Bloodhound™ BCR-ABL1 Panel – Product Overview

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

Technology Overview	Bloodhound™ is a proprietary set of RUO (Research Use Only) reagents used to detect the wild type (Negative) from Mutated (Positive) genes in a simplified workflow relative to alternative molecular testing technologies (RT-PCR or NGS).
BCR/ABL1	Bloodhound® BCR-ABL1 Reagents detect 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.

Isoforms	Coverage
Reaction #1	p210 b2a2 (e13a2), p210 b3a2 (e14a2) p203 b2a3 (e13a3), p203 b2a3 (e14a3)
Reaction #2	p190 (e1a2) p190 (e1a3)
Reaction #3	p230 (e19a2) p230 (e19a3)
Reaction #4	ABL1 (Internal control)

Results	The results from Bloodhound™ BCR-ABL1 are quantitative.
Associated WHO/NCCN Guidelines[1]	*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 }.

	Specificity	Sensitivity	LOD	Storage
Assay Specifications	>99%	99.9%	1 BCR/ABL1 fusion copy per 100,000 transcripts	-20 °C

SKU	Product Configuration	Assay Contents			
BH-4P-BCR	4 sample pre-plated plate	Primers/MasterMix	Positive controls	NTC	Wild Type
BH-8P-BCR	8 sample pre-plated plate	Primers/MasterMix	Positive controls	NTC	Wild Type
BH-12P-BCR	12 sample pre-plated plate	Primers/MasterMix	Positive controls	NTC	Wild Type
BH-20R-BCR	20 sample free-flow reagents	Primers/MasterMix	Positive controls		

Instrument Required	HRM-enabled RT-PCR (example ThermoFisher Quantstudio 3 or higher)
Contact	For further questions, contact our technical support team at techsupport@precipiodx.com or call 203-787-7888
Disclaimer	*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 Bloodhound. Laboratory managers and medical directors should seek their own information independently through their CLIA inspector and any other state and federal regulatory body available.*

1 World Health Organization. World Health Organization. Available at: https://tumourclassification.iarc.who.int/chaptercontent/63/10