BIOMÉRIEUX

REF **422010**

050049 - 02 - 2018-12

EN

VIDAS® PTH (1-84) (PTH)

IVD

INTENDED USE

VIDAS® PTH (1-84) (PTH) is a third generation automated quantitative assay for use on the VIDAS® family of instruments, for the quantitative measurement of the biologically active parathyroid hormone PTH (1-84) in human serum or plasma using the ELFA (Enzyme Linked Fluorescent Assay) technique.

Used in conjunction with other laboratory findings and clinical assessments, this assay is intended for use as follows:

- As an aid in the diagnosis of hyper or hypoparathyroidism.
- As an aid for the monitoring of calcium homeostasis in patients with chronic kidney disease.

SUMMARY AND EXPLANATION

Parathyroid hormone (PTH) is the main hormone involved in calcium and phosphorus homeostasis. PTH is formed in the parathyroid glands (essentially four, located on the back of the thyroid gland) and secreted as an 84 amino-acid peptide [1-84 according to the universal numbering convention beginning with the N-terminus] when the extracellular calcium concentration decreases.

The main function of the PTH is to maintain the ionized calcium level within a narrow range by a powerful hypercalcemic effect, by stimulating calcium release from bone and distal tubular reabsorption of calcium by the kidney, and by increasing renal production of 1,25-dihydroxyvitamin D-3 (calcitriol) which stimulates intestinal calcium absorption.

PTH increases urine phosphate levels and decreases serum phosphate levels. PTH stimulates bone remodeling by mobilizing osteoblasts, thus justifying its use in osteoporosis treatment to reduce the risk of vertebral fractures.

The secretion of PTH is promoted by low calcium concentrations and high phosphate concentrations, and is inhibited by high calcium concentrations and low phosphate concentrations. It is also inhibited by calcitriol, PTH (7-84) fragment, and magnesium deficiency.

In the bloodstream, the half-life of PTH (1-84) does not exceed 4 minutes. PTH is rapidly degraded by the liver into non-(1-84) C-terminal fragments, essentially (7-84) and (53-84) with long half-lives, and which are eliminated by the kidneys. These fragments accumulate in the blood when the kidneys fail to function.

Parathyroid gland disorders lead to either hyperparathyroidism (primary, secondary or tertiary) or hypoparathyroidism. Apart from bone fragility[1] or nephrolithiasis, the associated symptoms may not be very specific, and asymptomatic parathyroid disorder may be unexpectedly detected during a routine blood test[2].

This biological assay contributes in determining a patient's status regarding the function of the parathyroid glands as normal or hyper- or hypoparathyroidism, when interpreted with other biological parameters (such as calcium, phosphate, vitamin D) and clinical signs.

PTH measurement is indicated when performing a differential diagnosis for hypercalcemia or hypocalcemia. It enables the diagnosis of primary or secondary hyperparathyroidism[3], and the diagnosis of hypoparathyroidism[4] mainly after parathyroid surgery. It is also prescribed for patients with chronic kidney disease, in particular in the follow-up of dialysis patients[5].

In case of kidney failure, medical monitoring is guided by the KDOQI (Kidney Disease Outcomes Quality Initiative) and KDIGO (Kidney Disease Improving Global Outcomes) recommendations.

In non-kidney disorders, PTH levels in blood are one of the results of routine biological tests investigated by a healthcare specialist (for example: Endocrinology, Rheumatology, Geriatrics, Metabolic Diseases).

PRINCIPLE

The assay principle combines a 2-step sandwich enzyme immunoassay method with a final fluorescence detection (ELFA). VIDAS® PTH (1-84) is a third generation assay traced to the WHO International Standard for Parathyroid Hormone 1-84, recombinant, coded 95/646.

The single-use Solid Phase Receptacle (SPR) serves as the solid phase as well as the pipetting device. Reagents for the assay are ready-to-use and pre-dispensed in the sealed single-use reagent strips.

All of the assay steps are performed automatically by the instrument. The reaction medium is cycled in and out of the SPR several times.

The sample is collected and then diluted in a suitable diluent. The mixture is cycled in and out of the SPR several times. This operation enables PTH to bind with the capture antibodies fixed to the interior wall of the SPR. Unbound components are eliminated during washing steps.

The conjugate mixture is cycled in and out of the SPR several times. This operation enables the conjugate to bind with the immune complexes that are fixed to the interior wall of the SPR and to form a sandwich. Unbound components are eliminated during washing steps.

During the final detection step, the substrate (4-Methyl-umbelliferyl phosphate) is cycled in and out of the SPR. The conjugate enzyme catalyzes the hydrolysis of this substrate into a fluorescent product (4-Methyl-umbelliferone), the fluorescence of which is measured at 450 nm. The intensity of the fluorescence is proportional to the concentration of PTH in the sample.

At the end of the assay, the results are automatically calculated and reported in pg/mL by the instrument according to the calibration curve stored in memory. The results can then be printed out.

CONTENT OF THE KIT (30 TESTS)

30 PTH Strips	STR	Ready-to-use.
30 PTH Solid Phase Receptacles (SPR) 1 x 30	SPR	Ready-to-use. Interior of SPR coated with mouse monoclonal anti-PTH immunoglobulins (specific to the N-terminal (1-6) fragment).
PTH Calibrator 1 x 4.4 mL (liquid)	S1	Ready-to-use. Buffer containing recombinant PTH (1-84) + Stabilizer of animal origin + preservative. MLE (Master Lot Entry) data indicate the acceptable range in "Relative Fluorescence Value" ("Calibrator (S1) RFV Range").
PTH Control 1 x 2.3 mL (liquid)	C1	Ready-to-use. Buffer containing recombinant PTH (1-84) + Stabilizer of animal origin + preservative. MLE data indicate the acceptable range in pg/mL ("Control C1 Dose Value Range").
Specifications for the factory master data required to calibrate the assay: MLE barcode printed on the box label.		
1 package insert provided in the kit or downloadable from www.biomerieux.com/techlib.		

SPR
The interior of the SPR is coated during production with mouse monoclonal anti-PTH N-ter (1-6) fragment immunoglobulins. Each SPR is identified by the "PTH" code.

Only remove the required number of Solid Phase Receptacles (SPR) from the pouch and carefully reseal the pouch after opening.

Reagent Strip
The strip consists of 10 wells covered with a labeled foil seal. The label comprises a bar code which mainly indicates the assay code, kit lot number and expiration date. The foil of the first well is perforated to facilitate the introduction of the sample. The last well of each strip is a cuvette in which the fluorometric reading is performed. The wells in the center section of the strip contain the various reagents required for the assay.

Description of the VIDAS® PTH (1-84) (PTH) strip

Well	Reagents
1	Sample well: dispense 300 µL of calibrator, control, or sample.
2	Sample diluent: Buffer + Protein stabilizer of animal origin + preservative (300 µL).
3	Empty well.
4 - 5	Wash buffers: Buffer + preservative (600 µL).
6	Conjugate: Buffer containing anti-(7-84) PTH antibodies + Stabilizer of animal origin + preservative (400 µL).
7 - 8	Wash buffers: Buffer + preservative (600 µL).
9	Empty well.

Well	Reagents
10	Reading cuvette with substrate: 4-Methyl-umbelliferyl phosphate (0.6 mmol/L) + diethanolamine (DEA*) (0.62 mol/L or 6.6%, pH 9.2) + 1 g/L sodium azide (300 µL).

*Signal word: **DANGER**

Hazard statements
- H318: Causes serious eye damage.

Precautionary statements
- P280: Wear protective gloves/protective clothing/eye protection/face protection.
- P305 + P351 + P338: IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.

For further information, consult the Safety Data Sheet.

MATERIALS AND DISPOSABLES REQUIRED BUT NOT PROVIDED
- Single-use pipette and/or micropipettes to dispense the appropriate volumes.
- Powderless disposable gloves.
- For other specific materials and disposables, please refer to the Instrument User Manual.
- Instruments of the VIDAS® family: VIDAS®, MINI VIDAS® or VIDAS® 3.

WARNINGS AND PRECAUTIONS
- **For *in vitro* diagnostic use only.**
- **For professional use only, by qualified laboratory personnel, in clinical laboratories.**
- This kit does not contain products of human origin.
- This kit contains products of animal origin. Certified knowledge of the origin and/or sanitary state of the animals does not totally guarantee the absence of transmissible pathogenic agents. It is therefore recommended that these products be treated as potentially infectious, and handled observing the usual safety precautions (do not ingest; do not inhale).
- Handle all patient specimens as potentially infectious material and follow the usual safety precautions.
- Although the PTH (1-84) recombinant proteins present in the S1 Calibrator and C1 Control are inactive, handle the tubes as potentially infectious products.
- Do not use the Solid Phase Receptacles (SPR) if the pouch is pierced or if the dot sealing a SPR has come unstuck.
- Do not use visibly deteriorated STRs (damaged foil or plastic).
- Do not use reagents after the expiration date indicated on the box label.
- Do not mix reagents (or disposables) from different lots.
- VIDAS® PTH (1-84) assay reagents are only for use with the instruments of the VIDAS® family.
- Use powderless gloves, as powder has been reported to cause false results for certain enzyme immunoassay tests.
- Kit reagents contain sodium azide which can react with lead or copper plumbing to form explosive metal azides. If any liquid containing sodium azide is disposed of in the plumbing system, drains should be flushed with water to avoid build-up.
- The substrate in well 10 contains an irritant agent (diethanolamine 6.6%). Refer to the hazard statements “H” and precautionary statements “P” indicated above.
- Spills should be wiped up thoroughly after treatment with liquid detergent or a solution of household bleach containing at least 0.5% sodium hypochlorite. See the User Manual for cleaning spills on or in the instrument. Do not autoclave solutions containing bleach.
- The instrument should be regularly cleaned and decontaminated (refer to the User Manual for user and preventive maintenance operations).

STORAGE CONDITIONS
- Store the VIDAS® PTH (1-84) kit at +2°C/+8°C.
- **Do not freeze reagents.**
- **Store all unused reagents at +2°C/+8°C.**
- After opening the kit, check that the SPR pouch is correctly sealed and undamaged. If not, do not use the Solid Phase Receptacles (SPR).

- **After use, carefully reseal the pouch with the desiccant inside to maintain stability of the Solid Phase Receptacles (SPR), and return the complete kit to +2°C/+8°C.**
- If stored according to the recommended conditions, all components are stable until the expiration date indicated on the box label.

SAMPLES

Sample type and collection

Human serum or plasma.

Types of tubes validated:

- Plastic tube with clot activator
- Plastic tube with clot activator and separation gel
- Plastic tube with lithium heparin
- Plastic EDTA tube

It is recommended to validate collection tubes before use as some contain substances which interfere with test results.

Note: Blood sampling tube results may vary from one manufacturer to another depending on the materials and additives used.

It is the responsibility of each laboratory to validate the type of sample tube used and to follow the manufacturer's recommendations for use.

Sample Preparation

The current WHO/DIL/LAB/99.1 document provides recommendations for sample preparation. (6)

For use of sample tubes, refer to the tube manufacturer's recommendations for use.

The pre-analytical step, including the preparation of blood samples, is an essential first step when performing medical analyses. In accordance with Good Laboratory Practice, this step is performed under the responsibility of the laboratory manager.

Insufficient clot time can result in the formation of fibrin with micro-clots that are invisible to the naked eye. The presence of fibrin, red blood cells, or suspended particles can lead to erroneous results.

Samples containing suspended fibrin particles or erythrocyte stroma should be centrifuged before testing.

For serum samples, ensure that complete clot formation has taken place prior to centrifugation. Some specimens, especially those from patients receiving anticoagulant or thrombolytic therapy, may exhibit increased clotting times.

Sample stability

Samples (serum and plasma) can be stored in closed primary tubes at +18°C/+25°C for up to 8 hours and at +2°C/+8°C for up to 48 hours. If longer storage is required, freeze the serum or plasma at -19°C/-31°C.

A study performed on samples frozen for 6 months at -19°C/-31°C showed that the quality of results is not affected. Three freeze/thaw cycles were validated.

Sample-related interference

None of the following factors have been found to significantly influence this assay:

- hemolysis (after spiking samples with hemoglobin, up to 5 g/L (monomer)),
- lipemia (after spiking samples with lipids, up to 30 g/L equivalent in triglycerides),
- bilirubinemia (after spiking samples with bilirubin, up to 0.3 g/L).

It is recommended not to use hemolyzed, lipemic, icteric samples, and, if possible, to collect a new sample.

Refer to the section **PERFORMANCE – Study of drugs and other potentially interfering substances** for the compounds tested.

INSTRUCTIONS FOR USE

For complete instructions, see the Instrument User Manual.

Reading VIDAS® PTC (Protocol Test Change) data and MLE data

When using the assay for the first time:

With the external instrument barcode reader, **scan the barcodes (PTC and MLE) in the following order**:

1. According to the instrument used, scan the PTC barcode(s) downloadable from www.biomerieux.com/techlib. This reading allows VIDAS® PTC protocol data to be transferred to the instrument software for its update.
2. Scan the MLE data on the box label.

When opening a new lot of reagents:

With the external instrument barcode reader, scan the MLE data on the box label before performing the test.

Note: The master lot data need only be entered once for each lot.

It is possible to enter MLE data **manually or automatically** depending on the instrument (refer to the User Manual).

Calibration

The calibrator is traceable to the WHO International Standard 95/646 for PTH (1-84).[7]

Calibration, using the Calibrator provided in the kit, must be performed each time a new lot of reagents is opened, after the MLE data have been entered, and then every **84 days**. This operation provides instrument-specific calibration curves and compensates for possible minor variations in assay signal throughout the shelf-life of the kit.

The Calibrator identified by S1 must be tested in **duplicate** (refer to the User Manual). The Calibrator value must be within the set RFV (Relative Fluorescence Value) range. If this is not the case, recalibrate using S1.

Caution: The assay Calibrator (S1) and Control (C1) are ready-to-use reagents made liquid by the addition of a tension-active stabilizer. When pipetting the 300 µL calibration and calibration control portion, make sure that the entire 300 µL volume is dispensed out of the pipet tip.

Kit controls

One Control is included in each VIDAS® PTH (1-84) (PTH) kit. This Control must be performed immediately after opening a new kit to ensure that reagent performance has not been altered.

Each calibration must also be checked using this Control. The instrument will only be able to check the control value if it is identified by C1.

Results cannot be validated if the control value deviates from the expected values.

Note: The aim of the VIDAS® PTH (1-84) Quality Control (C1) is to validate calibrations. The use of the VIDAS® PTH (1-84) Quality Control (C1) as an Internal Quality Control is under the customer's responsibility.

Procedure

1. **Remove the kit from storage at +2°C/+8°C and take out the required reagents. Carefully reseal the SPR pouch and return the kit to +2°C/+8°C. The reagents can be used immediately.**
2. Use one "PTH" strip and one "PTH" SPR for each sample, control, or calibrator to be tested. Make sure the SPR pouch has been carefully resealed after the required Solid Phase Receptacles have been removed.
3. The test is identified by the "PTH" code on the instrument. The calibrator must be identified by "S1" and tested in duplicate. The control identified by "C1" must be tested singly.
4. Mix the calibrator, control, and samples using a vortex-type mixer (for serum or plasma separated from the pellet).
5. For optimal results, refer to all the paragraphs in the **SAMPLES** section.
6. Before pipetting, ensure that the samples, calibrator, control, and diluent are free of bubbles.
7. **For this test, the calibrator, control, and sample test portion is 300 µL.**
8. Insert the "PTH" Solid Phase Receptacles and "PTH" strips into the instrument. Check to make sure that the color labels with the assay code on the Solid Phase Receptacles and the Reagent Strips match.
9. Initiate the assay as directed in the User Manual. All the assay steps are performed automatically by the instrument.
10. Reclose the vials and return them to the required temperature after pipetting.
11. The assay will be completed within approximately **24 minutes**. After the assay is completed, remove the Solid Phase Receptacles (SPR) and strips from the instrument.
12. Dispose of the used Solid Phase Receptacles (SPR) and strips into an appropriate recipient.

QUALITY CONTROL

Additional quality controls can be performed in accordance with local regulations or requirements related to accreditation, as well as requirements defined in the laboratory's quality control procedure.

Note: It is the responsibility of the user to perform Quality Control in accordance with any applicable local regulations.

RESULTS AND INTERPRETATION

Once the assay is completed, results are analyzed automatically by the computer. Fluorescence is measured twice in the Reagent Strip's reading cuvette for each sample tested. The first reading is a background reading of the substrate cuvette before the SPR is introduced into the substrate.

The second reading is taken after incubating the substrate with the enzyme bound to the interior of the SPR. The RFV (Relative Fluorescence Value) is calculated by subtracting the background reading from the final result. This calculation appears on the result sheet.

The results are automatically calculated by the instrument using calibration curves which are stored by the instrument (predefined mathematical model) and are expressed as pg/mL.

Interpretation of test results should be made taking into consideration the patient's clinical history, and the results of any other tests performed.

The instrument displays the VIDAS® PTH (1-84) (PTH) assay results from 4.0 to 1500.0 pg/mL.

Sample dilution
Samples with VIDAS® PTH (1-84) concentrations greater than 1500.0 pg/mL must be retested after 1/2 dilution (dilution factor = 2) in saline solution (1 volume of sample + 1 volume of saline solution) in order to obtain a result within the measurement range.

The dilution must be performed manually on the VIDAS®, MINI VIDAS®, and VIDAS® 3 instruments.

If the dilution factor (= 2) was entered when the Work List was created, the result is calculated automatically. If the dilution factor was not entered, multiply the result by the dilution factor to obtain the sample concentration.

LIMITATIONS OF THE METHOD

- Interference may be encountered with certain sera containing antibodies directed against reagent components. For this reason, assay results should be interpreted taking into consideration the patient's clinical history and the results of any other tests performed.
- Refer to the section **PERFORMANCE – Study of drugs and other potentially interfering substances** for the compounds tested.
- Any results that do not correspond to the patient's clinical history may be due to inadequate instrument maintenance (see the Instrument User Manual).

REFERENCE VALUES
These results are given as a guide. It is recommended that each laboratory establish its own reference values from a rigorously selected population.

Reference values were determined in a clinical study using 491 samples from apparently healthy individuals. The population was divided into 3 groups, depending on the vitamin D status. For each group, a 95% reference value range (or reference interval, according to CLSI EP28-A3c Guideline) was determined, as well as for the total of the apparently healthy population as described below:

	N	Median (in pg/mL)	PTH (1-84) reference interval (in pg/mL)	90% CI*of the Lower reference limit (in pg/mL)	90% CI of the Upper reference limit (in pg/mL)
Healthy population	491	20.8	9.2 - 44.6	[8.7 ; 9.7]	[42.5 ; 46.7]

Healthy population by Vitamin D level	N	Median (in pg/mL)	PTH (1-84) reference interval (in pg/mL)	90% CI of the Lower reference limit (in pg/mL)	90% CI of the Upper reference limit (in pg/mL)
Deficient ≤ 20 ng/mL	176	21.5	8.9 - 45.3	[8.0 ; 9.9]	[42.1 ; 48.8]
Insufficient > 20 and < 30 ng/mL	213	20.7	8.8 - 47.8	[7.6 ; 9.9]	[41.6 ; 57.3]
Normal ≥ 30 ng/mL	102	21.3	9.6 - 47.3	[8.7 ; 10.6]	[41.6 ; 54.1]

* CI: Confidence Interval.

According to the KDIGO guidelines, the PTH concentration of the patients treated by dialysis should be maintained within two and nine times the upper normal limit of the assay.

PERFORMANCE
Studies performed using the VIDAS® PTH (1-84) (PTH) assay gave the following results.

Measurement range
The measurement range (or analytical measuring interval, according to CLSI EP36-Ed1 Guideline) is the range of values corresponding to the acceptable performance limits (precision and linearity).

The measurement range of the VIDAS® PTH (1-84) (PTH) assay is 4.0 to 1500.0 pg/mL.

Linearity
Linearity was evaluated according to CLSI EP06-A recommendations. The VIDAS® PTH (1-84) assay is linear between 4.0 and 1500.0 pg/mL.

Detection limits

Limit of Blank (LoB)	0.8 pg/mL
Limit of Detection (LoD)	2.2 pg/mL
Limit of Quantitation (LoQ)	4.0 pg/mL

LoB, LoD and LoQ values were determined according to CLSI EP17-A2 recommendations.

The Limit of Blank (LoB) is the concentration below which 95% of analyte-free samples are found.

The Limit of Detection (LoD) is the lowest concentration of analyte in a sample that can be distinguished from the analyte-free sample with a probability of 95% (observed result greater than the LoB with a 95% probability).

The Limit of Quantitation (LoQ) is the lowest concentration of analyte that can be detected and measured with an acceptable level of precision. All results under 4.0 pg/mL are printed ≤ 4.0 pg/mL. For the VIDAS® PTH (1-84) assay, the acceptable level of precision corresponds to within-lot precision fixed at 20% CV.

Hook effect
The assay uses a 2-step immunoassay sandwich method. Hook effect can therefore be excluded by design.

Precision
A precision study was performed according to CLSI EP05-A3 recommendations. A panel of human samples representing 6 concentration levels in the measurement interval was analyzed on the VIDAS® instrument to include the following main sources of variability: repeatability, run, day, calibration, and lot.

Repeatability (within-run precision), intermediate precision (total within-lot) and within-laboratory precision (between-lot within-instrument) were estimated for each sample. The values obtained are reported in the following table, as a guide.

Sample	Concentration level (pg/mL)	Repeatability		Intermediate precision		Within-laboratory	
		Standard deviation (pg/mL)	CV (%)	Standard deviation (pg/mL)	CV (%)	Standard deviation (pg/mL)	CV (%)
Sample 1	14.7	0.9	6.0	1.1	7.3	1.2	7.9
Sample 2	46.3	2.8	6.1	3.0	6.5	5.7	12.4
Sample 3	106.7	4.0	3.8	5.1	4.8	5.6	5.2
Sample 4	299.0	10.3	3.4	13.1	4.4	16.2	5.4
Sample 5	590.0	15.3	2.6	25.4	4.3	30.7	5.2
Sample 6	1130.1	42.5	3.8	51.1	4.5	62.4	5.5

These results are an indicator showing the ability to monitor chronic kidney disease patients in the routine mode.

Analytical specificity
The analytical specificity of the VIDAS® PTH (1-84) (PTH) assay was established by testing cross-reactive compounds according to CLSI document EP7-A2 recommendations. Cross-reactivity was evaluated by spiking serum samples with cross-reactive compounds (about 50 pg/mL and about 400 pg/mL of PTH).

The results of this study are reported in the following table.

Tested substance	Tested concentration (pg/mL)	Cross-reactivity %
PTH (7-84)	100 000	0.11%
PTH (1-34)	100 000	0.04%
PTH (13-34)	100 000	0.0004%
PTH (39-68)	100 000	0.0004%
PTH (44-68)	100 000	0.009%
PTH (39-84)	100 000	0.002%
PTH (53-84)	100 000	0.006%
Calcitonin	100 000	0.005%

Tested substance	Tested concentration (pg/mL)	Cross-reactivity %
Osteocalcin	100 000	0.014%
C-telopeptid	100 000	0.023%

Study of drugs and other potentially interfering substances

Potential interference by commonly used drugs and other substances was studied according to CLSI EP7-A2 recommendations. No significant interference was detected up to the maximum concentrations tested.

Tested drug	Maximum concentration	Tested drug	Maximum concentration
Acetaminophen	35 mg/dL	Etidronate	105 mg/dL
Acetylsalicylic acid	65 mg/dL	Ibuprofen	50 mg/dL (242.5 µmol/dL)
Alendronate	8 mg/dL	Lanthanum chloride	40 mg/dL
Alfacalcidol	2.5 µg/mL	Magnesium chloride	40 mg/dL
Aluminum sulfate	40 mg/dL	Pamidronate	18 mg/dL
Biotin	2 µg/mL	Risedronate	6 mg/dL
Calcitriol	1 ng/mL	Salicylic acid	60 mg/dL
Calcium acetate	40 mg/dL	Vitamin D2	1800 ng/mL
Calcium citrate	40 mg/dL	Vitamin D3	240 ng/mL

Tested substance	Maximum concentration
Bilirubin (unconjugated)	0.3 g/L (510 µmol/L)
Cholesterol	4.21 g/L
Hemoglobin	5 g/L (310 µmol/L)
Human Albumin	60 g/L
Human Anti Mouse Antibodies (HAMA)	2 µg/mL
Lipids (intralipids)	30 g/L
Rheumatoid factor	800 IU/mL

Method comparison

The comparison studies were performed according to CLSI EP09-A3 recommendations.

All the intended populations covering the measuring interval from 4.0 to 1500.0 pg/mL have been tested with VIDAS® PTH (1-84) (PTH) assay. Among the 215 patients enrolled, the following populations were represented:

- Adenoma
- Bone disorder
- Dialysis
- Non parathyroidian hypercalcemia
- Parathyroidectomy
- Renal failure stage 3
- Renal failure stage 4
- Renal failure stage 5
- Renal transplanted
- Apparently healthy population with 20 < Vit D < 30 ng/mL
- Apparently healthy population with Vit D ≥ 30 ng/mL

The comparison of the VIDAS® PTH (1-84) assay (Y) with another commercially available PTH (1-84) immunoassay (X) gave the following results:

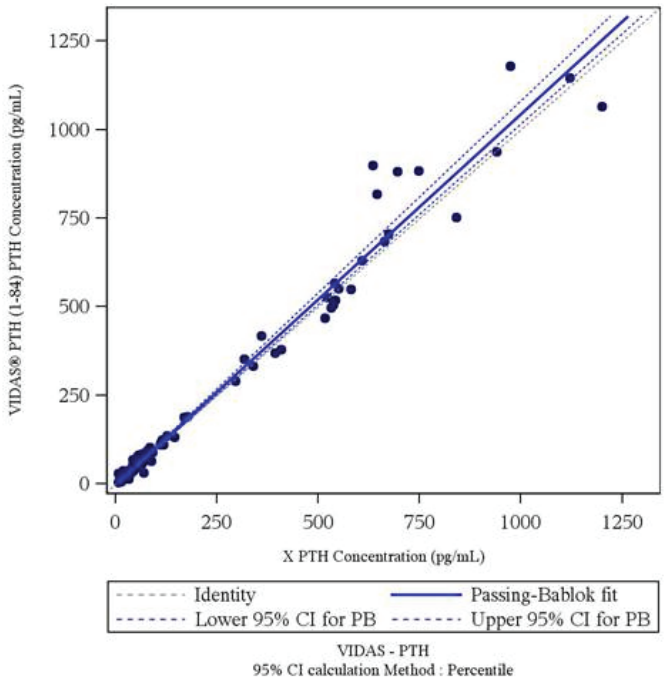
Number of samples tested: 215

Samples tested between 4.1 pg/mL and 1179.4 pg/mL for the VIDAS® PTH (1-84) (PTH) assay.

Samples tested between 6.68 pg/mL and 1200.00 pg/mL for the other commercially available immunoassay.

Equation for Passing-Bablok regression: Y = 1.0460 X - 2.2489

Correlation Coefficient: 0.9889



Monitoring performance

A total number of 21 patients were enrolled with 3 different time points. In conclusion a total of 63 samples were collected and tested with VIDAS® PTH (1-84) (PTH) assay (Y) and another commercially available PTH (1-84) immunoassay (X).

According to the KDIGO guidelines, the PTH concentration of the patients treated by dialysis should be maintained within two and nine times the upper normal limit of the assay. For information, the highest reference value established in a clinical study was 44.6 pg/mL, meaning an interval of PTH values between 89.2 and 401.4 pg/mL. Correspondence was defined by a concordant interpretation between both methods.

The global (all subjects and time points mixed) frequency and percent of concordant interpretation between the 2 assays regarding the KDIGO criterion was calculated.

Criteria	% Concordance
Concordant interpretation between the 2 assays regarding the KDIGO criterion	88.89 %

WASTE DISPOSAL

Dispose of used or unused reagents as well as any other contaminated disposable materials following procedures for infectious or potentially infectious products.

It is the responsibility of each laboratory to handle waste and effluents produced, according to their nature and degree of hazardousness, and to treat and dispose of them (or have them treated and disposed of) in accordance with any applicable regulations.

LITERATURE REFERENCES

1. Camacho PM *et al.* – American Association of Clinical Endocrinologists and American College of Endocrinology Clinical Practice Guidelines for the Diagnosis and Treatment of Postmenopausal Osteoporosis - 2016. – *Endocrine Practice* – 2016 September; 22 (Suppl 4): 1-42.
2. Khan AA *et al.* – Primary hyperparathyroidism: review and recommendations on evaluation, diagnosis, and management. A Canadian and international consensus. – *Osteoporos Int*. – 2017; 28: 1-19.
3. Wilhelm SM *et al.* – The American Association of Endocrine Surgeons Guidelines for Definitive Management of Primary Hyperparathyroidism. – *JAMA Surg*. – 2016 Oct; 151 (10): 959-68.
4. Bollerslev J *et al.* – European Society of Endocrinology Clinical Guideline: Treatment of chronic hypoparathyroidism in adults. – *European Journal of Endocrinology* – 2015; 173, G1-20.
5. KDIGO 2017 Clinical Practice Guideline Update for the Diagnosis, Evaluation, Prevention, and Treatment of Chronic Kidney Disease-Mineral and Bone Disorder (CKD-MBD). – *Kidney International Supplements* – 2017 July; 7 (1): 1-59.

6. WORLD HEALTH ORGANIZATION, USE OF ANTICOAGULANTS IN DIAGNOSTIC, LABORATORY INVESTIGATIONS, 2002, WHO/DIL/LAB/99.1 Rev.2
7. WORLD HEALTH ORGANIZATION, Parathyroid Hormone 1-84, human, recombinant (1st International Standard) - WHO_BS_09.2115.

INDEX OF SYMBOLS

Symbol	Meaning
	Catalogue number
	In Vitro Diagnostic Medical Device
	Manufacturer
	Temperature limit
	Use by date
	Batch code
	Consult Instructions for Use
	Contains sufficient for <n> tests
	Date of manufacture

LIMITED WARRANTY

bioMérieux warrants the performance of the product for its stated intended use provided that all procedures for usage, storage and handling, shelf life (when applicable), and precautions are strictly followed as detailed in the instructions for use (IFU).

Except as expressly set forth above, bioMérieux hereby disclaims all warranties, including any implied warranties of merchantability and fitness for a particular purpose or use, and disclaims all liability, whether direct, indirect or consequential, for any use of the reagent, software, instrument and disposables (the "System") other than as set forth in the IFU.

REVISION HISTORY

Change type categories

N/A	Not applicable (First publication)
Correction	Correction of documentation anomalies
Technical change	Addition, revision and/or removal of information related to the product
Administrative	Implementation of non-technical changes noticeable to the user

Note: *Minor typographical, grammar, and formatting changes are not included in the revision history.*

Release Date	Part Number	Change Type	Change Summary
2018-10	050049-01	N/A	Not applicable (First publication)
2018-12	050049-02	Correction	PERFORMANCE - Method comparison

bioMérieux SA
376 Chemin de l'Orme
69280 Marcy-l'Etoile - France

673 620 399 RCS LYON
Tel. 33 (0)4 78 87 20 00
Fax 33 (0)4 78 87 20 90
www.biomerieux.com