TECHNISCHE UNIVERSITÄT WIEN

A Study of the Accuracy (= Trueness and Precision) of the KetoScan Mini Ketosis Measurement Device ('Breathalyzer')

Report TUW CTA 2022/02 EN

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KETOSCAN

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1.4 DURATION OF THE STUDY

The experimental work reported in this study has been perfomed in the time frame of November 8, 2021 – January 24, 2022.

1.5 LIST OF ABBREVIATIONS

AcAc	acetyl acetonate
AcCoA	acetyl-coenzyme A
BMI	body mass index
BOHB	β-hydroxybutyrate
BrAce	breath acetone concentration
NAD+	nicotineamide adenine dinucleotide, oxidised form
NADH	nicotineamide adenine dinucleotide, reduced form

2 Introduction

2.1 OBJECTIVE OF THE STUDY

In order to assess the practical usability and reliability of small, portable devices for the determination of breath ketone levels for the private user, the company Sentech Korea Corp. as a large manufacturer of handheld ketosis measurement devices and the company ACE Handels- und Entwicklungs GmbH, a large distributor of testing devices for workplace safety, occupational and private uses located in Freilassing, Germany, together initiated in 2021 this study with the intention to objectively demonstrate the accuracy, that is, the precision and trueness of measurements performed with these instruments under controlled laboratory conditions.

Continuing the collaboration between the Laboratory of Trace Organic Analysis at the institute of Chemical Technologies and Analytics of the TU Wien (Vienna University of Technology) and the two commissioning companies which already earlier has led to the production of two reports on the accuracy testing of breath alcohol measurement devices ('breathalyzers') [1,21], this report presents and summarizes the findings of the current study of the accuracy testing for the *Ketoscan mini* ketosis measurement devices.

The present report describes in detail the design of the current study, its execution and it is summarizing the most relevant results.

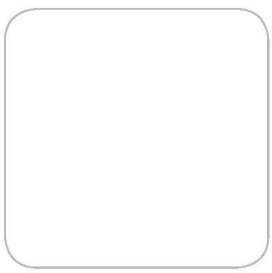
2.2 INTRODUCTION

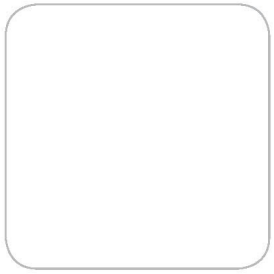
Breath Ketosis Level as Indicator of Physical Activity

The possibility of measuring endogenous acetone in breath for diagnostic purposes is already known for long [2]. In these early studies, the effect of caloric intake (fasting and calorie restriction diets), dietary macronutrient composition, and exercise on breath acetone was investigated [2,3,4,5,6]. While people of different weight classes participated in these investigations, the focus was on the effects of fasting and diabetes. The *breath acetone concentration* (BrAce) was understood to be a non-invasive measure of ketosis.

Ketosis describes the elevation of ketone bodies in the blood. Various distinguishable ketosis levels exist. Healthy individuals with standard dietary habits (i.e., moderate to high carbohydrate content) have a basal ketosis while individuals with uncontrolled diabetes have extremely elevated ketosis, also known as *ketoacidosis*. In all cases, ketosis describes the level of ketone bodies that are circulating in an individual. Increases in ketosis correspond to increases in ketone bodies.

Ketone bodies are produced as a by-product of the fat metabolism process. These acids are transformed into acetyl-CoA, an important intermediary molecule in the production of energy when the liver metabolizes circulating free fatty acids. Depending on the glucose level, acetyl-CoA can be diverted to produce acetoacetate, the first of three ketone bodies.





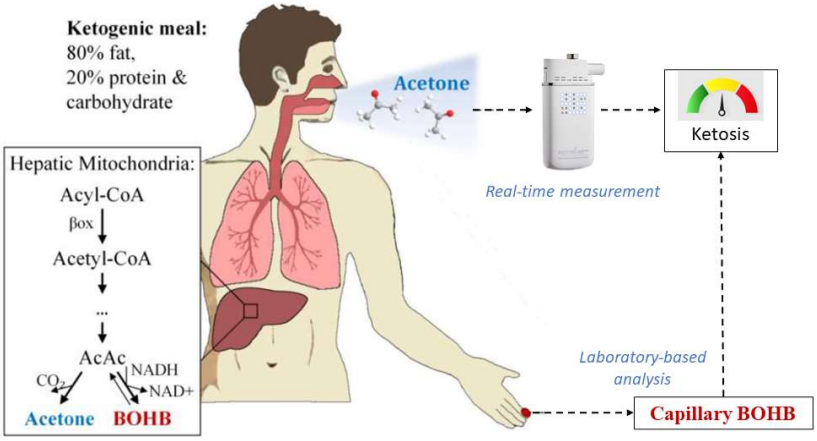


Figure 1: Graphical representation of the production and exhalation of acetone as a result of the human metabolism (modified after a graphics taken from Güntner et al. [18])

From acetoacetate (AcAc), two other ketone bodies, β-hydroxybutyrate (BOHB) and acetone, are produced by enzymatic degradation, but can also be formed by spontaneous decarboxylation [7,8]. While all three ketone bodies circulate in the bloodstream, it predominatly is acetone that diffuses into the air spaces of the lung and appears in the exhaled breath, because of its small size and high voaltility.

Endogenous acetone production is closely related to fat metabolism through the intermediary acetoacetate. For more than two decades, efforts were directed to elucidate the relationship between BrAce and fat loss. The overarching motivation behind this research was to develop a tool to quickly quantify the rate of fat loss. This type of measurement would inform and motivate weight loss patients whose daily weight fluctuations result primarily from variations in water content [9].

We will explain in the following the relationship between BrAce and the rate of fat loss. An important aspect in this context is the correlation between breath acetone and BOHB. The healthy ranges of BrAce corresponding to common ketotic and physiologic states are presented. We will also identify multiple dietary, metabolic, and respiratory factors that affect BrAce and quantify their effects, as far as possible. The understanding of the physiologic conditions and factors affecting BrAce in healthy subjects together with valid BrAce measurements will allow to optimize fat loss.

Breath Acetone Spectrum

As a small molecule of low molecular weight, acetone moves easily from blood into lung air and into exhaled breath [10]. Being a by-product of fat metabolism, acetone is present in blood and breath of all humans. There are a number of factors that increase BrAce including diet and exercise.

Blood concentrations can be converted to breath concentrations using the following relationship [11]. Calculated values often overestimate measured breath values due to airway gas exchange.

$$C_a = \frac{C_b V_M}{\lambda_{b:a} MW} \qquad \text{(eq. 1)}$$

Variable definitions are provided in Table 1. An overview of breath acetone concentrations for multiple conditions is given in Figure 1. Typical BrAce concentrations in normal healthy individuals range from 0.5 to 2.0 ppm. Adults on

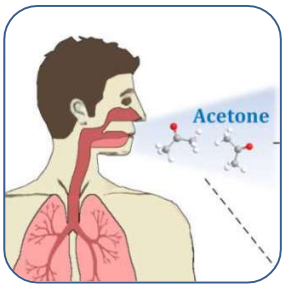


Table 1 Description of abbreviations and variables used in eq. (1)

Variable	Unit	Description
BOHB	mM	β-hydroxybutyrate (concentration)
BrAce	ppm, nM	Breath acetone concentration (relative / absolute)
C_a	ppm	Acetone concentration in air
C_b	µg l^{-1}	Acetone concentration in blood
$\lambda_{b:a}$		Blood to air partition coefficient for acetone, non-dimensional (= 341)
MW	g mol^{-1}	Molecular weight of acetone (= 58.08 g mol^{-1})
V_M	L mol^{-1}	Molar volume of air at 37°C and 1 atm (= 25.4 L mol^{-1})

ketogenic diets (e.g., high fat with low carbohydrate) can have elevated levels of up to *ca.* 40 ppm. Children with epilepsy can be treated with ketogenic diets to reduce the incidence of seizures. In these children, studies BrAce as high as 360 ppm have been reported. Fasting is a well known strategy to prompt the body to primarily utilize fats for energy production. Due to this change in the substrate for energy production BrAce levels can rise up to ~170 ppm. In case of poorly controlled diabetes, ketoacidosis can result with BrAce levels increasing up to 1,250 ppm.

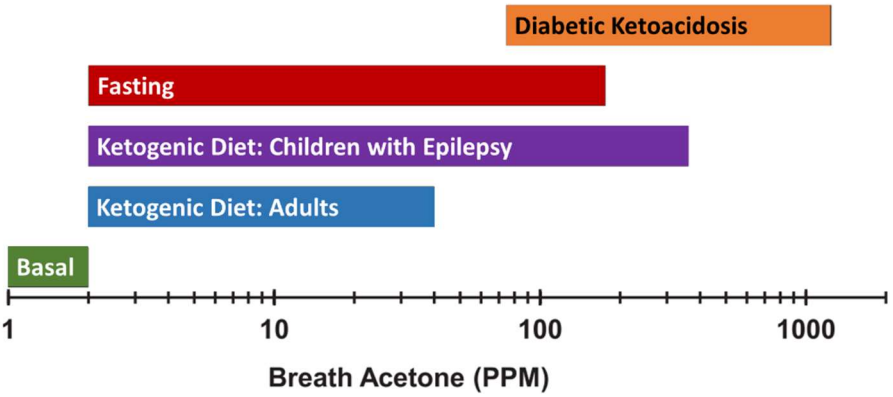
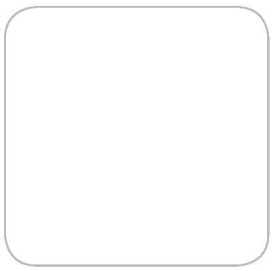
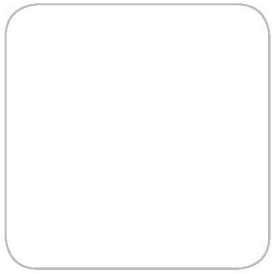


Figure 2 Breath acetone spectrum. The range of breath acetone concentration (BrAce) for a variety of physiologic states and ketosis ranges [].





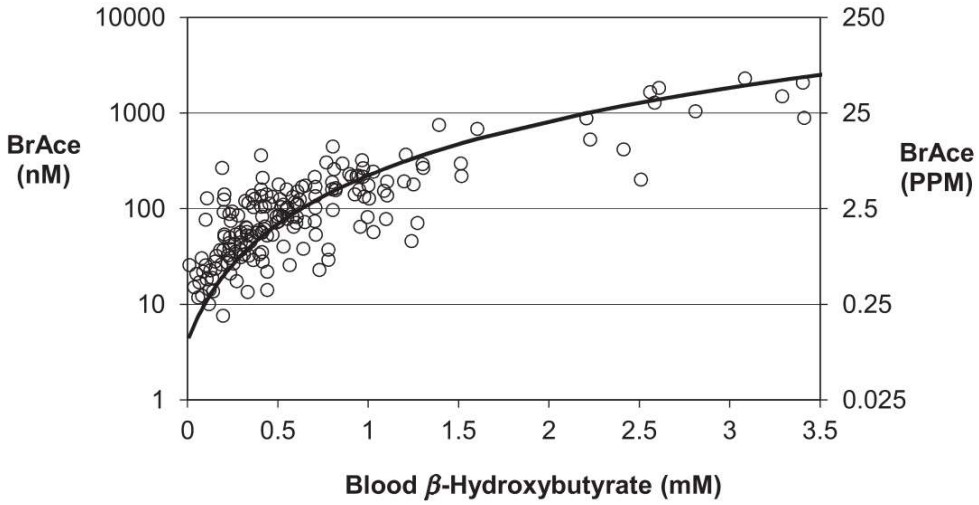


Figure 3 Breath acetone concentration (BrAce) has a non-linear relationship with blood b-hydroxybutyrate. Experimental data (open circles) were taken from multiple studies (and fit (black line) using an exponential relationship. For acetone the following relation holds: 1 ppm = 39.7 nM (molar basis). Graph taken from: J.C. Anderson (12).

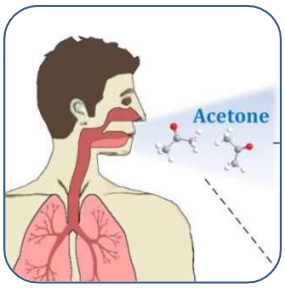
Breath Acetone and BOHB

BrAce levels relate to BOHB levels in blood, and thus to ketosis levels. A great number of studies have reported strong correlations between BrAce and BOHB with an average R^2 = 0.77 [Range: 0.54 to 0.94]. To demonstrate this relationship, blood-breath data from multiple studies were captured and plotted (Figure 3). The data was fit with an exponential relationship. Although data was taken from multiple sources and experimental conditions, the non-linear relationship between BrAce and BOHB appears to correlate well. BrAce is most sensitive to changes in BOHB between 0 and 1 mM. It is important to stress that the correlation shown in Figure 3 is only informative and empiric, and not due to a parmetrized model [12].

Breath Acetone and Fat Loss

It is known that acetone levels in blood and breath increase with fasting and caloric restriction as stored fat is mobilized to meet energy demands. This relationship has been known for more than 50 years. In the last three decades, however, studies aimed at better quantifying the relationship between BrAce and the rate of fat loss. Some representative findings shall be mentioned here:

- Initial weight loss in a restricted calorie diet is often related to (reversible) water loss
- If the restricted calorie-diet is continued, a further weight loss is observed that correlates to breath acetone concentration levels.
- If breath acetone levels from 85 to 500 nM (corresponding to ~2.1 – 12.6 ppm) can be maintained, a weight loss in the range of 227 g week^{-1} (0.5 lbs week^{-1}) can be observed – strongly depending on other factors such as composition (carbohydrate/fat ratio) of diet, body weight/obesity and physical activity.



Factors Affecting BrAce

BrAce can vary on short (hourly) and longer term (daily) time scales by a variety of physiologic factors including diet, obesity, and exercise; furthermore chemical factors and environmental factors. The physiology of acetone exchange in the lung affects BrAce in the breath sample. Understanding these factors and their impact on an individual's BrAce will improve the utility of BrAce for use in monitoring fat loss.

Dietary step-change and the time course of BrAce

When a dietary step-change is induced, such as starting a calorie restriction diet, fat metabolism is typically increased which also causes BrAce to increase. The time needed for BrAce to reach a new steady state depends on the dietary change. After initiating a calorie restriction diet, BrAce has been reported to rise for 3-8 days (in subjects that were losing fat) before achieving a new steady state. Also for fasting subjects, a similar time course appears to apply. In the pertinent literature on fasting it was noted that the rate of BrAce increase appears to have two phases. During the first 2-3 days of starvation, BrAce increases slowly. With continued fasting, BrAce rises rapidly, which is interpreted as an indication that liver glycogen is exhausted [2]. The time and reaction pathway that BrAce takes to achieve a new steady state is similar to the onset of fasting ketosis which is a result of the different processes of glycogenolysis (= the production of glucose 6-phosphate by tranfering an inorganic phosphate moiety to a glucose monomer split from glycogen), gluconeogenesis (= the metabolic process by which glucose is formed from non-carbohydrate precursors in the liver), lipolysis (= the metabolic pathway through which lipid triglycerides are hydrolyzed into a glycerol and three fatty acids), and ketogenesis changing their reaction rates to assume a new balance.

While it takes several days for acetone levels to increase, BrAce returns to baseline within hours of eating a high-calorie meal. This was observed for subjects fasting for a longer or shorter time. To indicate the typical time frame, after a 12 h overnight fast, a protein rich meal caused BrAce to return to pre-fasting levels within 4-5 h. In contrast to this, the termination of a prolonged fast with a heavy meal caused BrAce to return to baseline within 16 h.

Obesity

Obesity has a strong effect on both BrAce and fat loss. It appears that BrAce is inversely proportional to BMI, causing subjects with obesity to have lower BrAce; although this opinion is not completely uncontadicted. If true, caloric restriction may result in smaller BrAce increases for overweight subjects relative to thinner subjects. Additionally, individuals with obesity become ketotic at slower rates, experience a lower rate of fat loss, and exhale lower BrAce when starting a calorie restriction diet. It is assumed that as the weight of these individuals decreases, BrAce and the rate of fat loss will increase.

Exercise

In a similar way as a reduced calorie diet can increase BrAce, also exercise can increase BrAce levels. Many studies report BrAce being ca. twofold greater at the end than the beginning of exercise. BrAce is expected to increase during exercise. During graded exercise tests, BrAce increased (roughly twofold) with exercise intensity, maximum BrAce corresponded to the onset of the lactate threshold [13], and the fat oxidation rate was shown to be logarithmically related to BrAce [14]. Additionally, the fat oxidation rate and BrAce were shown to have parallel increases over 2 h of steady treadmill exercise [14].

Exercise is known to affect day-to-day measurements of BrAce. Subjects that are submitted to both caloric restriction and daily exercise had greater daily BrAce than caloric restriction alone. While few studies have investigated the impact of exercise on BrAce, multiple investigations have shown the effect of exercise on ketosis and fat oxidation. Because BrAce has been shown to correlate with ketosis and fat oxidation, it is expected that exercise will impact BrAce in a similar fashion to its effect on ketosis (i.e., BOHB) and fat oxidation.

Additional factors

In addition to the primary factors discussed above, other factors may affect ketonemia, fat oxidation, or BrAce directly. These factors are of minor importance or effect due to minimal supporting data, smaller impact on BrAce, or smaller


duration of effect. While some studies exist on changes to BrAce, most available data describes the impact of these factors on fat oxidation, fat mobilization, or ketosis. Changes in these three outcomes may alter BrAce but have to be confirmed yet in further studies.

Although many substances are suspected to increase breath acetone, this is not sufficiently well documented by expetrimental studies. The ingestion of large amounts of garlic can increase BrAce 24-30 h later [15]. Increased BrAce correlated with elevated allyl methyl sulfide, a product of garlic metabolism. The proposed mechanism of action which may increase BrAce is the inhibition of the hepatic acetone metabolism [15]. Another chemical, disulfiram, an acetaldehyde dehydrogenase inhibitor, blocked acetone metabolism which caused BrAce to increase 10- to 15-fold over baseline values [16].

Caffeine and green tea are also considered "fat burners" for their ability to promote fat metabolism [17]. Caffeine acts directly on the sympathetic nervous system and thereby increases circulating fatty acids and fat oxidation. The impact of caffeine on fat metabolism is expected to be small (<20%) and to become smaller with habitual ingestion. Green tea contains large amounts of catechin polyphenols. One prominent example is epigallocatechin-3-gallate which appears to promote lipolysis and increase fat oxidation [17]. Green tea consumption (>100 mg) can increase fat oxidation both acutely and chronically but its effects can be modulated by caffeine intake [17].

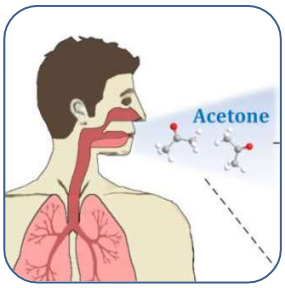
Breath sample

Measurement of acetone in breath depends on both an accurate and reliable measurement device and a well-defined breath sample. Many instruments (e.g., mass spectrometers, gas chromatographs, UV or near-IR light detection, and metal oxide sensors) can measure parts- per-million concentrations of acetone in breath under laboratory conditions [2,18]. In addition to the large number of available measurement instruments, there also exist a variety of breathing maneuvers (e.g., tidal breathing, vital capacity exhalation, and rebreathing) to provide a breath sample. It is important to be aware that the chosen breathing maneuver affects BrAce in the breath sample. Moreover, the portion of exhaled air collected (e.g., early or late in exhalation) and human factors affect BrAce.

There are a number of factors that affect BrAce, primarily, because acetone exchanges predominately in the lung airways and not in the alveoli like oxygen and carbon dioxide. Airway gas exchange requires highly blood soluble chemicals, has a temporal and spatial exchange pattern, and is affected by energy exchange in the lung. As a result, breath tests involving chemicals that exchange in the airways (e.g., acetone) must be designed and interpreted differently from breath tests of chemicals participating in alveolar exchange.

Human factors such as exhaled air volume, breathing pattern, and breath temperature affect chemical exchange in the lung airways. These factors have to be accounted for when sampling, measuring, and interpreting BrAce. During a single exhalation, BrAce increases with exhaled volume. Thus, the more air volume exhaled, the greater the acetone concentration [10]. The breathing pattern prior to breath sampling can affect the concentration. It is expected that BrAce will increase with breath holding and decrease with hyperventilation in a manner similar to ethanol [19]. Another factor casuing increase in BrAce is breath temperature [13]. This underpins the importance of controlling the conditions under which samples are taken for BrAce measurement.

A tidal breath (typical *ca.* 500 ml; large *ca.* 1,000 ml) is a commonly used breathing maneuver for providing a breath sample. Based on a normal breathing pattern, a tidal breath requires minimal effort, inhalation from and exhalation to functional residual capacity, and is completed within 5-8 s. The maximum BrAce (at the end of the exhalation) is at most two-thirds of the blood acetone value (Figure 4), however, when captured in a bag, the mixed-exhaled sample is less than end-exhaled BrAce. BrAce from tidal breath is susceptible to alteration by human factors and typically provides the poorest representation of blood acetone of the maneuvers listed here. On the contrary, BrAce measurements from tidal breaths are generally repeatable.



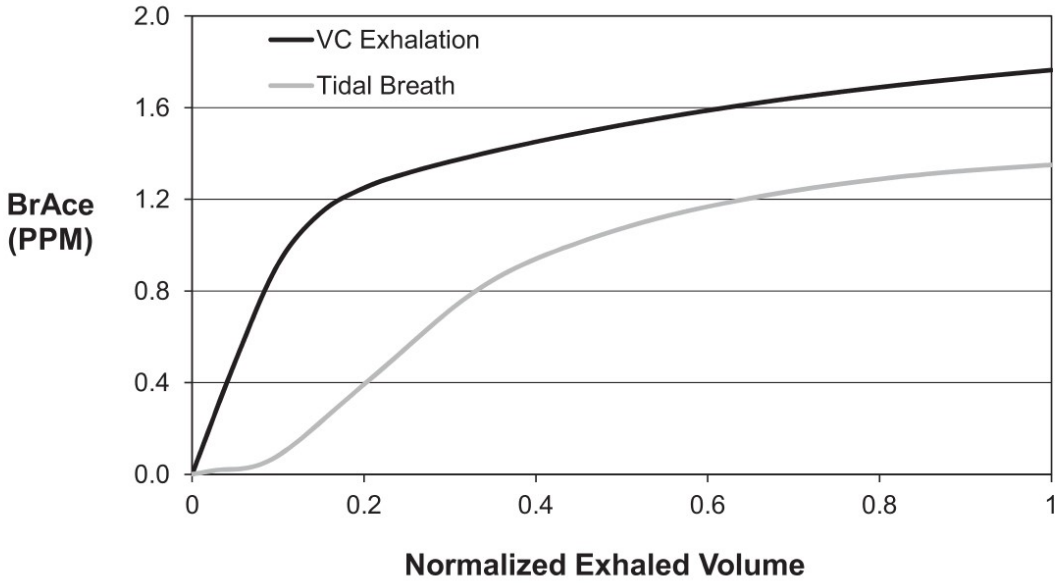


Figure 4 Acetone expirograms for vital capacity (VC, black) and tidal (gray) exhalation. Exhaled volume is ~10-fold greater for VC versus tidal exhalation.

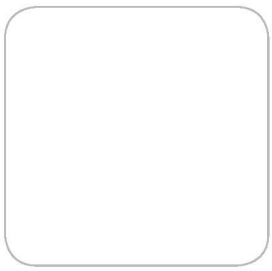
The vital capacity manoeuvre (~5000 ml), typically requested for alcohol breath testing, requires inhalation to total lung capacity and exhalation for 10 to 25 s against a fixed resistance until subjects are unable to exhale, stopping at residual volume. While this maneuver provides a better representation of blood acetone than the tidal maneuver, end-exhaled BrAce is *ca.* 85% of that in the blood (Figure 4). This maneuver is more sensitive to human factors because of the greater exhaled volume needed and the need to sample the end-exhaled air. This maneuver can provide better accuracy than tidal breathing. However, accuracy and repeatability may suffer unless human factors are controlled.

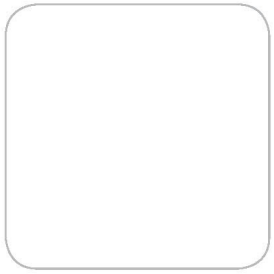
For rebreathing, subjects breathe ~1,000 ml into and out of a sealed bag over six breath cycles. This maneuver typically lasts from 30 to 50 s and, for some subjects, can become uncomfortable as carbon dioxide concentration increases throughout the maneuver , making breathing less efficient. With rebreathing, air is in close contact with blood for up to 10 times longer than with other breathing maneuvers. Thus, acetone exchange is more complete which mini- mizes the effects of human factors and causes BrAce to more closely resemble blood acetone. Although rebreathing may be diffi- cult for some subjects, it provides the best accuracy and repeatabil- ity of the three possibilities presented.

Summary

Endogenous breath acetone is correlated with the rate of fat loss and can be used to understand this process in healthy subjects. Maintaining a 2 ppm BrAce while on a calorie restriction diet should cause a fat loss of ca. 227 g week^{-1}. Acetone is correlated with fat loss because it is strongly correlated with the blood ketone body BOHB. Breath acetone is strongly correlated with the blood ketone body BOHB. Breath acetone can span the concentration range from 1 ppm in healthy non-dieting subjects to 1,250 ppm in diabetic ketoacidosis. In healthy individuals, breath acetone is affected by multiple factors.

Dietary macronutrient composition has the greatest impact and is followed, according to importance, by caloric restriction, exercise, pulmonary factors, and other factors. Because of its relationship to fat metabolism, a high-fat, low-carbohydrate diet will lead to higher breath acetone levels than a standard mixed diet. A reduction in consumed calories relative to that needed for weight maintenance can increase breath acetone and fat loss.





Exercise can promote the effects of caloric restriction. Consequently, exercise can cause breath acetone elevation during a workout. Human respiratory factors can affect the acetone concentration in the breath sample. Other foods (e.g., garlic), drugs (e.g., disulfiram), and environmental conditions can increase breath acetone due to their ability to increase fat metabolism or block acetone metabolism. It can thus be summerized that the relationship between breath acetone and fat loss is well established, however, that additional research is needed to better understand these factors and advance this area of integrative physiology.

3 Study Design

3.1 STUDY DESIGN

Unlike for the use of breath alcohol testing devices, there are no generally agreed protocols for the testing of breath ketone measurement devices. The present study follows thus a protocol that was defined by the commissioning parties and accepted by the contractor.

The purpose of the tests performed was:

a) to check the accuracy of the *Ketoscan mini* breath ketone measurement device
b) to check of the calibration stability of the *Ketoscan mini* breath ketone measurement device

Tests were performed at three different acetone concentration levels (0 ppm (= blank), 5 ppm and 10 ppm) according to a precisely defined protocol within five subsequent days.

Measurements on Day 1 and Day 2 were intended to test the accuracy of the instruments, while the continuation of the measurements for three further days (Day 3, Day 4, Day 5) was performed to check the stability of the calibration of these instruments. A graphical representation of the test protocol is reported in Figure 5.

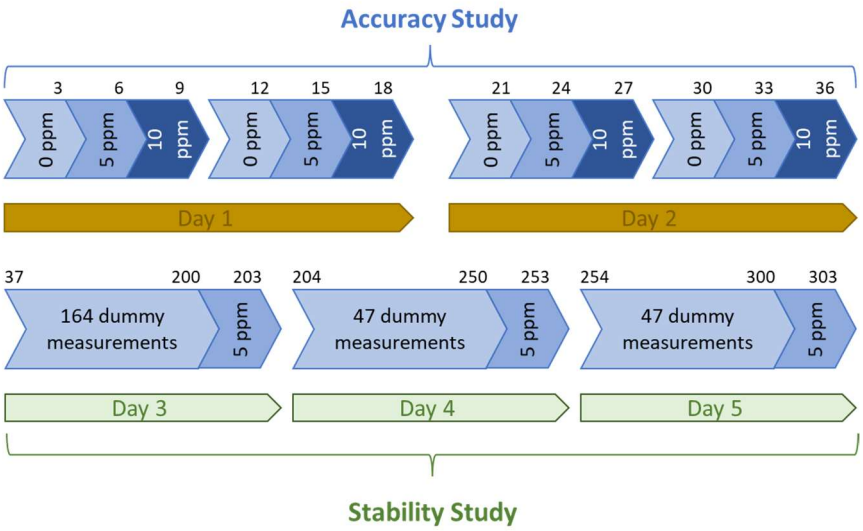


Figure 5: Graphical representation of the experimental design of the performed study, assessing the accuracy and the calibration stability of *Ketoscan mini* breath ketone measurement devices. The numbers above the arrows represent the cumulative number of measurements performed with each individual instrument.

The data produced was statistically evaluated with regard to accuracy and precision and is presented in this report in the following sections.

Statistical Data Evaluation

The **precision** of a dataset of individual measurements is a measure of the mutual approximation of each datapoint x_i of this dataset. It is usually reported as the relative standard deviation (RSD) of the dataset and calculated according to:

Standard deviation: $$s = \sqrt{\frac{\sum (x_i - \bar{x})^2}{(n-1)}} \quad \text{(eq. 2)}$$

Relative standard deviation: $$RSD = s/\bar{x}\ [\%] \quad \text{(eq. 3)}$$

The **accuracy** is defined as the agreement of known and measured concentrations. It is typically given as the ratio of the measured and the known concentration of the analyte:

Trueness [%]: $$Trueness = x_{\text{measured}}/x_{\text{known}}\ [\%] \text{ with } x_{\text{measured}} < x_{\text{known}}, \quad \text{(eq. 4)}$$

otherwise: $$Trueness = x_{\text{known}}/x_{\text{measured}}\ [\%] \text{ with } x_{\text{measured}} > x_{\text{known}}, \quad \text{(eq. 4')}$$

or it is expressed as a lack of agreement (= difference) between measured and known value, which we will further on denote as **"Bias"**:

Bias [in ppm]: $$Bias = x_{\text{measured}} - x_{\text{known}}\ [\text{ppm}] \quad \text{(eq. 5)}$$

To facilitate interpretation, the measurement deviation (bias) is often expressed as relative deviation (**Relative Bias**).

Relative Bias [%]: $$Relative\ Bias = \frac{x_{measured} - x_{known}}{x_{known}}\ [\%] \quad \text{(eq. 6)}$$

These data are reported in the tables given for each instrument analysed, as a result of the "Mid-term stability study": In this study, the acetone standards with $c_{\text{Acetone}} = 5$ ppm were analysed at seven occasions during five consecutive days in triplicate $(n = 3)$. The relative standard deviation (RSD%) of these replicates is also reported in these tables.

The turquoise bars represent the average readings of the instruments (with the error bars representing ±1 standard deviation (left scale of the graphs), while the red dots represent the relative standard deviation (right scale). The hatched orange lines represent the fixed deviation of ±1 ppm, corresponding to ±20%RSD at this concentration level.

In order to obtain a more robust estimate of the actual accuracy of the test results, trueness or bias was not determined (and then averaged) over all individual test results and different concentration levels, but instead the accuracy was determined as the slope of the recovery function, that is, regression line of the measured *versus* the known concentrations of the acetone standards.

A recovery function allows to assess the quality of the data in twofold respect:

- The slope of the (linear) graph is an indication for the systematic error if different from 1, indicating a higher than expected (slope > 1) or lower than expected (slope < 1) recovery. In fact, in the absence of a constant systematic error, the slope of the recovery function can be considered as a representation of the *proportional systematic error* of the measurements.
- If the intercept of the calibration line is significantly different from zero, then also the presence of a *constant systematic error* must be assumed.

The second important conmclusion that can be drawn from the recovery function is one on the precision of the measurements. This information is based on the calculation of the prediction band of a linear calibration function.

When calculating a linear regression line from experimental data, then that curve is searched, for which the squares of the deviations of the distance of the individual data points from the calibration line is minimsed ('least-square method').

Still, individual data points will show a deviation from the calibration line (which is considered the best estimate of the result), and the squared deviation of individual data points from the calibration line is used to calculate the so-called residual standard deviation s_y according to the following formula:

$$s_y = \sqrt{\frac{\sum(y_i - \hat{y})^2}{(n-2)}} \text{ [signal units]} \qquad \text{(eq. 7)}$$

While the residual standard deviation is an useful indicator for how well the experimental data (measurments) are described by the model, its drawback is that it is expressed in signal units or units of the dependant variable (y) which often is not easily interpretable. By relating the residual standard deviation s_y to the slope of the calibration line b, the standard deviation of the method s_{x0} is calculated:

$$s_{x0} = \frac{s_y}{b} \text{ [concentration units]} \qquad \text{(eq. 8)}$$

The standard deviation of the method s_{x0} is expressed in units of the independent variable x, mostly a concentration (e.g., ppm). In order to have a more objective and more easily comparable measure of the standard deviation of the method, this quantity is related to the midpoint of the calibration range, $\bar{x}$, leading to the variation coefficient of the method, V_{x0}:

$$V_{x0} = \frac{s_{x0}}{\bar{x}} \text{ [\%]} \qquad \text{(eq. 9)}$$

We will use this variation coefficient of the method, V_{x0}, in the subsequent tables to assess the precision of the measurements.

The standard deviation of the method, s_y, is also used to calculate the *prediction bands* or *prediction intervals* for acetone measurements. The prediction interval represents that interval within which the individual measurements are expected to occur with a given probability, typically 95%.

The calculation of the prediction interval is according to the following formula:

$$\Delta y_p(x) = \pm t_{f,\alpha} \cdot s_{x0} \sqrt{\frac{1}{m} + \frac{1}{n} + \frac{(x-\bar{x})^2}{Q_{xx}}} \text{ [ppm]} \qquad \text{(eq. 10)}$$

In this formula, the symbols denote the following parameters: $t_{f,\alpha}$...*t*-factor for a calibration with *n* individual measurments and the confidence level α, s_{x0}...residual standard deviation of the method, m...number of calibration measurments; n...number of sample measurements, Q_{xx}...sum of squares of the difference of concentration values and concentration midpoint. The calculation and the nomenclature follows the German standard DIN 38402, Part 51 [20].

This formula denotes the interval above and below the calibration line, indicated as the two dotted lines in the recovery graphs that surround the calibration line.

All statistical calculations were carried out using Microsoft Excel® 2019.

The results of the study are presented in both tabular and graphic form in the section “4 Results of the Study”.

Table 2: Explanation of the terms and abbreviations used in the graphs and tables in the presentation of the study results.

Level [‰]	Nominal value of blood alcohol concentration (BAC) [‰]
Reference value [ppm]	Concentration of the calibration gas at the considered concentration level [ppm]
Mean value [ppm]	Mean value of each set of BrAce measurements [ppm]
Accuracy	Ratio of mean and reference value, reported in [%]

RSD%	Relative standard deviation of the mean values of the BrAce, expressed in [%]
Bias [ppm]	Absolute difference between the reference value and the mean value of the BrAce, expressed in [ppm]
SD of Bias [ppm]	Absolute standard deviation of the bias, expressed in [ppm]
Rel. Bias [%]	Relative difference between reference and mean value, expressed in [%]
SD of Rel. Bias [%]	Standard deviation of the relative bias, expressed in [%]
Residual standard deviation, s_y	Parameter expressing the deviation of the indivual measurement values from the regression model
Standard deviation of the method, s_{x0}	Parameter expressing the deviation of the indivual measurement values from the regression model, expressed in concentration units
Variation coefficient of the method, V_{x0}	Parameter indicating the spread of the datapoints around the calibration line, related to the midpoint of the calibration, expressed in %
Prediction band / prediction interval	Interval around the recovery function within which the individual measurements are expected to appear at a confidence level of 95%

3.2 PERFORMANCE OF THE STUDY

This study was devoted to assessing the performance of the *KetoScan mini* (Sentech GMI Corp.) breath acetone measurement instrument (breathalyzer). The instruments with the following serial numbers were tested in this study:

Table 3: Identification of the KetoScan mini breathalyzers used in this study.

KetoScan mini instrument serial numbers (SN)				
KMAL9B0001	KMAL9B0002	KMAL9B0003	KMAL9B0004	KMAL9B0005
KMAL9B0006	KMAM1F0001	KMAM1F0002	KMAL9B0008	KMAL9B0010

Generation of Test Gas Atmosphere

The performance of this study requires the generation of calibration gas atmospheres with precisely known and constant acetone concentration. The dynamic generation of suitable test gas atmospheres was performed in analogy to the setup used earlier in the accuracy study of alcohol breathalyzer [21]. The experimental set-up consisted of two *simulators* coupled in series, as well as one membrane pump that was used to generate the stream of air enriched with a precisely controlled level of acetone needed to test the breath acetone measurement devices.

A *simulator* is a device that is filled with a dilute aqueous solution of the analyte – in this case: acetone – through which a stream of pure air (zero air) is passed. The air flow is saturated with water vapour and equilibrates with gaseous acetone according to the precisely set temperature of the device. Both simulators were thermostated to 34.00±0.02°C [22]. When passing air through the simulators, the temperature could drop briefly by up to 0.05°C. However, it returned again to the target value of 34.00°C within a short period of time which typically was much shorter than the time in between two measurements and hence was considered an insignificant factor of influence for the quality of the meaurements. The operation of both simulators in series ensures that the set gas phase concentration of acetone remains constant over a period of 30 subsequent measurements.

The two simulators used in this study were devices of the type Dräger X-Cal 2000 (Dräger Safety AG & Co. KGaA, Lübeck, Germany), part no. 8326 000 with serial numbers ARJL-0016 and ARJL-0023.

Furthermore, one Hi-Blow DongYang DY-20L membrane pump with the type designation HB07016-1001B was used to pass the zero air (at a flow rate exceding 10 L min^{-1}) through the acetone solutions, thereby generating the gas stream necessary for the activation of the breath acetone measuring devices (Figure 6).

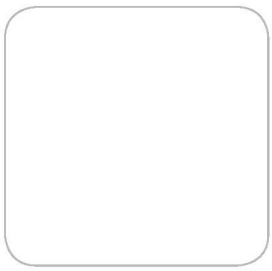
The concentration of acetone in the test gas stream (expressed in µL L^{-1} or in µmol mol^{-1}, hence in both cases as ppm) is a function of the acetone concentration in solution. It can be calculated according to Raoult's law:

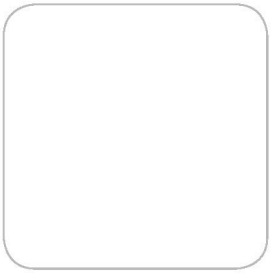
$$p_{\text{Acetone}} = x_{\text{Acetone}} \cdot p^{\circ}_{\text{Acetone}} \text{ [Pa]} \qquad \text{(eq. 11)}$$

The standard vapour pressure p° of a substance at a given temperature can be calculated from the Antoine equation (7) as an approximation for a given temperature interval.

$$p_{\text{Acetone}} = (10^{A-\frac{B}{C+T}}) \times \frac{101\,325}{760} \text{ [Pa]} \qquad \text{(eq. 12)}$$

With the parameters for *A*, *B* and *C* being as follows: $A = 7.1327$, $B = 1219.27$ and $C = 230.653$ which are applicable within the temperature range -64°C < T < 70°C, the value of $p_{\text{Acetone}}(34°\text{C}) = 44454$ Pa results.



While the above mentioned equations make it possible to calculate the gas phase concetration of acetone, the reported values refer to the acetone concentration in the liquid phase. Below described is the two-step procedure suggested by the manufacturer of the ketosis measurement devices which was used to prepare the acetone standard used for calibration:

1. Prepare a 0.1% (v/v) solution of acetone in organic-free, deionized water by adding 1 mL of acetone to 999 mL of water and filling to the exact volume of 1 L. Considering the density of acetone, this solution contains 0.788 g acetone/L solution.
2. Add 8 mL of this solution to 992 mL of organic-free, deionized water and make up to exact volume of 1 L.
3. The resulting solution has a concentration of 5 ppm acetone.

For the 10 ppm acetone standard, the concentration of the stock solution must be doubled (16 ml acetone/L).

Figure 6: Experimental setup for the conduction of the accuracy study for breath acetone measuring devices. The membrane pump is visible on the left side, the two simulators operated in series are located to the right of it. The test gas is delivered to the Ketoscan breathalyzer through the hose seen in the foreground. The droplet trap at the end of tube was not used; instead the mouth pieces of the breathalyzers were exchanged frequently.

All measurements were carried out according to the instruction manual of the respective alcotesters.

4 Results of the Study

4.1 PRESENTATION OF RESULTS

The following pages show, for each instrument separately, the results of the accuracy check. The presentation of the results includes a plot of the measurement results achieved at the three investigated concentration levels (0, 5 and 10 ppm) in the four measurement series done. The graph reports the individual data points, as well as the regression line of known *versus* found concentrations. Obviously, this graph (recovery function) should ideally have the slope = 1 and the intercept = 0. Further to the calibration line and the individual data points, the prediction interval of the recovery function is plotted (the dotted lines above and below the regression line). This prediction band or prediction interval represents the interval within which, at a given sample concentration, the measurement signal can be expected at a confidence level of 95%. The width of the prediction interval is directly related to the standard deviation of the method and thus a good illustration of the quality of the measurement.

The second graph presented for each instrument is the plot which summarizes the results of the stability study. This study included seven measurement series of the 5 ppm standard and should illustrate the midterm stability of the instrument over its lifecycle of 300 measurements. The graph presents both the average of the three measurements $\bar{x}$ at each occasion including the error bars (which represent ±1 standard deviation s in this case, and also the relative standard deiviation ($RSD\%$) for each measurement series. The parallel lines denote a ±20% interval from the nominal value (5±1 ppm) which may be considered a satisfactory measurement result.

Two tables support and complement the information given in the graphs, in that they present:

- the recovery function data for all individual four experiments and for the grand average (slope, intercept, coefficient of determination),
- the residual standard deviation s_y, the standard deviation of the method s_{x0}, and the variation coefficient of the method V_{x0}, and in the cecond table
- the bias, relative bias and RSD% values.

Instrument 1: KMAL9B0001

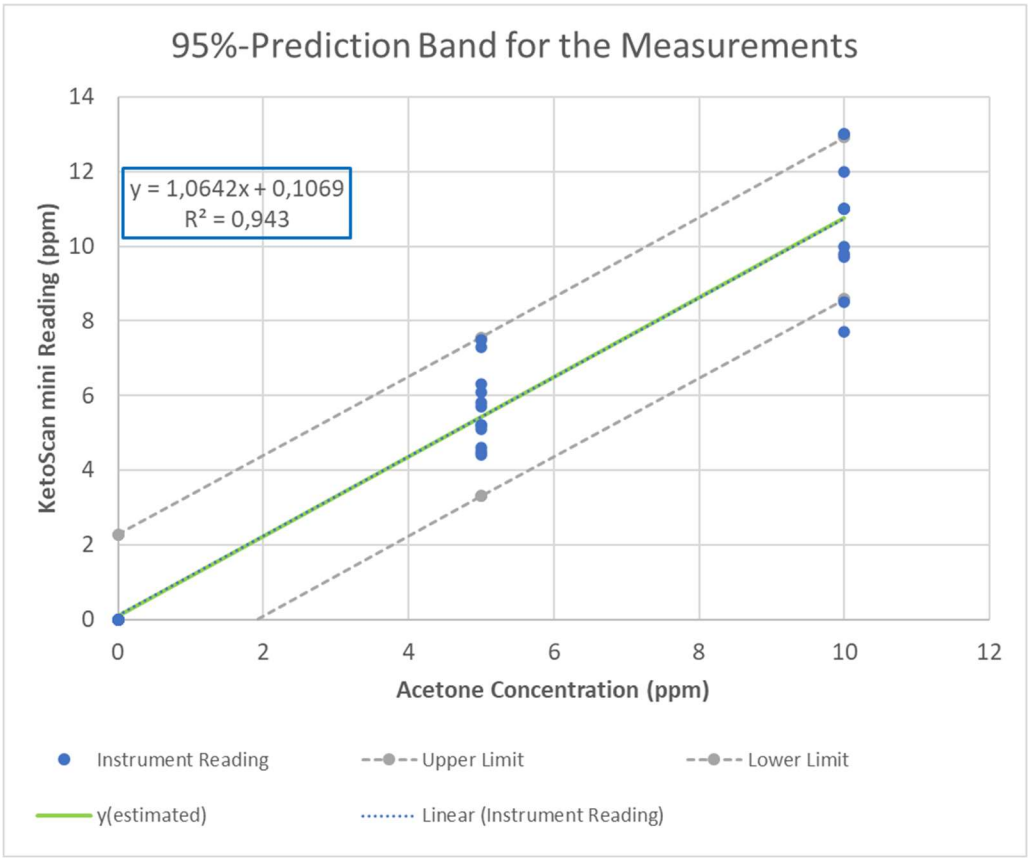


Figure 7: Graphical presentation of results from the accuracy check of Ketoscan mini, S/N KMAL9B0001. The dotted lines represent the prediction interval or prediction band for individual measurements.

Table 4: Summary of the results for the Ketoscan mini ketosis measurement device: individual test and overall results.

Parameter	1st Test	2nd Test	3rd Test	4th Test	Overall
Slope	1.100	1.267	0.913	0.977	1.064
Intercept	0.19	0.17	0.07	0.01	0.11
Coeff. of Determin. R^2	0.9958	0.9872	0.9728	0.9761	0.9430
No. of Measurments, n	9	9	9	9	36
Residual standard deviation s_y [ppm]					1.099
Standard deviation of the method s_{x0} [ppm]					1.032
Variation coefficient of the method V_{x0} [%]					20.6

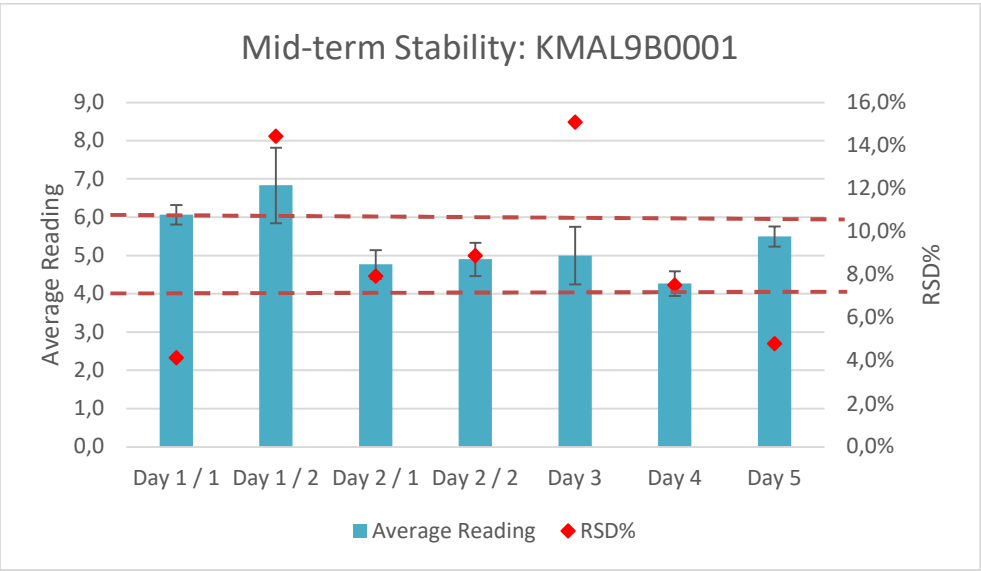
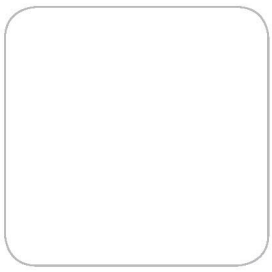
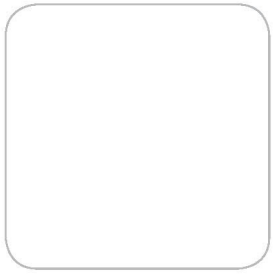


Figure 8: Graphical presentation of results from the mid-term stability study of Ketoscan mini, S/N KMAL9B0001.

Table 5: Tabular presentation of the Bias (absolute and relative deviation) of the masurements of the 5 ppm acetone standard

KMAL9B001	Bias (ppm)	Rel. Bias (%)	RSD%
Day 1 / 1	1.1	21%	4.1%
Day 1 / 2	1.8	37%	14.4%
Day 2 / 1	-0.2	5%	7.9%
Day 2 / 2	-0.1	2%	8.9%
Day 3	0.0	0%	15.1%
Day 4	-0.7	15%	7.5%
Day 5	0.5	10%	4.8%
Average:	**0.6**	**13%**	**9%**



Instrument 2: KMAL9B0002

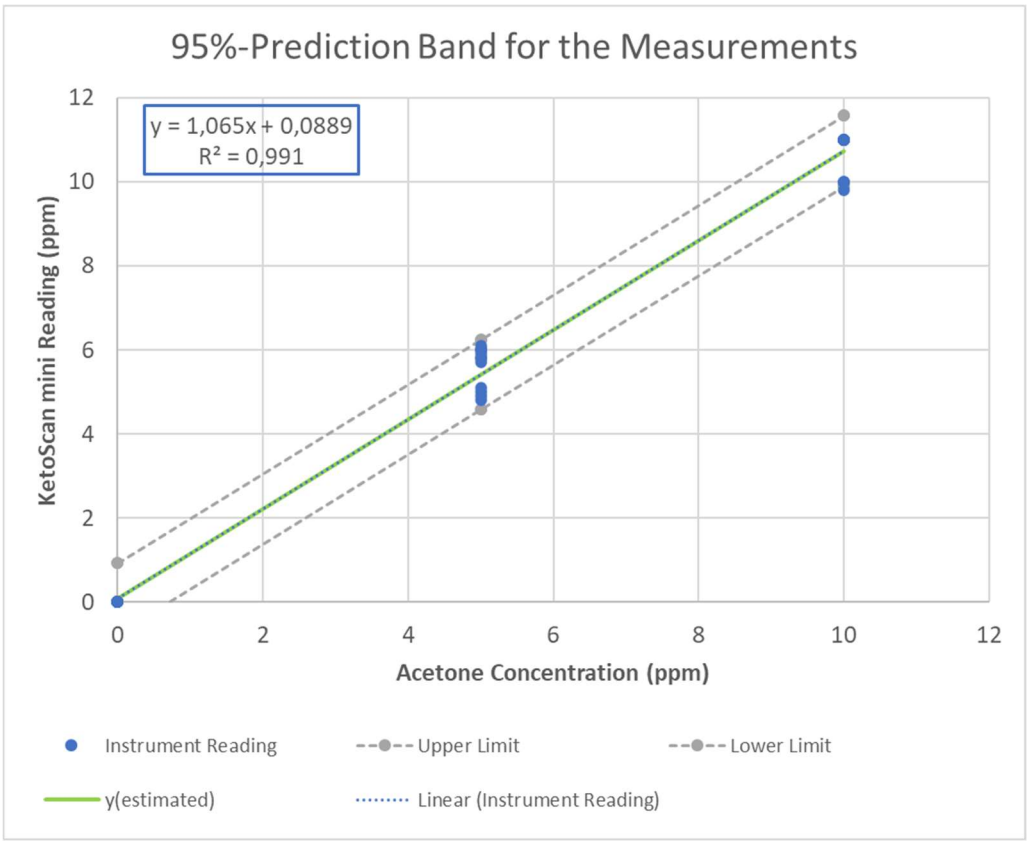


Figure 9: Graphical presentation of results from the accuracy check of Ketoscan mini, S/N KMAL9B0002. The dotted lines represent the prediction interval or prediction band for individual measurements.

Table 6: Summary of the results for the Ketoscan mini ketosis measurement device: individual test and overall results.

Parameter	1st Test	2nd Test	3rd Test	4th Test	Overall
Slope	1.067	1.100	1.067	1.027	1.065
Intercept	0.21	0.16	-0.12	0.11	0.089
Coeff. of Determin. R^2	0.9912	0.9976	0.9943	0.9904	0.9910
No. of Measurments. n	9	9	9	9	36
Residual standard deviation s_y [ppm]					0.427
Standard deviation of the method s_{x0} [ppm]					0.401
Variation coefficient of the method V_{x0} [%]					8.0

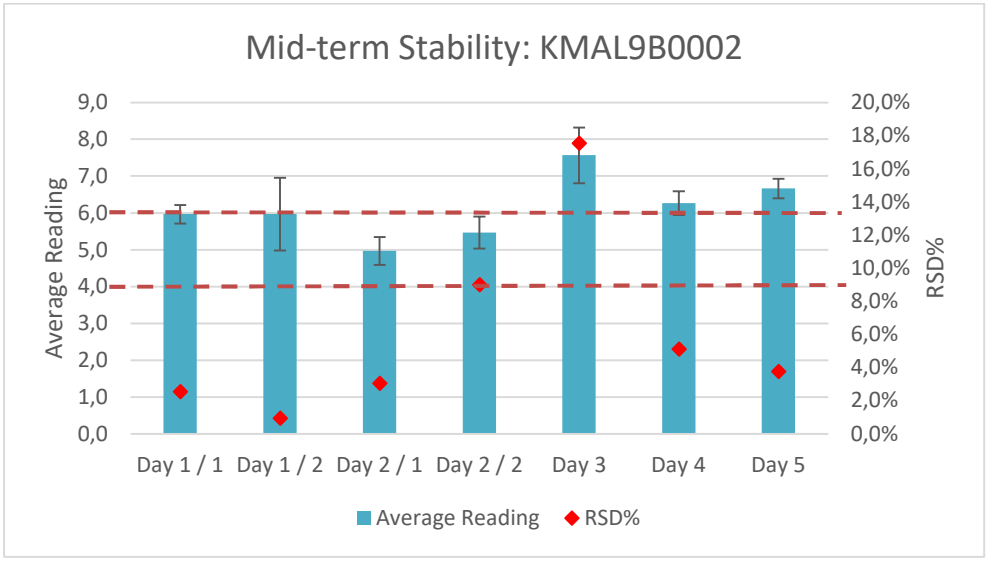


Figure 10: Graphical presentation of results from the mid-term stability study of Ketoscan mini, S/N KMAL9B0002.

Table 7: Tabular presentation of the Bias (absolute and relative deviation) of the masurements of the 5 ppm acetone standard

KMAL9B002	Bias (ppm)	Rel. Bias (%)	RSD%
Day 1 / 1	1.0	19%	2.6%
Day 1 / 2	1.0	19%	1.0%
Day 2 / 1	0.0	1%	3.1%
Day 2 / 2	0.5	9%	9.0%
Day 3	2.6	51%	17.5%
Day 4	1.3	25%	5.1%
Day 5	1.7	33%	3.8%
Average:	**1.1**	**23%**	**6%**

Instrument 3: KMAL9B0003

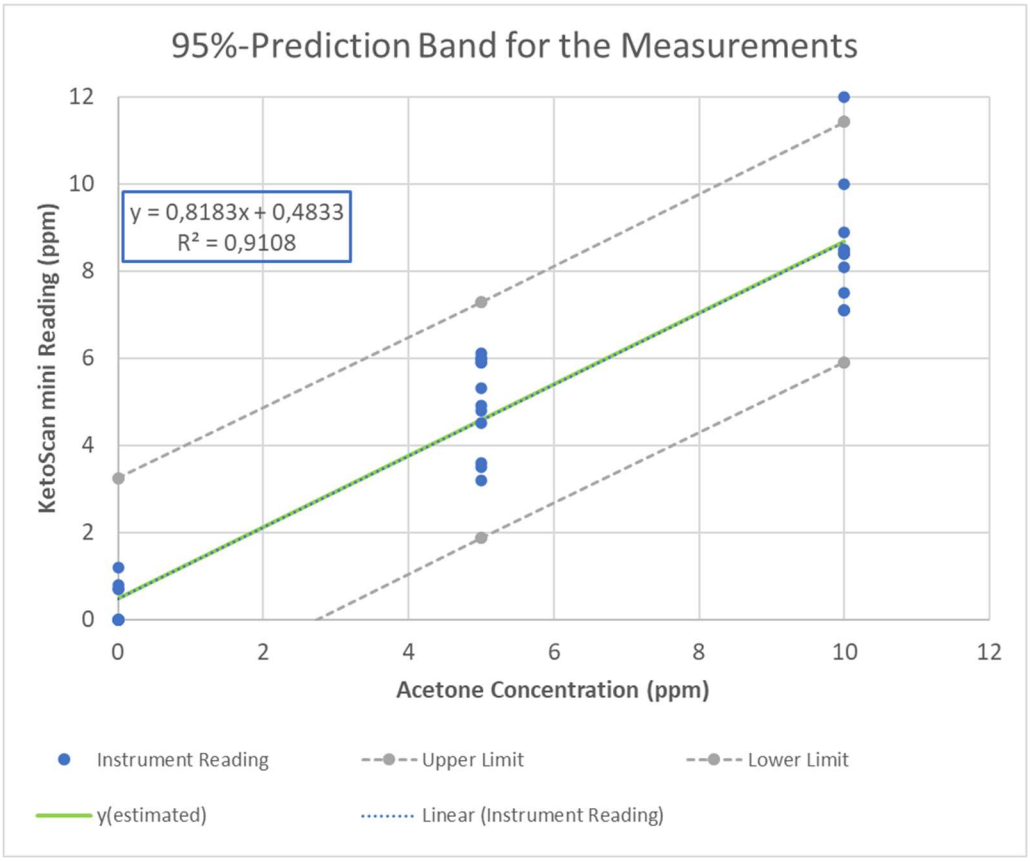


Figure 11: Graphical presentation of results from the accuracy check of Ketoscan mini, S/N KMAL9B0003. The dotted lines represent the prediction interval or prediction band for individual measurements.

Table 8: Summary of the results for the Ketoscan mini ketosis measurement device: individual test and overall results.

Parameter	1st Test	2nd Test	3rd Test	4th Test	Overall
Slope	0.957	0.833	0.670	0.813	0.818
Intercept	0.717	0.367	0.294	0.556	0.483
Coeff. of Determin. R^2	0.9380	0.9921	0.9818	0.9390	0.9108
No. of Measurments. n	9	9	9	9	36
Residual standard deviation s_y [ppm]					1.076
Standard deviation of the method s_{x0} [ppm]					1.315
Variation coefficient of the method V_{x0} [%]					26.3

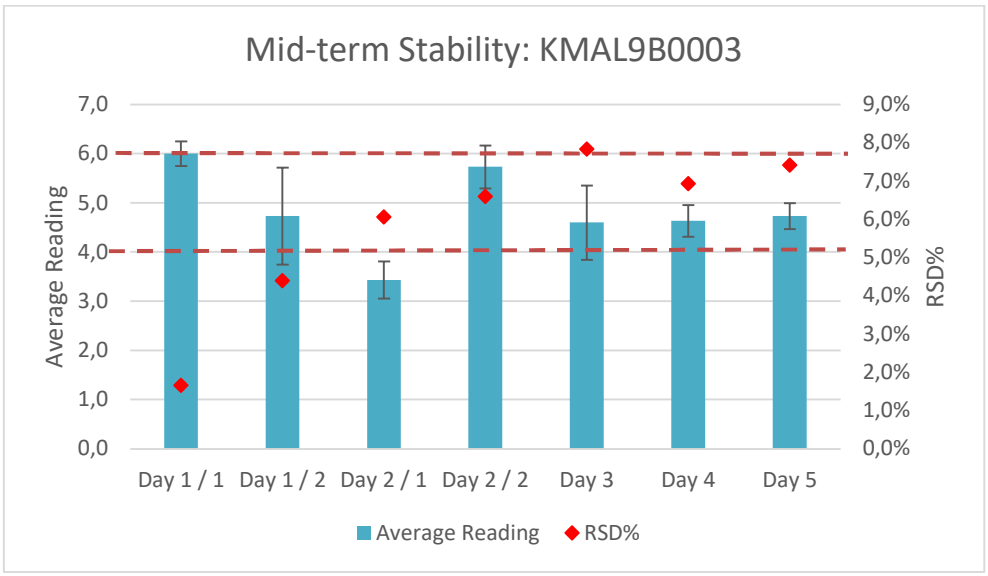
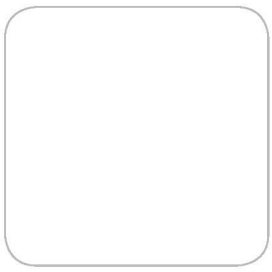
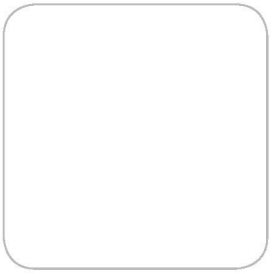


Figure 12: Graphical presentation of results from the mid-term stability study of Ketoscan mini, S/N KMAL9B0003.

Table 9: Tabular presentation of the Bias (absolute and relative deviation) of the masurements of the 5 ppm acetone standard

KMAL9B003	Bias (ppm)	Rel. Bias (%)	RSD%
Day 1 / 1	1.0	20%	1.7%
Day 1 / 2	-0.3	5%	4.4%
Day 2 / 1	-1.6	31%	6.1%
Day 2 / 2	0.7	15%	6.6%
Day 3	-0.4	8%	7.8%
Day 4	-0.4	7%	6.9%
Day 5	-0.3	5%	7.4%
Average:	**0.7**	**13%**	**6%**



Instrument 4: KMAL9B0004

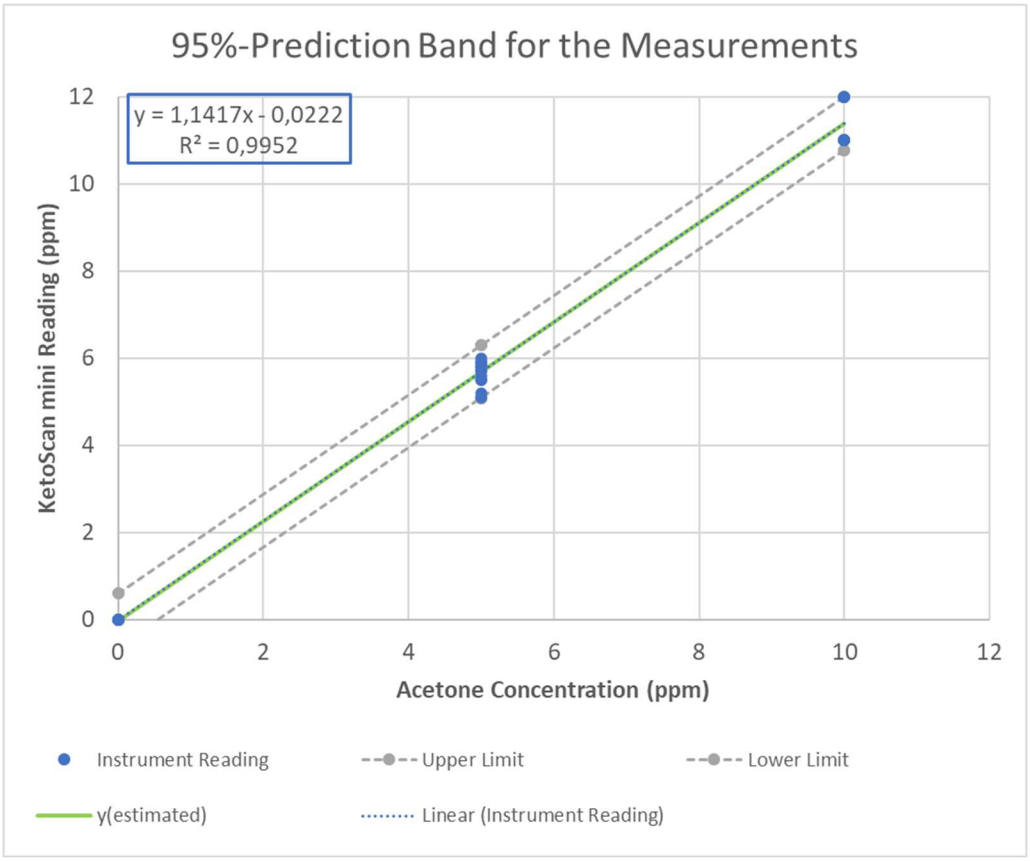


Figure 13: Graphical presentation of results from the accuracy check of Ketoscan mini, S/N KMAL9B0004. The dotted lines represent the prediction interval or prediction band for individual measurements.

Table 10: Summary of the results for the Ketoscan mini ketosis measurement device: individual test and overall results.

Parameter	1st Test	2nd Test	3rd Test	4th Test	Overall
Slope	1.167	1.100	1.167	1.133	1.142
Intercept	0.011	0.067	-0.189	0.022	-0.022
Coeff. of Determin. R^2	0.9965	0.9991	0.9932	0.9964	0.9952
No. of Measurments, n	9	9	9	9	36
Residual standard deviation s_y [ppm]					0.334
Standard deviation of the method s_{x0} [ppm]					0.293
Variation coefficient of the method V_{x0} [%]					5.9

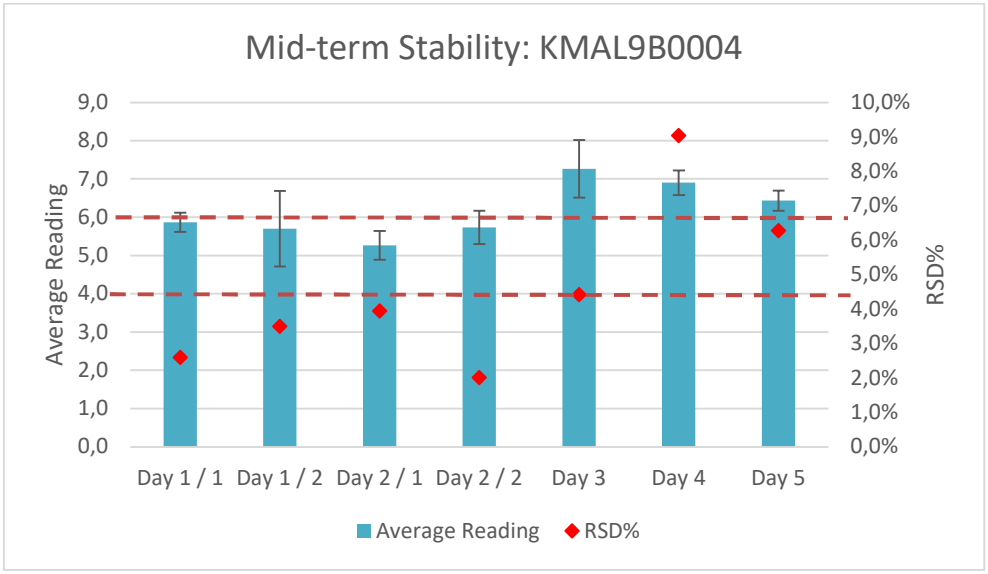


Figure 14: Graphical presentation of results from the mid-term stability study of Ketoscan mini, S/N KMAL9B0004

Table 11: Tabular presentation of the Bias (absolute and relative deviation) of the masurements of the 5 ppm acetone standard

KMAL9B004	Bias (ppm)	Rel. Bias (%)	RSD%
Day 1 / 1	0.9	17%	2.6%
Day 1 / 2	0.7	14%	3.5%
Day 2 / 1	0.3	5%	4.0%
Day 2 / 2	0.7	15%	2.0%
Day 3	2.3	45%	4.4%
Day 4	1.9	38%	9.1%
Day 5	1.4	29%	6.3%
Average:	**1.2**	**23%**	**5%**

Instrument 5: KMAL9B0005

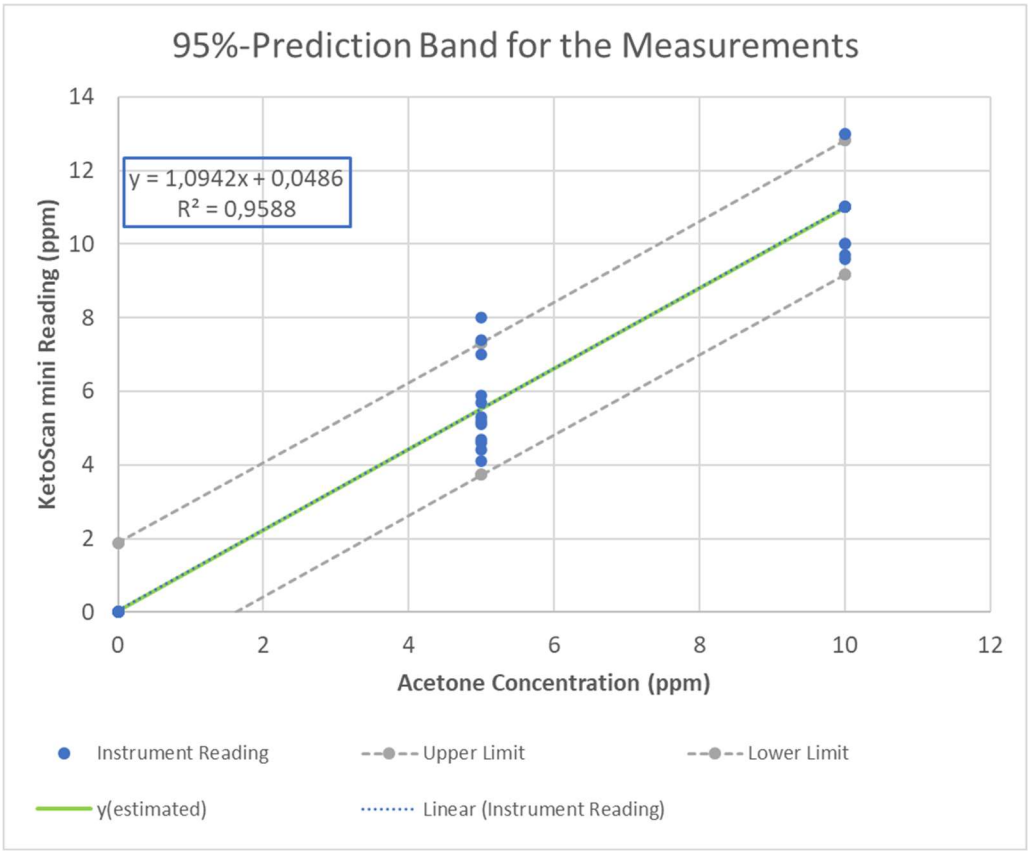


Figure 15: Graphical presentation of results from the accuracy check of Ketoscan mini, S/N KMAL9B0005. The dotted lines represent the prediction interval or prediction band for individual measurements.

Table 12: Summary of the results for the Ketoscan mini ketosis measurement device: individual test and overall results.

Parameter	1st Test	2nd Test	3rd Test	4th Test	Overall
Slope	1.100	1.233	1.020	1.023	1.094
Intercept	0.66	-0.18	-0.21	-0.07	0.05
Coeff. of Determin. R^2	0.9566	0.9852	0.9870	0.9912	0.9588
No. of Measurments. n	9	9	9	9	36
Residual standard deviation s_y [ppm]					0.952
Standard deviation of the method s_{x0} [ppm]					0.870
Variation coefficient of the method V_{x0} [%]					17.4

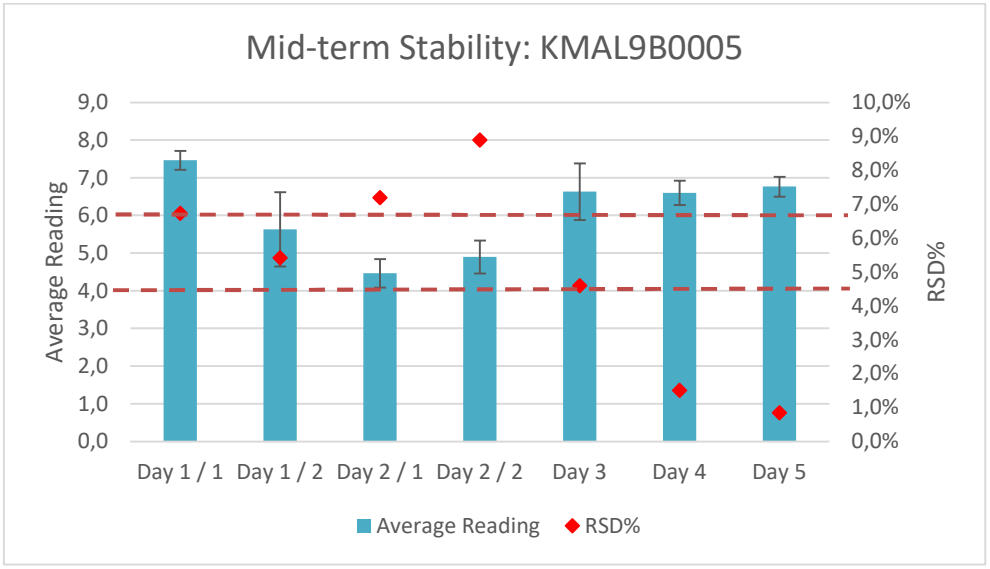
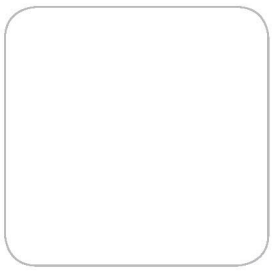
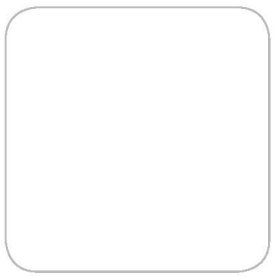


Figure 16: Graphical presentation of results from the mid-term stability study of Ketoscan mini, S/N KMAL9B0005.

Table 13: Tabular presentation of the Bias (absolute and relative deviation) of the masurements of the 5 ppm acetone standard

KMAL9B005	Bias (ppm)	Rel. Bias (%)	RSD%
Day 1 / 1	2.5	49%	6.7%
Day 1 / 2	0.6	13%	5.4%
Day 2 / 1	-0.5	11%	7.2%
Day 2 / 2	-0.1	2%	8.9%
Day 3	1.6	33%	4.6%
Day 4	1.6	32%	1.5%
Day 5	1.8	35%	0.9%
Average:	**1.2**	**25%**	**5%**



Instrument 6: KMAL9B0006

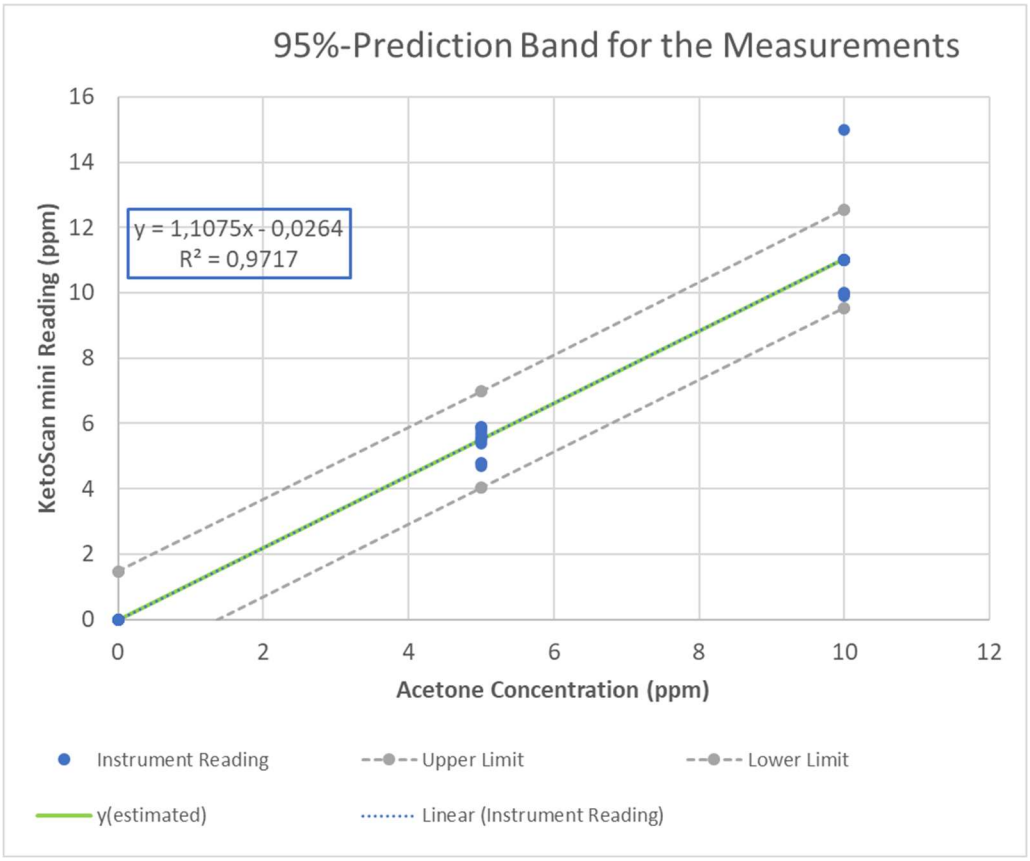


Figure 17: Graphical presentation of results from the accuracy check of Ketoscan mini, S/N KMAL9B0006. The dotted lines represent the prediction interval or prediction band for individual measurements.

Table 14: Summary of the results for the Ketoscan mini ketosis measurement device: individual test and overall results.

Parameter	1st Test	2nd Test	3rd Test	4th Test	Overall
Slope	1.063	1.233	1.033	1.100	1.108
Intercept	0.183	-0.189	-0.067	-0.033	-0.03
Coeff. of Determin. R^2	0.9917	0.9527	0.9936	0.9965	0.9717
No. of Measurments, n	9	9	9	9	36
Residual standard deviation s_y [ppm]					0.952
Standard deviation of the method s_{x0} [ppm]					0.870
Variation coefficient of the method V_{x0} [%]					14.3

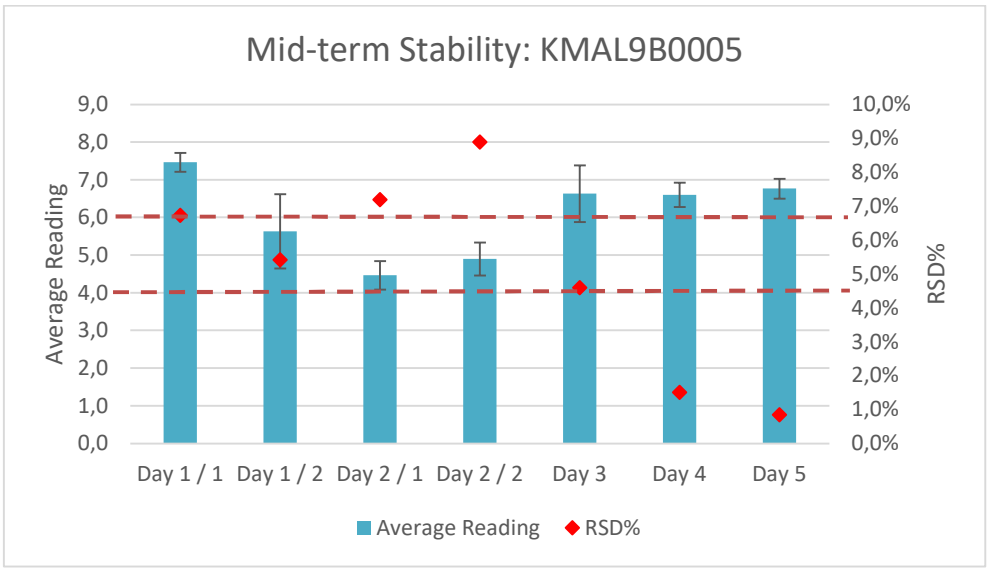
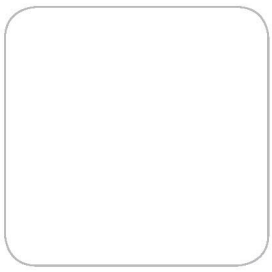
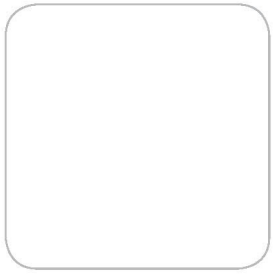


Figure 18: Graphical presentation of results from the mid-term stability study of Ketoscan mini, S/N KMAL9B0005.

Table 15: Tabular presentation of the Bias (absolute and relative deviation) of the masurements of the 5 ppm acetone standard

KMAL9B006	Bias (ppm)	Rel. Bias (%)	RSD%
Day 1 / 1	0.9	17%	1.0%
Day 1 / 2	0.6	12%	1.8%
Day 2 / 1	0.0	1%	7.6%
Day 2 / 2	0.4	8%	10.3%
Day 3	1.4	29%	12.5%
Day 4	1.6	31%	0.9%
Day 5	1.3	25%	5.1%
Average:	**0.9**	**18%**	**6%**



Instrument 7: KMAM1F0001

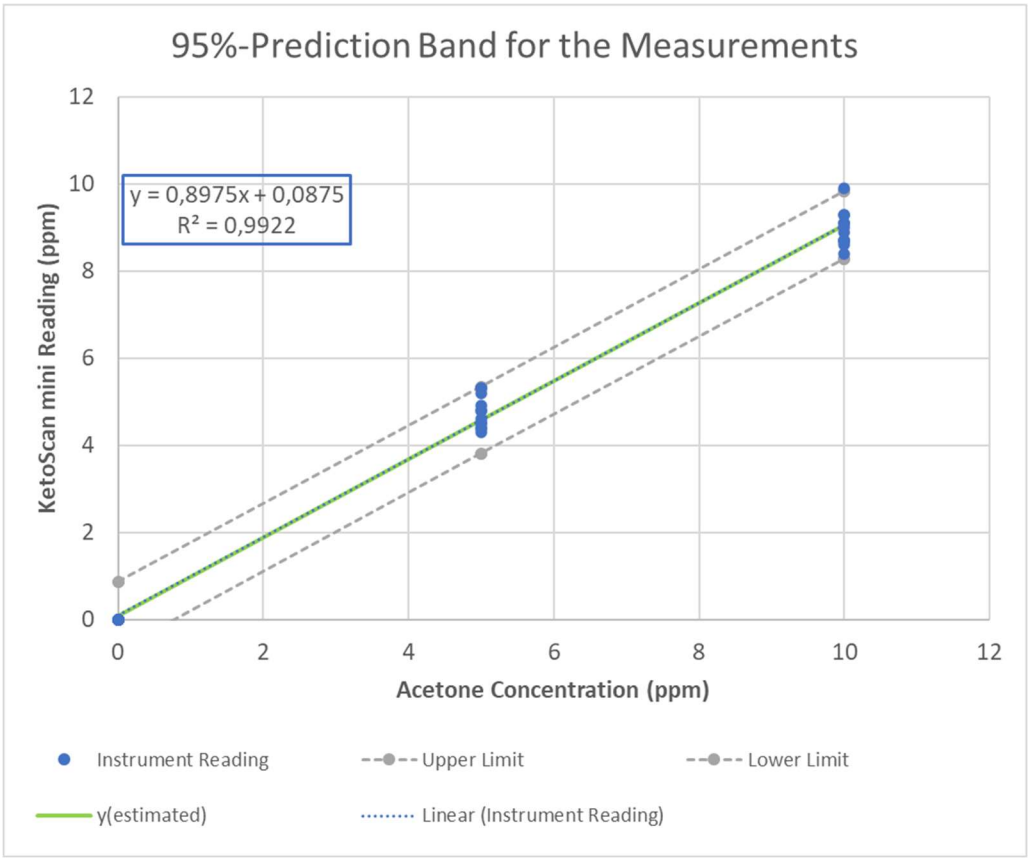


Figure 19: Graphical presentation of results from the accuracy check of Ketoscan mini, S/N KMAM1F0001. The dotted lines represent the prediction interval or prediction band for individual measurements.

Table 16: Summary of the results for the Ketoscan mini ketosis measurement device: individual test and overall results.

Parameter	1st Test	2nd Test	3rd Test	4th Test	Overall
Slope	0.900	0.900	0.887	0.903	0.898
Intercept	0.256	0.000	0.078	0.017	0.088
Coeff. of Determin. R^2	0.9803	0.9997	0.9958	0.9969	0.9922
No. of Measurments, n	9	9	9	9	36
Residual standard deviation s_y [ppm]					0.334
Standard deviation of the method s_{x0} [ppm]					0.372
Variation coefficient of the method V_{x0} [%]					7.4

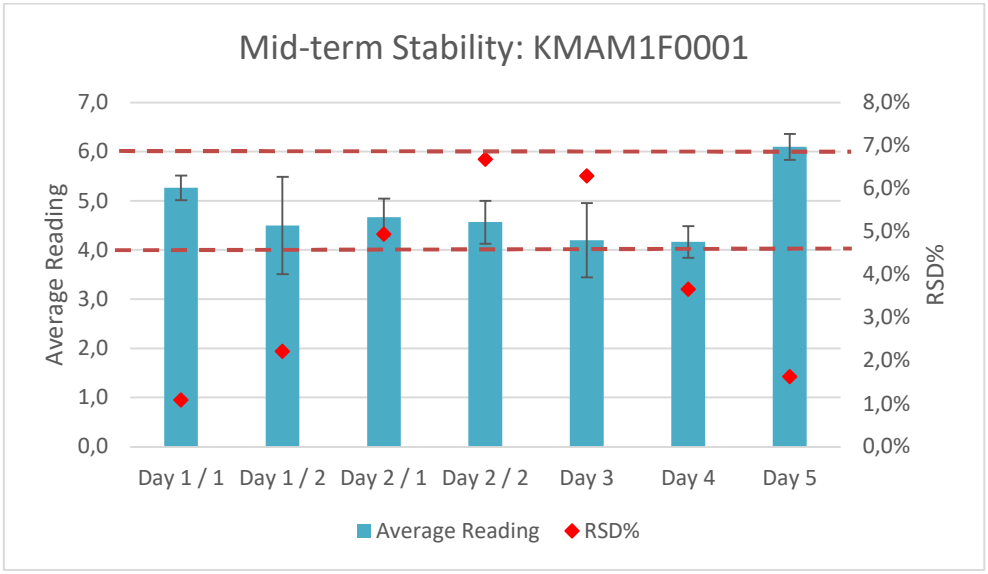


Figure 20: Graphical presentation of results from the mid-term stability study of Ketoscan mini, S/N KMAL9B0005.

Table 17: Tabular presentation of the Bias (absolute and relative deviation) of the masurements of the 5 ppm acetone standard

KMAM1F0001	Bias (ppm)	Rel. Bias (%)	RSD%
Day 1 / 1	0.3	5%	1.1%
Day 1 / 2	-0.5	10%	2.2%
Day 2 / 1	-0.3	7%	4.9%
Day 2 / 2	-0.4	9%	6.7%
Day 3	-0.8	16%	6.3%
Day 4	-0.8	17%	3.7%
Day 5	1.1	22%	1.6%
Average:	**0.6**	**12%**	**4%**

Instrument 8: KMAM1F0002

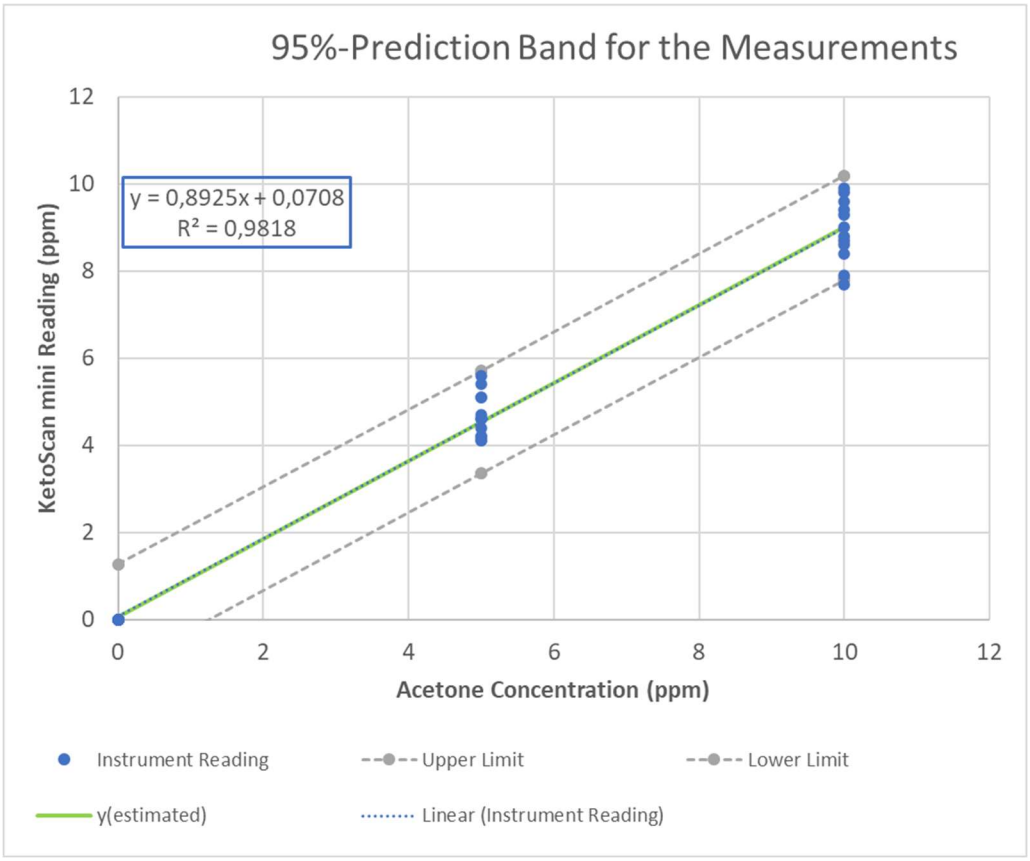


Figure 21: Graphical presentation of results from the accuracy check of Ketoscan mini, S/N KMAM1F0002. The dotted lines represent the prediction interval or prediction band for individual measurements.

Table 18: Summary of the results for the Ketoscan mini ketosis measurement device: individual test and overall results.

Parameter	1st Test	2nd Test	3rd Test	4th Test	Overall
Slope	0.943	0.923	0.830	0.873	0.893
Intercept	0.161	-0.094	0.250	-0.033	0.071
Coeff. of Determin. R^2	0.9883	0.9944	0.9679	0.9967	0.9818
No. of Measurments, n	9	9	9	9	36
Residual standard deviation s_y [ppm]					0.510
Standard deviation of the method s_{x0} [ppm]					0.572
Variation coefficient of the method V_{x0} [%]					11.4

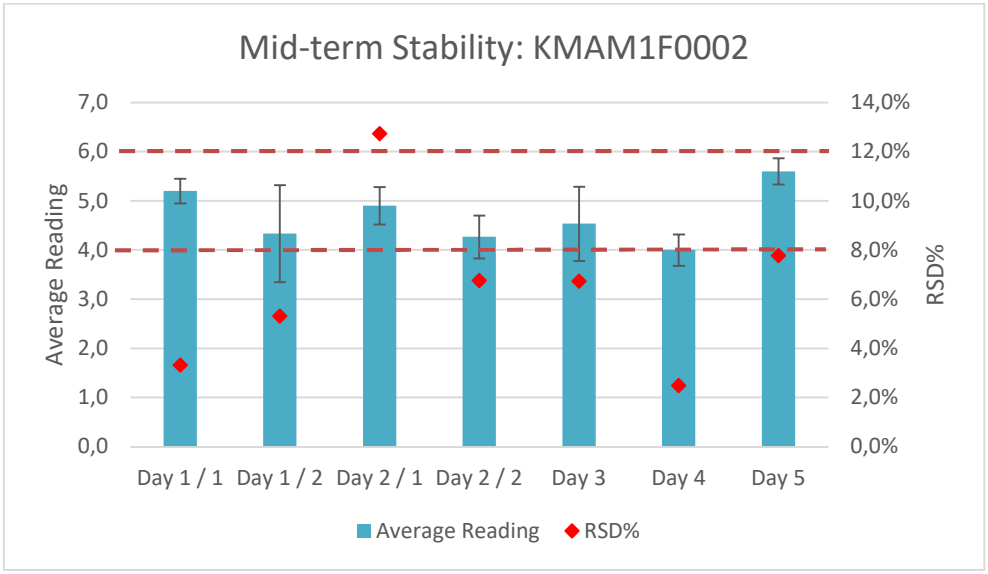


Figure 22: Graphical presentation of results from the mid-term stability study of Ketoscan mini, S/N KMAM1F0002.

Table 19: Tabular presentation of the Bias (absolute and relative deviation) of the masurements of the 5 ppm acetone standard

KMAM1F0002	Bias (ppm)	Rel. Bias (%)	RSD%
Day 1 / 1	0.2	4%	3.3%
Day 1 / 2	-0.7	13%	5.3%
Day 2 / 1	-0.1	2%	12.7%
Day 2 / 2	-0.7	15%	6.8%
Day 3	-0.5	9%	6.7%
Day 4	-1.0	20%	2.5%
Day 5	0.6	12%	7.8%
Average:	**0.5**	**11%**	**6%**

Instrument 9: KMAL9B0009

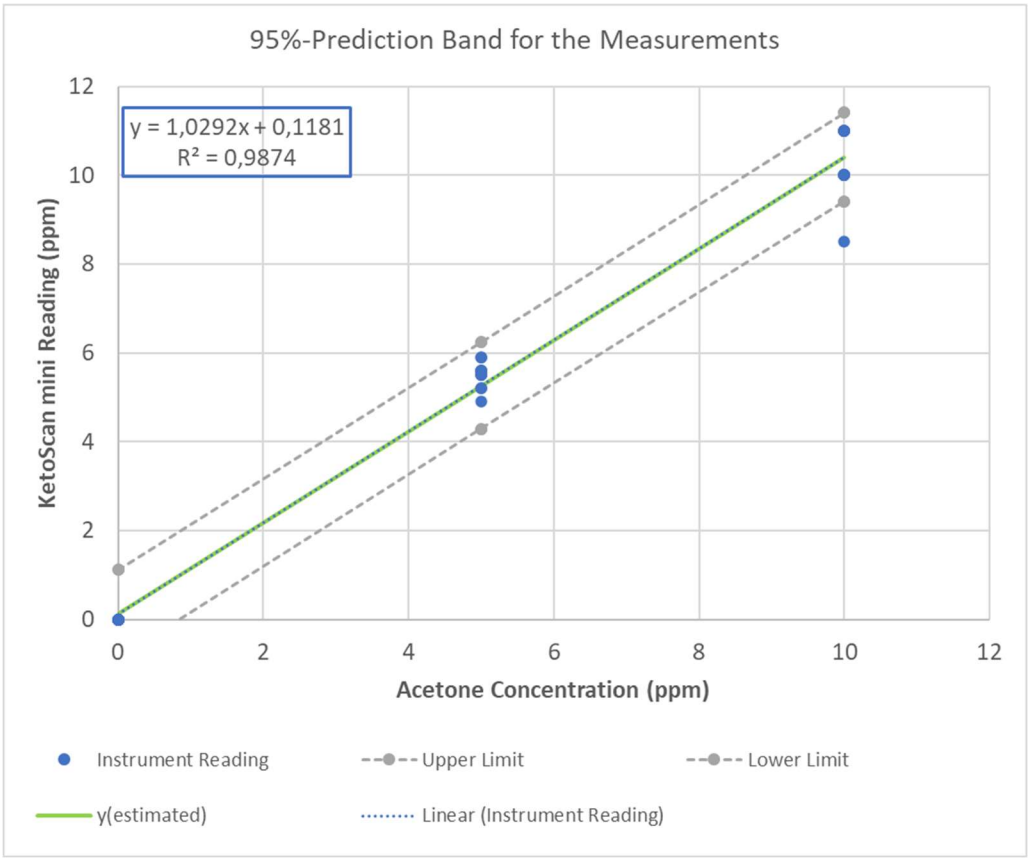


Figure 23: Graphical presentation of results from the accuracy check of Ketoscan mini, S/N KMAL9B0009. The dotted lines represent the prediction interval or prediction band for individual measurements.

Table 20: Summary of the results for the Ketoscan mini ketosis measurement device: individual test and overall results.

Parameter	1st Test	2nd Test	3rd Test	4th Test	Overall
Slope	1.033	1.067	0.950	1.067	1.029
Intercept	0.089	-0.011	0.272	0.122	0.118
Coeff. of Determin. R^2	0.9944	0.9947	0.9778	0.9942	0.9874
No. of Measurments, n	9	9	9	9	36
Residual standard deviation s_y [ppm]					0.489
Standard deviation of the method s_{x0} [ppm]					0.475
Variation coefficient of the method V_{x0} [%]					9.5

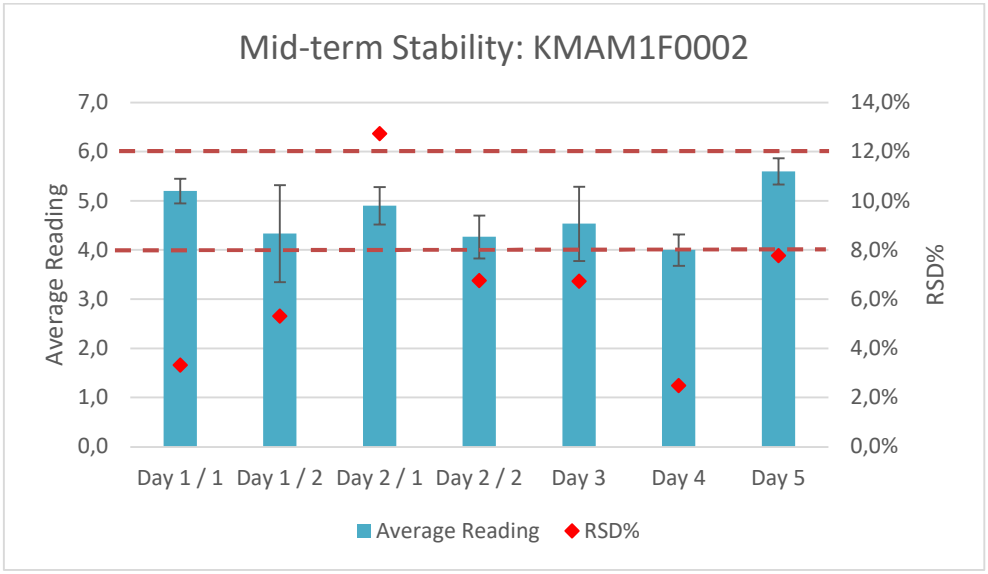


Figure 24: Graphical presentation of results from the mid-term stability study of Ketoscan mini, S/N KMAM1F0002.

Table 21: Tabular presentation of the Bias (absolute and relative deviation) of the masurements of the 5 ppm acetone standard

KMAM1F0002	Bias (ppm)	Rel. Bias (%)	RSD%
Day 1 / 1	0.2	4%	3.3%
Day 1 / 2	-0.7	13%	5.3%
Day 2 / 1	-0.1	2%	12.7%
Day 2 / 2	-0.7	15%	6.8%
Day 3	-0.5	9%	6.7%
Day 4	-1.0	20%	2.5%
Day 5	0.6	12%	7.8%
Average:	**0.5**	**11%**	**6%**

Instrument 10: KMAL9B0010

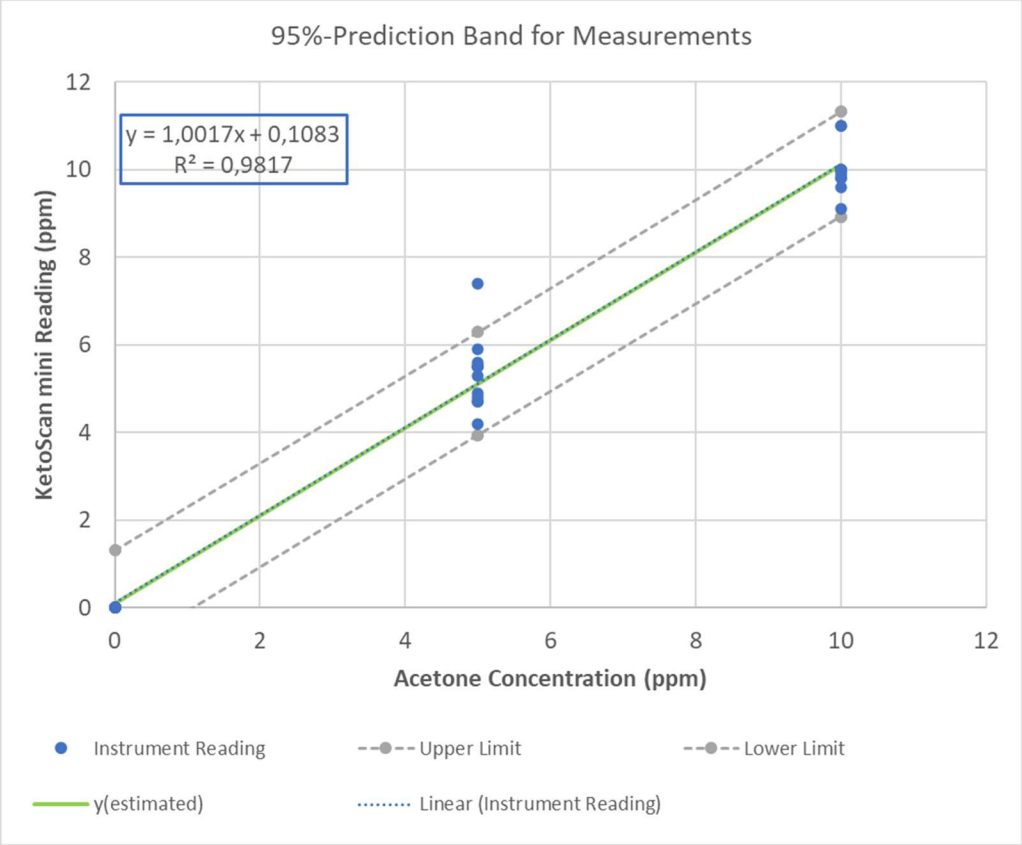


Figure 25: Graphical presentation of results from the accuracy check of Ketoscan mini, S/N KMAL9B0010. The dotted lines represent the prediction interval or prediction band for individual measurements.

Table 22: Summary of the results for the Ketoscan mini ketosis measurement device: individual test and overall results.

Parameter	1st Test	2nd Test	3rd Test	4th Test	Overall
Slope	1.000	1.067	0.953	0.987	1.002
Intercept	0.078	0.267	-0.011	0.100	0.108
Coeff. of Determin. R^2	0.9980	0.9751	0.9975	0.9875	0.9817
No. of Measurments, n	9	9	9	9	36
Residual standard deviation s_y [ppm]					0.574
Standard deviation of the method s_{x0} [ppm]					0.573
Variation coefficient of the method V_{x0} [%]					11.5

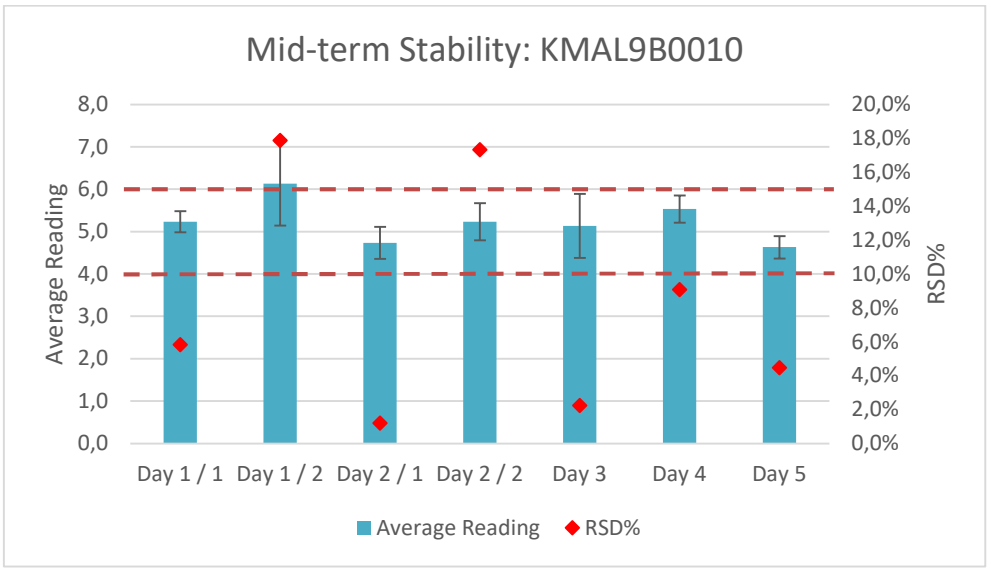
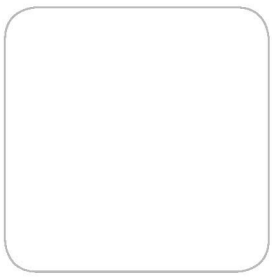
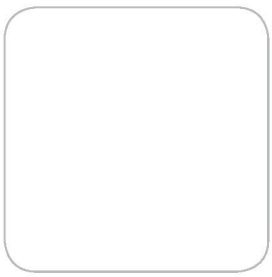
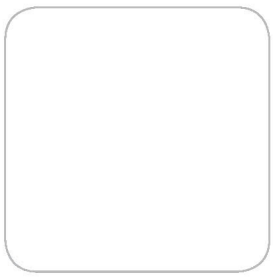


Figure 26: Graphical presentation of results from the mid-term stability study of Ketoscan mini, S/N KMAL9B0010.

Table 23: Tabular presentation of the Bias (absolute and relative deviation) of the masurements of the 5 ppm acetone standard

KMAL9B0010	Bias (ppm)	Rel. Bias (%)	RSD%
Day 1 / 1	0.2	5%	5.8%
Day 1 / 2	1.1	23%	17.9%
Day 2 / 1	-0.3	5%	1.2%
Day 2 / 2	0.2	5%	17.3%
Day 3	0.1	3%	2.2%
Day 4	0.5	11%	9.1%
Day 5	-0.4	7%	4.5%
Average:	0.4	8%	8%


5 Summary and Conclusion

In order to provide an overview of and to summarize the measurements that were performed, a cumulative evaluation of the ten instruments tested shall be given in the following.

The first graphical presentation (Figure 27) demonstrates the uniformity of response, given in the form of the regression parameters (slope and intercept of the recovery functions). The blue bars, representing the slope in this graph, should be close to 1,00 = 100%, and to support the assessment, guiding lines at 100±10% have been plotted as orange hatched lines into the graph. It is seen that 6 out of 10 instruments fall within the accuracy range of target value 100±10%, while the four other instruments do not and deviate by 10 to almost 20%.

The intercept for 9 out of 10 measurement instruments is insignificant, and only in one case is somewhat (significantly) larger than zero. Since even under conditions of low ketosis, the breath acetone level would normally exceed 0.5 ppm, this should, however, be a minor concern.

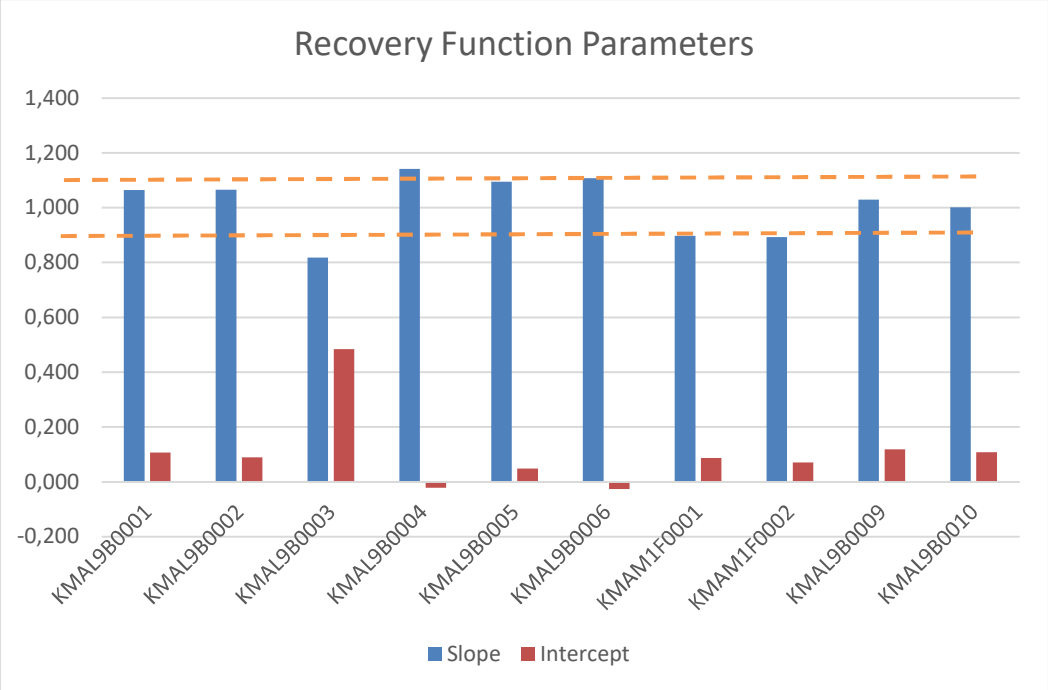


Figure 27: Graphical summary of the uniformity of response (comparability) of the ten Ketoscan mini instruments investigated: The blue bars represent the slope and thus the accuracy of the recovery. The orange lines denote an interval of ±10% around the target value of 100%. The red bars represent the intercept which ideally should be equal to zero.

As a further possibility of representing the accuracy of the Ketoscan mini devices, the variation coefficients of the method, V_{x0}, are reported together with the coefficents of determination R^2 for each instrument (Figure 28). It is seen that the variation coefficient and the coefficient of determination are inversely proportional.

Four out of the ten instruments tested have variation coefficients lower than 10% which is considered good. Four more instruments have variation coefficients between 10 and 20% which is considered acceptable. Two instruments exhibit variation coefficients exceedimg 20% which is considered less satisfactory.

The coefficient of determination exceeds 0.95 in eight out of 10 cases, and only in two cases is between 0.91 and 0.94.

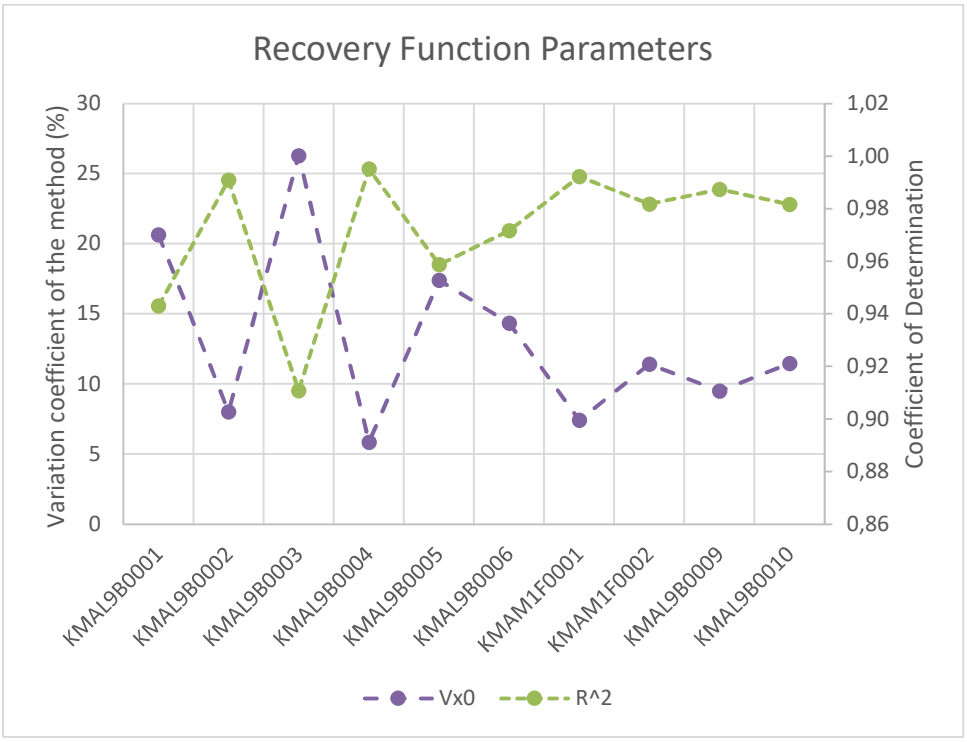


Figure 28: Graphical presentation and comparison of the variation coefficient of the method (V_{x0}) and the coefficient of determination R^2 for each individual measurement device.

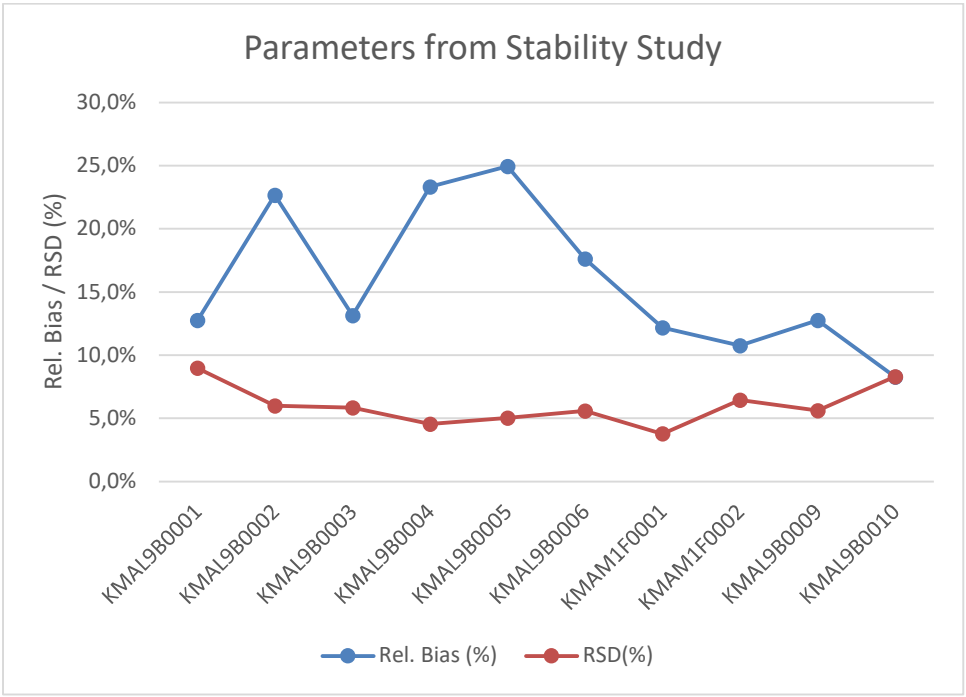


Figure 29: Relative Bias (%) and RSD% values for the repeated determination of a 5 ppm standard measured over the calibration lifecycle of the Ketoscan mini instrument (300 measurements). Values represent the average of seven measurement series with each *n* = 3 measurements.

In Figure 29, a summary of the stability of the Ketoscan mini instruments is given in the form of the relative bias (in %) and the relative standard deviation (RSD%), calculated as an average over the seven measurement series at the concentration level of 5 ppm, performed with each three measurements ($n = 3$) over the instruments' calibration lifecycle of 300 measurements.

While the relative standard deviation in all cases is below 10%, the relative bias exceeds 10% in all cases but one, and even exceeds 20% in three of the ten cases.

Note that the accuracy at this concentration level can be expressed as 100% - Relative Bias (%).

6 References

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