



# CADET® *BRAF* and CADET *BRAF-PLUS*

## Leaders in Molecular Diagnostics

We strive to provide products for accurate and early Cancer DETection (CADET) that will help to enhance the health and welfare of our canine companions. Our products are supported by robust research, proven science and leading genetics and oncology experts.

**To learn more and how AVD/Antech can benefit your veterinary organization**

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## Convenient

The free-catch urine system is non-invasive, allowing specimens to be collected while the patient is at the clinic, or by the owner at home; allows pooling of multiple urine collections. Collected urine in the *BRAF* urine container with preservative is stable at room temperature for weeks.

## Affordable

Timely detection of TCC/UC allows pet owners to direct their resources towards effective treatment of the cancer itself, rather than non-specific clinical signs.

## Sensitive

The assay permits forensic-level limit of sensitivity for earliest detection of emerging TCC/UC.

## Robust

CADET *BRAF* testing is unaffected by the presence of blood, protein, sugars, bacteria, urine stones and crystals, or other interfering substances in the urine.

## Specific

CADET *BRAF* and *BRAF-PLUS*, compared to other TCC/UC diagnostic tests, has the highest specificity, eliminating the risk of false-positive cancer diagnoses.

## Rapid

Results are available in just 3-6 days from receipt of the sample.

## Research Offers a New DNA-Based Strategy for Detection of TCC/UC from Free-Catch Urine

Research has shown that a single mutation in the canine b-raf gene is present in 85% of confirmed cases of canine transitional carcinoma/urothelial carcinoma (TCC/UC).<sup>1,2</sup> Detection of the mutation is performed by the CADET *BRAF* DNA test. A second DNA test called CADET *BRAF*-PLUS detects chromosomal copy number variation linked to the presence of TCC/UC in 2 out of 3 b-raf mutation negative patients. This additional testing increases

the diagnostic sensitivity of the combined CADET *BRAF* and *BRAF*-PLUS to 95%.<sup>3</sup> Both tests can be run on a single free-catch urine sample containing malignant cells shed naturally into the urine of a tumor-bearing dog.

Rigorous validation through university and industry research indicates that the b-raf mutation has not been found in the urine of healthy dogs, or from dogs that have benign bladder polyps, inflammation or chronic cystitis. In cases that have undergone biopsy of a visible mass, there was concordance between the presence of the b-raf mutation in free catch urine and pathology-based confirmation of a TCC/UC. Presence of the mutation in canine urine therefore is a highly specific indicator of the presence of TCC/UC.<sup>1,2</sup>

## How CADET *BRAF* and *BRAF*-PLUS are Used in the Clinical Setting

CADET *BRAF* evaluates urine samples from dogs for the presence of cells harboring the b-raf mutation or specific copy number variations associated with TCC/UC. The assays identify 95% of TCC/UC cases. The extremely low limit of detection of 10 mutation-bearing cells in a urine sample allows early diagnosis of a developing TCC/UC, often several months before any advanced clinical signs associated with the cancer become evident. This enables veterinarians to initiate appropriate treatment very early in the course of the disease, potentially before the mass has become invasive. Dogs presenting with abnormal urinary signs, such as hematuria, can be tested for the presence of a TCC/UC by submitting a free-catch urine sample. Urine can be submitted to Antech Diagnostics in a dedicated *BRAF* urine specimen container that contains a stabilizing reagent.

CADET *BRAF* is a highly sensitive test to monitor the b-raf mutation in TCC/UC cases during the course of their treatment, for therapeutic response and relapse. CADET *BRAF* testing can be used for both the rapid, non-invasive assessment of dogs displaying clinical signs consistent with TCC/UC, and for confirmed cases undergoing treatment.

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## Clinical Indications When to Use the CADET *BRAF* and *BRAF*-PLUS

1. Clinical cases presenting with hematuria, stranguria, and/or urinary incontinence with diagnostic imaging evidence of a mass in the bladder.
2. During chemotherapy to monitor treatment success by decreased levels of b-raf mutation detection, or to monitor cancer relapse by re-occurrence of b-raf mutation tumorbearing cells.
3. Early diagnosis in clinical cases with recurrent, complicated or antibiotic-resistant urinary tract infections presenting with hematuria without ultrasonographic evidence of a bladder mass.
4. Confirmation of the TCC/UC diagnosis of a bladder mass from a stained cytology slide following ultrasonography and cytological examination of a fine-needle aspirate from tumor-bearing cells.
5. Early detection in high-risk dog breeds such as Terriers, Shetland and Australian sheep dogs, cattle dogs, Beagles and Border collies that are six years and older.

### References:

1. Mochizuki H, Kennedy K, Shapiro SG, Breen M. *BRAF* Mutations in Canine Cancers. PLoS One. 2015 Jun 8;10(6):e0129534
2. Mochizuki H, Shapiro SG, Breen M. Detection of *BRAF* Mutation in Urine DNA as a Molecular Diagnostic for Canine Urothelial and Prostatic Carcinoma. PLoS One. 2015 Dec 9;10(12):e0144170
3. Mochizuki H, Shapiro SG, Breen M. Detection of Copy Number Imbalance in Canine Urothelial Carcinoma With Droplet Digital Polymerase Chain Reaction. Vet Pathol. 2016 Jul;53(4):764-72



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