TEST INFORMATION SHEET: DiGeorge Syndrome (DGS) / Velocardiofacial Syndrome (VCFS) / 22q11.2 Deletion Syndrome

CLINICAL FEATURES / DISEASE OVERVIEW
22q11.2 deletion syndrome, also known as DiGeorge (DGS) or velo-cardio-facial syndrome (VCFS), is a genetic disorder caused by a deletion from chromosome 22 at the q11 location. It is one of the most frequent chromosomal defects found in newborns, causing developmental delay and a spectrum of physical findings including heart abnormalities, cleft palate, and immune deficiency. Early diagnosis is important for treatment of the disorder. Clinical phenotypic features may be subtle or absent in newborns, making molecular testing an important diagnostic adjunct.

GENETICS
The typical deleted region on chromosome 22q11.2 contains more than 35 genes, including T-box gene 1 (TBX1) and v-crk sarcoma virus CT10 oncogene homolog (avian)-like gene (CRKL). The TBX1 gene is considered to be a major genetic determinant in the phenotype of 22q11.2 deletion syndrome. CRKL haploinsufficiency is associated with some phenotypes observed in 22q11.2 deletion syndrome. Both the TBX1 and CRKL genes are located within the 3 Mb region most commonly deleted in 22q11.2 deletion syndrome.

METHODS
TAI Diagnostics analyzes specimens using a real-time quantitative PCR based genotyping platform that detects and measures copy number variation for TBX1 and CRKL in relation to a housekeeping gene known to exist in two copies in a diploid genome.

SENSITIVITY / SPECIFICITY FOR DETECTION OF TARGETED DELETION

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<th>Analytical Sensitivity</th>
<th>Analytical Specificity</th>
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<tr>
<td>TBX1</td>
<td>&gt;99% (95% Confidence Interval (77.1-100%))</td>
<td>&gt;99% (95% Confidence Interval (93.8-100%))</td>
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<tr>
<td>CRKL</td>
<td>&gt;99% (95% Confidence Interval (74.7-100%))</td>
<td>&gt;99% (95% Confidence Interval (93.9-100%))</td>
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TEST LIMITATIONS
This assay tests for copy number variations of the TBX1 and CRKL genes by using probes that specifically target the overlap region intron 11/exon 12 within the human TBX1 gene and exon 3 of the human CRKL gene. Other genetic variations in TBX1 and/or CRKL such as point mutations and other deletions, may exist which are not detected by this assay. In addition, microdeletions of chromosome 22q11.2 may be present that do not include TBX1 or CRKL sequences. Thus, a negative result does not eliminate the possibility of a mutation, gene deletion, gene duplication, or chromosome abnormality not tested for in this assay. False negative or positive results may also occur due to mosaicism, presence of underlying polymorphisms or mutations, or prior bone marrow transplantation or blood transfusion. Full gene sequencing and determination of chromosomal origin are not performed as part of this assay.

REFERENCES