. HemaVision®-Screen is a qualitative test intended for use on total RNA samples from human blood or bone marrow for presence of chromosomal translocations associated with leukemia. Tests should be performed and results should be analysed by professionals only. The test is intended for use as an adjunct to evaluation of Leukemia in conjunction with other clinicopathological factors (aid to diagnosis).

It is a fast one day test based on the method described by Pallisgard et al. (Ref 58). The HemaVision®-Screen test has very high sensitivity (>99%) and specificity (>99%) (Ref 59, 60).

Limit of detection is 10^{-9} µg of fusion RNA in a sample of 1 µg total RNA when the RNA quality is good.

This test provides a more detailed description of the exon organization of fusion genes originating from chromosome translocations.

HemaVision®-Screen is a qualitative test using total RNA extracted from human whole blood or bone marrow cells as starting material in the test. The test uses reverse transcription of RNA to cDNA followed by multiplex nested polymerase chain reactions (RT-PCR), agarose gel electrophoresis, and interpretation.

HemaVision®-Screen identifies chromosomes, genes and exons at the breakpoint in fusion genes. Furthermore, the test identifies mRNA splice variants from fusion genes.

The HemaVision®-Screen kit contains primers for 25 cDNA reactions and 25 (master) nested PCR tests.

The HemaVision®-Screen kit is identical to the BOX 1 of HemaVision®-28N kit (Cat No HV01-28N). Therefore, positive master reactions from HemaVision®-Screen tests must be characterized further by split-out reactions from BOX2 of the HemaVision®-28N kit.

The test is for professional use only.

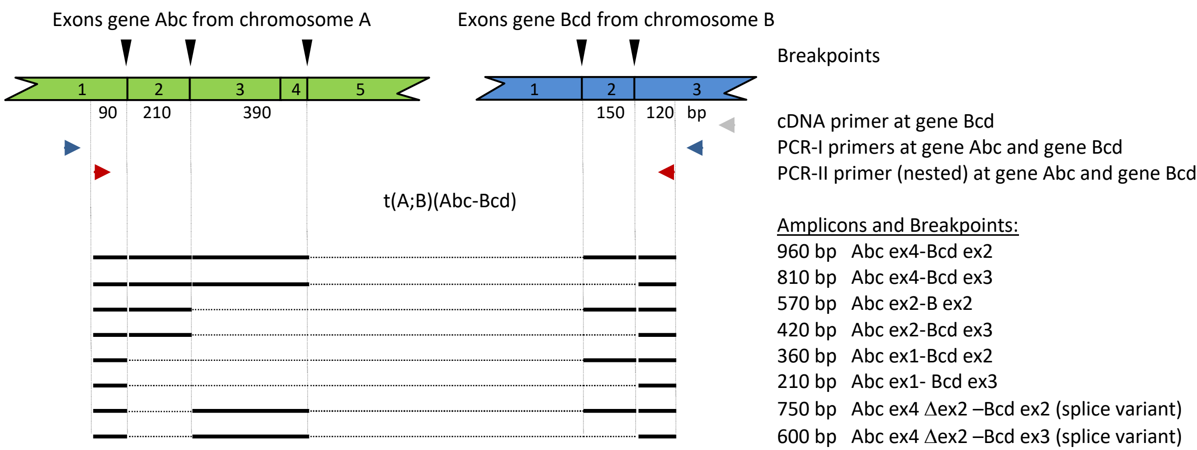


Figure 1 illustrates how HemaVision® kit HV01-Screen identifies chromosomes, fusion genes and exons at the breakpoint among 28 chromosome translocations causing leukemia. Only breakpoints for fusion genes maintaining the original translational reading frame are presented.

2. PRINCIPLES OF TEST

RNA is template for synthesis of cDNA in a reaction using Reverse Transcriptase (RT) and specific cDNA primers. The cDNA is template for PCR amplification using a hot start Taq DNA Polymerase and specific PCR primers. Many of the fusion genes have several breakpoints. Therefore, the PCR primers are designed to bind at positions enabling screening for all these breakpoints as illustrated in figure 1. The workflow of the test and an example of test results are shown in figure 2.

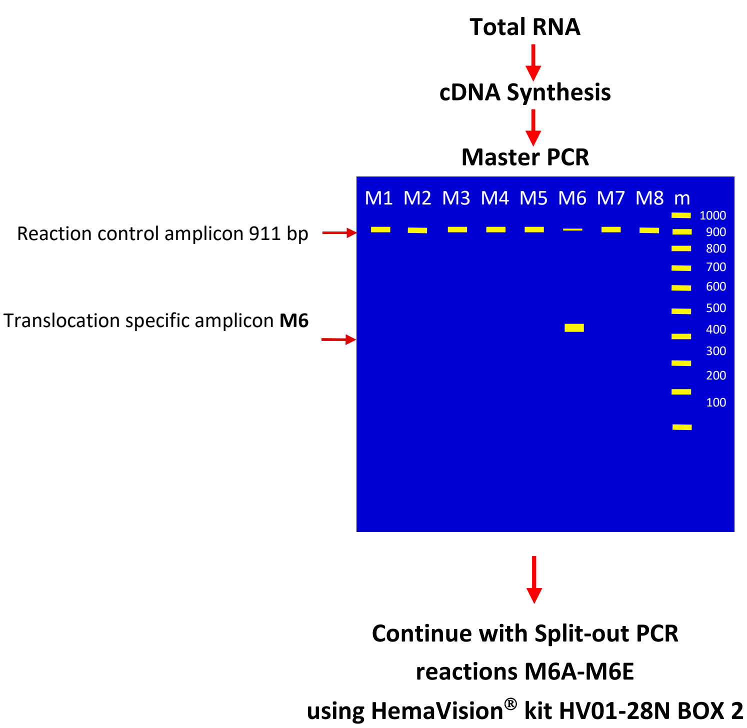


Figure 2. Workflow and results from a test with HemaVision® Cat. No. HV01-Screen.
Result: All reactions M1-M8 are positive for the reaction control amplicon of 911 bp. M6 is also positive for an amplicon approximately 400 bp.
Conclusion: Patient is positive for a translocation. Continue testing with the split-out reactions M6A-M6E from BOX 2 in HemaVision® kit HV01-28N for identification of the translocation.

RNA Preparation

Total RNA is prepared from whole blood, cell lines, or bone marrow cells with the QIAamp® RNA Blood Mini Kit (Qiagen Cat. No. 52304).

cDNA Synthesis

cDNA is synthesized in a reaction containing the isolated RNA using the cDNA Mix (primers) from the HemaVision® HV01-Screen kit and Reverse Transcriptase, 5x RT Buffer, DTT, and dNTP, DTT from the reagent module HemaVision® kit Cat. No. HV06-RMP.

Master PCR

The cDNA is used as a template for eight multiplex PCR amplification reactions (Master PCR-I) subsequently followed by eight nested PCR reactions (Master PCR-II). All reactions use primer mixes from the HemaVision® HV01-Screen kit and HemaVision DNA Polymerase, 10xbuffer, and dNTP from HemaVision® kit Cat. No. HV06-RMP. Each Master PCR reaction contains four, five or six pairs of translocation specific primers and one pair of reaction control primers specific for the housekeeping gene biotinidase. The Master PCR-II products are analyzed by agarose gel electrophoresis. The 911 bp reaction control band is a positive control for using intact RNA and functionality of the RT-PCR reactions. A translocation specific band show the test is positive for a translocation. The identity of this translocation is established in the split-out PCR using HemaVision® kit HV01-28N BOX 2.

Split-out PCR

Use HemaVision® kit HV01-28N BOX 2 primer mixes and HemaVision® kit HV06-RMP for split-out tests as described in the HemaVision® kit HV01-28N User Manual.

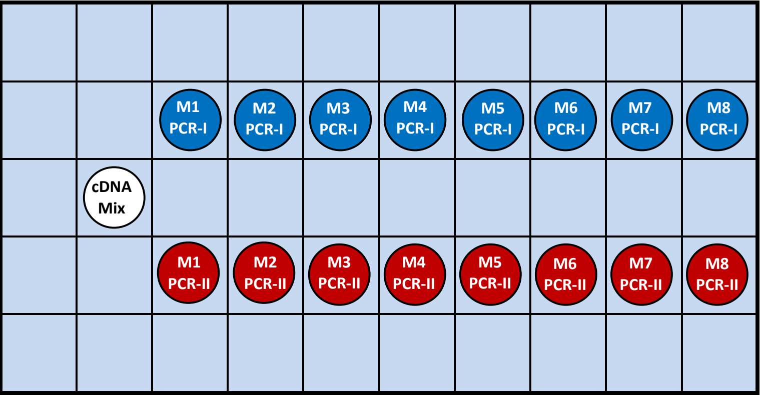
Interpretation of results

A sample is positive for a translocation when both master and split-out PCR produce bands with identical molecular size. The breakpoint is identified by the reaction number of the split-out and the molecular size of the translocation specific amplicon using Interpretation Table 11 of HemaVision® kit HV01-28N. More than one translocation specific band in both Master and Split-out PCR reactions shows presence of alternative spliced mRNA from the fusion gene.

Figure 2 shows workflow for testing blood or bone marrow samples with HemaVision® test HV01-Screen. In this example the test is positive in Master M6 showing an amplicon of approximately 400 bp. The identity of the translocation is established in a test using HemaVision® kit HV01-28N BOX 2 split-out primer mixes M6A-M6E.

3. KIT COMPONENTS AND STORAGE

The HemaVision® kit Cat. No. HV01-Screen contains one box with Primer Mixes (see figure 3) and a User Manual for instruction. The kit is shipped at -20°C or below and both boxes must be stored at -20°C by the customer. While performing the test always keep test components on ice (0°C). Each kit contains sufficient material for 25 Master tests.



BOX 1:
cDNA and Master PCR primer mixes:
1x 200 µL cDNA Mix (white cap)
8x 155 µL Master PCR-I (blue caps)
8x 155 µL Master PCR-II (red caps)

Figure 3 shows content of HemaVision® kit Cat. No. HV01-Screen.

NOTE: It is essential for functionality of the multiplex RT-PCR test using HemaVision® kit HV01-Screen also to obtain and use the reagents provided in HemaVision® kit **Cat. No. HV06-RMP** containing: MMLV-Reverse Transcriptase; 5x RT buffer; DTT; dNTP, HemaVision DNA Polymerase, 10x PCR buffer.

4. EQUIPMENT AND MATERIALS REQUIRED BUT NOT PROVIDED

RNA extraction:
QIAamp® RNA Blood Mini Kit from Qiagen Cat. No. 52304.

Reagent Module:
HemaVision® kit Cat. No. HV06-RMP containing: MMLV-RT; 5x RT buffer; DTT; dNTP, HemaVision DNA Polymerase, 10x PCR buffer. Use four HV06-RMP kits together with each HV01-Screen kit.

Or as an alternative use: HemaVision® kit Cat. No. HV04-RM containing: MMLV-RT; 5x RT buffer; DTT; dNTP and from Qiagen HotStarTaq DNA Polymerase 5 Units/ µL and 10x PCR buffer. Use four HV04-RM kits and 1000 Units HotStarTaq DNA Polymerase together with each HV01-Scree kit.

Master Mix room – No templates in this room:
Micropipettes, 0.5-10 µL, 20-200 HemaVision® kit Cat. No. HV06-RMP containing: MMLV-RT; 5x RT buffer; DTT; dNTP, HemaVision DNA Polymerase, 10x PCR buffer
Aerosol barrier micropipette tips, 0.5-10 µL, and 20-200 µL
Micro centrifuge
Ice bath
RNase free tubes
Disposable gloves
RNase free water
-20°C freezer for storage of kits (HV01-28N and HV06-RMP)

cDNA room:
Micropipettes, 0.5-10 µL, 20-200 µL
Aerosol barrier micropipette tips, 0.5-10 µL, and 20-200 µL
Micro centrifuge
Heating block/Water bath
Ice bath
RNase free tubes
Disposable gloves
RNase free water
-80°C freezer for storage of RNA samples

PCR room:
Micropipettes, 0.5-10 µL, 20-200 µL
Aerosol barrier micropipette tips, 0.5-10 µL, and 20-200 µL
Micro centrifuge
Thermal Cycler
Ice bath
PCR tubes (0.1 mL or 0.2 mL) and lids
Disposable gloves

Gel electrophoresis room:
Micropipettes, 0.5-10 µL
Aerosol barrier micropipette tips, 0.5-10 µL
Micro centrifuge
Equipment for agarose gel electrophoresis
Disposable gloves
Molecular size marker (e.g. 100 bp ladder)

5. PRECAUTIONS

General precautions

- The quality and concentration of the RNA sample greatly affects the results of this test. To minimize the risk of degradation by ribonucleases, we strongly recommend purification of total RNA immediately after blood or bone marrow extraction. Optionally, mononuclear cells can be purified prior to RNA extraction using Ficoll Hypaque. Do not freeze Ficoll purified cells without adding a denaturing solution [e.g. containing guanidinium isothiocyanate (GTC)] immediately after isolation and before freezing.
- Use blood from venipuncture collected into a tube containing EDTA. Alternatively, use bone marrow collected into a tube containing EDTA. Do not freeze the blood or bone marrow sample.
- Do NOT use Heparin for stabilization of blood samples.
- Always store cell samples and aqueous RNA solutions at -80°C. Even an overnight storage at -20°C may result in RNA degradation.
- When working with RNA always use gloves, as hands are a major source of ribonuclease contamination.
- The integrity and purity of RNA is important for the efficiency of the cDNA synthesis and thus detection of translocations. The quality of RNA can be checked by OD 260/280 nm measurements, agarose gel electrophoresis, or using RIN number from the Agilent Bioanalyzer.
- For more guidance on specimen collection, RNA isolation and storage please refer to “ISO 20186:2019 Molecular in vitro diagnostic examinations – Specifications for pre-examination processes for venous whole blood – Part 1: isolated cellular RNA” and CLSI guidance MM13-A “Collection, Transport, Preparation and Storage of Specimens for Molecular Methods; Approved guideline.
- RT-PCR is a very sensitive technique. Therefore, precautions must be taken to avoid false positive results caused by contamination with RNA, cDNA or PCR products from other samples.
- Dedicate four separate rooms/areas to the following activities:
    - Master mix production – no templates in here
    - cDNA synthesis
    - PCR
    - Gel electrophoresis
- A set of micropipettes, aerosol barrier pipette tips, disposable gloves and clean lab coats should be kept in each of the four rooms. The work must be organized so that mixes and reaction products only moves in the direction from 1-4. NEVER move mixes or reaction products in the opposite direction.
- Laboratory workbenches, pipettes, and lab coats must be cleaned on a regular basis.
- Use of aerosol barrier pipette tips is highly recommended during the entire procedure. It is essential to change gloves very often when handling tubes containing RNA or cDNA.
- For more general guidance on best practice in PCR testing please refer to the CLSI guidance document MM01: Molecular Methods for Clinical Genetics and Oncology Testing, 3rd Edition

Safety

- Read and understand the procedure before starting.
- Normal laboratory aseptic technique should be followed at all times.
- Treat each sample as if it is infectious.
- Wear eye protection and disposable gloves during all steps of the assay.
- The products can be discarded as normal laboratory waste
- Check the safety data sheet for the product on our website for further information or ask for a copy of it.

6. PROCEDURE

Procedural notes

- Store all test components as described in section *3: Kit Components and Storage*.
- Do not mix reagents from different lots.
- Careful pipetting technique is essential for accurate results.
- This protocol is optimized with enzymes and buffers from HemaVision® kit Cat. No. HV06-RMP.
- This protocol is optimized for the Perkin Elmer GeneAmp 9600/9700 thermal cycler. Use of another thermal cycler may require optimization by the user.
- As a positive control for RNA quality and functionality of each RT-PCR reaction a 911 bp fragment of the housekeeping gene biotinidase must be present in all lanes except in reactions positive for a translocation specific amplicon where it may be weak or missing.
- As a negative control make the cDNA reaction without RNA template.

RNA preparation

- Use blood from venipuncture collected into a tube containing EDTA. Alternatively, use bone marrow collected into a tube containing EDTA. Do not freeze the blood or bone marrow sample or use samples collected in heparin tubes.
- Prepared mononuclear cells from whole blood or bone marrow by the Ficoll Hypaque method.
- Within 24 hours of collection, extract total RNA with QIAamp® RNA Blood Mini Kit (Qiagen Cat. No. 52304). Typically 5-10 μg total RNA is extracted from 1 $x10^7$ mononuclear blood cells.
- Measure the RNA concentration by reading the optical density at 260 nm. An absorbance of 1 unit at 260 nm corresponds to 40 μg of RNA per mL. Adjust the concentration of RNA to 0.1 μg/μL with RNase free H_2O.
- Make 20 μL (0.1 μg/μL) RNA aliquots in RNase free tubes. Store RNA aliquots at –80°C or use RNA immediately for cDNA synthesis.

Master test

Step 1 cDNA Synthesis

1.1 In the Master Mix room prepare *cDNA Synthesis Mix* according to Table 1 using reagents from HemaVision® reagent module Cat. No. HV06-RMP.

Do not add additional volume to compensate for liquid loss during liquating. This has already been factored into the table numbers.

Table 1: *cDNA Synthesis Mix*

Number of samples	1	2
5x MMLV-RT Buffer (μL)	11.0	22.0
100 mM DTT (μL)	5.5	11.0
10 mM dNTP Mix (μL)	5.5	11.0
MMLV-RT (μL)	2.2	4.4
Total volume (μL):	24.2	48.4

1.2 In the cDNA room add 8 μL cDNA Mix (primers) from white capped tube in the HemaVision® HV01-28N kit to one tube containing 20 μL total RNA (2 μg). Mix gently and spin down for 10 seconds.

1.3 In a separate RNase free tube, add 8 μL of cDNA Mix to 20 μL H_2O (negative control).

1.4 Incubate the tubes in a heating block or water bath at 65°C for 5 minutes. Chill and hold on ice.

1.5 Add 22 μL of the *cDNA Synthesis Mix* to the tube with 28 μL RNA+cDNA Mix and the negative control tube from step 1.4. Mix gently and spin down for 10 seconds.

1.6 Incubate at 37°C for 45 minutes.

1.7 Add 50 μL H_2O to each cDNA tube.

1.8 Incubate at 95°C for 5 min to inactivate the MMLV-RT enzyme.

1.9 Chill and hold the cDNA tube on ice (0°C, do not freeze) for a maximum of three days before use in Master PCR and Split-out PCR.

Step 2 Master PCR-I

To achieve maximal sensitivity and specificity each sample is tested with both a first and a nested Master PCR reaction.

2.1 In the Master Mix room prepare the *Master Mix PCR-I* according to Table 2 using HemaVision® reagent module Cat. No. HV06-RMP. Mix and spin down for 10 seconds.

Do not add additional volume to compensate for liquid loss during liquating. This has already been factored (+10 %) into the table numbers.

Table 2: *Master Mix PCR-I*

Number of samples	**1**	**2**
Number of PCR reactions	**8**	**16**
10x PCR buffer (μL)	22.0	44.0
dNTP mix (μL)	4.4	8.8
HemaVision DNA Polymerase (μL)	3.5	7.0
H_2O (μL)	102.1	204.2
Total volume (μL):	132.0	264.0

2.2 For each sample label the tubes in an 8-microtube strip M1 to M8.

2.3 Aliquot 15 μL *Master Mix PCR-I* to each of the PCR tubes in the 8-microtube strip(s).

2.4 To these tubes add 5 μL Master PCR-I primers from blue capped tubes M1-M8 to the corresponding PCR tubes. E.g. to PCR tube labeled M1 add 5 μL M1 PCR-I.

2.5 In the PCR room add 5 μL cDNA (from step 1.9) to each of the PCR tubes from step 2.4. Close the tubes, mix and spin for 10 seconds. Volume per tube 25 μL.

2.6 Transfer the tubes to a thermal cycler and start the PCR amplification using the PCR cycling parameters in Table 3.

Table 3: Master PCR-I Amplification Parameters

Step	Time/Temperature	Cycles
1	15 minutes at 95°C	1
2	30 seconds at 95°C 30 seconds at 58°C 1 minute 30 seconds at 72°C	25
3	Hold at 4°C	1

Step 3 Master PCR-II (nested)

3.1 In the Master Mix room prepare the *Master Mix PCR-II* according to Table 4 using HemaVision® reagent module Cat. No. HV06-RMP. Mix and spin down for 10 seconds.

Do not add additional volume to compensate for liquid loss during liquating. This has already been factored (+10 %) into the table numbers.

Table 4: *Master Mix PCR-II*

Number of samples	1	2
Number of PCR reactions	**8**	**16**
10x PCR buffer (μL)	22.0	44.0
dNTP mix (μL)	4.4	8.8
HemaVision DNA Polymerase (μL)	3.5	7.0
H_2O (μL)	137.3	274.6
Total volume (μL):	167.2	334.4

3.2 For each sample label the tubes in an 8-microtube strip M1 to M8.

3.3 Aliquot 19 μL *Master Mix PCR-II* to each of the PCR tubes in the 8-microtube strip(s).

3.4 To these tubes add 5 μL Master PCR-II primers from red capped tubes M1-M8 to the corresponding PCR tubes. E.g. to PCR tube labeled M1 add 5 μL M1 PCR-II.

3.5 In the PCR room carefully open without spillage the PCR tubes containing the Master PCR-I reactions. From these tubes transfer 1 μL to the corresponding Master PCR-II tubes from step 3.3. An eight channel pipette can be used for this transfer. Close the tubes, mix and spin for 10 seconds. Volume per tube 25 μL.

3.6 Transfer the tubes to a thermal cycler and start the PCR amplification using the PCR cycling parameters in Table 5.

Table 5: Master PCR-II Amplification Parameters

Step	Time/Temperature	Cycles
1	15 minutes at 95°C	1
2	30 seconds at 95°C 30 seconds at 58°C 1 minute 30 seconds at 72°C	20
3	10 minutes at 72°C	1
4	Hold at 4°C	1

Step 4 Gel electrophoresis

4.1 Prepare a 1.5 % (w/v) agarose gel at least 10 cm long in 1X TBE buffer. Add ethidium bromide to a final concentration of 0.5 μg/mL.

4.2 In the Gel Electrophoresis room carefully open the PCR tubes with Master PCR-II without contaminating gloves and surroundings with drops containing high copy numbers of amplicon.

Add 3 μL of 10x loading buffer into each PCR tube. Load approximately 14 μL per slot in the gel (lane 1-8). Finally load a molecular size marker to lane 9.

4.3 Run the gel in 1X TBE buffer until the Bromophenol blue dye has migrated approximately 3/4 of the gel.

4.4 Examine the gel with UV-light and document result by photography.

Step 5 Interpretation of results from Master PCR-II

- Positive for one (or more) translocation specific band(s). Continue with the corresponding Split-out reactions to identify translocation. Use HemaVision® kit HV01-28N BOX 2 and reagent module HemaVision® kit HV06-RMP.
- Positive for a translocation specific band but it is very weak or a smear. Positive for reaction control band (911 bp) in all lanes. Continue with the relevant Split-out reactions to identify translocation. Use HemaVision® kit HV01-28N BOX 2 and reagent module HemaVision® kit HV06-RMP.
- Negative for a translocation specific band and positive for reaction control band (911 bp) in all lanes M1-M8. The patient is negative for the 28 translocations shown in Table 10.
- Negative for a translocation specific band and negative for reaction control band (911 bp) in all lanes M1-M8. The test failed most likely due to 1) poor quality of RNA, or 2) use of thermal cycler with temperature profile (ramp speed) differing from ABI 9600/9700, or 3) incorrect mixing of reactions. Correct and repeat test.
- Negative for a translocation specific band and positive for reaction control band (911 bp) in some of the lanes M1-M8. The test failed most likely due to 1) use of thermal cycler with temperature profile (ramp speed) differing from ABI 9600/9700, or 2) incorrect mixing of some reactions. Correct and repeat test.
- Negative Control test is positive (band(s) present): Reaction(s) have been contaminated with DNA. Identify contamination and repeat test.

Table 10: List of translocations detected by HemaVision® kit HV01-Screen

PCR	TRANSLOCATION	GENES	REFERENCE
M1	t(X;11)(q13;q23)	KMT2A(11q23) FOXO4(Xq13.1)	1
	t(6;11)(q27;q23)	KMT2A(11q23) AFDN(6q27)	2; 3
	t(11;19)(q23;p13.1)	KMT2A(11q23) ELL(19p13.1)	4; 5; 6
	t(10;11)(p12;q23)	KMT2A(11q23) MLLT10(10p12)	9; 10

Note: The interpretation table has been updated according to the HUGO Gene Nomenclature Committee (HGNC).

For a list of the changes made see section “7. GENE ABBREVATIONS ACCCORDING TO THE HGNC”.

PCR	TRANSLOCATION	GENES	REFERENCE
M2	t(1;11)(p32;q23)	KMT2A(11q23) EPS15 (1p32)	7
	t(11;17)(q23;q12-21)	KMT2A(11q23) MLLT6(17q21)	8
	t(11;19)(q23;p13.3)	KMT2A(11q23) MLLT1(19p13.3)	30; 32; 34
	t(10;11)(p12;q23)	KMT2A(11q23) MLLT10(10p12)	9; 10; 12
	t(9;11)(p22;q23)	KMT2A(11q23) MLLT3(9p22)	3; 30; 35

PCR	TRANSLOCATION	GENES	REFERENCE
M3	t(1;19)(q23;p13)	TCF3(19p13.3) PBX1(PRL)(1q23.3)	13; 14; 15
	t(17;19)(q22;p13)	TCF3(19p13.3) HLF(17q22)	16; 17; 18
	t(12;21)(p13;q22)	ETV6(12p13) RUNX1(21q22.3)	19; 20; 21; 55
	TAL1[d] 40kbp deletion 1p32	STIL(1p32) TAL1(1p32)	22; 23

PCR	TRANSLOCATION	GENES	REFERENCE
M4	t(8;21)(q22;q22)	RUNX1(21q22.3) RUNX1T1(8q22)	24; 25; 26
	t(3;21)(q26;q22)	RUNX1(21q22.3) MECOM(3q26)	25; 27; 28
	t(16;21)(p11;q22)	FUS(16p11.2) ERG(21q22.3)	29; 57
	t(15;17)(q24;q21)	PML(15q24) RARA(17q21)	50; 51; 52

PCR	TRANSLOCATION	GENES	REFERENCE
M5	t(4;11)(q21;q23)	KMT2A(11q23) AFF1(4q21.3)	30; 31; 32; 33
	t(10;11)(p12;q23)	KMT2A(11q23) MLLT10(10p12)	9; 10; 11
	t(11;19)(q23;p13.3)	KMT2A(11q23) MLLT1(19p13.3)	30; 34
	t(9;11)(p22;q23)	KMT2A(11q23) MLLT3(9p22)	3; 30; 35
	t(1;11)(q21;q23)	KMT2A(11q23) MLLT11(1q21)	36

PCR	TRANSLOCATION	GENES	REFERENCE
M6	inv(16)(p13;q22)	CBFB (16q22.1) MYH11 (16p13.11)	47
	t(9;22)(q34;q11)	BCR(22q11) ABL1(9q34.1)	37; 38; 39
	t(9;12)(q34;p13)	ETV6(12p13) ABL1(9q34.1)	40; 41
	t(5;12)(q33;p13)	ETV6(12p13) PDGFRB(5q33)	42
	t(12;22)(p13;q11-12)	ETV6(12p13) MN1(22q12.1)	43

PCR	TRANSLOCATION	GENES	REFERENCE
M7	t(6;9)(p23;q34)	DEK(6p23) NUP214(9q34)	44
	t(9;9)(q34;q34)	SET(9q34) NUP214(9q34)	45; 46
	inv(16)(p13;q22)	CBFB (16q22.1) MYH11 (16p13.11)	47
	t(3;21)(q26;q22) or ------------------------- t(1;21)(p36;q22)	RUNX1(21q22.3) RPL22P1(pseudogene) (3q26.2) ------------------------- RUNX1(21q22.3) RPL22 (1p36.3)	25; 27; 28; 56

PCR	TRANSLOCATION	GENES	REFERENCE
M8	t(11;17)(q23;q12)	ZBTB16(11q23) RARA(17q12)	48; 49
	t(3;21)(q26;q22)	RUNX1(21q22.3) MECOM(3q26)	25; 27; 28
	t(15;17)(q24;q21)	PML(15q24) RARA(17q21)	50; 51; 52
	t(5;17)(q35;q12)	NPM1(5q35) RARA(17q12)	53
	t(3;5)(q25.1;q35)	NPM1(5q35) MLF1(3q25.1)	54
	t(9;22)(q34;q11)	BCR(22q11) ABL1(9q34.1)	37; 38; 39

7. GENE ABBREVIATIONS ACCORDING TO THE HGNC:

The HUGO Gene Nomenclature Committee (HGNC) approves a *unique* and *meaningful* name for every known human gene (read more at www.genenames.org). Table 11 contains a list of all relevant genes for the HemaVision® product series, with the old abbreviation and the corresponding HGNC abbreviation.

Table 11

Old Abbreviation	HGNC Abbreviation	Chromosome	HGNC ID
ABL	ABL1	9q34.1	HGNC:76
AF10	MLLT10	10p12	HGNC:16063
AF17	MLLT6	17q21	HGNC:7138
AF1p	EPS15	1p32	HGNC:3419
AF1q	MLLT11	1q21	HGNC:16997
AF4	AFF1	4q21.3	HGNC:7135
AF6 or MLLT4	AFDN	6q27	HGNC:7137
AF9	MLLT3	9p22	HGNC:7136
AFX1	FOXO4	Xq13.1	HGNC:7139
AML1	RUNX1	21q22.3	HGNC:10471
BCR	BCR	22q11	HGNC:1014
CAN	NUP214	9q34	HGNC:8064
CBFβ	CBFB	16q22.1	HGNC:1539
DEK	DEK	6p23	HGNC:2768
EAP	RPL22	1p36.3	HGNC:10315
E2A	TCF3	19p13.3	HGNC:11633
ELL	ELL	19p13.1	HGNC:23114
ENL	MLLT1	19p13.3	HGNC:7134
ERG	ERG	21q22.3	HGNC:3446
ETO	RUNX1T1	8q22	HGNC:1535
FUS	FUS	16p11.2	HGNC:4010
HLF	HLF	17q22	HGNC:4977
MDS1- EVI1	MECOM	3q26	HGNC:3498
MLF1	MLF1	3q25	HGNC:7125
MLL	KMT2A	11q23	HGNC:7132
MN1	MN1	22q12.1	HGNC:7180
MYH11	MYH11	16p13.11	HGNC:7569
NPM	NPM1	5q35	HGNC:7910
PBX1	PBX1	1q23.3	HGNC:8632
PDGFRβ	PDGFRB	5q31-q32	HGNC:8804
PLZF	ZBTB16	11q23	HGNC:12930
PML	PML	15q24	HGNC:9113
RARα	RARA	17q21	HGNC:9864
SET	SET	9q34	HGNC:10760
SIL1	STIL	1p32	HGNC:10879
Tal1	TAL1	1p32	HGNC:11556
TEL	ETV6	12p13	HGNC:3495
TLS	FUS	16p11.2	HGNC:4010

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REVISION HISTORY

REVISION NUMBER	SECTION CHANGED	DATE
9	Updated intended use to more precisely describe. Updated 5. Precautions with more details on specimen collection and RNA extraction. Updated 6. procedure with more details on RNA extraction.	2019.09.19
10	Corrected mistakes in precautions where qPCR was mentioned and it should be PCR	2020.09.15
11	Minor editions in precautions section	2020.10.19
12	Changed from User Manual to Instruction For Use	2021.04.23

Symbols used on tubes and boxes

CE	"Conformité Européenne" ("European Conformity")	IVD	In vitro Diagnostic Medical Device		Consult instructions for use
REF	Catalogue Number	LOT	Lot number	CONT	Contents
	Storage temperature		Expiry Date		Manufacturer

DNA
DIAGNOSTIC

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