

Use of Zoetis Premium Lipase (DGGR) for the Diagnosis of Canine and Feline Pancreatitis



Pancreatitis is one of the most common diseases of the exocrine pancreas in dogs and cats.^{1,4,7,8,10} Diagnosis of pancreatitis remains a challenge not only because of its variability in disease process and severity, but also due to the lack of highly sensitive and specific, non-invasive ante-mortem diagnostic tests.^{4,5} Currently, the gold standard in diagnosis and classification is histopathological evaluation.^{2,4,6,8,9,12} However, this is rarely performed due to its invasive nature, cost, and other inherent limitations.⁸ As a result, the diagnosis of pancreatitis is commonly determined based on patient history, clinical signs, and physical exam findings, combined with laboratory data and abdominal ultrasound abnormalities. Clinical signs can vary depending on the severity of disease. Moderate to severe presentations may include vomiting, diarrhea, hypovolemia, abdominal pain, and anorexia.¹⁵ Mild presentations can be subclinical. Currently, no blood test provides 100% accuracy for diagnosing pancreatitis.

Development of laboratory assays for the diagnosis of pancreatitis has focused on the enzyme lipase, which functions to break down fats, allowing the body to digest and utilize the components. Lipase is produced by several tissues, including the liver, intestine, and pancreas. Pancreatic lipase is more specifically produced by pancreatic acinar cells, stored in zymogen granules, and excreted into the duodenum to hydrolyze dietary triglycerides.^{7,8} In health, less than 1% of pancreatic lipase diffuses into the vascular system.^{7,8} However, a large amount of pancreatic lipase is released into the bloodstream of patients suffering from acute pancreatitis.^{7,8} Thus, measuring lipase has proven to be useful in diagnosis of pancreatitis.

There are two methods by which serum lipase is measured: immunological and colorimetry.⁸ Immunologic assays can target pancreatic lipase specifically, generally increasing assay specificity.⁸ The original immunological assays were cumbersome radioimmunoassays, replaced by ELISAs specific for feline and canine pancreatic lipase in more recent years.^{7,8} These tests are currently considered to be the most sensitive and specific laboratory tests available for detecting pancreatitis.^{4,10} That being said, note that the assay has variably sensitivity and specificity depending on the study and patient population. According to one study, the sensitivity of fPLI is about 79% and the specificity is 82% in cats.¹⁰ While the sensitivity of cPLI is 64-94% and specificity is 70-94% in dogs.⁴ Despite the targeted nature of pancreatic lipase immunoassays, this test lacks the consistently high sensitivity and specificity desired in a true gold standard assay and pancreatitis remains a clinical diagnosis in many cases.

Additionally, the fPLI and cPLI assays have other limitations, including longer turnaround times due to the inherent assay methodology and high cost. As a result, much industry investment has occurred to develop point-of-care, semiquantitative tests, including the Vetscan® Rapid cPL test. With a sensitivity of 73.9-83.3% and a specificity of 76.9-83.8%, this convenient-to-use assay has proven to be a useful screening test for pancreatitis.¹ Comparison studies between cPLI and Vetscan® Rapid cPL suggest good agreement.¹ The flexibility of having rapid, cost-effective, and accurate point-of-care testing for pancreatitis is a key advancement in the diagnosis of pancreatitis for veterinary patients.¹

Colorimetric assays are run on traditional chemistry analyzers. The assay premise is based on hydrolysis of a substrate, resulting in color development, the degree of which correlates to the

concentration of the target analyte. Historically, 1,2-diglyceride was used as a substrate to measure serum lipase activity on high-throughput chemistry analyzers.⁸ However, this assay substrate was found to lack analytical specificity for pancreatic lipase because extrapancreatic lipases (e.g. hepatic lipase, lipoprotein lipases, etc.) were included in the assay measurement.^{8,9} Ultimately, this general lipase assessment has not proven to be clinically useful in helping to diagnose pancreatitis and has fallen out of routine use for many laboratories.

A newer colorimetric assay using an alternative substrate, 1,2-o-dilauryl-rac-glycero-3-glutaric acid (6'-methyl-resorufin) ester (referred to as DGGR), was more recently introduced for use in human medicine.^{3,8} This new substrate has proven to be more analytically specific for measuring pancreatic lipase, even though the assay does not immunologically target pancreatic lipase.^{2,3,4}

In the mid-2000's, the veterinary community began exploring the utility of DGGR lipase in dog and cat populations.^{2,5,6,8} Various validation studies have since shown good precision, linearity, and agreement with cPLI.^{3,10} Sensitivity and specificity of DGGR lipase varies by study. The study design, including specific DGGR reagent brand, analytical cut-offs for diagnosing disease, and assessment for acute versus chronic disease can affect study outcomes.^{3,10,11,13} The sensitivity of DGGR lipase is as high as 78.6% in cats and 93.0% in dogs, while the specificity tops out at 100% in felines and 74.3% in canines.^{7,11} Cumulatively, the scientific literature supports the conclusion that DGGR lipase is a reliable alternative to pancreatic lipase immunoassays (PLI) for the diagnosis of pancreatitis in dogs and cats.^{2,3,5,10,11}

This sensitive and specific assay for pancreatitis is available as **Zoetis Premium Lipase (DGGR)** with a next day by 8 am turnaround time and a competitive price point.

References:

1. Cridge H., MacLeod A. G., Pachtinger G. E., et. al. Evaluation of SNAP cPL, Spec cPL, VetScan cPL Rapid Test, and Precision PSL Assays for the diagnosis of clinical pancreatitis. *J Vet Intern Med* 2018;32:658-664.
2. Goodband E. L., Serrano G., Constantino-Casas F., et. al. Validation of a commercial 1,2-o-dilauryl-rac-glycero glutaric acid-(6'-methylresorufin) ester lipase assay for diagnosis of canine pancreatitis. *Veterinary Record Open* 2018;5:e000270.
3. Graca R., Messick J., McCullough S., et. al. Validation and diagnostic efficacy of a lipase assay using the substrate 1,2-o-dilauryl-rac-glycero glutaric acid-(6'-methylresorufin) ester for the diagnosis of acute pancreatitis in dogs. *Vet Clinl Pathol* 2005;34:39-43.
4. Hope A., Bailen E. L., Sheil R. E., et. al. Retrospective study evaluation of DGGR lipase for diagnosis, agreement with pancreatic lipase and prognosis in dogs with suspected acute pancreatitis. *J of Small Animal Practice* 2021;62:1092-1100.
5. Kook P. H., Kohler N, Hartnack S., et. al. Agreement of serum Spec cPL with the 1,2-o-dilauryl-rac-glycero glutaric acid-(6'-methylresorufin) ester (DGGR) lipase assay and with pancreatic ultrasonography in dogs with suspected pancreatitis. *J Vet Intern Med* 2014;28:863-870.

6. Krasztel, M. M., Czopowicz M., Szalus-Jordanow O., et. al. The agreement between feline pancreatic lipase immunoreactivity and DGGR-lipase assay in cats-preliminary results. *Animals* 2021;11,3172.
7. Lim S. Y., Steiner J. M., Cridge H. Understanding lipase assays in the diagnosis of pancreatitis in veterinary medicine. *JAVMA* 2022;260(11):1249-1258.
8. Lim S. Y., Xenoulis P. G., Stavroulaki E. M., et. al. The 1,2-o-dilauryl-rac-glycero glutaric acid-(6'-methylresorufin) ester (DGGR) lipase assay in cats and dogs is not specific for pancreatic lipase. *Vet Clin Patholo.* 2020;49:6097-613.
9. Linari G., Francesco D., Segatore S., et. al. Evaluation of 1,2-o-dilauryl-rac-glycero glutaric acid-(6'-methylresorufin) ester (DGGR) and 1,2-diglyceride lipase assays in dogs with naturally occurring hypercortisolism. *Journal of Veterinary Diagnostic Investigation* 2021;33(5):817-824.
10. Oppliger S., Hartnack S., Riond B., et. al. Agreement of the serum Spec fPL and 1,2-o-dilauryl-rac-glycero glutaric acid-(6'-methylresorufin) ester lipase assay for determination of serum lipase in cats with suspicion of pancreatitis. *J Vet Intern Med* 2013;27:1077-1082.
11. Oppliger S., Hilbe M., Hartnack S., et. al. Comparison of serum Spec fPL and 1,2-o-dilauryl-rac-glycero glutaric acid-(6'-methylresorufin) ester assay in 60 cats using standardized assessment of pancreatic histology. *J Vet Intern Med* 2016;30:764-770.
12. Serrano G., Paepe D., Williams T., et. al. Increased canine pancreatic lipase immunoreactivity (cPL) and 1,2-o-dilauryl-rac-glycero glutaric acid-(6'-methylresorufin) ester (DGGR) lipase in dogs with evidence of portal hypertension and normal pancreatic histology: a pilot study. *J of Veterinary Diagnostic Investigation* 2021;33(3):548-553.
13. Wolfer L. A., Howard J., Peters L. M. Accuracy of 1,2-o-dilauryl-rac-glycero glutaric acid-(6'-methylresorufin) ester (DGGR) lipase to predict canine pancreas-specific lipase (cPL) and diagnostic accuracy of both tests for canine acute pancreatitis. *Vet Sci* 2022;9(177):1-13.