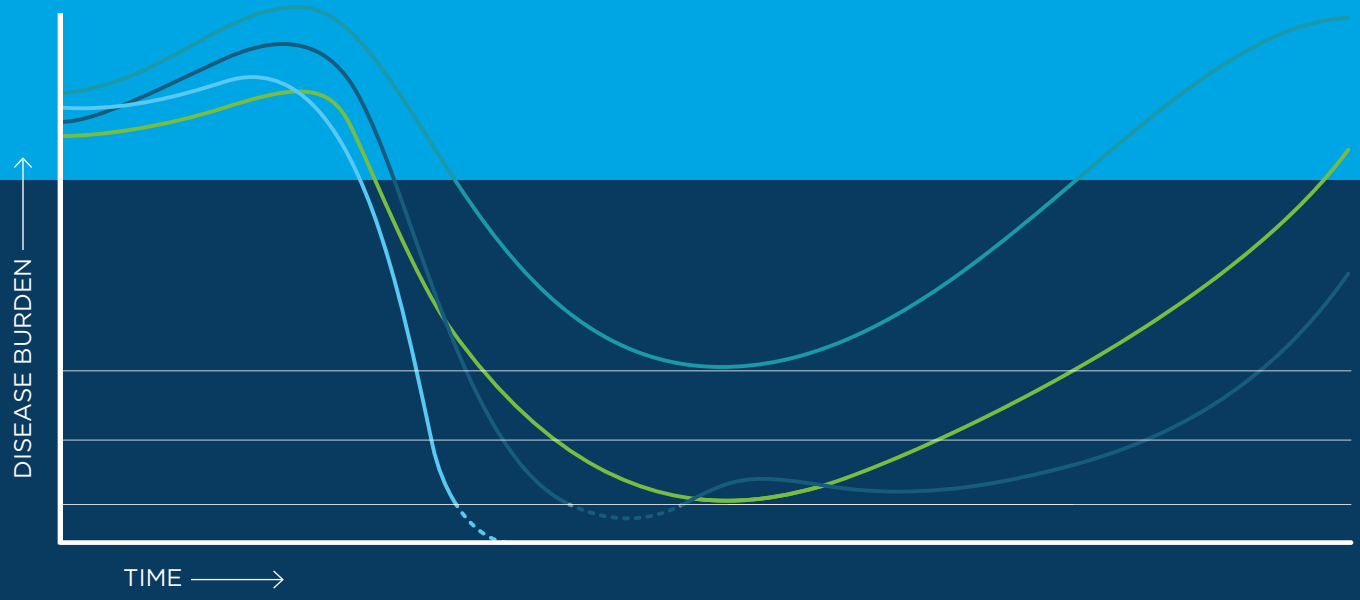
FOR HEALTHCARE PROVIDERS

clonoSEQ® By Adaptive

UNDERSTANDING THE CLONOSEQ ASSAY B-CELL REAGENT SET CLINICAL REPORT

B-cell Clonality (ID) and B-cell Tracking (MRD) Reports



The clonoSEQ Assay is CE marked as an *in vitro* diagnostic (IVD) for assessing the MRD status and changes in disease burden during and after treatment in B-cell malignancies in DNA extracted from blood and/or bone marrow samples.

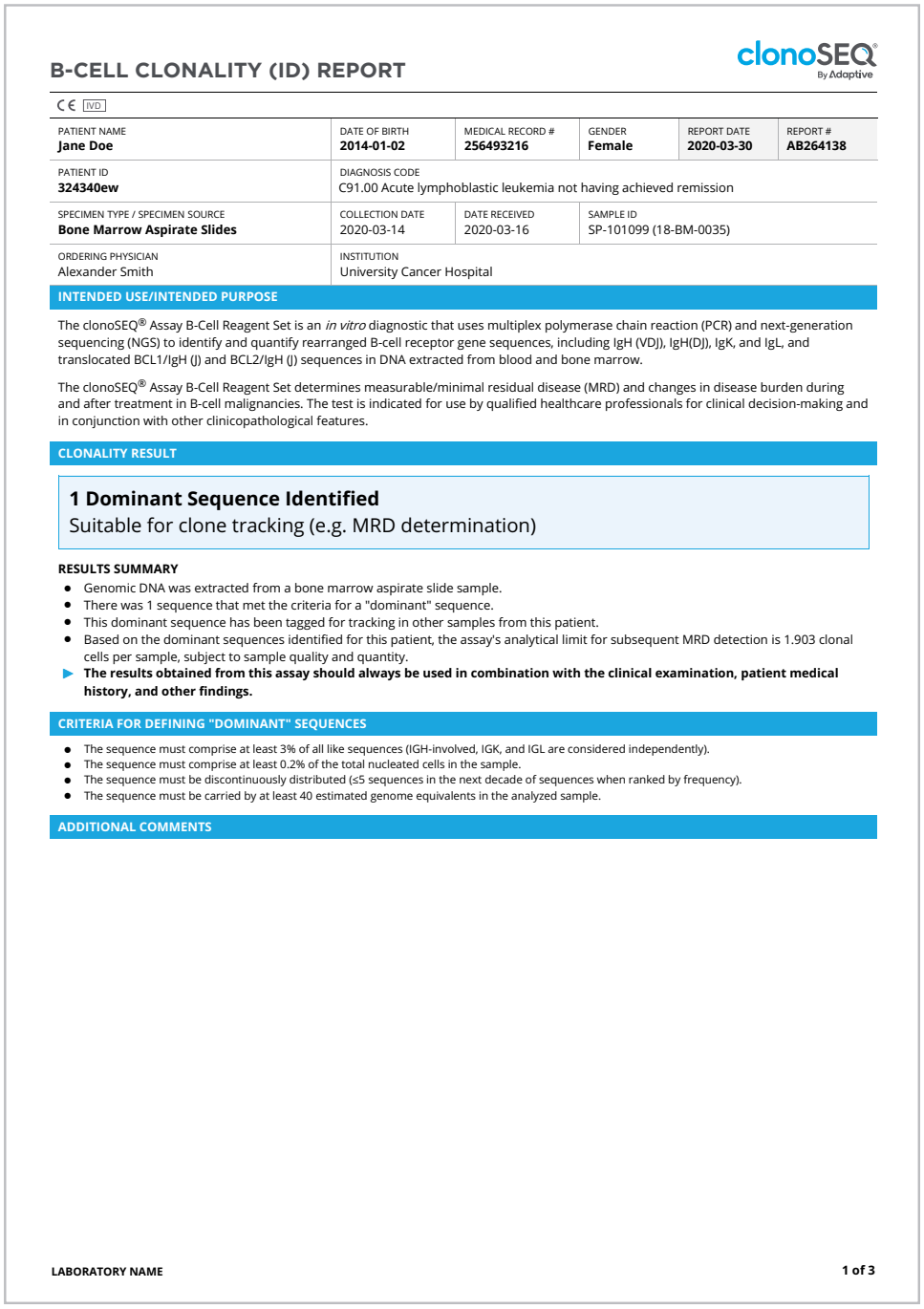
clonoSEQ® By Adaptive

B-CELL CLONALITY (ID) REPORT:

The B-cell Clonality (ID) Test is used to identify dominant DNA sequence(s) in a high disease load diagnostic sample. Identification of at least one dominant DNA sequence is a prerequisite to future monitoring of MRD.

After the dominant DNA sequence(s) has been identified utilizing the B-cell Clonality (ID) Test, subsequent monitoring of the associated clone(s) can be completed by ordering B-cell Tracking (MRD) Tests.

clonoSEQ results should always be used in combination with clinical examination, patient medical history, and other findings. Results may vary according to sample time within the course of disease or by sampling site location. False positive or false negative results may occur for reasons including, but not limited to: contamination, technical, and/or biological factors.



B-CELL CLONALITY (ID) REPORT

clonoSEQ By Adaptive

CE IVD

PATIENT NAME	DATE OF BIRTH	MEDICAL RECORD #	GENDER	REPORT DATE	REPORT #
Jane Doe	**2014-01-02**	**256493216**	**Female**	**2020-03-30**	**AB264138**

PATIENT ID	DIAGNOSIS CODE
324340ew	C91.00 Acute lymphoblastic leukemia not having achieved remission

SPECIMEN TYPE / SPECIMEN SOURCE	COLLECTION DATE	DATE RECEIVED	SAMPLE ID
Bone Marrow Aspirate Slides	2020-03-14	2020-03-16	SP-101099 (18-BM-0035)

ORDERING PHYSICIAN	INSTITUTION
Alexander Smith	University Cancer Hospital

INTENDED USE/INTENDED PURPOSE

The clonoSEQ® Assay B-Cell Reagent Set is an *in vitro* diagnostic that uses multiplex polymerase chain reaction (PCR) and next-generation sequencing (NGS) to identify and quantify rearranged B-cell receptor gene sequences, including IgH (VDJ), IgH(DJ), IgK, and IgL, and translocated BCL1/IgH (J) and BCL2/IgH (J) sequences in DNA extracted from blood and bone marrow.

The clonoSEQ® Assay B-Cell Reagent Set determines measurable/minimal residual disease (MRD) and changes in disease burden during and after treatment in B-cell malignancies. The test is indicated for use by qualified healthcare professionals for clinical decision-making and in conjunction with other clinicopathological features.

CLONALITY RESULT

1 Dominant Sequence Identified
Suitable for clone tracking (e.g. MRD determination)

RESULTS SUMMARY

- Genomic DNA was extracted from a bone marrow aspirate slide sample.
- There was 1 sequence that met the criteria for a "dominant" sequence.
- This dominant sequence has been tagged for tracking in other samples from this patient.
- Based on the dominant sequences identified for this patient, the assay's analytical limit for subsequent MRD detection is 1.903 clonal cells per sample, subject to sample quality and quantity.
- ▶ **The results obtained from this assay should always be used in combination with the clinical examination, patient medical history, and other findings.**

CRITERIA FOR DEFINING "DOMINANT" SEQUENCES

- The sequence must comprise at least 3% of all like sequences (IGH-involved, IGK, and IGL are considered independently).
- The sequence must comprise at least 0.2% of the total nucleated cells in the sample.
- The sequence must be discontinuously distributed (≤5 sequences in the next decade of sequences when ranked by frequency).
- The sequence must be carried by at least 40 estimated genome equivalents in the analyzed sample.

ADDITIONAL COMMENTS

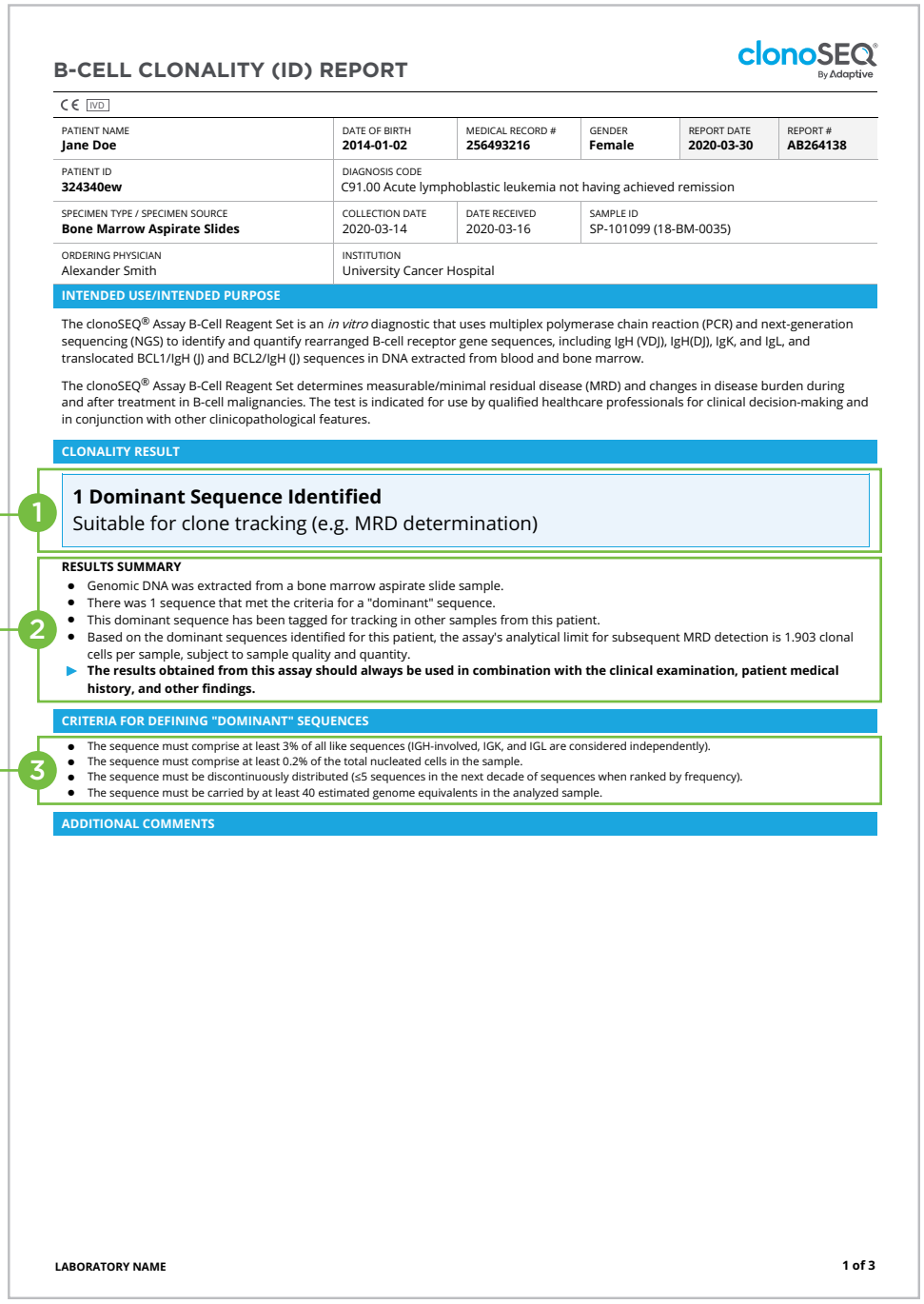
LABORATORY NAME **1 of 3**

B-cell Clonality (ID) Report with Dominant Sequences Identified

This is an example B-cell Clonality (ID) Report. The clonoSEQ B-cell Clonality (ID) Report provides results based on analysis of the IgH, IgK and IgL loci as well as Bcl1 and Bcl2 translocations.

Page 1 of the report shows that dominant DNA sequences were identified from the submitted sample (1). A more detailed description of the results for this sample can be found in the "Results Summary" section (2). A summary of the criteria used to determine which DNA sequences are dominant and thus can be followed as markers of malignancy is provided for reference (3). Additional observations provided by a licensed medical professional relating to the report result may be included in the "Additional Comments" section.

Page 1



B-CELL CLONALITY (ID) REPORT

clonoSEQ By Adaptive

CE IVD

PATIENT NAME	DATE OF BIRTH	MEDICAL RECORD #	GENDER	REPORT DATE	REPORT #
Jane Doe	**2014-01-02**	**256493216**	**Female**	**2020-03-30**	**AB264138**

PATIENT ID	DIAGNOSIS CODE
324340ew	C91.00 Acute lymphoblastic leukemia not having achieved remission

SPECIMEN TYPE / SPECIMEN SOURCE	COLLECTION DATE	DATE RECEIVED	SAMPLE ID
Bone Marrow Aspirate Slides	2020-03-14	2020-03-16	SP-101099 (18-BM-0035)

ORDERING PHYSICIAN	INSTITUTION
Alexander Smith	University Cancer Hospital

INTENDED USE/INTENDED PURPOSE

The clonoSEQ® Assay B-Cell Reagent Set is an *in vitro* diagnostic that uses multiplex polymerase chain reaction (PCR) and next-generation sequencing (NGS) to identify and quantify rearranged B-cell receptor gene sequences, including IgH (VDJ), IgH(DJ), IgK, and IgL, and translocated BCL1/IgH (J) and BCL2/IgH (J) sequences in DNA extracted from blood and bone marrow.

The clonoSEQ® Assay B-Cell Reagent Set determines measurable/minimal residual disease (MRD) and changes in disease burden during and after treatment in B-cell malignancies. The test is indicated for use by qualified healthcare professionals for clinical decision-making and in conjunction with other clinicopathological features.

CLONALITY RESULT

Result — 1

1 Dominant Sequence Identified
Suitable for clone tracking (e.g. MRD determination)

RESULTS SUMMARY

Additional result information — 2

- Genomic DNA was extracted from a bone marrow aspirate slide sample.
- There was 1 sequence that met the criteria for a "dominant" sequence.
- This dominant sequence has been tagged for tracking in other samples from this patient.
- Based on the dominant sequences identified for this patient, the assay's analytical limit for subsequent MRD detection is 1.903 clonal cells per sample, subject to sample quality and quantity.

▶ **The results obtained from this assay should always be used in combination with the clinical examination, patient medical history, and other findings.**

CRITERIA FOR DEFINING "DOMINANT" SEQUENCES

Criteria for defining a dominant sequence — 3

- The sequence must comprise at least 3% of all like sequences (IGH-involved, IGK, and IGL are considered independently).
- The sequence must comprise at least 0.2% of the total nucleated cells in the sample.
- The sequence must be discontinuously distributed (≤5 sequences in the next decade of sequences when ranked by frequency).
- The sequence must be carried by at least 40 estimated genome equivalents in the analyzed sample.

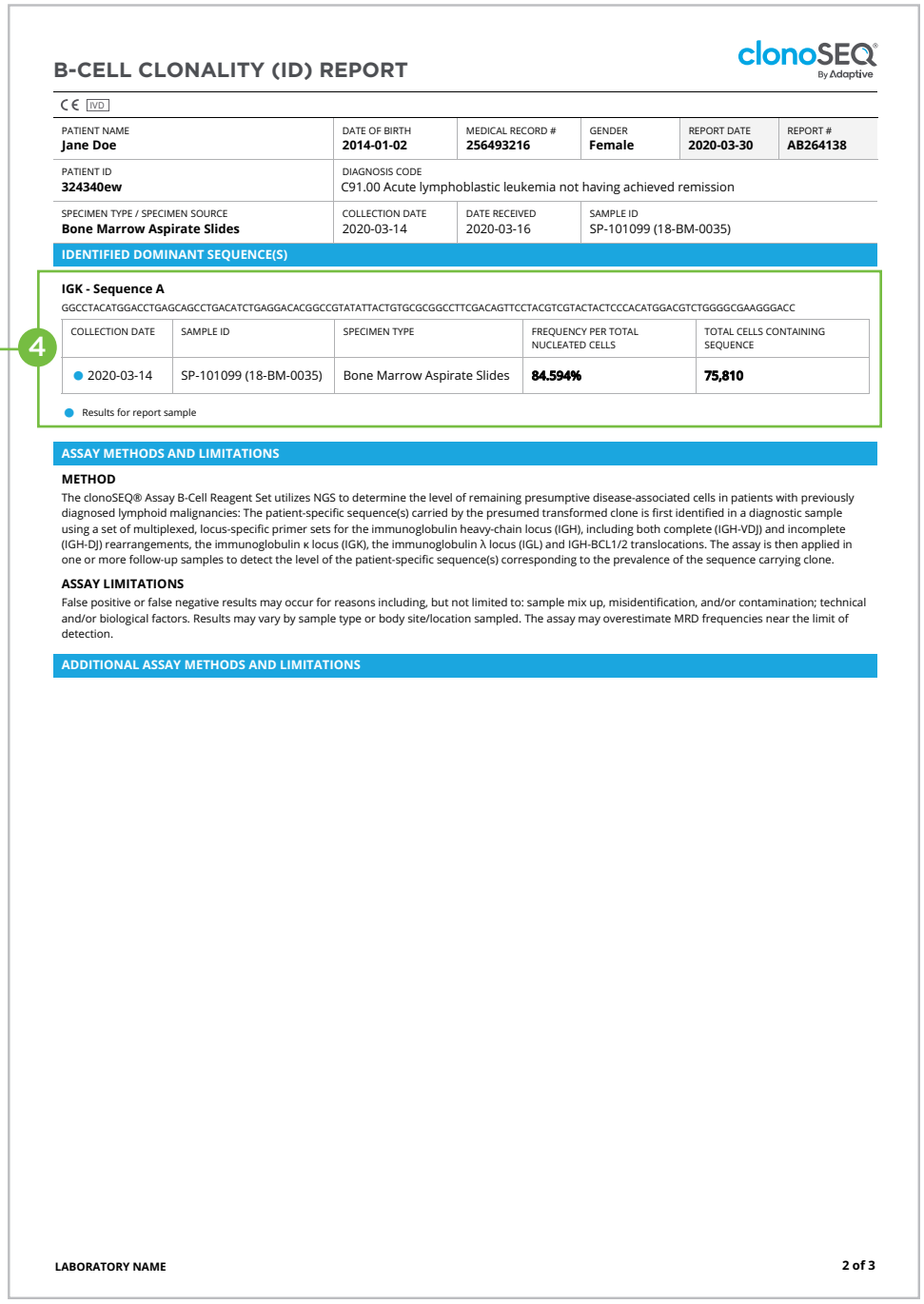
ADDITIONAL COMMENTS

LABORATORY NAME **1 of 3**

B-cell Clonality (ID) Report with Dominant Sequences Identified (continued)

Page 2 of the report shows detailed information relating to the sample (4) including the actual rearranged DNA nucleotide sequence or sequences identified, the sample collection date, the receptor locus in which each dominant sequence was found, the specimen type analyzed, the frequency of the dominant sequence as a fraction of the total nucleated cells assessed, and the total number of cells carrying the rearranged DNA sequence.

Page 2



B-CELL CLONALITY (ID) REPORT

clonoSEQ By Adaptive

CE IVD

PATIENT NAME	DATE OF BIRTH	MEDICAL RECORD #	GENDER	REPORT DATE	REPORT #
Jane Doe	**2014-01-02**	**256493216**	**Female**	**2020-03-30**	**AB264138**

PATIENT ID	DIAGNOSIS CODE
324340ew	C91.00 Acute lymphoblastic leukemia not having achieved remission

SPECIMEN TYPE / SPECIMEN SOURCE	COLLECTION DATE	DATE RECEIVED	SAMPLE ID
Bone Marrow Aspirate Slides	2020-03-14	2020-03-16	SP-101099 (18-BM-0035)

IDENTIFIED DOMINANT SEQUENCE(S)

IGK - Sequence A

GGCCTACATGGACCTGAGCAGCCTGACATCTGAGGACACGGCCGTATATTACTGTGCGCGGCCTTCGACAGTTCCTACGTCGTACTACTCCCACATGGACGTCTGGGGCGAAGGGACC

COLLECTION DATE	SAMPLE ID	SPECIMEN TYPE	FREQUENCY PER TOTAL NUCLEATED CELLS	TOTAL CELLS CONTAINING SEQUENCE
● 2020-03-14	SP-101099 (18-BM-0035)	Bone Marrow Aspirate Slides	**84.594%**	**75,810**

● Results for report sample

ASSAY METHODS AND LIMITATIONS

METHOD

The clonoSEQ® Assay B-Cell Reagent Set utilizes NGS to determine the level of remaining presumptive disease-associated cells in patients with previously diagnosed lymphoid malignancies: The patient-specific sequence(s) carried by the presumed transformed clone is first identified in a diagnostic sample using a set of multiplexed, locus-specific primer sets for the immunoglobulin heavy-chain locus (IGH), including both complete (IGH-VDJ) and incomplete (IGH-DJ) rearrangements, the immunoglobulin κ locus (IGK), the immunoglobulin λ locus (IGL) and IGH-BCL1/2 translocations. The assay is then applied in one or more follow-up samples to detect the level of the patient-specific sequence(s) corresponding to the prevalence of the sequence carrying clone.

ASSAY LIMITATIONS

False positive or false negative results may occur for reasons including, but not limited to: sample mix up, misidentification, and/or contamination; technical and/or biological factors. Results may vary by sample type or body site/location sampled. The assay may overestimate MRD frequencies near the limit of detection.

ADDITIONAL ASSAY METHODS AND LIMITATIONS

LABORATORY NAME

2 of 3

4 Specific DNA sequences identified

B-cell Clonality (ID) Report with Dominant Sequences Identified (continued)

Page 3 of the report provides more details on the immune repertoire of the analyzed sample, including the sample clonality, the number of sequences assessed for each locus, and the number of unique sequences assessed (5).

Page 3

B-CELL CLONALITY (ID) REPORT

clonoSEQ® By Adaptive

CE IVD

PATIENT NAME	DATE OF BIRTH	MEDICAL RECORD #	GENDER	REPORT DATE	REPORT #
Jane Doe	**2014-01-02**	**256493216**	**Female**	**2020-03-30**	**AB264138**

PATIENT ID	DIAGNOSIS CODE
324340ew	C91.00 Acute lymphoblastic leukemia not having achieved remission

SPECIMEN TYPE / SPECIMEN SOURCE	COLLECTION DATE	DATE RECEIVED	SAMPLE ID
Bone Marrow Aspirate Slides	2020-03-14	2020-03-16	SP-101099 (18-BM-0035)

APPENDIX

SUPPLEMENTAL SAMPLE INFORMATION

SAMPLE CLONALITY [1]	TOTAL NUCLEATED CELLS [2]
0.85	89,617

LOCI	TOTAL SEQUENCES [3]	TOTAL UNIQUE SEQUENCES [4]
IGH	76,872	1,007
IGK	5,856	5,362
IGL	>=2,610	2,610

5 Details on immune repertoire of analyzed sample

[1] Sample Clonality	A measure of the lymphocyte population diversity (distinct lymphocyte clonal sub-populations or "clones") comprising the immune repertoire in a given biological sample. Values for clonality vary from 0 to 1. Values close to 1 represent samples with one or a few predominant clones. Values near zero represent a more polyclonal sample.
[2] Total Nucleated Cells	The total number of nucleated cells calculated within the sample, based on quantitation of non-immune receptor loci contained in the reaction and the assumption that the DNA content per cell is diploid.
[3] Total Sequences	A measure of the number of nucleotide sequences detected in the sample for each defined immune receptor locus.
[4] Total Unique Sequences	A measure of the number of unique nucleotide sequences detected in the sample for each defined immune receptor locus.
Limit of Detection (LOD)	The lowest level of residual tracked sequence(s) that can be reliably detected by the clonoSEQ® Assay B-Cell Reagent Set in ≥95% of samples tested. LOD is independently calculated for each trackable sequence and hence can vary by sequence based on factors including the amount of input DNA, the uniqueness of the sequence, and/or relative amplification due to nucleotide sequence polymorphism or mutation.

REFERENCES

- Armand P, et al. Br J Haematol. 2013; 163:123-126.
- Carlson CS, et al. Nat Commun. 2013;4:2680.
- Faham M, et al. Blood. 2012;120(26):5173-80.
- Kurtz D, et al. Blood 2015; 125:3679-3687.
- Logan AC, et al. Leukemia. 2013;27(8):1659-65.
- Martinez-Lopez J, et al. Blood. 2014;123(20):3073-9.
- Paietta E. Bone Marrow Transplantation. 2002;29(6):459-465.
- Pulsipher M, et al. Blood. 2015;125(22):3501-8.
- Rawstron AC, et al. Leukemia. 2016;30(4):929-36.
- Roschewski M, et al. Lancet Oncol. 2015;16:541-49.
- Wu D, et al. Clin Cancer Res. 2014;20(17):4540-8.

REPORT APPROVAL

REVIEWED AND RELEASED BY	SIGNATURE	DATE & TIME
Maria C Santos, MD	Maria C Santos	2020-03-30 12:22 PM

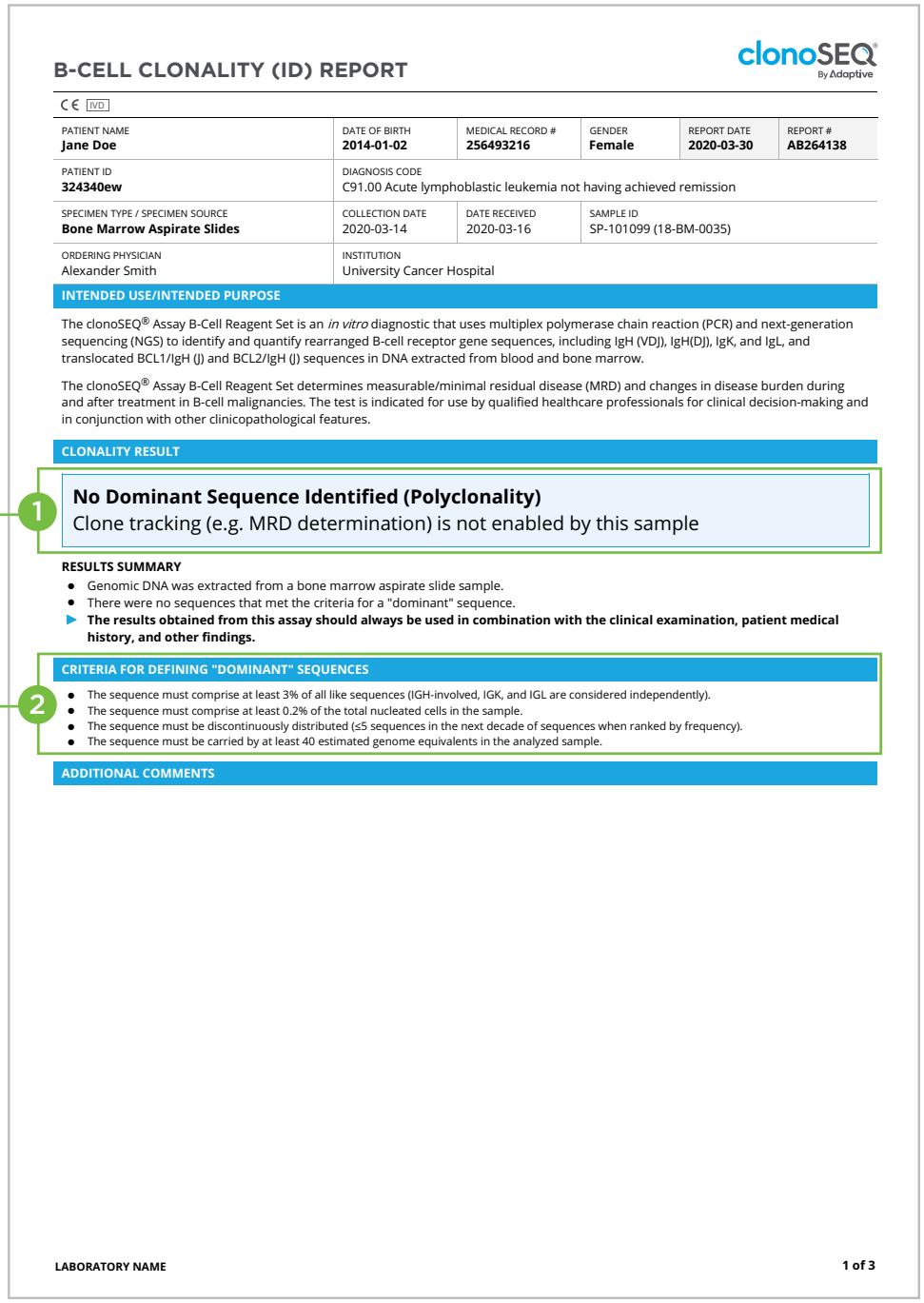
The proprietary reagents and computational algorithms used for the clonoSEQ® Assay B-Cell Reagent Set are provided by Adaptive Biotechnologies Corporation.

B-cell Clonality (ID) Report with No Dominant Sequence Identified

This is an example B-cell Clonality (ID) Report. The clonoSEQ B-cell Clonality (ID) Report provides results based on analysis of the IgH, IgK and IgL loci as well as Bcl1 and Bcl2 translocations.

In this sample report, no dominant DNA sequences were identified from the submitted sample so the result is described as "Polyclonality" (1). This result is often encountered when a sample of insufficient disease load is supplied for testing, so it is important to ensure that samples sent for B-cell Clonality (ID) testing are high disease load diagnostic samples. For reference, information about the criteria for defining a sequence as dominant is also provided at the bottom of the page (2).

Page 1



B-CELL CLONALITY (ID) REPORT

clonoSEQ By Adaptive

CE IVD

PATIENT NAME	DATE OF BIRTH	MEDICAL RECORD #	GENDER	REPORT DATE	REPORT #
Jane Doe	**2014-01-02**	**256493216**	**Female**	**2020-03-30**	**AB264138**

PATIENT ID	DIAGNOSIS CODE
324340ew	C91.00 Acute lymphoblastic leukemia not having achieved remission

SPECIMEN TYPE / SPECIMEN SOURCE	COLLECTION DATE	DATE RECEIVED	SAMPLE ID
Bone Marrow Aspirate Slides	2020-03-14	2020-03-16	SP-101099 (18-BM-0035)

ORDERING PHYSICIAN	INSTITUTION
Alexander Smith	University Cancer Hospital

INTENDED USE/INTENDED PURPOSE

The clonoSEQ® Assay B-Cell Reagent Set is an *in vitro* diagnostic that uses multiplex polymerase chain reaction (PCR) and next-generation sequencing (NGS) to identify and quantify rearranged B-cell receptor gene sequences, including IgH (VDJ), IgH(DJ), IgK, and IgL, and translocated BCL1/IgH (J) and BCL2/IgH (J) sequences in DNA extracted from blood and bone marrow.

The clonoSEQ® Assay B-Cell Reagent Set determines measurable/minimal residual disease (MRD) and changes in disease burden during and after treatment in B-cell malignancies. The test is indicated for use by qualified healthcare professionals for clinical decision-making and in conjunction with other clinicopathological features.

CLONALITY RESULT

No Dominant Sequence Identified (Polyclonality)
Clone tracking (e.g. MRD determination) is not enabled by this sample

RESULTS SUMMARY

- Genomic DNA was extracted from a bone marrow aspirate slide sample.
- There were no sequences that met the criteria for a "dominant" sequence.
- **The results obtained from this assay should always be used in combination with the clinical examination, patient medical history, and other findings.**

CRITERIA FOR DEFINING "DOMINANT" SEQUENCES

- The sequence must comprise at least 3% of all like sequences (IGH-involved, IGK, and IGL are considered independently).
- The sequence must comprise at least 0.2% of the total nucleated cells in the sample.
- The sequence must be discontinuously distributed (≤5 sequences in the next decade of sequences when ranked by frequency).
- The sequence must be carried by at least 40 estimated genome equivalents in the analyzed sample.

ADDITIONAL COMMENTS

LABORATORY NAME **1 of 3**

1 A 'Polyclonality' result is reported when no dominant sequences are identified in the supplied sample

2 Criteria for defining a dominant sequence

B-cell Clonality (ID) Report with No Dominant Sequence Identified (continued)

Since no dominant sequences were identified in the B-cell Clonality (ID) test, a sequences table is not shown on Page 2 of the report. Instead, Page 3 provides more details on the immune repertoire of the analyzed sample, including sample clonality, the number of sequences assessed for each locus, and the number of unique sequences assessed (3).

Page 3

B-CELL CLONALITY (ID) REPORT

clonoSEQ® By Adaptive

CE IVD

PATIENT NAME	DATE OF BIRTH	MEDICAL RECORD #	GENDER	REPORT DATE	REPORT #
Jane Doe	**2014-01-02**	**256493216**	**Female**	**2020-03-30**	**AB264138**

PATIENT ID	DIAGNOSIS CODE
324340ew	C91.00 Acute lymphoblastic leukemia not having achieved remission

SPECIMEN TYPE / SPECIMEN SOURCE	COLLECTION DATE	DATE RECEIVED	SAMPLE ID
Bone Marrow Aspirate Slides	2020-03-14	2020-03-16	SP-101099 (18-BM-0035)

APPENDIX

SUPPLEMENTAL SAMPLE INFORMATION

3 Details on immune repertoire of analyzed sample

SAMPLE CLONALITY [1]	TOTAL NUCLEATED CELLS [2]
0.13	82,497

LOCI	TOTAL SEQUENCES [3]	TOTAL UNIQUE SEQUENCES [4]
IGH	158	114
IGK	>=43	43
IGL	>=13	13

[1] Sample Clonality	A measure of the lymphocyte population diversity (distinct lymphocyte clonal sub-populations or "clones") comprising the immune repertoire in a given biological sample. Values for clonality vary from 0 to 1. Values close to 1 represent samples with one or a few predominant clones. Values near zero represent a more polyclonal sample.
[2] Total Nucleated Cells	The total number of nucleated cells calculated within the sample, based on quantitation of non-immune receptor loci contained in the reaction and the assumption that the DNA content per cell is diploid.
[3] Total Sequences	A measure of the number of nucleotide sequences detected in the sample for each defined immune receptor locus.
[4] Total Unique Sequences	A measure of the number of unique nucleotide sequences detected in the sample for each defined immune receptor locus.
Limit of Detection (LOD)	The lowest level of residual tracked sequence(s) that can be reliably detected by the clonoSEQ® Assay B-Cell Reagent Set in ≥95% of samples tested. LOD is independently calculated for each trackable sequence and hence can vary by sequence based on factors including the amount of input DNA, the uniqueness of the sequence, and/or relative amplification due to nucleotide sequence polymorphism or mutation.

REFERENCES

- Armand P, et al. Br J Haematol. 2013; 163:123-126.
- Carlson CS, et al. Nat Commun. 2013;4:2680.
- Faham M, et al. Blood. 2012;120(26):5173-80.
- Kurtz D, et al. Blood 2015; 125:3679-3687.
- Logan AC, et al. Leukemia. 2013;27(8):1659-65.
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- Rawstron AC, et al. Leukemia. 2016;30(4):929-36.
- Roschewski M, et al. Lancet Oncol. 2015;16:541-49.
- Wu D, et al. Clin Cancer Res. 2014;20(17):4540-8.

REPORT APPROVAL

REVIEWED AND RELEASED BY	SIGNATURE	DATE & TIME
Maria C Santos, MD	Maria C Santos	2020-03-30 12:22 PM

The proprietary reagents and computational algorithms used for the clonoSEQ® Assay B-Cell Reagent Set are provided by Adaptive Biotechnologies Corporation.

LABORATORY NAME

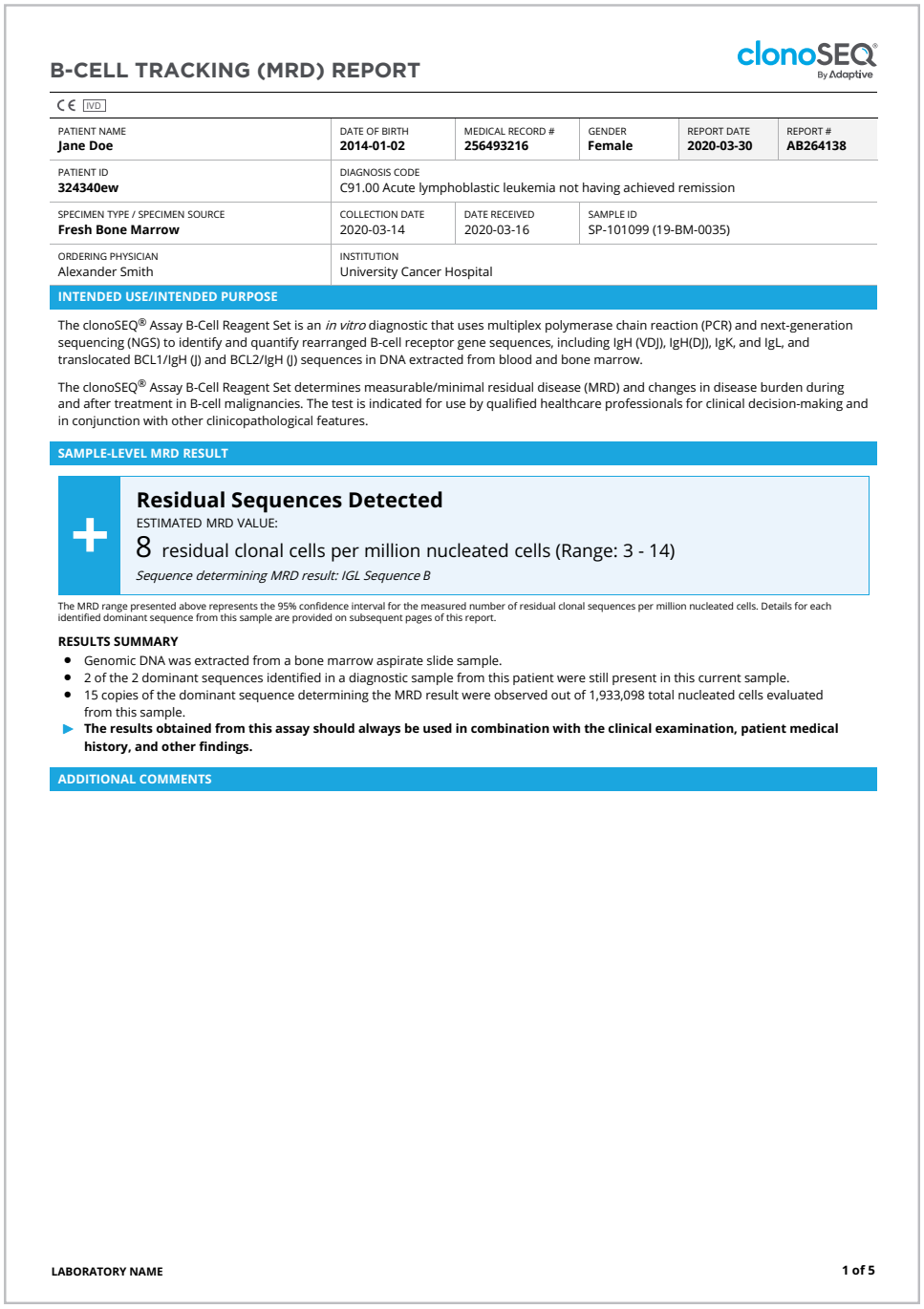
3 of 3

clonoSEQ® By Adaptive

B-CELL TRACKING (MRD) REPORT:

MRD Detection and Monitoring

After the dominant DNA sequence(s) has been identified utilizing the B-cell Clonality (ID) Test, subsequent monitoring of the associated clone(s) can be completed by ordering B-cell Tracking (MRD) Tests throughout treatment.



B-CELL TRACKING (MRD) REPORT

clonoSEQ® By Adaptive

CE IVD

PATIENT NAME	DATE OF BIRTH	MEDICAL RECORD #	GENDER	REPORT DATE	REPORT #
Jane Doe	**2014-01-02**	**256493216**	**Female**	**2020-03-30**	**AB264138**

PATIENT ID	DIAGNOSIS CODE
324340ew	C91.00 Acute lymphoblastic leukemia not having achieved remission

SPECIMEN TYPE / SPECIMEN SOURCE	COLLECTION DATE	DATE RECEIVED	SAMPLE ID
Fresh Bone Marrow	2020-03-14	2020-03-16	SP-101099 (19-BM-0035)

ORDERING PHYSICIAN	INSTITUTION
Alexander Smith	University Cancer Hospital

INTENDED USE/INTENDED PURPOSE

The clonoSEQ® Assay B-Cell Reagent Set is an *in vitro* diagnostic that uses multiplex polymerase chain reaction (PCR) and next-generation sequencing (NGS) to identify and quantify rearranged B-cell receptor gene sequences, including IgH (VDJ), IgH(DJ), IgK, and IgL, and translocated BCL1/IgH (J) and BCL2/IgH (J) sequences in DNA extracted from blood and bone marrow.

The clonoSEQ® Assay B-Cell Reagent Set determines measurable/minimal residual disease (MRD) and changes in disease burden during and after treatment in B-cell malignancies. The test is indicated for use by qualified healthcare professionals for clinical decision-making and in conjunction with other clinicopathological features.

SAMPLE-LEVEL MRD RESULT

\+ **Residual Sequences Detected**

ESTIMATED MRD VALUE:

8 residual clonal cells per million nucleated cells (Range: 3 - 14)

Sequence determining MRD result: IGL Sequence B

The MRD range presented above represents the 95% confidence interval for the measured number of residual clonal sequences per million nucleated cells. Details for each identified dominant sequence from this sample are provided on subsequent pages of this report.

RESULTS SUMMARY

- Genomic DNA was extracted from a bone marrow aspirate slide sample.
- 2 of the 2 dominant sequences identified in a diagnostic sample from this patient were still present in this current sample.
- 15 copies of the dominant sequence determining the MRD result were observed out of 1,933,098 total nucleated cells evaluated from this sample.

▶ **The results obtained from this assay should always be used in combination with the clinical examination, patient medical history, and other findings.**

ADDITIONAL COMMENTS

LABORATORY NAME **1 of 5**

MRD DETECTION AND MONITORING

B-cell Tracking (MRD) Report With Residual Sequences Detected

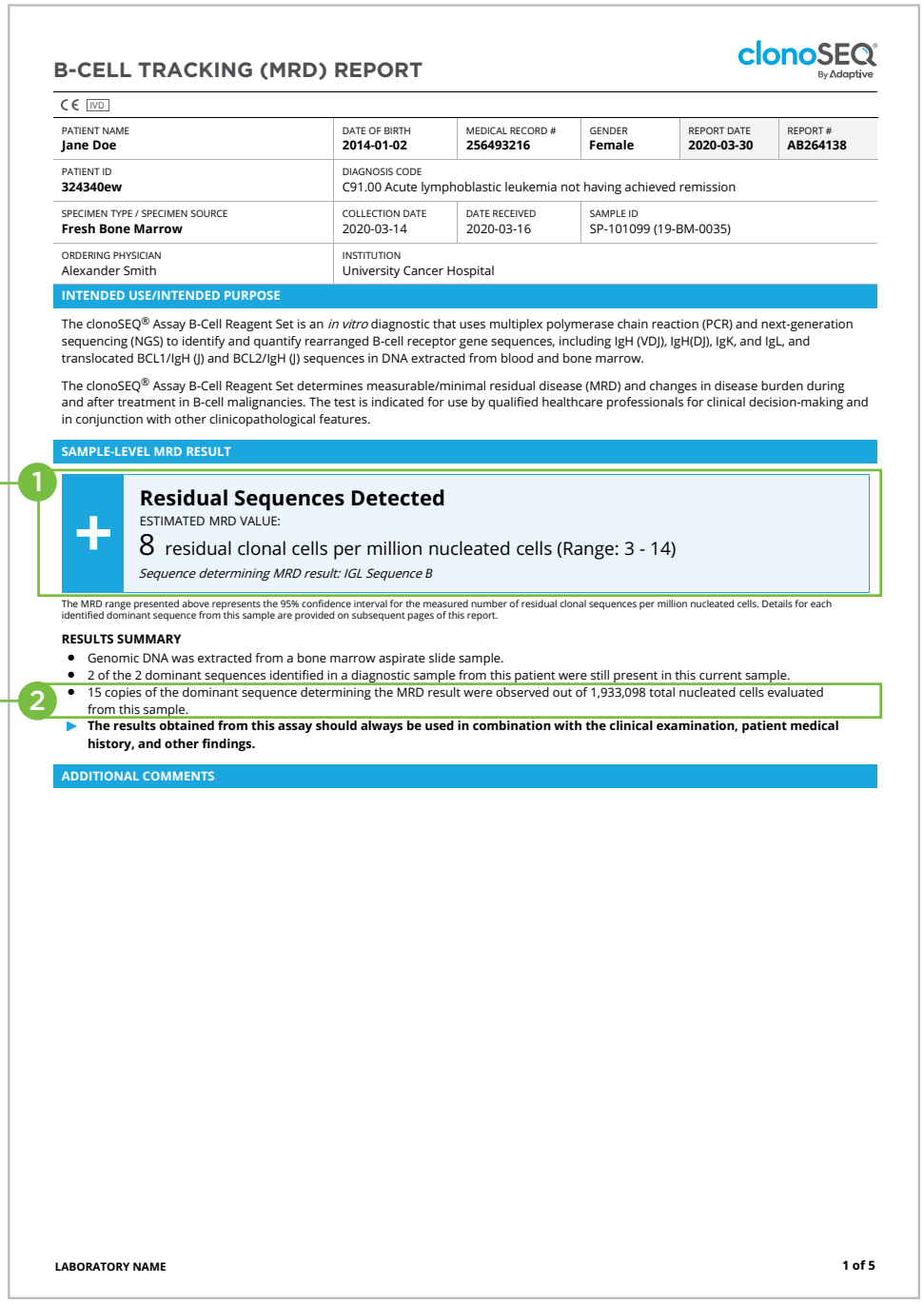
This is an example B-cell Tracking (MRD) Report. The clonoSEQ B-cell Tracking (MRD) Report provides results based on analysis of the IgH, IgK and IgL loci as well as Bcl1 and Bcl2 translocations.

In this sample, residual disease (MRD) was detected by the clonoSEQ Assay. This is indicated by the "plus" sign as well as the language stating "Residual Sequence(s) Detected" in the blue box on page 1 of the report (1). Also in the blue box, the report provides a quantitative assessment of the number of detected residual cells containing that sequence, displayed as a number per 1 million cells in the sample.

Note that a range is also included to the right of the quantitative MRD value. This range represents the 95% confidence interval for the measured number of residual clonal sequences per million nucleated cells. The size of the range varies depending on the total number of input cells assessed and the limit of detection of the sequence determining the MRD result.

Further down the page, the Results Summary states the actual number of sequences observed by the assay and the total number of nucleated cells assessed in the sample (2).

Page 1



B-CELL TRACKING (MRD) REPORT

clonoSEQ® By Adaptive

CE IVD

PATIENT NAME	DATE OF BIRTH	MEDICAL RECORD #	GENDER	REPORT DATE	REPORT #
Jane Doe	**2014-01-02**	**256493216**	**Female**	**2020-03-30**	**AB264138**

PATIENT ID	DIAGNOSIS CODE
324340ew	C91.00 Acute lymphoblastic leukemia not having achieved remission

SPECIMEN TYPE / SPECIMEN SOURCE	COLLECTION DATE	DATE RECEIVED	SAMPLE ID
Fresh Bone Marrow	2020-03-14	2020-03-16	SP-101099 (19-BM-0035)

ORDERING PHYSICIAN	INSTITUTION
Alexander Smith	University Cancer Hospital

INTENDED USE/INTENDED PURPOSE

The clonoSEQ® Assay B-Cell Reagent Set is an *in vitro* diagnostic that uses multiplex polymerase chain reaction (PCR) and next-generation sequencing (NGS) to identify and quantify rearranged B-cell receptor gene sequences, including IgH (VDJ), IgH(DJ), IgK, and IgL, and translocated BCL1/IgH (J) and BCL2/IgH (J) sequences in DNA extracted from blood and bone marrow.

The clonoSEQ® Assay B-Cell Reagent Set determines measurable/minimal residual disease (MRD) and changes in disease burden during and after treatment in B-cell malignancies. The test is indicated for use by qualified healthcare professionals for clinical decision-making and in conjunction with other clinicopathological features.

SAMPLE-LEVEL MRD RESULT

1

\+

Residual Sequences Detected

ESTIMATED MRD VALUE:

8 residual clonal cells per million nucleated cells (Range: 3 - 14)

Sequence determining MRD result: IGL Sequence B

The MRD range presented above represents the 95% confidence interval for the measured number of residual clonal sequences per million nucleated cells. Details for each identified dominant sequence from this sample are provided on subsequent pages of this report.

RESULTS SUMMARY

- Genomic DNA was extracted from a bone marrow aspirate slide sample.
- 2 of the 2 dominant sequences identified in a diagnostic sample from this patient were still present in this current sample.
- 15 copies of the dominant sequence determining the MRD result were observed out of 1,933,098 total nucleated cells evaluated from this sample.

2

▶ **The results obtained from this assay should always be used in combination with the clinical examination, patient medical history, and other findings.**

ADDITIONAL COMMENTS

LABORATORY NAME **1 of 5**

Result indicating whether residual sequences were detected and quantifying MRD level as a fraction per 1 million cells

Number of residual sequences observed out of total nucleated cells assessed

MRD DETECTION AND MONITORING

B-cell Tracking (MRD) Report With Residual Sequences Detected (continued)

At the top of page 2, a chart (3) provides a longitudinal view of the sample-level MRD result for the current sample as well as for past samples sent for clonoSEQ testing for this patient. Each result is shown as a point on the chart with a corresponding test date; each MRD time point also has an associated confidence interval displayed. Note that the results shown in this chart are “sample level” results, meaning that they reflect the MRD result for the highest frequency dominant sequence in each tested sample. For sequence-level MRD results, see the table on the bottom half of the page and/or the chart on page 3 of the report.

Page 2

B-CELL TRACKING (MRD) REPORT

clonoSEQ By Adaptive

CE IVD

PATIENT NAME	DATE OF BIRTH	MEDICAL RECORD #	GENDER	REPORT DATE	REPORT #
Jane Doe	**2014-01-02**	**256493216**	**Female**	**2020-03-30**	**AB264138**

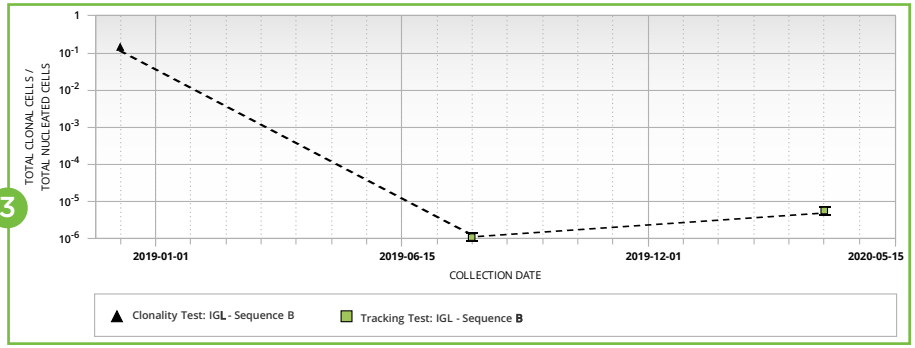
PATIENT ID	DIAGNOSIS CODE
324340ew	C91.00 Acute lymphoblastic leukemia not having achieved remission

SPECIMEN TYPE / SPECIMEN SOURCE	COLLECTION DATE	DATE RECEIVED	SAMPLE ID
Fresh Bone Marrow	2020-03-14	2020-03-16	SP-101099 (19-BM-0035)

SAMPLE-LEVEL MRD TRACKING *(shows only the sequence determining the MRD result for each time point)*

Chart showing sample-level MRD results over time

3



IDENTIFIED DOMINANT SEQUENCE(S)

The number of clonal cells may vary by sample type. As such, changes in clonal cell values over time are best compared using the same sample type.

IGH - Sequence A

GGCCTACATGGACCTGAGCAGCCTGACATCTGAGGACACGGCCGTATATTACTGTGCGCGGCCTTCGACAGTTCCTACGTCGTACTACTCCCACATGGACGTCTGGGGCGAAGGGACC

COLLECTION DATE	SAMPLE ID	SPECIMEN TYPE	ESTIMATED SEQUENCE ABUNDANCE (RESIDUAL CLONAL CELLS PER MILLION NUCLEATED CELLS)	95% CONFIDENCE INTERVAL
● 2020-03-14	SP-657843	Fresh Bone Marrow	**7**	3 - 13
2019-08-30	SP-563745	Fresh Bone Marrow	**0**	0 - 1
2018-11-30	SP-758362	Bone Marrow Aspirate Slides	**119,534**	-

IGL - Sequence B SEQUENCE DETERMINING CURRENT MRD RESULT

TCAGTAGACAAGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCCGCGGACACGGCCGTGTATTACTGTGCCCTTGGGGGATATTAGTAGTAGTACCAGCTGCTATCCTGAGGCCCAGACACCAAC
TGGTTCGACCCCTGGGGCCAGGGAACC

COLLECTION DATE	SAMPLE ID	SPECIMEN TYPE	ESTIMATED SEQUENCE ABUNDANCE (RESIDUAL CLONAL CELLS PER MILLION NUCLEATED CELLS)	95% CONFIDENCE INTERVAL
● 2020-03-14	SP-657843	Fresh Bone Marrow	**8**	3 - 14
✔ 2019-08-30	SP-563745	Fresh Bone Marrow	**0**	0 - 1
✔ 2018-11-30	SP-758362	Bone Marrow Aspirate Slides	**120,256**	-

● Results for report sample ✔ Sequence determining previous MRD result

LABORATORY NAME **2 of 5**

MRD DETECTION AND MONITORING

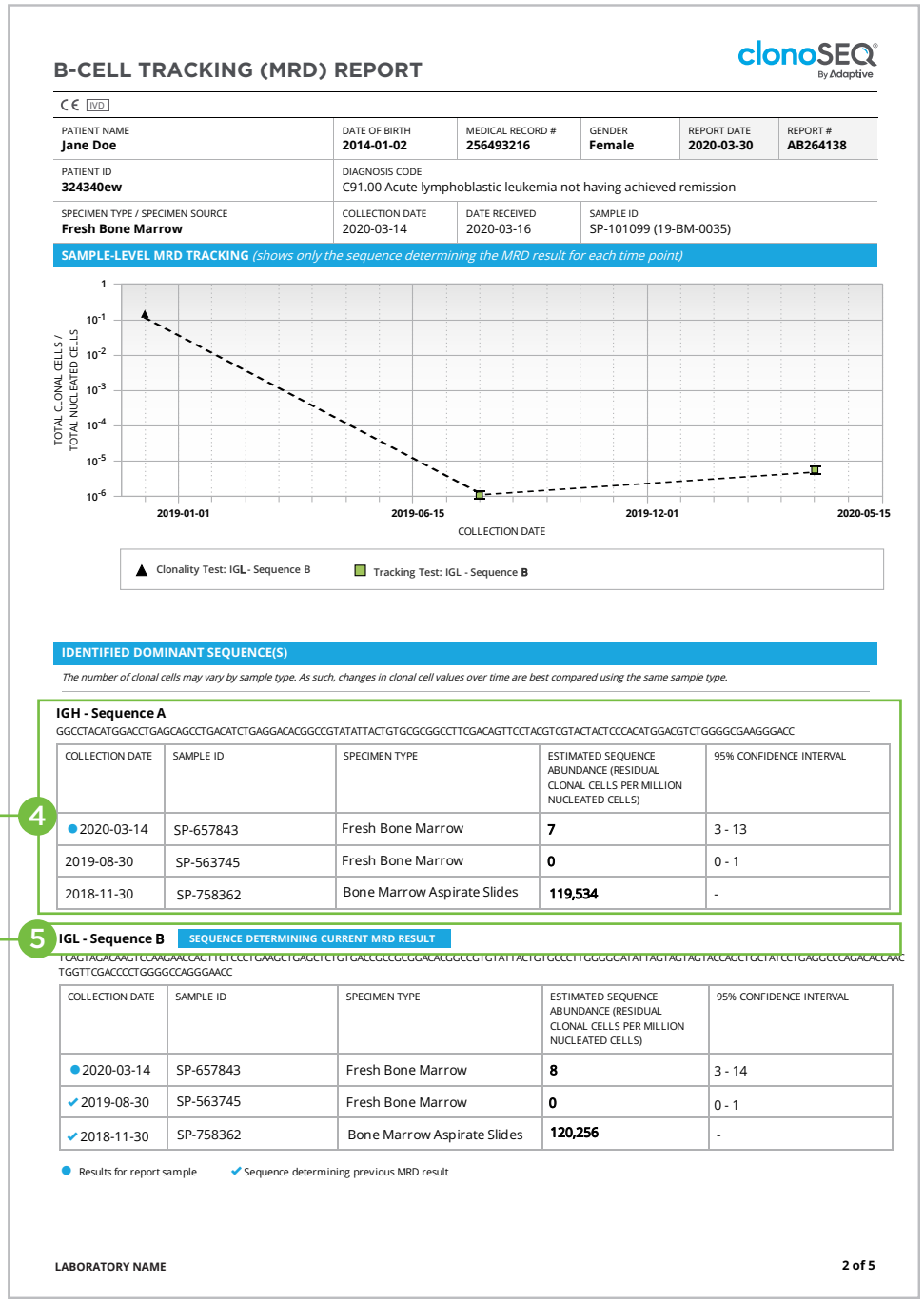
B-cell Tracking (MRD) Report With Residual Sequences Detected (continued)

Page 2 of the report shows detailed information relating to the current and previous samples (4) including the actual rearranged DNA nucleotide sequence or sequences identified, sample collection dates the receptor locus which each dominant DNA sequence was found, the specimen type analyzed, the estimated sequence abundance (i.e., the number of residual clonal cells per million nucleated cells), and the 95% confidence interval for each MRD result.

A blue bar (5) will be placed next to one of the sequences listed on this page to indicate that it is the sequence determining the MRD result for the current sample. The sequence(s) that determined the MRD result for previous samples are noted with a blue check mark.

Any MRD result which falls below the limit of detection (LOD) for a particular sequence is indicated with a double-cross which will be displayed in the estimated sequence abundance column next to the relevant result(s).

Page 2



B-CELL TRACKING (MRD) REPORT

clonoSEQ By Adaptive

CE IVD

PATIENT NAME	DATE OF BIRTH	MEDICAL RECORD #	GENDER	REPORT DATE	REPORT #
Jane Doe	2014-01-02	256493216	Female	2020-03-30	AB264138

PATIENT ID	DIAGNOSIS CODE
324340ew	C91.00 Acute lymphoblastic leukemia not having achieved remission

SPECIMEN TYPE / SPECIMEN SOURCE	COLLECTION DATE	DATE RECEIVED	SAMPLE ID
Fresh Bone Marrow	2020-03-14	2020-03-16	SP-101099 (19-BM-0035)

SAMPLE-LEVEL MRD TRACKING *(shows only the sequence determining the MRD result for each time point)*

IDENTIFIED DOMINANT SEQUENCE(S)

The number of clonal cells may vary by sample type. As such, changes in clonal cell values over time are best compared using the same sample type.

IGH - Sequence A

GGCCTACATGGACCTGAGCAGCCTGACATCTGAGGACACGGCCGTATATTACTGTGCGCGGCCTTCGACAGTTCCTACGTCGTACTACTCCCACATGGACGTCTGGGGCGAAGGGACC

COLLECTION DATE	SAMPLE ID	SPECIMEN TYPE	ESTIMATED SEQUENCE ABUNDANCE (RESIDUAL CLONAL CELLS PER MILLION NUCLEATED CELLS)	95% CONFIDENCE INTERVAL
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2019-08-30	SP-563745	Fresh Bone Marrow	**0**	0 - 1
2018-11-30	SP-758362	Bone Marrow Aspirate Slides	**119,534**	-

IGL - Sequence B SEQUENCE DETERMINING CURRENT MRD RESULT

TCAGTAGACAAGTCCAAGAACACAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCCGCGGACACGGCCGTGTATTACTGTGCCCTTGGGGGATATTAGTAGTAGTACCAGCTGCTATCCTGAGGCCCAGACACCAAC
TGGTTCGACCCCTGGGGCCAGGGAACC

COLLECTION DATE	SAMPLE ID	SPECIMEN TYPE	ESTIMATED SEQUENCE ABUNDANCE (RESIDUAL CLONAL CELLS PER MILLION NUCLEATED CELLS)	95% CONFIDENCE INTERVAL
● 2020-03-14	SP-657843	Fresh Bone Marrow	**8**	3 - 14
✔ 2019-08-30	SP-563745	Fresh Bone Marrow	**0**	0 - 1
✔ 2018-11-30	SP-758362	Bone Marrow Aspirate Slides	**120,256**	-

● Results for report sample ✔ Sequence determining previous MRD result

LABORATORY NAME 2 of 5

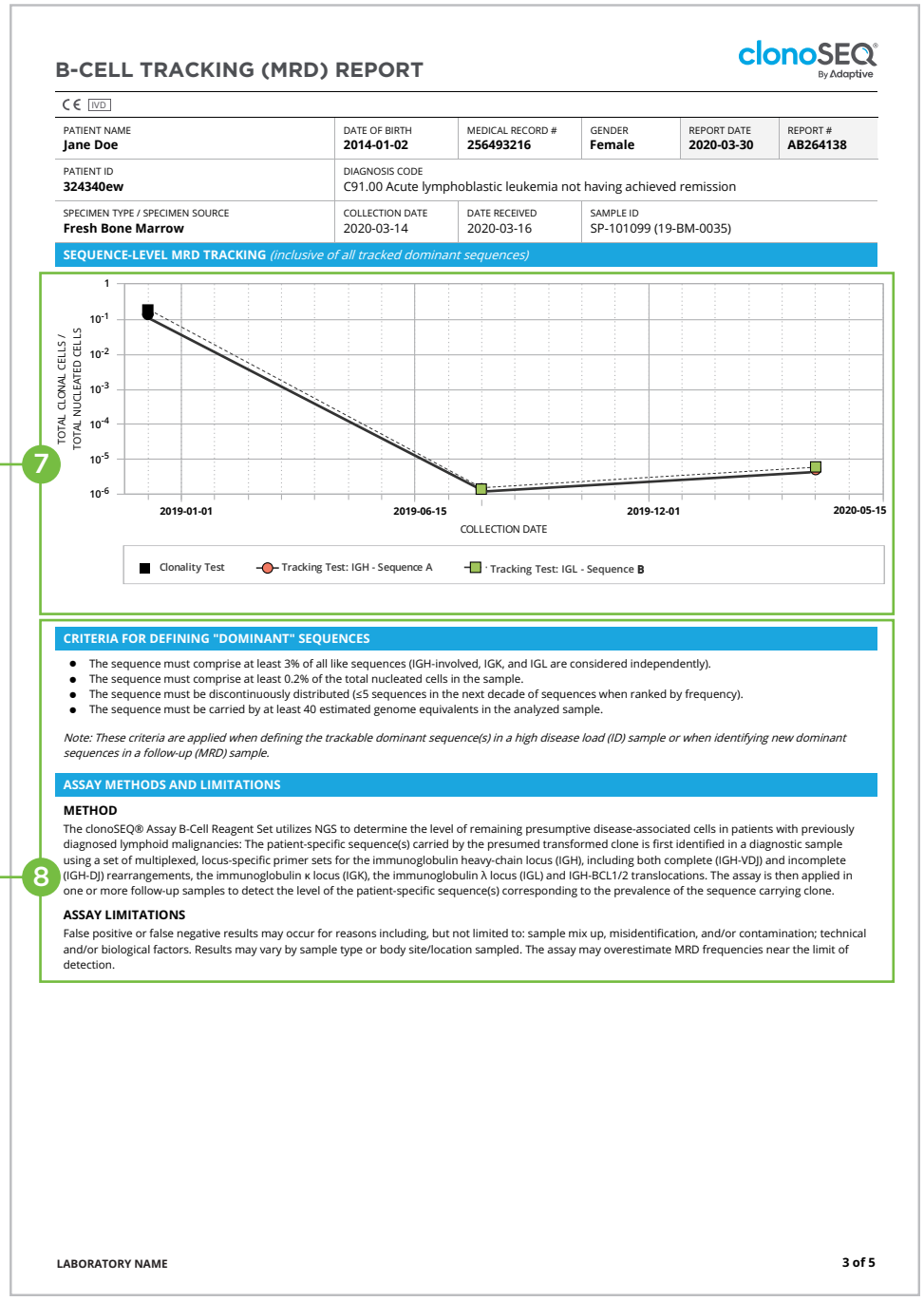
MRD DETECTION AND MONITORING

B-cell Tracking (MRD) Report With Residual Sequences Detected (continued)

Page 3 of the report displays the sequence-level information from Page 2 in a chart format (7). This "sequence-level MRD" chart provides a longitudinal view of results for each individual tracked sequence, for the current sample as well as for past samples sent for clonoSEQ testing for this patient. Similar to the "sample-level" chart on Page 1, the sequence-level chart includes a point on the chart for each test with a corresponding test date, but on this chart, each individual sequence is displayed separately.

In addition to the sequence-level chart, this page lists the criteria used by the clonoSEQ Assay to define dominant sequences, as well as a summary of the assay method and limitations (8).

Page 3



B-CELL TRACKING (MRD) REPORT

clonoSEQ By Adaptive

CE IVD

PATIENT NAME	DATE OF BIRTH	MEDICAL RECORD #	GENDER	REPORT DATE	REPORT #
Jane Doe	**2014-01-02**	**256493216**	**Female**	**2020-03-30**	**AB264138**

PATIENT ID	DIAGNOSIS CODE
324340ew	C91.00 Acute lymphoblastic leukemia not having achieved remission

SPECIMEN TYPE / SPECIMEN SOURCE	COLLECTION DATE	DATE RECEIVED	SAMPLE ID
Fresh Bone Marrow	2020-03-14	2020-03-16	SP-101099 (19-BM-0035)

SEQUENCE-LEVEL MRD TRACKING *(inclusive of all tracked dominant sequences)*

Chart showing sequence-level MRD results over time

7

CRITERIA FOR DEFINING "DOMINANT" SEQUENCES

- The sequence must comprise at least 3% of all like sequences (IGH-involved, IGK, and IGL are considered independently).
- The sequence must comprise at least 0.2% of the total nucleated cells in the sample.
- The sequence must be discontinuously distributed (≤5 sequences in the next decade of sequences when ranked by frequency).
- The sequence must be carried by at least 40 estimated genome equivalents in the analyzed sample.

Note: These criteria are applied when defining the trackable dominant sequence(s) in a high disease load (ID) sample or when identifying new dominant sequences in a follow-up (MRD) sample.

ASSAY METHODS AND LIMITATIONS

METHOD

The clonoSEQ® Assay B-Cell Reagent Set utilizes NGS to determine the level of remaining presumptive disease-associated cells in patients with previously diagnosed lymphoid malignancies: The patient-specific sequence(s) carried by the presumed transformed clone is first identified in a diagnostic sample using a set of multiplexed, locus-specific primer sets for the immunoglobulin heavy-chain locus (IGH), including both complete (IGH-VDJ) and incomplete (IGH-DJ) rearrangements, the immunoglobulin κ locus (IGK), the immunoglobulin λ locus (IGL) and IGH-BCL1/2 translocations. The assay is then applied in one or more follow-up samples to detect the level of the patient-specific sequence(s) corresponding to the prevalence of the sequence carrying clone.

Summary of assay method and limitations

8

ASSAY LIMITATIONS

False positive or false negative results may occur for reasons including, but not limited to: sample mix up, misidentification, and/or contamination; technical and/or biological factors. Results may vary by sample type or body site/location sampled. The assay may overestimate MRD frequencies near the limit of detection.

LABORATORY NAME **3 of 5**

MRD DETECTION AND MONITORING

B-cell Tracking (MRD) Report With Residual Sequences Detected (continued)

The appendix provides more details on the immune repertoire of the analyzed sample, including the sample clonality, the number of sequences assessed for each locus, and the number of unique sequences assessed (9).

Page 4 of the report continues details on the immune repertoire of the analyzed sample, noting the limit of detection and limit of quantitation for each sequence tracked (10). The limit of detection (LOD) and limit of quantitation (LOQ) are independently calculated for each trackable sequence and hence can vary by sequence based on factors including the amount of input DNA, the uniqueness of the sequence, and/or relative amplification due to nucleotide sequence polymorphism or mutation.

A glossary of terms and references relevant to the report is also provided on this page (11).

Within the glossary, the assay's limit of blank, which is zero, is stated and defined (12). A limit of blank equal to zero indicates that in tests of assay performance on samples that were known to have zero residual disease, the clonoSEQ Assay did not generate any false-positive results.

Note: False positive or false negative results may still occur, for reasons including contamination, technical and/or biological factors.

Page 4

B-CELL TRACKING (MRD) REPORT

clonoSEQ® By Adaptive

CE IVD

PATIENT NAME	DATE OF BIRTH	MEDICAL RECORD #	GENDER	REPORT DATE	REPORT #
Jane Doe	**2014-01-02**	**256493216**	**Female**	**2020-03-30**	**AB264138**

PATIENT ID	DIAGNOSIS CODE
324340ew	C91.00 Acute lymphoblastic leukemia not having achieved remission

SPECIMEN TYPE / SPECIMEN SOURCE	COLLECTION DATE	DATE RECEIVED	SAMPLE ID
Fresh Bone Marrow	2020-03-14	2020-03-16	SP-101099 (19-BM-0035)

ADDITIONAL ASSAY METHODS AND LIMITATIONS

APPENDIX

SUPPLEMENTAL SAMPLE INFORMATION

SAMPLE CLONALITY [1]	TOTAL NUCLEATED CELLS [2]
0.04	1,933,098

LOCI	TOTAL SEQUENCES [3]	TOTAL UNIQUE SEQUENCES [4]
IGH	≥78,588	78,588
IGK	20,064	12,181
IGL	859	785

SUPPLEMENTAL SEQUENCE INFORMATION

SEQUENCE	LIMIT OF DETECTION (PER MILLION CELLS) [5]	LIMIT OF QUANTITATION (PER MILLION CELLS) [6]
IGH - Sequence A	1	1
IGK - Sequence B	1	1

[1] Sample Clonality	A measure of the lymphocyte population diversity (distinct lymphocyte clonal sub-populations or "clones") comprising the immune repertoire in a given biological sample. Values for clonality vary from 0 to 1. Values close to 1 represent samples with one or a few predominant clones. Values near zero represent a more polyclonal sample.
[2] Total Nucleated Cells	The total number of nucleated cells calculated within the sample, based on quantitation of non-immune receptor loci contained in the reaction and the assumption that the DNA content per cell is diploid.
[3] Total Sequences	A measure of the number of nucleotide sequences detected in the sample for each defined immune receptor locus.
[4] Total Unique Sequences	A measure of the number of unique nucleotide sequences detected in the sample for each defined immune receptor locus.
[5] Limit of Detection (LOD)	The lowest level of residual tracked sequence(s) that can be reliably detected by the clonoSEQ® Assay B-Cell Reagent Set in ≥95% of samples tested. LOD is independently calculated for each trackable sequence and hence can vary by sequence based on factors including the amount of input DNA, the uniqueness of the sequence, and/or relative amplification due to nucleotide sequence polymorphism or mutation.
[6] Limit of Quantitation (LOQ)	The lowest level of residual tracked sequence(s) that can be reliably quantified by the clonoSEQ® Assay B-Cell Reagent Set (within 70% total RMS error). LOQ is independently calculated for each trackable sequence and hence can vary by sequence based on factors including the amount of input DNA, the uniqueness of the sequence, and/or relative amplification due to nucleotide sequence polymorphism or mutation.
Limit of Blank (LOB)	The level of residual tracked sequence(s) at or below which 95% of true MRD-negative samples will fall. The LOB for the clonoSEQ® Assay B-Cell Reagent Set was determined during analytical validation to be 0.

REFERENCES

- Armand P, et al. Br J Haematol. 2013; 163:123-126.
- Carlson CS, et al. Nat Commun. 2013;4:2680.
- Faham M, et al. Blood. 2012;120(26):5173-80.
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- Wu D, et al. Clin Cancer Res. 2014;20(17):4540-8.

LABORATORY NAME

9 Details on immune repertoire of analyzed sample

10 Limit of detection and limit of quantitation for each tracked sequence

11 Glossary of terms and references

12 Limit of blank

MRD DETECTION AND MONITORING

B-cell Tracking (MRD) Report With No Residual Sequences Detected

This is an example B-cell Tracking (MRD) Report. The clonoSEQ B-cell Tracking (MRD) Report provides results based on analysis of the IgH, IgK and IgL loci as well as Bcl1 and Bcl2 translocations.

In this sample, residual disease was NOT detected by the clonoSEQ Assay. This is indicated by the language "Residual Sequence(s) Not Detected" in the blue box on page 1 of the report (1). Also in the blue box, the report provides a quantitative assessment of the number of detected residual cells containing that sequence, displayed as a number per 1 million cells in the sample. In this example, the number of detected residual cells is zero.

Note that a range is also included to the right of the quantitative MRD value. This range represents the 95% confidence interval for the measured number of residual clonal sequences per million nucleated cells. The size of the range varies depending on the total number of input cells assessed and the limit of detection of the sequence determining the MRD result. For a test in which residual disease was not detected, the range reflects the fact that there was zero disease in the tested sample, but that some disease could still be present in the patient (due to sampling bias).

Further down the page, the Results Summary states the actual number of sequences observed by the assay and the total number of nucleated cells assessed in the sample (2).

Page 1

B-CELL TRACKING (MRD) REPORT

clonoSEQ® By Adaptive

CE IVD

PATIENT NAME	DATE OF BIRTH	MEDICAL RECORD #	GENDER	REPORT DATE	REPORT #
Jane Doe	**2014-01-02**	**256493216**	**Female**	**2020-03-30**	**AB264138**

PATIENT ID	DIAGNOSIS CODE
324340ew	C91.00 Acute lymphoblastic leukemia not having achieved remission

SPECIMEN TYPE / SPECIMEN SOURCE	COLLECTION DATE	DATE RECEIVED	SAMPLE ID
Fresh Bone Marrow	2020-03-14	2020-03-16	SP-101099 (19-BM-0035)

ORDERING PHYSICIAN	INSTITUTION
Alexander Smith	University Cancer Hospital

INTENDED USE/INTENDED PURPOSE

The clonoSEQ® Assay B-Cell Reagent Set is an *in vitro* diagnostic that uses multiplex polymerase chain reaction (PCR) and next-generation sequencing (NGS) to identify and quantify rearranged B-cell receptor gene sequences, including IgH (VDJ), IgH(DJ), IgK, and IgL, and translocated BCL1/IgH (J) and BCL2/IgH (J) sequences in DNA extracted from blood and bone marrow.

The clonoSEQ® Assay B-Cell Reagent Set determines measurable/minimal residual disease (MRD) and changes in disease burden during and after treatment in B-cell malignancies. The test is indicated for use by qualified healthcare professionals for clinical decision-making and in conjunction with other clinicopathological features.

SAMPLE-LEVEL MRD RESULT

No Residual Sequences Detected

ESTIMATED MRD VALUE:

0 residual clonal cells (Range: 0 - 2) **

Sequence determining MRD result: IGH Sequence A

The MRD range presented above represents the 95% confidence interval for the measured number of residual clonal sequences per million nucleated cells. Details for each identified dominant sequence from this sample are provided on subsequent pages of this report.

RESULTS SUMMARY

- Genomic DNA was extracted from a bone marrow aspirate slide sample.
- The 3 dominant sequences identified in a diagnostic sample from this patient were not detected in this current sample.

** The sensitivity of this assay is directly related to the total number of cells (or cellular equivalents of genomic DNA) analyzed. There were 1,331,826 total nucleated cells evaluated from this sample.

▶ **The results obtained from this assay should always be used in combination with the clinical examination, patient medical history, and other findings.**

ADDITIONAL COMMENTS

LABORATORY NAME **1 of 5**

1 Result indicating whether residual sequences were detected

2 Number of residual sequences observed out of total nucleated cells assessed

MRD DETECTION AND MONITORING

B-cell Tracking (MRD) Report With No Residual Sequences Detected (continued)

At the top of page 2, a chart (3) provides a longitudinal view of the sample-level MRD result for the current sample as well as for past samples sent for clonoSEQ testing for this patient. In this example, the patient was MRD-positive in previous tests, but no residual disease was detected in the current sample. Each result is shown as a point on the chart with a corresponding test date; each MRD time point also has an associated confidence interval displayed. Note that the results shown in this chart are "sample level" results, meaning that they reflect the MRD result for the highest frequency dominant sequence in each tested sample. For sequence-level MRD results, see the table on the bottom half of the page and/or the chart on page 3 of the report.

Page 2

B-CELL TRACKING (MRD) REPORT

clonoSEQ® By Adaptive

CE IVD

PATIENT NAME	DATE OF BIRTH	MEDICAL RECORD #	GENDER	REPORT DATE	REPORT #
Jane Doe	**2014-01-02**	**256493216**	**Female**	**2020-03-30**	**AB264138**

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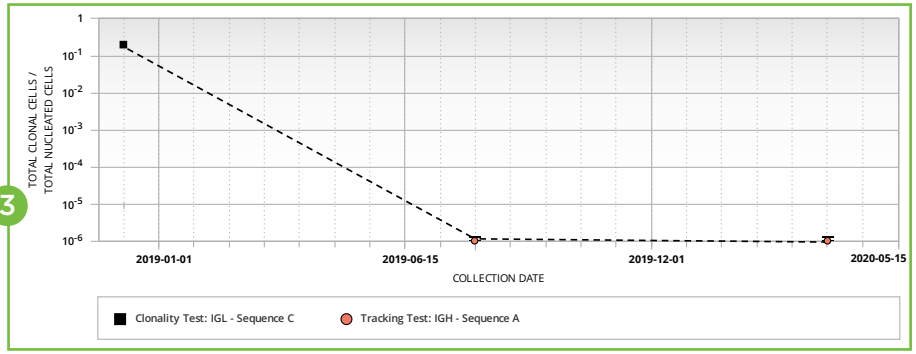
SPECIMEN TYPE / SPECIMEN SOURCE	COLLECTION DATE	DATE RECEIVED	SAMPLE ID
Fresh Bone Marrow	2020-03-14	2020-03-16	SP-101099 (19-BM-0035)

SAMPLE-LEVEL MRD TRACKING *(shows only the sequence determining the MRD result for each time point)*

Chart showing sample-level MRD results over time

3



IDENTIFIED DOMINANT SEQUENCE(S)

The number of clonal cells may vary by sample type. As such, changes in clonal cell values over time are best compared using the same sample type.

IGH - Sequence A SEQUENCE DETERMINING CURRENT MRD RESULT

GGCCTACATGGACCTGAGCAGCCTGACATCTGAGGACACGGCCGTATATTACTGTGCGCGGCCTTCGACAGTTCCTACGTCGTACTACTCCCACATGGACGTCTGGGGCGAAGGGACC

COLLECTION DATE	SAMPLE ID	SPECIMEN TYPE	ESTIMATED SEQUENCE ABUNDANCE (RESIDUAL CLONAL CELLS PER MILLION NUCLEATED CELLS)	95% CONFIDENCE INTERVAL
● 2020-03-14	SP-237584	Bone Marrow Aspirate Slides	*not detected*	0- 2
✔ 2019-08-30	SP-546732	Bone Marrow Aspirate Slides	*not detected*	0 - 2
2018-11-30	SP-974563	Fresh Bone Marrow	**62,222**	-

IGK - Sequence B

CGATGTCAGACTGTGGTGGATATAGTGGCTACGATTAGGGTCTTTGACTACTGGGGCCAGGGAACC

COLLECTION DATE	SAMPLE ID	SPECIMEN TYPE	ESTIMATED SEQUENCE ABUNDANCE (RESIDUAL CLONAL CELLS PER MILLION NUCLEATED CELLS)	95% CONFIDENCE INTERVAL
● 2020-03-14	SP-237584	Bone Marrow Aspirate Slides	*not detected*	0 - 2
2019-08-30	SP-546732	Bone Marrow Aspirate Slides	*not detected*	0 - 2
2018-11-30	SP-974563	Fresh Bone Marrow	**106,978**	-

LABORATORY NAME

2 of 5

MRD DETECTION AND MONITORING

B-cell Tracking (MRD) Report With No Residual Sequences Detected (continued)

Page 2 of the report shows detailed information relating to the current and previous samples (4) including the actual rearranged DNA nucleotide sequence or sequences identified, sample collection dates, the receptor locus which each dominant sequence was found, the specimen type analyzed, the estimated sequence abundance (i.e., the number of residual clonal cells per million nucleated cells), and the 95% confidence interval for each MRD result.

Since no residual sequences were detected in the current sample, the estimated sequence abundance is zero.

Page 2

B-CELL TRACKING (MRD) REPORT

clonoSEQ® By Adaptive

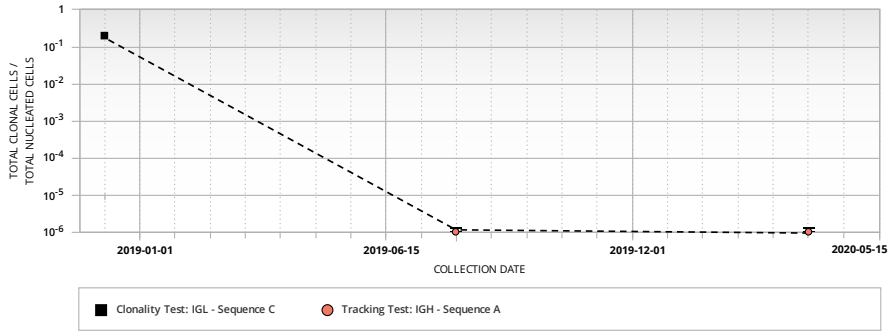
CE IVD

PATIENT NAME	DATE OF BIRTH	MEDICAL RECORD #	GENDER	REPORT DATE	REPORT #
Jane Doe	**2014-01-02**	**256493216**	**Female**	**2020-03-30**	**AB264138**

PATIENT ID	DIAGNOSIS CODE
324340ew	C91.00 Acute lymphoblastic leukemia not having achieved remission

SPECIMEN TYPE / SPECIMEN SOURCE	COLLECTION DATE	DATE RECEIVED	SAMPLE ID
Fresh Bone Marrow	2020-03-14	2020-03-16	SP-101099 (19-BM-0035)

SAMPLE-LEVEL MRD TRACKING *(shows only the sequence determining the MRD result for each time point)*



IDENTIFIED DOMINANT SEQUENCE(S)

The number of clonal cells may vary by sample type. As such, changes in clonal cell values over time are best compared using the same sample type.

IGH - Sequence A SEQUENCE DETERMINING CURRENT MRD RESULT

GGCCTACATGGACCTGAGCAGCCTGACATCTGAGGACACGGCCGTATATTACTGTGCGCGGCCTTCGACAGTTCCTACGTCGTACTACTCCCACATGGACGTCTGGGGCGAAGGGACC

COLLECTION DATE	SAMPLE ID	SPECIMEN TYPE	ESTIMATED SEQUENCE ABUNDANCE (RESIDUAL CLONAL CELLS PER MILLION NUCLEATED CELLS)	95% CONFIDENCE INTERVAL
● 2020-03-14	SP-237584	Bone Marrow Aspirate Slides	*not detected*	0- 2
✔ 2019-08-30	SP-546732	Bone Marrow Aspirate Slides	*not detected*	0 - 2
2018-11-30	SP-974563	Fresh Bone Marrow	**62,222**	-

4 Specific DNA sequences identified

IGK - Sequence B

CGATGTCAGACTGTGGTGGATATAGTGGCTACGATTAGGGTCTTTGACTACTGGGGCCAGGGAACC

COLLECTION DATE	SAMPLE ID	SPECIMEN TYPE	ESTIMATED SEQUENCE ABUNDANCE (RESIDUAL CLONAL CELLS PER MILLION NUCLEATED CELLS)	95% CONFIDENCE INTERVAL
● 2020-03-14	SP-237584	Bone Marrow Aspirate Slides	*not detected*	0 - 2
2019-08-30	SP-546732	Bone Marrow Aspirate Slides	*not detected*	0 - 2
2018-11-30	SP-974563	Fresh Bone Marrow	**106,978**	-

MRD DETECTION AND MONITORING

B-cell Tracking (MRD) Report With No Residual Sequences Detected (continued)

Page 3 of the report displays the sequence-level information from Page 2 in a chart format (5). This "sequence-level MRD" chart provides a longitudinal view of results for each individual tracked sequence, for the current sample as well as for past samples sent for clonoSEQ testing for this patient. Similar to the "sample-level" chart on Page 1, the sequence-level chart includes a point on the chart for each test with a corresponding test date, but on this chart, each individual sequence is displayed separately.

In addition to the sequence-level chart, this page lists the criteria used by the clonoSEQ Assay to define dominant sequences, as well as a summary of the assay method and limitations (6).

Page 3

B-CELL TRACKING (MRD) REPORT

clonoSEQ® By Adaptive

CE IVD

PATIENT NAME	DATE OF BIRTH	MEDICAL RECORD #	GENDER	REPORT DATE	REPORT #
Jane Doe	**2014-01-02**	**256493216**	**Female**	**2020-03-30**	**AB264138**

PATIENT ID	DIAGNOSIS CODE
324340ew	C91.00 Acute lymphoblastic leukemia not having achieved remission

SPECIMEN TYPE / SPECIMEN SOURCE	COLLECTION DATE	DATE RECEIVED	SAMPLE ID
Fresh Bone Marrow	2020-03-14	2020-03-16	SP-101099 (19-BM-0035)

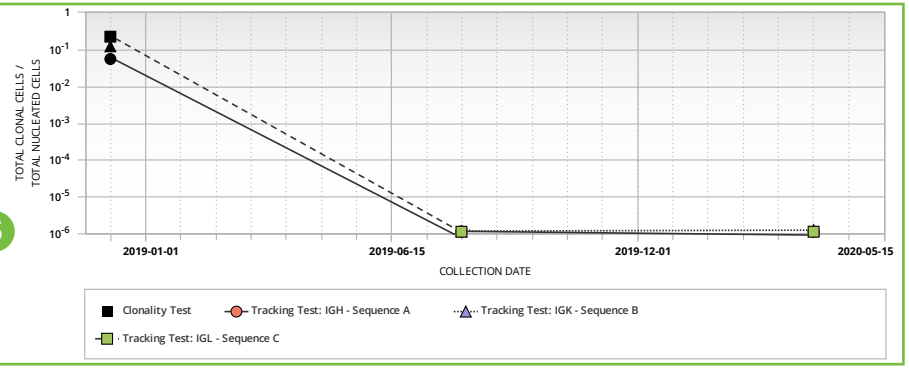
IGL - Sequence C

TCAGTAGACAAGTCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCCGCGGACACGGCCGTGTATTACTGTGCCCTTGGGGGATATTAGTAGTAGTACCAGCTGCTATCCTGAGGCCCAGACACCAAC
TGGTTCGACCCCTGGGGCCAGGGAACC

COLLECTION DATE	SAMPLE ID	SPECIMEN TYPE	ESTIMATED SEQUENCE ABUNDANCE (RESIDUAL CLONAL CELLS PER MILLION NUCLEATED CELLS)	95% CONFIDENCE INTERVAL
● 2020-03-14	SP-237584	Bone Marrow Aspirate Slides	*not detected*	0 - 2
2019-08-30	SP-546732	Bone Marrow Aspirate Slides	*not detected*	0 - 2
✔ 2018-11-30	SP-974563	Fresh Bone Marrow	**133,763**	-

● Results for report sample ✔ Sequence determining previous MRD result

SEQUENCE-LEVEL MRD TRACKING *(inclusive of all tracked dominant sequences)*



5 Chart showing sequence-level MRD results over time

CRITERIA FOR DEFINING "DOMINANT" SEQUENCES

- The sequence must comprise at least 3% of all like sequences (IGH-involved, IGK, and IGL are considered independently).
- The sequence must comprise at least 0.2% of the total nucleated cells in the sample.
- The sequence must be discontinuously distributed (≤5 sequences in the next decade of sequences when ranked by frequency).
- The sequence must be carried by at least 40 estimated genome equivalents in the analyzed sample.

Note: These criteria are applied when defining the trackable dominant sequence(s) in a high disease load (ID) sample or when identifying new dominant sequences in a follow-up (MRD) sample.

ASSAY METHODS AND LIMITATIONS

METHOD

The clonoSEQ® Assay B-Cell Reagent Set utilizes NGS to determine the level of remaining presumptive disease-associated cells in patients with previously diagnosed lymphoid malignancies: The patient-specific sequence(s) carried by the presumed transformed clone is first identified in a diagnostic sample using a set of multiplexed, locus-specific primer sets for the immunoglobulin heavy-chain locus (IGH), including both complete (IGH-VDJ) and incomplete (IGH-DJ) rearrangements, the immunoglobulin κ locus (IGK), the immunoglobulin λ locus (IGL) and IGH-BCL1/2 translocations. The assay is then applied in one or more follow-up samples to detect the level of the patient-specific sequence(s) corresponding to the prevalence of the sequence carrying clone.

6 Summary of assay method and limitations

ASSAY LIMITATIONS

False positive or false negative results may occur for reasons including, but not limited to: sample mix up, misidentification, and/or contamination; technical and/or biological factors. Results may vary by sample type or body site/location sampled. The assay may overestimate MRD frequencies near the limit of detection.

LABORATORY NAME

3 of 5

MRD DETECTION AND MONITORING

B-cell Tracking (MRD) Report With No Residual Sequences Detected (continued)

The appendix provides more details on the immune repertoire of the analyzed sample, including the sample clonality, the number of sequences assessed for each locus, and the number of unique sequences assessed (7).

Page 4 of the report continues details on the immune repertoire of the analyzed sample, noting the limit of detection and limit of quantitation for each sequence tracked (8). The limit of detection (LOD) and limit of quantitation (LOQ) are independently calculated for each trackable sequence and hence can vary by sequence based on factors including the amount of input DNA, the uniqueness of the sequence, and/or relative amplification due to nucleotide sequence polymorphism or mutation.

A glossary of terms and references relevant to the report is also provided on this page (9).

Within the glossary, the assay's limit of blank, which is zero, is stated and defined (10). A limit of blank equal to zero indicates that in tests of assay performance on samples that were known to have zero residual disease, the clonoSEQ Assay did not generate any false-positive results.

Note: False positive or false negative results may still occur, for reasons including contamination, technical and/or biological factors.

Page 4

B-CELL TRACKING (MRD) REPORT

clonoSEQ® By Adaptive

CE IVD

PATIENT NAME	DATE OF BIRTH	MEDICAL RECORD #	GENDER	REPORT DATE	REPORT #
Jane Doe	**2014-01-02**	**256493216**	**Female**	**2020-03-30**	**AB264138**

PATIENT ID	DIAGNOSIS CODE
324340ew	C91.00 Acute lymphoblastic leukemia not having achieved remission

SPECIMEN TYPE / SPECIMEN SOURCE	COLLECTION DATE	DATE RECEIVED	SAMPLE ID
Fresh Bone Marrow	2020-03-14	2020-03-16	SP-101099 (19-BM-0035)

ADDITIONAL ASSAY METHODS AND LIMITATIONS

APPENDIX

SUPPLEMENTAL SAMPLE INFORMATION

SAMPLE CLONALITY [1]	TOTAL NUCLEATED CELLS [2]
0.09	1,331,826

LOCI	TOTAL SEQUENCES [3]	TOTAL UNIQUE SEQUENCES [4]
IGH	≥120,400	120,400
IGK	160,834	68,357
IGL	48,683	21,795

Details on immune repertoire of analyzed sample — 7

SUPPLEMENTAL SEQUENCE INFORMATION

SEQUENCE	LIMIT OF DETECTION (PER MILLION CELLS) [5]	LIMIT OF QUANTITATION (PER MILLION CELLS) [6]
IGH - Sequence A	1	2
IGK - Sequence B	7	9
IGL - Sequence C	143	179

Limit of detection and limit of quantitation for each tracked sequence — 8

[1] Sample Clonality	A measure of the lymphocyte population diversity (distinct lymphocyte clonal sub-populations or "clones") comprising the immune repertoire in a given biological sample. Values for clonality vary from 0 to 1. Values close to 1 represent samples with one or a few predominant clones. Values near zero represent a more polyclonal sample.
[2] Total Nucleated Cells	The total number of nucleated cells calculated within the sample, based on quantitation of non-immune receptor loci contained in the reaction and the assumption that the DNA content per cell is diploid.
[3] Total Sequences	A measure of the number of nucleotide sequences detected in the sample for each defined immune receptor locus.
[4] Total Unique Sequences	A measure of the number of unique nucleotide sequences detected in the sample for each defined immune receptor locus.
[5] Limit of Detection (LOD)	The lowest level of residual tracked sequence(s) that can be reliably detected by the clonoSEQ® Assay B-Cell Reagent Set in ≥95% of samples tested. LOD is independently calculated for each trackable sequence and hence can vary by sequence based on factors including the amount of input DNA, the uniqueness of the sequence, and/or relative amplification due to nucleotide sequence polymorphism or mutation.
[6] Limit of Quantitation (LOQ)	The lowest level of residual tracked sequence(s) that can be reliably quantified by the clonoSEQ® Assay B-Cell Reagent Set (within 70% total RMS error). LOQ is independently calculated for each trackable sequence and hence can vary by sequence based on factors including the amount of input DNA, the uniqueness of the sequence, and/or relative amplification due to nucleotide sequence polymorphism or mutation.

Glossary of terms and references — 9

Limit of Blank (LOB)	The level of residual tracked sequence(s) at or below which 95% of true MRD-negative samples will fall. The LOB for the clonoSEQ® Assay B-Cell Reagent Set was determined during analytical validation to be 0.

Limit of blank — 10

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LABORATORY NAME

Intended Use/Intended Purpose:
The clonoSEQ Assay B-Cell Reagent Set is a quantitative *in vitro* diagnostic (IVD) assay that uses multiplex polymerase chain reaction (PCR) and next-generation sequencing (NGS) to identify and quantify rearranged B-cell receptor gene sequences, including IgH (VDJ), IgH (DJ), IgK, and IgL and translocated BCL1/IgH (J) and BCL2/IgH (J) sequences in DNA extracted from blood and bone marrow.

The clonoSEQ Assay is a manual test that determines measurable/minimal residual disease (MRD) and monitors changes in disease burden during and after treatment in B-cell malignancies. The test is indicated for use by qualified healthcare professionals as an aid to clinical decision making in conjunction with other clinicopathological features.

Limitations:
The limitations of the clonoSEQ Assay include the following:

- The clonoSEQ Assay is for *in vitro* diagnostic use.
- This device is for use by healthcare professionals only.
- MRD values obtained with different assay methods may not be interchangeable due to differences in assay methods and reagent specificity.
- The results obtained from this assay should always be used in combination with the clinical examination, patient medical history, and other findings.
- Use of samples derived from specimen types outside of those listed in this document may produce inaccurate results.
- Results may vary according to sample type, time within the course of disease or by body site/location sampled.
- The assay may overestimate MRD frequencies near the limit of detection (LoD).
- The MRD frequency LoD varies based on the amount of DNA that is tested and using lower DNA input may prevent MRD detection at low frequencies.
- Sample processing and cell enrichment strategies may affect the measured MRD frequency.
- The volume and cellularity of sampled input material may affect the ability to detect low levels of disease.
- False positive or false negative results may occur for reasons including, but not limited to: contamination; technical and/or biological factors such as the type of rearrangement or the size of the junction region.
- The assay has been validated with the Illumina NextSeq 500 and 550.

clonoSEQ Clinical Services

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CE IVD

PNL-10085 Rev 2

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