AlphaTrak® 3 Blood Glucose Monitoring System for Dogs and Cats

Section 1.
Overview of Diabetes Mellitus in Dogs and Cats

Section 2.
AlphaTrak 3 Blood Glucose Monitor

Diabetes mellitus (DM) is a disorder of carbohydrate metabolism due to a deficiency of insulin in the body (decreased pancreatic production, type 1) or cells being unable to respond to insulin that is present in the body (type 2), resulting in elevated blood glucose (BG). Type 1 DM is characterized by damage to pancreatic islet beta cells, is insulin-dependent, requires life-long insulin therapy, and is most commonly seen in dogs. Type 2 DM is characterized by insulin resistance, is not insulin-dependent but may be treated with oral medications or insulin, and is most commonly seen in cats. Clinical signs of DM in dogs and cats include fatigue/weakness, excessive thirst, frequent urination, increased appetite without accompanying weight gain, and weight loss. Clinical progression of DM in dogs and cats can include diabetic ketoacidosis, diabetic neuropathy, cataracts, and systemic hypertension. If DM is suspected, a physical examination and full laboratory evaluation should be performed to confirm the diagnosis and rule out other diseases. Clinical signs typically develop when hyperglycemia and glucosuria persist; a definitive diagnosis is based on a combination of persistent glucosuria, persistent hyperglycemia, and the presence of characteristic clinical signs.

Management of DM in dogs and cats often involves a comprehensive approach: administration of insulin, dietary changes, exercise/active play, and weight management. The goals of treatment are to maintain BG levels below the renal threshold (200 mg/dL in dogs and 250-300 mg/dL in cats) for as much of a 24-hour period as possible and to avoid clinically significant hypoglycemia. Insulin is the primary therapy for DM in dogs and may be part of the initial therapy for DM in cats.

Regular monitoring of clinical signs of DM in dogs and cats, including home monitoring of pet drinking and urinating, body weight trends, and physical examinations are important for patient management. Laboratory testing of blood and or urine, including real-time BG levels, are a cornerstone of monitoring. BG can be determined in reference labs, with an in-house analyzer, or using point-of-care BG devices. Serial BG curves (BGCs), generated by taking BG measurements regularly, can provide important information about insulin dose, onset of action, and duration of action. Trends in fructosamine levels can also help assess glycemic control. At-home monitoring of BG can identify hypoglycemic events and contribute to improved glycemic control. Generating at-home BGCs is strongly recommended for owners of dogs and cats with DM.

The AlphaTrak 3 is a next generation system developed for in vitro diagnostic monitoring of BG levels in dogs and cats and is intended for veterinary and home use. AlphaTrak 3 is specifically calibrated and validated for use in dogs and cats. AlphaTrak 3 accounts for the differences in the distribution of glucose in whole blood to plasma in dogs and cats to accurately calculate glucose levels, whereas a BG meter intended for use with human blood does not make these adjustments. AlphaTrak 3 works by first attaching a new test strip to the meter and then touching the test strip to a blood sample obtained from a dog or cat. The test strip takes up the blood sample and a chemical reaction inside the meter produces a BG result within a few seconds. AlphaTrak 3 is Bluetooth enabled and can link to a mobile app. At-home recording of a dog's or cat's BG levels may reduce the risk of complications due to DM.

This technical bulletin reviews key information about the clinical features of DM in dogs and cats, the clinical management of DM; guidelines and resources for at-home monitoring of BG; and an in-depth review of the unique attributes and performance of AlphaTrak 3, a new Bluetooth enabled BG monitor specifically designed and calibrated for use in dogs and cats.

Section 1. Overview of Diabetes Mellitus in Dogs and Cats

Definition of Disease

Diabetes mellitus affects the body's ability to convert glucose into energy. Diabetes mellitus occurs when there is a deficiency of insulin in the body (the pancreas does not produce enough insulin) or when the cells are unable to react to the insulin that is present in the body (**Figure 1**). More specifically, increased BG that occurs with DM is due to the loss or dysfunction of insulin secretion by pancreatic beta cells, decreased insulin sensitivity in tissues, or both. Beta cell loss is usually caused by immune-mediated

Figure 1.

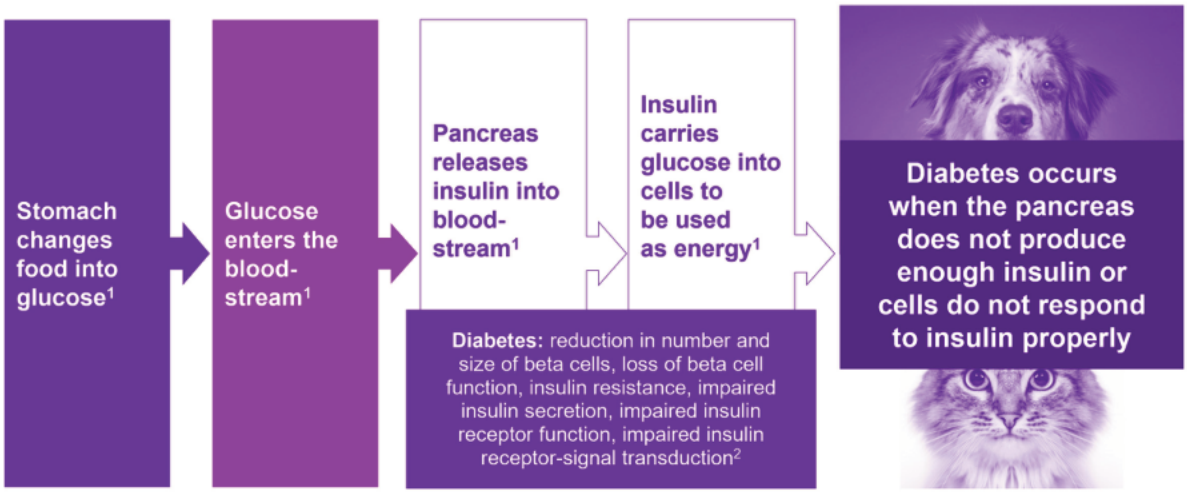

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Figure 1. Pathophysiology of Diabetes Mellitus

destruction, vacuolar degeneration, or pancreatitis in dogs, and by insulin resistance, islet amyloidosis, or chronic lymphoplasmacytic pancreatitis in cats.[1] The most common types of DM include: Type 1, which is characterized by destruction of pancreatic beta cells, is insulin-dependent, requires life-long insulin therapy, and is most commonly seen in dogs; and Type 2, which is characterized by the failure of cells to use insulin properly, is not insulin-dependent but may be treated with oral medications or insulin, and is most commonly seen in cats. Cats with type 2 DM may achieve clinical remission if diagnosed early and tight glycemic control is maintained.[2]

Clinical Signs in Dogs and Cats

The most common clinical signs of DM in dogs and cats include fatigue/weakness, excessive thirst, frequent urination, increased appetite without accompanying weight gain, and weight loss.[1-7] In some predisposed cases, an unrelated comorbidity may reduce insulin sensitivity and put the animal over the threshold into diabetes as a result of the additional reduction in insulin sensitivity.[2-3]

Clinical Sequalae

As DM progresses, if left untreated, clinical complications typically seen in diabetic dogs and cats include diabetic ketoacidosis, diabetic neuropathy, cataracts, and systemic hypertension.[2-7] Additional complications that have been observed in dogs include lens-induced uveitis, corneal ulceration, nephropathy, and diabetic retinopathy and hypoglycemia (with treatment).[2-3]

Diagnosis

In cats and dogs who present with clinical signs suggestive of DM, a physical examination and full laboratory evaluation should be performed to confirm the diagnosis as well as rule out other diseases. Clinical signs will typically develop when hyperglycemia and glucosuria persist; a definitive diagnosis is based on a combination of persistent glucosuria, persistent hyperglycemia, and the presence of characteristic clinical signs. Laboratory workup for diabetes could include a complete blood count, chemistry with electrolytes, fructosamine, urinalysis with culture, urine protein:creatinine ratio, triglycerides, and thyroxine. Stress hyperglycemia should be ruled out before making a definitive diagnosis. In cats, documentation of an increased fructosamine level may be necessary to confirm the diagnosis.[1,4]

Diabetes Management

Diabetes mellitus is a treatable condition that requires a committed effort by veterinarian, veterinary staff, and pet parent.[1] Management of diabetic dogs and cats often involves the administration of insulin, dietary changes, exercise/active play, and weight management. **In most cases the goals of treatment are to maintain the BG levels below the renal threshold (200 mg/dL in dogs and 250-300 mg/dL in cats) for as much of a 24-hour period as possible (in order to improve clinical signs) and to avoid clinically significant hypoglycemia.** All dogs require exogenous insulin therapy to treat DM. In cats, insulin therapy is used as part of the initial approach to diabetic management.[1,4]

Insulins Commonly Used in Dogs and Cats[1]

Product	Brand Name (Manufacturer)	Concentration*	Comments
NPH: Neutral Protamine Hagedorn (isophane) Insulin (intermediate-acting)	Humulin N® (Lilly), Novolin N® (Novo Nordisk)	100 U/mL	Commonly used twice-daily insulin for dogs. Duration can be short for some dogs. Also used in cats as twice-daily but duration of action often insufficient.
Porcine Lente Insulin (intermediate-acting)	Vetsulin®, Caninsulin® (Merck)	40 U/mL	Commonly used twice-daily insulin worldwide, and in cats in Europe. Some cats can be controlled with twice-daily, average length is 8 hours in cats. Twice-daily with a low-carbohydrate diet in cats observed 25% and 43% remission. In dogs, the manufacturer recommends a starting dose of 0.5 U/kg every 24 hours. FDA-approved for dogs and cats.
PZI: Protamine Zinc Insulin (long-acting)	ProZinc® (Boehringer Ingelheim)	40 U/mL	Commonly used as a twice-daily insulin in cats due to longer duration. Remission rate of 38% has been reported with low-carbohydrate diet in cats. Also used twice-daily in dogs not controlled with Lente (some clinicians believe that the starting dose should be 0.25 U/kg in dogs, with 0.5 U/kg reserved for potentially challenging diabetics). FDA-approved for cats and dogs.
Glargine (long-acting)	Lantus® (Sanofi Aventis)	100 U/mL	Long-acting (prolonged release) recombinant insulin analog. Popular twice-daily maintenance insulin in cats. Remission rates of 14%, 40%, 64%-100% with low-carbohydrate diets in cats.
Detemir (long-acting)	Levemir® (Novo Nordisk)	100 U/mL	Long-acting insulin recombinant insulin analog. Effective twice-daily insulin in cats; 67% remission rate with low-carbohydrate diet reported. Second study 21%. Published use in dogs is limited; caution required (very potent in dogs). Suitable for dogs in which NPH and porcine lente insulins have short duration of activity.

**U, units.*

It is important to regularly monitor clinical signs of DM in dogs and cats to determine if the disease is well controlled and to promptly identify the need for a change in insulin dose. Feedback from the pet parent about how much the pet is drinking and urinating, as well as monitoring body weight trends and considering physical examination findings are essential to appropriately manage each diabetic patient (**Table 1**). Laboratory testing of blood and/or urine plays a significant role in the long-term management of DM. Real-time BG levels are a cornerstone of monitoring and can be determined in reference labs, with an in-house analyzer, or using point-of-care BG devices.

Table 1.

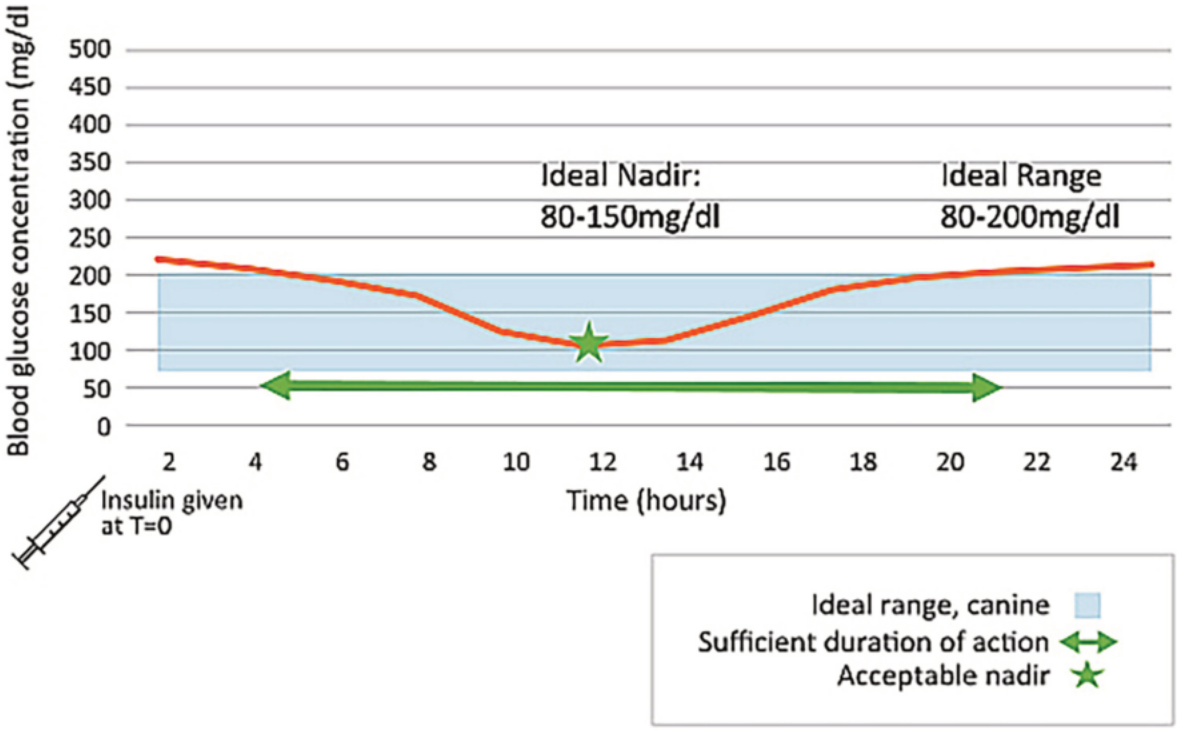
Suggested Home Monitoring for Pet Owners[1]
Log insulin, food and water intake, and appetite daily
Note any signs suggestive of hypoglycemia; contact veterinarian if persistent
Periodically test urine; record glucose level and ketones. If ketones are present, contact veterinarian

Serial BG curves (BGCs), which are a very useful tool for monitoring diabetic animals (especially those that are not well controlled), are generated by taking BG measurements regularly depending on the insulin administration schedule (usually every 2 hours for 12-24 hours). Serial BGCs provide important information about the insulin dose, onset, and duration, and are particularly helpful in the early stages of insulin treatment.

- Insulin dose adjustments are generally performed using BGCs instead of spot checks (which are considered to be unreliable)
- BGCs can identify clinically undetectable hypoglycemia and allow for the insulin dose to be adjusted before development of clinical hypoglycemia[1]
- To run a BGC, BG is generally measured every 2 hours for one interval between injections; exceptions to this recommendation are when glargine is used in cats (measure BG every 3 to 4 hours) and when BG is less than 150 mg/dL in both cats and dogs during any BGC (measure BG hourly)
- It is important to consider that BGCs can vary from day to day and can be affected by changes in the patient's normal routine; therefore, BGCs should always be interpreted in light of clinical signs[8]

For diabetics that appear to be well controlled, testing fructosamine levels can help assess glycemic control.[9] Fructosamine is formed by binding to serum proteins (mainly albumin) and is affected by the half-life of albumin; therefore, fructosamine levels reflect glycemic control over the previous 1 to 2 weeks in cats and 1 to 3 weeks in dogs.[2-3] Trends in fructosamine levels are more valuable than isolated values when determining glycemic control.[1] Urine testing is sometimes used for monitoring but is not ideal, because the renal threshold of glucose is higher than the desired control range for most animals. Glycosylated hemoglobin represents BG over the lifespan of a red blood cell (~110 days in dogs, ~70 days in cats).[2-3] Although glycosylated hemoglobin is used to monitor glycemic control in humans, more studies are warranted to determine its clinical use in cats and dogs.[1]

BGCs serve two very useful purposes that other monitoring parameters do not. They identify clinically undetectable hypoglycemia so that the insulin dose can be decreased before clinical signs of hypoglycemia develop. The only way to know how to appropriately change an insulin dose is to perform a BGC. Thus, a periodic BGC is recommended for seemingly well-controlled patients. More importantly, BGCs can help identify factors, including an insulin dose that is too low or high, that may contribute to poor glucose control that other techniques or clinical signs cannot determine.[3,8]



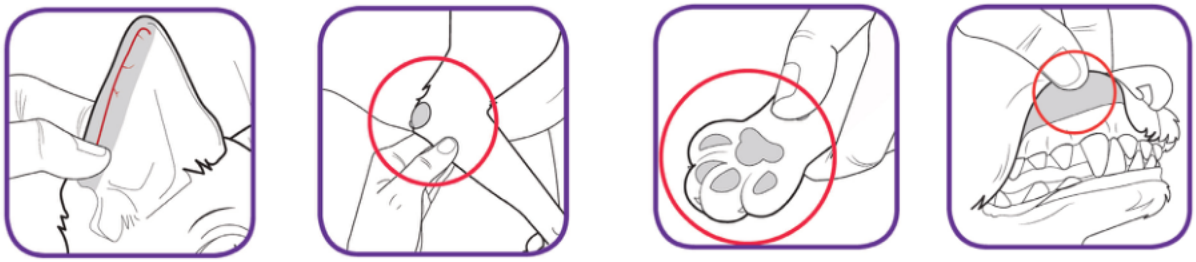
Source: Optimal Canine Glucose Curve (www.aaha.org/aaha-guidelines/diabetes-management/resource-center/interpreting-glucose-curves)

At-home monitoring of BG helps provide more control over disease by helping identify hypoglycemic events and providing better glycemic control.[4] During at-home monitoring, clinical signs should be evaluated. Pet parents should keep a diary to record overall well-being, water and food intake, urine production, insulin doses, and body weight.[1,4] For both dog and cat owners, at-home BGCs are strongly recommended. At-home monitoring is especially important for cats due to the risk of stress hyperglycemia in the hospital setting.[1] Pets should be monitored for signs of low BG, such as lethargy, abnormal behavior, weakness, tremors, anorexia, vomiting, and seizures.[1,4]

Guidelines/Resources for At-Home Monitoring
AAHA: www.aaha.org/aaha-guidelines/diabetes-management/monitoring[8]
AAHA: www.aaha.org/aaha-guidelines/diabetes-management/client-education[10]
AAHA: www.aaha.org/aaha-guidelines/diabetes-management/resource-center[11]
ISFM: journals.sagepub.com/doi/full/10.1177/1098612X15571880[4,12]

Where Is the Best Place on a Pet to Obtain a Capillary Sample?

The ear is the most common location for both cats and dogs, due to easy access. Other locations include the paw pad for cats and dogs, the elbow callus for some dogs, and the inner or outer lip for dogs only.



Marginal ear vein | Elbow callus (dog only) | Paw pad | Inner lip (dog only)

Source: AlphaTrak 3 Quick User Guide

Links to Instructional Resources:
For the pet owner: www.zoetispetcare.com/products/alphatrak
For the veterinarian: www.zoetisus.com/products/dogs/alphatrakmeter/alphatrak-home.aspx#

Section 2. AlphaTrak 3 Blood Glucose Monitor

Overview

The AlphaTrak 3 is the next generation of the AlphaTrak BG monitoring system intended for use outside of the body only (*in vitro* diagnostic use) for monitoring glucose levels in blood samples. AlphaTrak 3 is intended for use in a veterinary professional setting to determine BG concentrations in dogs and cats. It is also intended for use in the home setting to determine BG concentrations in dogs and cats. AlphaTrak 3 is not indicated for diagnosis of DM.

The AlphaTrak 3 provides a BG measurement to pet owners and clinic staff. A veterinarian can use this information to determine if the insulin dose and insulin type are appropriate based on BG concentrations determined over several hours (generally every 2 to 4 hours), referred to as a BGC.

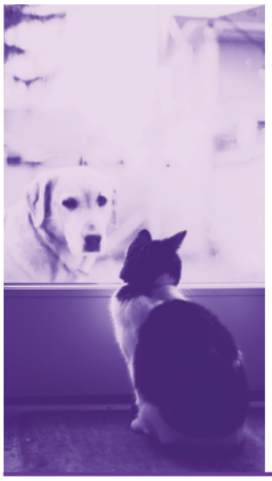
Specific uses of the AlphaTrak 3 include:

- Determining BG in dogs and cats
- Testing with fresh whole blood capillary or venous samples
- Testing with whole blood collected in a syringe or vacutainer tube with EDTA or heparin anticoagulant if testing within 10 minutes
- Testing with whole blood collected in a syringe or vacutainer tube without anticoagulant, if testing is performed immediately. The AlphaTrak 3 should **not** be used for: testing of arterial blood, testing with serum, testing with plasma, or diagnosis of DM

The AlphaTrak 3 is species specific; it has been specifically calibrated and validated for use in dogs and cats, and not for

use in humans, which is important for producing accurate results.[1] Portable BG meters use whole blood, which includes glucose in the plasma and red blood cells. The distribution of glucose in blood differs between humans, dogs, and cats (**Figure 2**). As a consequence, glucose meters calibrated for human use will underestimate the levels of glucose in blood samples obtained from dogs and cats. AlphaTrak 3 accounts for the differences in the distribution of glucose in whole blood to plasma in dogs and cats to accurately calculate glucose levels.[13] A meter intended for use exclusively for humans does not make those same adjustments.

Figure 2.



Species	Distribution	Reference
Humans	42% red blood cells 58% plasma	EM MacKay. The Distribution of Glucose in Human Blood. *J. Biol. Chem.* 1932, 97:685-689.
Dogs	12.5% red blood cells 87.5% plasma	MF Coldman and W Good. The Distribution of Sodium, Potassium and Glucose in the Blood of some mammals. *Comp. Biochem. Physiol.*, 1967, Vol 21. pp. 201-206.
Cats	7% red blood cells 93% plasma	MF Coldman and W Good. The Distribution of Sodium, Potassium and Glucose in the Blood of some mammals. *Comp. Biochem. Physiol.*, 1967, Vol 21. pp. 201-206.

Figure 2. The AlphaTrak 3 BG meter is calibrated for pets, not humans; this is important because not all blood is created equal.[14-15] **Photo:** alexis-chloe-dD75iU5UAU4-unsplash

Glucose concentrations are affected by stress, eating, exercise, health, and medication intake. Severe dehydration and excessive water loss may cause false low results. Additional factors that can impact or influence the glucose meter results include anemia (may cause falsely elevated BG), polycythemia (may cause falsely decreased BG), and alcohol/water (may cause dilution of sample).[5,16] Finally, the skin should not be squeezed or pinched to get a higher blood volume for testing. Squeezing or pinching the skin may result in hemodilution from the addition of interstitial fluid.

Mechanism of Action

The AlphaTrak 3 provides pet parents with a BG measurement based on the blood sample obtained from a dog or cat. The AlphaTrak 3 uses the chemical reagents glucose dehydrogenase (GDH) and the coenzyme, mediator, flavin adenine dinucleotide (FAD) to determine the glucose concentration in a sample (AlphaTrak 3 Product Specifications). In the first step in the process, a small blood sample (minimum 0.3 ul) is added to the test strip. The components and function of the test strip are described in **Figure 3**.

Home Monitoring Tools

There are several digital and physical tools available to the pet owner to help them perform BG monitoring at home. These include state regulations on insulin needle disposal, and manufacturer training videos and handouts on how to administer insulin. Pet owners are encouraged to complete a diary to collect important information to help guide their veterinarian's treatment decisions for their pet. This diary can

Figure 3.

Figure 3. Structure and function of a diabetes test strip. **1)** Plastic supports: two strips of thin plastic which contain the strip components, including the electrodes and chemical reagents. **2)** Spacer material (adhesive layer): this separates the two plastic supports, creating an internal space which can fill with blood so that the sample can interact with the chemical reagents. **3)** A working sample detection electrode; this is the portal through which electrons from glucose are transferred to the meter to be measured. **4)** The combination "counter/reference" electrode; this is the portal through which glucose derived electrons re-enter the strip after measurement. **5)** Chemical reagents: these include principally the enzyme and mediator (co-enzyme), as well as a host of other reagents, including preservatives (to improve shelf life), surfactants (to help blood fill the strip quickly) and film formers (to distribute all of the reagents evenly within the strip), among others.[17]

Image: Zoetis Stock Photo

be printed out or filled in electronically, and then should be shared with the veterinarian at each visit. Additionally, pet owners can track their diabetic pet's response to treatment or other useful parameters on home monitoring smart phone mobile applications. For clinics using Vetscan FUSE, blood glucose and patient activity data can be directly uploaded into the patient's medical record.

The AlphaTrak 3 will come equipped with a home monitoring mobile app. The digital interface for the AlphaTrak 3 is described in **Figure 4**.

Figure 4.

Figure 4. Digital tools for home monitoring and the home monitoring app. (Source: Zoetis Stock Photos)

For pet owners/pet parents who prefer not to use a mobile device to record BG readings, a journal in diary format is shown in **Figure 5**. At-home recording of a dog's or cat's BG levels in a diary or through the AlphaTrak 3 App serves as a valuable tool to help ensure that the levels remain within the target range. Pet owner identification of any significant changes can help the veterinarian to determine how to best adjust a dog's or cat's treatment protocol and reduce the risk of problems related to DM.

Figure 5.

AlphaTrak 3 Daily Journal					
Date	Time	Blood Glucose	Appetite	Units of Insulin	Time of Injection

Comments:

Figure 5. Example of a journal for at-home tracking of a dog's or cat's DM protocol. (Source: AlphaTrak 3 Diary)

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Section 1

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