MiraVista
VETERINARY DIAGNOSTICS

CLINICAL DIAGNOSIS

MVista® *Histoplasma* Antigen Quantitative EIA – All Antigen Tests are NOT Created Equal

Histoplasma antigen detection is commonly used for diagnosis, treatment monitoring, and detection of disease relapse in veterinary medicine. The gold-standard for *Histoplasma* antigen detection is the MVista® *Histoplasma* Antigen Quantitative enzyme immunoassay (EIA). First made commercially available almost 20 years ago, it has been modified since to optimize diagnostic performance, turnaround time, and cost-efficiency.

More recently a second *Histoplasma* Antigen EIA has been made available. The first iteration (Alpha, Immy) used a polyclonal capture antibody and had poor diagnostic performance in humans. Data for dogs and cats are not available. A modification of this test using a monoclonal capture antibody (Clarus, Immy) is now available. It is FDA cleared for detection of antigen in human urine but is not USDA approved for use in animals. To offer the test commercially, a veterinary diagnostic laboratory would need to develop/validate a test for veterinary species using the test kit components (analyte specific reagents, ASR). Peer-reviewed published data regarding the diagnostic performance of the Immy *Histo* EIA (ASR- now available as Clarus) are available for dogs and cats (see below).

Diagnostic Performance

The MVista® *Histoplasma* Antigen EIA has a high diagnostic sensitivity (92% and 94%) and specificity (99% and 98%) in dogs and cats (Table 1). This has been investigated in multiple studies including dogs and cats with various forms of histoplasmosis (localized and disseminated). The study findings have been reported in peer-reviewed publications [1-5]. In 2 separate peer-reviewed publications the Immy *Histo* EIA was shown to be inferior to the MVista *Histo* EIA. In dogs, the Immy *Histo* EIA lacked sensitivity, providing false negative results in 30% of cytology proven cases [2]. This was most problematic in dogs with GI involvement, which occurs in 1/3 of dogs with histoplasmosis [6]. Likewise in cats, the Immy *Histo* EIA lacked sensitivity, providing false negative results in 23% of cytology proven cases [1]. In attempt to decrease the number of false negative results, a lower diagnostic cutoff was investigated, which made the specificity unacceptable low- providing false positive results in 30% of cases. **Collectively, these findings clearly demonstrate that the MVista® *Histo* EIA is superior to the Immy *Histo* EIA for the diagnosis of histoplasmosis in dogs and cats.**

Table 1. Combined diagnostic performance of the MVista® *Histoplasma* Antigen EIA and Immy *Histoplasma* EIA reported in peer-reviewed publications.

Test	Sample	Species	Service Lab / Manufacturer	Sensitivity (%)	Range (%)	Specificity (%)	Range (%)	Ref
Antigen EIA	Urine	Canine	MVD*	92	89-95	99	99-100	2,4
			IMMY^	70	70	99	99	2
		Feline	MVD*	94	94	98	97-100	1,3
			IMMY^	77	77	97	97	1

MVD, MiraVista Diagnostics – MVista® *Histoplasma* Antigen Quantitative EIA; Immy, *Histoplasma* EIA- ASRs

HEADQUARTERS
4705 Decatur Blvd. | Indianapolis, Indiana 46241, USA

888-841-8387

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Treatment Monitoring

The MVista® *Histoplasma* Antigen EIA is useful for treatment monitoring. This has been investigated in a prospective study that was reported as a peer-reviewed publication [5]. In that study, antigen concentrations decreased with successful treatment and increased with disease relapse. Based on that report, it is recommended to monitor urine antigen concentrations at 3-month intervals and treat until no antigen is detected on the MVista® *Histo* IEA. Moreover, it is recommended to monitor for disease relapse by testing for antigen in urine 6-12 months after stopping antifungal treatment, then annually thereafter.

Since antigen concentrations decrease during antifungal treatment, detection of low antigen concentrations is vital for treatment monitoring. Two peer-reviewed publications have shown only moderate-poor overall agreement between the Immy *Histo* EIA and the MVista® *Histo* EIA during and after treatment (Table 2) [1,2]. As expected, due to the low diagnostic sensitivity of the Immy *Histo* EIA, agreement was especially poor for antigen concentrations <1.0 ng/ml [1]. For example, antigen was not detected by the Immy Histo EIA in 41% of samples from dogs where antigen was detected by the MVista® Histo EIA (Table 2). **Collectively, these studies suggest that only the MVista *Histo* EIA is useful for treatment monitoring in dogs and cats with histoplasmosis.**

Table 2. Overall agreement between the MVista® *Histoplasma* antigen EIA and Immy *Histoplasma* antigen EIA in dogs before, during, and after antifungal treatment.

		MVista® *Histoplasma* Antigen EIA	
		Positive	Negative
Immy *Histoplasma* Antigen EIA	Positive	54	2
	Negative	42	104

Sample Type – Versatility

The MVista® *Histoplasma* Antigen EIA has been validated for serum, plasma, urine, CSF, and BAL fluid. While urine is most commonly tested, there are times when testing a different sample type is needed. For example, approximately 4-5% of dogs and cats with histoplasmosis will test negative for antigen in urine but positive in serum. As such, testing serum for antigen is recommended if suspicion of histoplasmosis remains and no antigen is detected in urine. The Immy *Histo* EIA is only cleared for testing urine in humans, which is also the only sample type that has been investigated in dogs and cats.

Highest Quality Service

The MVista® *Histoplasma* Antigen EIA is performed at a single reference service laboratory following the highest industry standards- as demonstrated by CLIA and CAP (College of American Pathologists) certifications. It is run twice daily Tues-Fri and once on Monday and Saturday. This testing schedule provides same day results in >90% of samples. Moreover, MiraVista Diagnostics is supported by a robust clinical support team including experts in infectious disease and diagnostic medicine who are available for case consultation every weekday (p:888-841-8387 or labsupport@miravistalabs.com). Your questions and comments are encouraged.

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