

This document provides a general product overview of the HemeScreen BCR/ABL1 Assay. Additional information can be found on Precipio’s website at [www.precipiodx.com](http://www.precipiodx.com), and the associated IFU (Instructions For Use), available upon request.

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| <b>Technology Overview</b> | HemeScreen® is a proprietary set of RUO (Research Use Only) reagents used to screen the wild type (Negative) from Mutated (Positive) genes in a simplified workflow relative to alternative molecular testing technologies (RT-PCR or NGS). |
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| <b>BCR/ABL1</b> | HemeScreen® BCR-ABL1 Reagents screen for the three major BCR-ABL1 isoforms and one minor isoform associated with BCR-ABL1-induced leukemogenesis, including chronic myeloid leukemia (CML) and acute lymphocytic leukemia (ALL). These isoforms all contain the BCR and ABL1 genes but differ in the breakpoints and length of their BCR or ABL1 component. |
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| Isoforms | Coverage   |
|----------|--|
| Assay #1 | p210 b2a2 (e13a2), p210 b3a2 (e14a2)<br>p203 b2a3 (e13a3), p203 b2a3 (e14a3) |
| Assay #2 | p190 (e1a2)<br>p190 (e1a3)   |
| Assay #3 | p230 (e19a2)<br>p230 (219a3)   |

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| <b>Results</b> | The results from HemeScreen® BCR/ABL1 are qualitative and DNA sequencing is required to identify specific isoforms. |
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| <b>Associated WHO/NCCN Guidelines<sup>1</sup></b> | <i>Per the WHO: BCR::ABL1 exists in several different isoforms depending on the precise position of the t(9;22)(q34;q11) genomic breakpoints. The two most common isoforms are known as e13a2 and e14a2, i.e. BCR exon 13 or BCR exon 14, respectively, spliced to ABL1 exon 2. Historically, these two fusions were referred to as b2a2 and b3a2, with b2 (BCR exon 13) and b3 (BCR exon 14) corresponding to the second and third exons within the classically-defined 5.8kb major breakpoint cluster region (M-BCR) within BCR. Collectively, e13a2 and e14a2 BCR::ABL1 account for 98% of CML cases, with the majority of these expressing e14a2. About 10% of cases express both isoforms { 8839828 ; 30675008 }. Case reports have associated atypical BCR::ABL1 fusions with an unusually aggressive or benign clinical course, but these are likely subject to substantial ascertainment or publication bias, and in general atypical variants are not considered to be markers of prognosis. An exception appears to be the e1a2 transcript which encodes p190 BCR::ABL1, the predominant isoform in Ph chromosome-positive acute lymphoblastic leukaemia (Ph + ALL) that is also seen in 1% of CML cases. P190 CML was originally associated with a phenotype intermediate between CML and chronic myelomonocytic leukaemia (CMML) { 8289491 }, and recent data have indicated a relatively poor response to imatinib, possibly associated with frequent mutations in epigenetic modifier genes { 19531657 ; 28708130 ; 33168949 }.</i> |
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|                             | Specificity | Sensitivity | LOD  | Storage |
|-----------------------------|-------------|-------------|--|---------|
| <b>Assay Specifications</b> | >99%        | 99.9%       | 1 BCR/ABL1 fusion copy per 100,000 transcripts | -20 °C  |

| SKU         | Product Configuration         | Assay Contents        |                   |
|-------------|-------------------------------|-----------------------|-------------------|
| HS-20R-BCR  | 20-sample free-flow reagents  | Primers/MasterMix Mix | Positive controls |
| HS-100R-BCR | 100-sample free-flow reagents | Primers/MasterMix Mix | Positive controls |

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| <b>Instrument Required</b> | HRM-enabled RT-PCR (example ThermoFisher Quantstudio 3 or higher) |
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| <b>Contact</b> | For further questions, contact our technical support team at <a href="mailto:techsupport@precipiodx.com">techsupport@precipiodx.com</a> or call 203-787-7888 |
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| <b>Disclaimer</b> | <i>The information in this document represents the company's best understanding of the technical and regulatory landscape; however, it should not serve as any guidance to any laboratory seeking to implement HemeScreen. Laboratory managers and medical directors should seek their own information independently through their CLIA inspector and any other state and federal regulatory body available.</i> |
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