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VIDAS® AMH assay : optimized design to ensure reliability

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AMH is a dimeric glycoprotein produced as a precursor protein consisting of two monomers linked by a disulfide bond. It can be measured in the blood with the ELISA technique by monoclonal antibodies giving sensitivity performances suited to monitoring changes in ovarian reserves from birth to menopause (1) :

- Assessment of ovarian reserve in reproductive medicine for infertility investigation

- Help to select the best stimulation protocol:
  ⇒ Adapt treatment
  ⇒ Avoid unnecessary stimulation
  ⇒ Reduce risk of hyperstimulation syndrome

- better characterization of the type of ovarian dysfunction, particularly hypergonadotropic anovulation associated with ovarian insufficiency such as polycystic ovary syndrome (2)

- monitor the ovarian reserve in young girls and women who, for example, have undergone gonadotoxic treatment

The aim of this study was to evaluate the analytical and clinical performance of the VIDAS® AMH Assay, the new marker of VIDAS® fertility panel.

A sensitivity to conformational change of AMH has been reported, linked to specimen storage conditions that induced huge laboratory constraints. (3)

Consequently, bioMerieux developed its own antibodies for the VIDAS® AMH kit in order to address this AMH conformational issue .

The VIDAS® AMH assay principle combines a one-step enzyme immunoassay sandwich method with a final fluorescent detection (ELFA).

Literature references:

1. KELSEY TW, WRIGHT P et al. A validated model of serum anti-müllerian hormone from conception to menopause. PLoS ONE 2011,6(7):e22024

2. FONG SL, SCHIPPER I et al. The role of anti-Müllerian hormone in the classification of anovulatory infertility. European Journal of Obstetrics & Gynecology and Reproductive Biology. 2015,186:75-9

3 RUSTAMOV O, SMITH A.et al. Anti-Müllerian hormone: poor assay reproducibility in a large cohort of subjects suggests sample instability. Human Reproduction, Vol.0, N° 0 pp1-7,2012 .

VIDAS® AMH is not available in the following countries, states and regions: Armenia, Australia, Austria, Azerbaijan, Belarus, Belgium, Canada, Denmark, France, Germany, Hong-Kong, Ireland, Israel, Italy, Japan, Kazakhstan, Kyrgyzstan, Lichtenstein, Moldavia, New Zealand, Portugal, Russia, Spain, Tajikistan, The Netherlands, Turkey, Turkmenistan, United Kingdom, Switzerland.

SELECTION OF THE BEST ANTIBODIES TO ADDRESS AMH CONFORMATIONAL CHANGE

1/ Choice of the capture & detection antibodies:

Eight serum samples have been tested with a microtiterplate commercialized kit and with the VIDAS® anti-AMH antibodies. Samples have been assayed up to 3 hours after bleeding (T0), then after 24 hours or 7 days at 2-8° C and 7 days at -19/-31° C. The ratio of concentrations between each time and T0 have been calculated.

	Kit IA commercialized			VIDAS AMH Ab pair		
	AMH not stable			AMH stable		
	T24 hours 2-8°C	T7 days 2-8°C	T7 days -30°C	T24 hours 2-8°C	T7 days 2-8°C	T7 days -30°C
Ratio concentration at T/T0						
Mean 8 samples	**1.33**	**1.34**	**1.34**	**0.99**	**0.96**	**0.98**
Min	1.10	1.05	1.07	0.96	0.95	0.95
Max	1.58	1.66	1.73	1.01	0.97	1.01

The antibodies chosen for the VIDAS® AMH assay are not sensitive to the conformational change of the AMH molecule occurring during the first hours after bleeding (ratios close to 1), as seen in the microtiterplate commercialized kit .

2/ Sample stability study:

Three serum samples have been tested up to 3 hours after bleeding corresponding to the T0, then after 24 hours at 18-25° C, 7 days at 2-8° C, after one to four freeze/ thaw cycles with VIDAS® AMH assay.
The sample stability study was performed to evaluate the robustness of VIDAS® AMH assay results in relation to collection tube storage conditions

	T0	24 hours at 18-25°C		7 days at 2-8°C	
Id sample	Concentration	Concentration	ratio //T0	Concentration	ratio //T0
MFG0009	0.811	0.754	93%	0.703	87%
MFG0007	3.602	3.237	90%	3.115	86%
MFG0012	9.811	9.055	92%	8.565	87%

	T0	Cycle 1 freeze/ thaw		Cycle 2 freeze/ thaw		Cycle 3 freeze/ thaw		Cycle 4 freeze/ thaw	
Id sample	Concentration	Concentration	ratio //T0	Concentration	ratio //T0	Concentration	ratio //T0	Concentration	ratio //T0
MFG 27	1.18	1.147	97%	1.127	96%	1.094	93%	1.101	93%
MFG 23	3.751	3.628	97%	3.485	93%	3.464	92%	3.423	91%
MFG 26	9.226	8.961	97%	8.663	94%	8.787	95%	8.789	95%

Three pools of serum have been tested up to 3 hours after bleeding corresponding to the T0, then after 6 months at -19/-31° C and < -60° C.

	T0	Storage 6 months			
		-19/-31°C		< -60°C	
Id sample	Concentration	Concentration	ratio //T0	Concentration	ratio //T0
Pool B	0.83	0.83	100%	0.84	101%
Pool C	3.53	3.46	98%	3.68	104%
Pool D	11.18	10.98	98%	11.72	105%

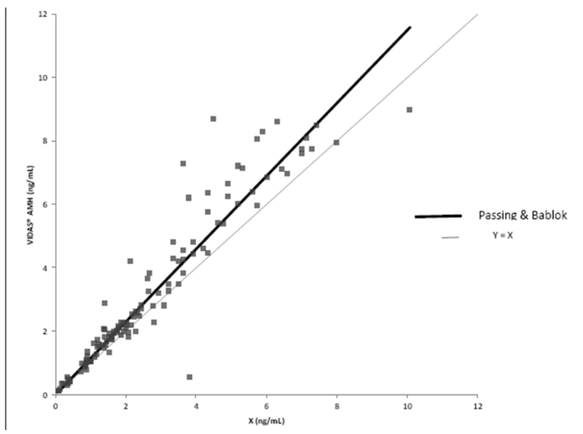
These results show that VIDAS® AMH assay has an excellent robustness in relation to collection tube storage conditions .

FINAL CHARACTERISTICS & PERFORMANCE

- Reportable range from 0.01 to 9.00 ng/mL
- Quantification detection limit: 0.02 ng/mL
- Dilution: ¼ recommended in the package insert ; 1/10 and 1/20 also possible.
- Precision:
  Within-run precision (repeatability) from 4.1 to 4.8%
  Within-lot precision from 6.6 to 8.2%
- Time to result: 35 minutes using Fertility protocol, as LH, FSH or prolactin
- Usable on VIDAS®, mini VIDAS® or VIDAS 3® platforms with same performance
- Calibration every 28 days
- Human AMH specificity
- VIDAS® AMH is robust to sample tube storage conditions: samples (serum and plasma) can be stored :
  - During 4 hours at +18/+25° C in open primary tubes ,
  - During 8 hours at +18/+25° C in closed primary tube,
  - for up to 5 days at +2/+8° C when aliquoted,
  - for up to 6 months at -25 ± 6° C, with up to 3 freeze/thaw cycles if longer storage is required.

Clinical trial study results with 118 serum samples:
Comparison of the VIDAS® AMH assay (Y) with another automated commercially available immunoassay (X)

Equation for Passing-Bablock regression:
Y = 1.15 X - 0.02
Correlation Coefficient:
r = 0.95



CONCLUSIONS

VIDAS® AMH assay was designed by selecting antibodies robust to the specimen storage conditions , and to AMH conformational change.

VIDAS® AMH, is particularly convenient, simple, and completes the fertility panel.

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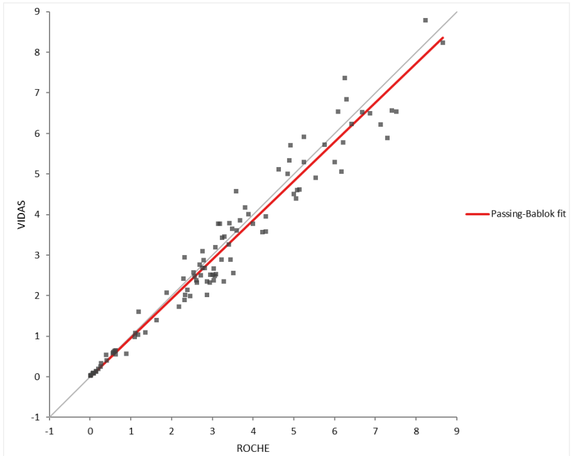
CORRELATION STUDIES

VIDAS®/ ELECSYS® ROCHE

Internal R&D study* with 101 serum samples:

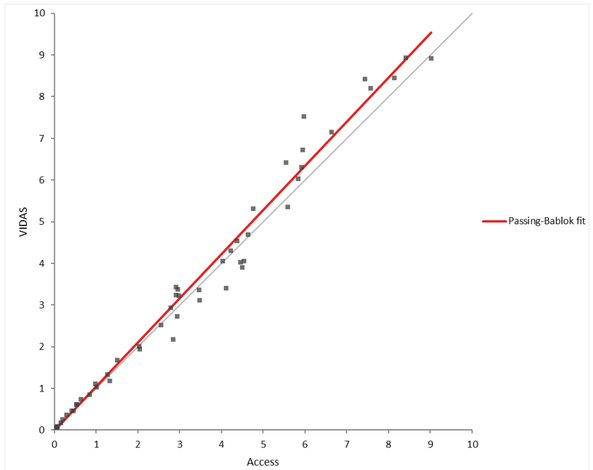
Equation for Passing-Bablock regression:
VIDAS® = 0.97 ROCHE - 0.02
Correlation Coefficient: r = 0.98



VIDAS®/ BECKMAN ACCESS

Internal R&D study * with 50 serum samples:

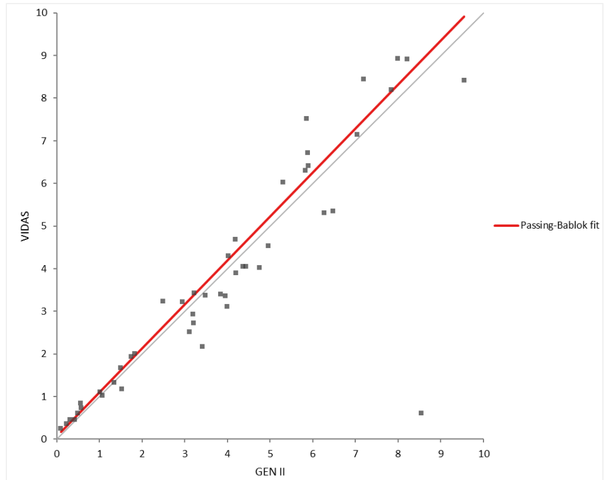
Equation for Passing-Bablock regression:
VIDAS® = 1.06 ACCESS - 0.02
Correlation Coefficient: r = 0.99



VIDAS®/ BECKMAN GEN II

Internal R&D study * with 46 serum samples:

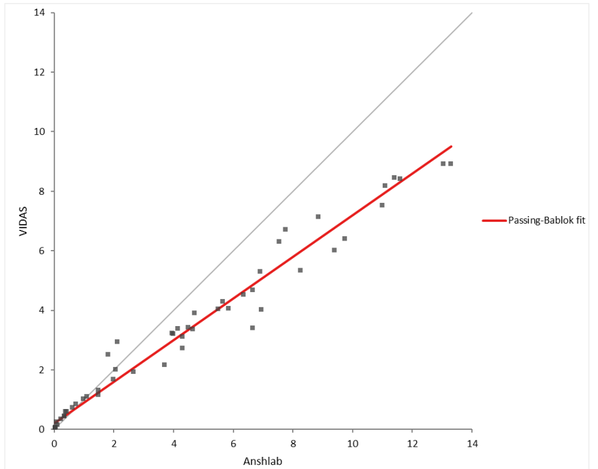
Equation for Passing-Bablock regression:
VIDAS® = 1.03 GEN II + 0.08
Correlation Coefficient: r = 0.87



VIDAS®/ ANSHLABS®

Internal R&D study * with 50 serum samples:

Equation for Passing-Bablock regression:
VIDAS® = 0.70 AnshLabs® + 0.21
Correlation Coefficient: r = 0.98



*: These correlation results are from internal R/D studies. For clinical method comparison results, refer to the package insert.

CONCLUSIONS

Correlation studies results performed with the VIDAS® AMH assay fit with the intended use: VIDAS® AMH is well correlated with the other commercially available immunoassays (ROCHE Elecsys®, BECKMAN Access, BECKMAN Gen II and AnshLabs®).

Based on the claimed intended use : assessment of the ovarian follicle reserve in young girls over 12 years of age and in women in the context of ovarian dysfunction or controlled or assisted procreation, the VIDAS® AMH is a new automated alternative.

Please check the availaibility of VIDAS AMH in your country on http://www.biomerieux-diagnostics.com/vidas-amh-countries-list