XL MYC BA triple-color

Break Apart Probe - Triple Color

Order No.:
D-6030-100-TC

Clinical performance

Clinical performance means the ability of a device to yield results that are correlated with a particular clinical condition or a physiological or pathological process or state in accordance with the target population and intended user. Relevant clinical performance parameters related to FISH probes are diagnostic sensitivity and diagnostic specificity.

Diagnostic sensitivity is defined as the ability of a device to identify the presence of a target marker. It is calculated as the quotient of true positive tests and the sum of true positive tests plus false negative tests. Diagnostic specificity is defined as the ability of a device to recognize the absence of a target marker. It is calculated as the quotient of true negative tests and the sum of true negative tests plus false positive tests.

The evaluations are based on the confirmation of the presence of the target marker in positive cases and the absence of the target marker in negative cases by FISH in cases confirmed by chromosome banding analysis. Specimens examined were bone marrow and peripheral blood. The test population consisted of patients with confirmed or suspected ALL, AML, CLL, CML/MPN, MDS, MM and NHL.

The composition and probe design regarding the green and orange parts of the probe of D-6030 is identical to D-6023, XL MYC BA and therefore can detect breaks in the MYC gene region in exactly the same way. The similarity of these 2 probes allows us to combine data from experience gained by routine diagnostic testing of D-6023 and D-6030.

Analyte	Total No. of Cases		Diagnostic Sensitivity	Diagnostic Specificity
	D-6023	427		
Breaks in the MYC gene region at 8q24	D-6030	1524	100 %	99.9 % *
	Σ	1951		

* Two cases using XL MYC BA triple-color showed a clear split in the blue-labeled probes, and the results could not be confirmed by cytogenetics. The two cases were considered false positive for FISH although it is unclear which of the two technologies generated the false result in these cases.

Breakpoint differentiation was evaluated on 20 positive cases with particular attention to the blue signal. The following aberrant patterns have been observed: 1OB1GB, 1OB1G, 2OB, 1O1GB. The color combinations observed in the aberrant signal patterns allow, within the resolution of the FISH technology, a conclusion about the location of the breakpoint on chromosome 8.

The determination of the clinical performance parameters diagnostic sensitivity and diagnostic specificity of XL MYC BA triple-color is based on data from a European routine laboratory accredited according to ISO 15189. This evaluation is based exclusively on existing data; no patient samples were taken for this purpose.

PERFORMANCE DATA

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Analytical performance

Analytical performance means the ability of a device to correctly detect or measure a particular analyte. Relevant analytical performance parameters related to FISH probes are analytical specificity, analytical sensitivity, reproducibility, and cut-off.

Analytical specificity is calculated as the percentage of correct targets detected on metaphases out of the total number of targets detected. Lymphocytes of 5 different chromosomally characterized males with no indication of the genetic aberration of interest were included in the analysis. Calculated analytical specificity is 100 % after 20 evaluated metaphases from 5 different chromosomally characterized males. The acceptance criterion for analytical specificity is ≥98 %.

Analytical sensitivity is calculated as the percentage of interphase nuclei that have the expected normal signal pattern out of the total number of interphase nuclei analyzed. The signal pattern of 400 nuclei of 10 karyotypically normal individuals each were analyzed. The degree of deviation from the mean is represented by the relative standard deviation (%RSD). The acceptance criterion for analytical sensitivity is ≥95 %.

Pattern	Sensitivity	%RSD
2GOB (normal)	99.3 %	0.6 %

Reproducibility is the degree of agreement between the results of analytical sensitivity studies conducted under different conditions (Day, Lot and Sample). For each condition three analyses with 100 nuclei each were performed. Reproducibility is given as degree of deviation from the mean by the relative standard deviation (%RSD). The acceptance criterion for reproducibility is relative standard deviation ≤5 %.

Conditions	Reproducibility (%RSD)
Day-to-Day (same lot and same individual at three days)	0.6 %
Lot-to-Lot (same individual and day with three lots)	0.6 %
Sample-to Sample (same lot and day with three individuals)	0.0 %

The cut-off for a qualitative test is the threshold above which the result is reported as positive and below which the result is reported negative. The cut-off value was calculated based on probe hybridizations on interphase nuclei of 10 karyotypically normal individuals. Cut-off values are based on 400 scored nuclei each.

Pattern	Cut-off
1GOB 1GB 1O	0.8 %
1GOB 1G 1OB	3.3 %
1GOB 1GB 1OB	1.9 %

The cut-off value is informative and depends on several laboratory-related parameters. Therefore, for diagnostic use, cut-off values have to be determined individually by each laboratory.

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