Azienda Ospedaliero Universitaria Careggi

VEQ Centro Regionale di Riferimento per la Verifica Esterna di Qualità

SST Servizio Sanitario della Toscana

« VEQ CICLO 2018 – RISULTATI 3 Allergologia, Biologia molecolare, Sieroimmunologia 1, 2, 3, Ormoni »

Consensus Meeting

Alessandro Terreni

Azienda Ospedaliero-Universitaria Careggi
Largo G.A. Brambilla, 3
Firenze 29 NOVEMBRE 2019

Criticità legate alla standardizzazione ormoni

- Forme molecolari complesse o che tendono a modificarsi in condizioni fisiopatologiche(es PSA, TSH, hCG, CEA LH, FSH..)
- Specificità analitica diversa

H.A. Morris / Clinical Biochemistry 42 (2009) 241–245

Joint Committee for Traceability in Laboratory Medicine (JCTLM)

Misure di riferimento per:

- ✓ cortisolo,
- ✓ aldosterone,
- ✓ 17beta-estradiolo,
- ✓ progesterone,
- ✓ testosterone
- ✓ acido Folico,
- ✓ Vit D,
- ✓ C-Peptide
- ✓ fT4,
- ✓ aldosterone

Consensus Statement

Sverre Sandberg*, Callum G. Fraser, Andrea Rita Horvath, Rob Jansen, Graham Jones, Wytze Oosterhuis, Per Hyltoft Petersen, Heinz Schimmel, Ken Sikaris and Mauro Panteghini

Defining analytical performance specifications: Consensus Statement from the 1st Strategic Conference of the European Federation of Clinical Chemistry and Laboratory Medicine

Il primo EFLM Strategic Conference tenutasi a Milan nel 2014, ha definito tre modelli per stabilire i limiti di accettabilità:

1. basato sull'effetto delle performance analitiche sull'outcome clinico
2. basato sulla variabilità biologica del misurando
3. basato sullo stato dell'arte delle misure

Clin Chem Lab Med 2015; 53(6): 833–835

Cosa possiamo dire

1. Obbiettivi basati sull'effetto delle performance: non esistono
2. Obbiettivi basati sulla variabilità biologica: vecchi scarsamente attendibili
3. Stato dell'arte unico valido attualmente

Cosa possiamo dire

Un “Task and Finish Group” dell’”European Federation of Clinical Chemistry and Laboratory Medicine” (EFLM) sta lavorando sul miglioramento dei dati di variabilità biologica:

- Valutazione dei dati presenti in letteratura in base ai criteri definiti per ottenere il dato
- Produzione di nuovi dati

Nuovo database che sostituisce WESTGARD

Working Group: Biological Variation

Back Home

Back to the main page of the WG-BV

News

We are happy to announce that the EFLM Biological Variation Database is now live! The database, available via the EFLM homepage and at https://biologicalvariation.eu/, was launched during the Euromedlab in Barcelona in May 2019 and delivers updated, evidence-based biological variation (BV) estimates to users worldwide. Please see below for more information.
Please also check into Resources / Educational Material to view and access articles on BV published by the WG-BV, mostly recently a systematic review on BV data for lipid markers; Diaz-Garzon J et al Biological variation data for lipid cardiovascular risk assessment biomarkers. A systematic review applying the biological variation data critical appraisal checklist (BIVAC). Clin Chim Acta 2019 doi: 10.1016/j.cca.2019.05.013. [Epub ahead of print] and EuBIVAS results for 15 frequently measured proteins; Carobene A et al European Biological Variation Study (EuBIVAS): Within- and Between-Subject Biological Variation Data for 15 Frequently Measured Proteins Clin Chem 2019 doi:10.1373/clinchem.2019.304618.

Current projects

Forthcoming EFLM events

EFLM webinars

3rd EFLM Strategic Conference

EuroMedLab Munich 2021

Partners

LAB TESTS ONLINE
Your Trusted Guide
Understand your tests. Empower your health.
A PROGRAM OF AACC

TRUSTED PARTNER
ETHICAL MEDTECH

Clinical Chemistry 63:6
1141–1150 (2017)

Other Areas of Clinical Chemistry

Biological Variation Estimates Obtained from 91 Healthy Study Participants for 9 Enzymes in Serum

Anna Carobene,[1,10*] Thomas Røraas,[2] Una Ørvim Sølvik,[3] Marit Sverresdotter Sylte,[4] Sverre Sandberg,[2,3,4,10] Elena Guerra,[1] Irene Marino,[1] Niels Jonker,[5,10] Gerhard Barla,[5] William A. Bartlett,[6,10] Pilar Fernandez-Calle,[7,10] Jorge Díaz-Garzón,[7] Francesca Tosato,[8] Mario Plebani,[8] Abdurrahman Coşkun,[9,10] Mustafa Serteser,[9] Ibrahim Unsal,[9] and Ferruccio Ceriotti[1] on behalf of the European Biological Variation Study of the EFLM Working Group on Biological Variation

DE GRUYTER

Clin Chem Lab Med 2018; 56(8): 1309–1318

Abdurrahman Coşkun[a,*], Anna Carobene[a], Meltem Kilercik, Mustafa Serteser, Sverre Sandberg[a], Aasne K. Aarsand[a], Pilar Fernandez-Calle[a], Niels Jonker[a], William A. Bartlett[a], Jorge Díaz-Garzón, Sibel Huet, Cansu Kızıltaş, Ilayda Dalgakıran, Esra Ugur and Ibrahim Unsal, on behalf of the European Biological Variation Study of the EFLM Working Group on Biological Variation

Within-subject and between-subject biological variation estimates of 21 hematological parameters in 30 healthy subjects

EuBIVAS: Within- and Between-Subject Biological Variation Data for Electrolytes, Lipids, Urea, Uric Acid, Total Protein, Total Bilirubin, Direct Bilirubin, and Glucose

Aasne K. Aarsand,[1,2,3*] Jorge Díaz-Garzón,[4] Pilar Fernandez-Calle,[3,4] Elena Guerra,[5] Massimo Locatelli,[5] William A. Bartlett,[3,6] Sverre Sandberg,[1,2,3] Thomas Røraas,[2,3] Ferruccio Ceriotti,[7] Una Ørvim Sølvik,[2,8] Marit Sverresdotter Sylte,[1] Abdurrahman Coşkun,[3,9] Mustafa Serteser,[9] Ibrahim Unsal,[9] Francesca Tosato,[10] Mario Plebani,[10] Niels Jonker,[3,11] Gerhard Barla,[11] and Anna Carobene,[3,5] on behalf of the European Federation of Clinical Chemistry and Laboratory Medicine Working Group on Biological Variation

Clinical Chemistry 63:9
1527–1536 (2017)

Other Areas of Clinical Chemistry

The EuBIVAS Project: Within- and Between-Subject Biological Variation Data for Serum Creatinine Using Enzymatic and Alkaline Picrate Methods and Implications for Monitoring

Anna Carobene,[1,11*] Irene Marino,[1] Abdurrahman Coşkun,[2,11] Mustafa Serteser,[2] Ibrahim Unsal,[2] Elena Guerra,[1] William A. Bartlett,[3,11] Sverre Sandberg,[4,5,11] Aasne Karine Aarsand,[4,11] Marit Sverresdotter Sylte,[4] Thomas Røraas,[5,11] Una Ørvim Sølvik,[6] Pilar Fernandez-Calle,[7,11] Jorge Díaz-Garzón,[7] Francesca Tosato,[8] Mario Plebani,[8] Niels Jonker,[9,11] Gerhard Barla,[9] and Ferruccio Ceriotti[10] on behalf of the European Biological Variation Study of the EFLM Working Group on Biological Variation

REFERENCE	REFERENCE	JOURNAL	PUBLICATION DATE	USED IN
Aziz N, Detels R, Quint JJ et al, 2019, BMC Immunology , , , Biological variation of immunological blood biomarkers in healthy individuals and quality goals for biomarker tests	Biological variation of immunological blood biomarkers in healthy individuals and quality goals for biomarker tests	BMC Immunology	2019	
Aziz N, Jamieson D, Quint JJ eta al, 2019, Medicine, 98:41, e17525 , Longitudinal Intra- and Inter-individual variation inT-cell subsets of HIV-infected and uninfected men participating in the LA Multi-Center AIDS Cohort Study	Longitudinal Intra- and Inter-individual variation inT-cell subsets of HIV-infected and uninfected men participating in the LA Multi-Center AIDS Cohort Study	Medicine	2019	
Bozzolino C, Vaglio S, Amante E et al., 2019, Steroids, , , Individual and cyclic estrogenic profile in women: Structure and variability of the data	Individual and cyclic estrogenic profile in women: Structure and variability of the data	Steroids	2019	
Braga F, Ferraro S, Borille S and Panteghini M, 2019, Clin Chem Lab Med, , , Biological variation of two serum markers for preeclampsia prediction	Biological variation of two serum markers for preeclampsia prediction	Clin Chem Lab Med	2019	
Carobene A, Aarsand AK, Guerra E et al, 2019, Clin Chem, 65 (8), 1031-41 , Within- and Between-Subject Biological VariationData for 15 Frequently Measured Proteins	Within- and Between-Subject Biological VariationData for 15 Frequently Measured Proteins	Clin Chem	2019	•Complement 3 (C3) •Albumin •Cystatin C
DeLuca A, Betz J, Bollinger R et al, 2019, BMJ Evid Based Med , , , Users beware! Biological variation in complete blood counts over short time intervals	Users beware! Biological variation in complete blood counts over short time intervals	BMJ Evid Based Med	2019	
Ercan M, Akbulut ED, Avci E et al, 2019, Biochem Med, 29(3), , Determining biological variation of serum parathyroid hormone in healthy adults	Determining biological variation of serum parathyroid hormone in healthy adults	Biochem Med	2019	
Falay M, Senes M, Korkmaz S et al, 2019, J Imm Methods, , , Biological variation of peripheral blood T-lymphocytes	Biological variation of peripheral blood T-lymphocytes	J Imm Methods	2019	
Jabor A, Kubicek Z, Komrskova J, et al, 2019, Ann Clin Biochem, , , Biological variation of intact fibroblast growth factor 23 measured on a fully automated chemiluminescent platform	Biological variation of intact fibroblast growth factor 23 measured on a fully automated chemiluminescent platform	Ann Clin Biochem	2019	•Fibroblast growth factor-23 level

I traguardi basati sullo stato dell'arte si riferiscono al più alto livello di performance tecnicamente raggiungibile

Criteri per la selezione dei limiti di accettabilità dei risultati nei programmi di Valutazione Esterna della Qualità

Maurizio Borsotti, Massimo Quercioli, Carlo Franzini
Centro Regionale di Riferimento per il Controllo di Qualità, Azienda Ospedaliero-Universitaria Careggi, Firenze

METODI

Elaborazione di 131431 risultati inviati da 285 Laboratori Lombardi e Toscani partecipanti al programma VEQ« Ormoni e marcatori tumorali« gestito dal Centro di Riferimento Regionale per la Qualità dei SMeL della Regione Lombardia in collaborazione con il Centro di Riferimento Regionale per la VEQ Regione Toscana; i risultati erano relativi a 24 misurandi prodotti in 48 esercizi nell'arco di 4anni (cicli 2014-2017)

METODI

1- RAGGRUPPAMENTO DEI RISULTATI PER ESERCIZIO E PER GRUPPO OMOGENEO

CRITICITA': la robustezza del valore di consenso dipende anche dalla numerosità del gruppo omogeneo; pertanto sono stati presi in considerazione solo i gruppi con numerosità superiore a 7 Laboratori

METODI

2- CALCOLO PER OGNI GRUPPO OMOGENEO DELLA MEDIA ROBUSTA (DOPO RIMOZIONE DEGLI OUTLIER SECONDO IL METODO DI HUBER-HAMPEL):

- per migliorare l'accuratezza dei parametri statistici è necessario eliminare i valori aberranti

- metodo di Huber-Hampel, che è uno di quelli consigliati nella norma ISO13528

In breve, vengono considerati aberranti quei valori che hanno una distanza dalla mediana:

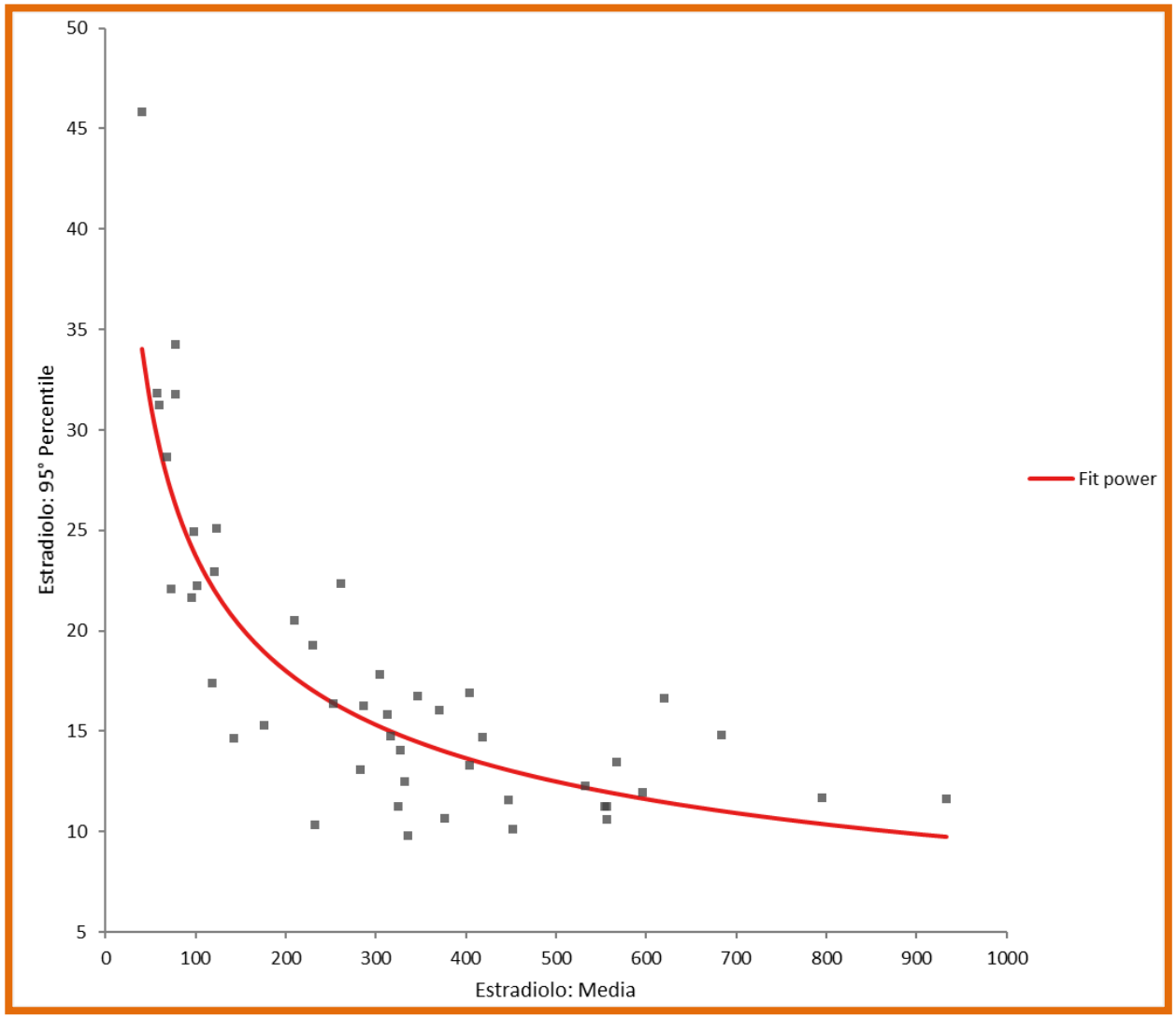
> a 3x Mediana x 1,483

METODI

3- CALCOLO DELLO SCOSTAMENTO % DI OGNI RISULTATO DALLA MEDIA ROBUSTA DEL PROPRIO GRUPPO OMOGENEO

4- COSTRUZIONE DI CURVE DI CORRELAZIONE FRA LA CONCENTRAZIONE E IL 95°PERCENTILE CALCOLATO PER OGNI ESERCIZIO

SCOPO: verificare, per ogni misurando, se c'è una evidente relazione fra la concentrazione e l'entità dell'errore totale commesso


50
45
40
35
30
25
20
15
10
5
Estradiolo: 95° Percentile
0
100
200
300
400
500
600
700
800
900
1000
Estradiolo: Media
Fit power

METODI

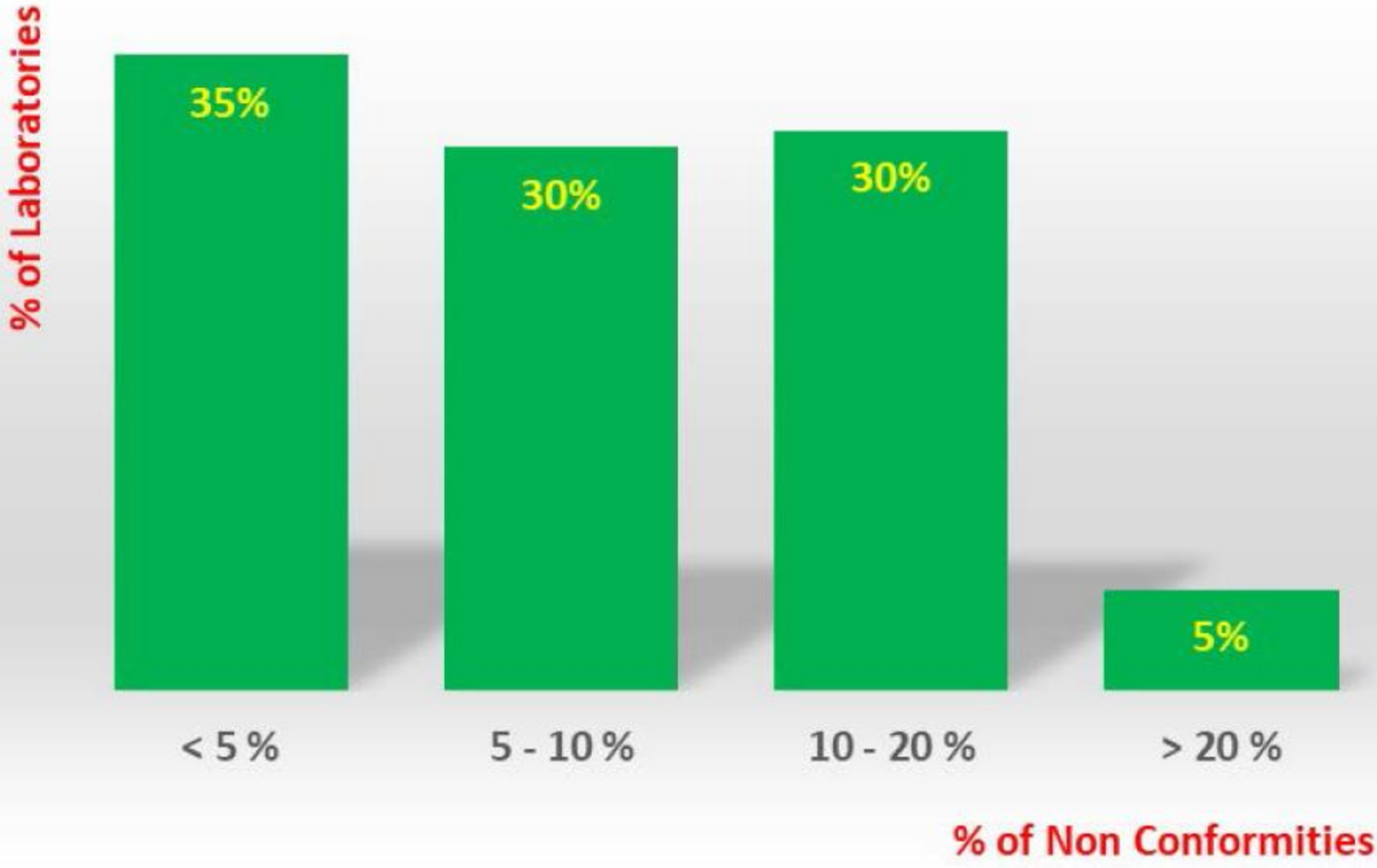
CALCOLO DEL 95°PERCENTILE DI TUTTI GLI SCOSTAMENTI (PER I MISURANDI IN CUI NON C'E' EVIDENZA DI DIPENDENZA DALLA CONCENTRAZIONE)

OPPURE

SUDDIVISIONE DEGLI SCOSTAMENTI IN GRUPPI DIVISI PER CONCENTRAZIONE E CALCOLO DEL 95°PERCENTILE PER OGNI SOTTOGRUPPO

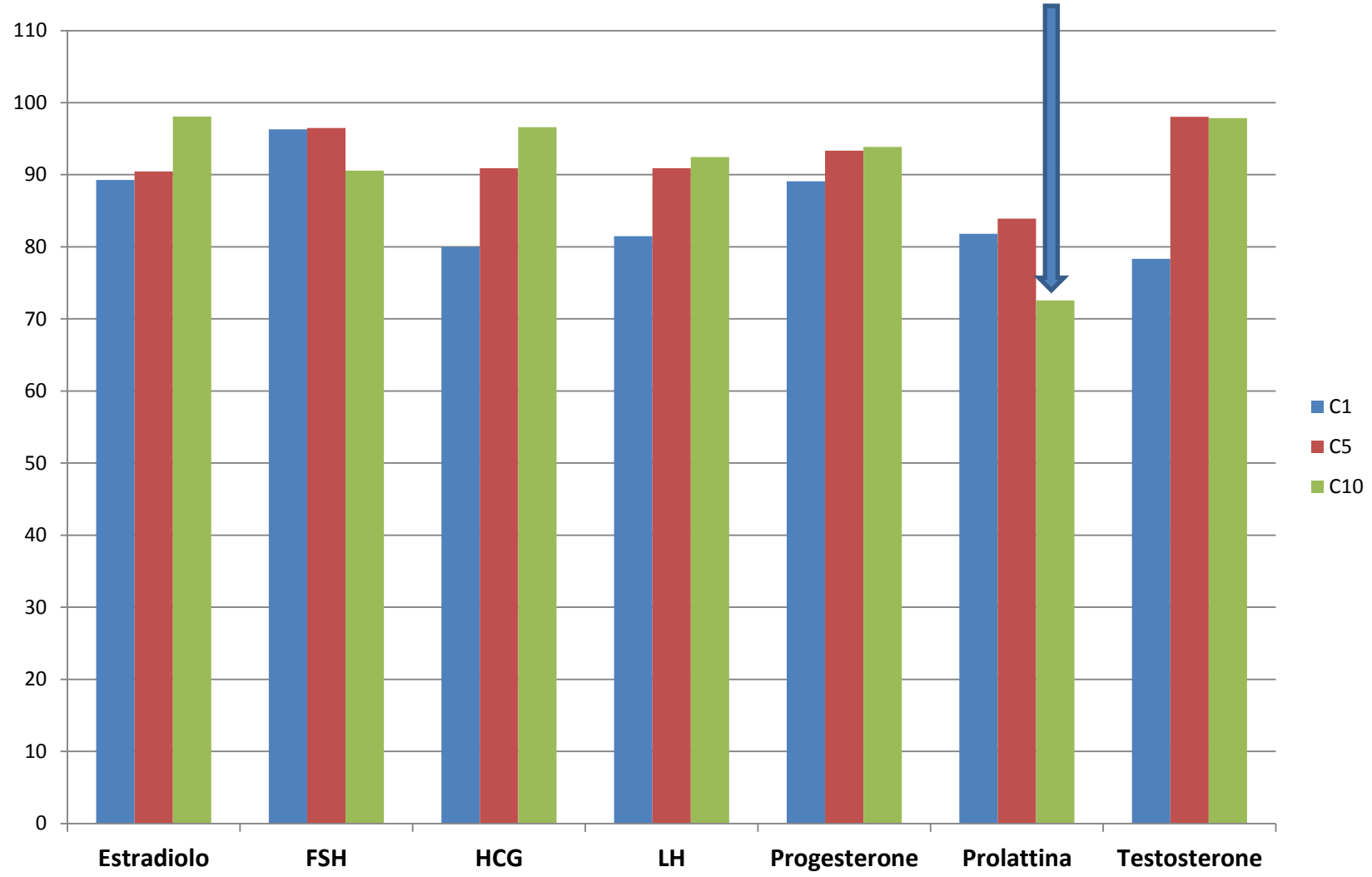
MEASURAND	APS (TEa%)	% NC 2014-2017
Alpha-fetoprotein	15,47 %	7,53 %
C-Peptide	15,86 %	8,24 %
CA 15.3	14,48 %	7,27 %
CA 19.9	14,04 %	7,81 %
CA 125	10,92 %	7,59 %
CEA	11,51 %	7,31 %
Cortisol	13,89 %	8,59 %
Estradiol (< 150 pg/mL)	28,23 %	6,25 %
Estradiol (> 150 pg/mL)	14,62 %	7,11 %
Ferritin	16,56 %	7,93 %
Folate (< 3 ng/mL)	40,44 %	6,16 %
Folate (> 3 ng/mL)	17,92 %	8,35 %
FSH	11,80 %	7,64 %
fT3	13,42 %	6,94 %
fT4	10,58 %	8,56 %
hCG	13,42 %	7,15 %
Insulin (< 10 µUI/mL)	18,68 %	7,50 %
Insulin (> 10 µUI/mL)	12,23 %	8,24 %
LH	12,19 %	7,98 %

MEASURAND	APS (TEa%)	% NC 2014-2017
Progesterone (< 3 ng/mL)	22,69 %	6,78 %
Progesterone (> 3 ng/mL)	14,38 %	7,35 %
Prolactin	11,47 %	7,75 %
Free PSA	13,38 %	7,83 %
Total PSA	12,31 %	7,59 %
PTH (< 70 pg/mL)	60,74 %	6,31 %
PTH (> 70 pg/mL)	26,08 %	7,04 %
Testosterone (< 1 ng/mL)	45,85 %	4,98 %
Testosterone (> 1 ng/mL)	17,07 %	7,84 %
TSH	10,62 %	7,32 %
Vitamin B12 (< 300 pg/mL)	17,48 %	7,80 %
Vitamin B12 (> 300 pg/mL)	13,97 %	7,60 %


% of Laboratories
35%
30%
30%
5%
< 5 %
5 - 10 %
10 - 20 %
> 20 %
% of Non Conformities

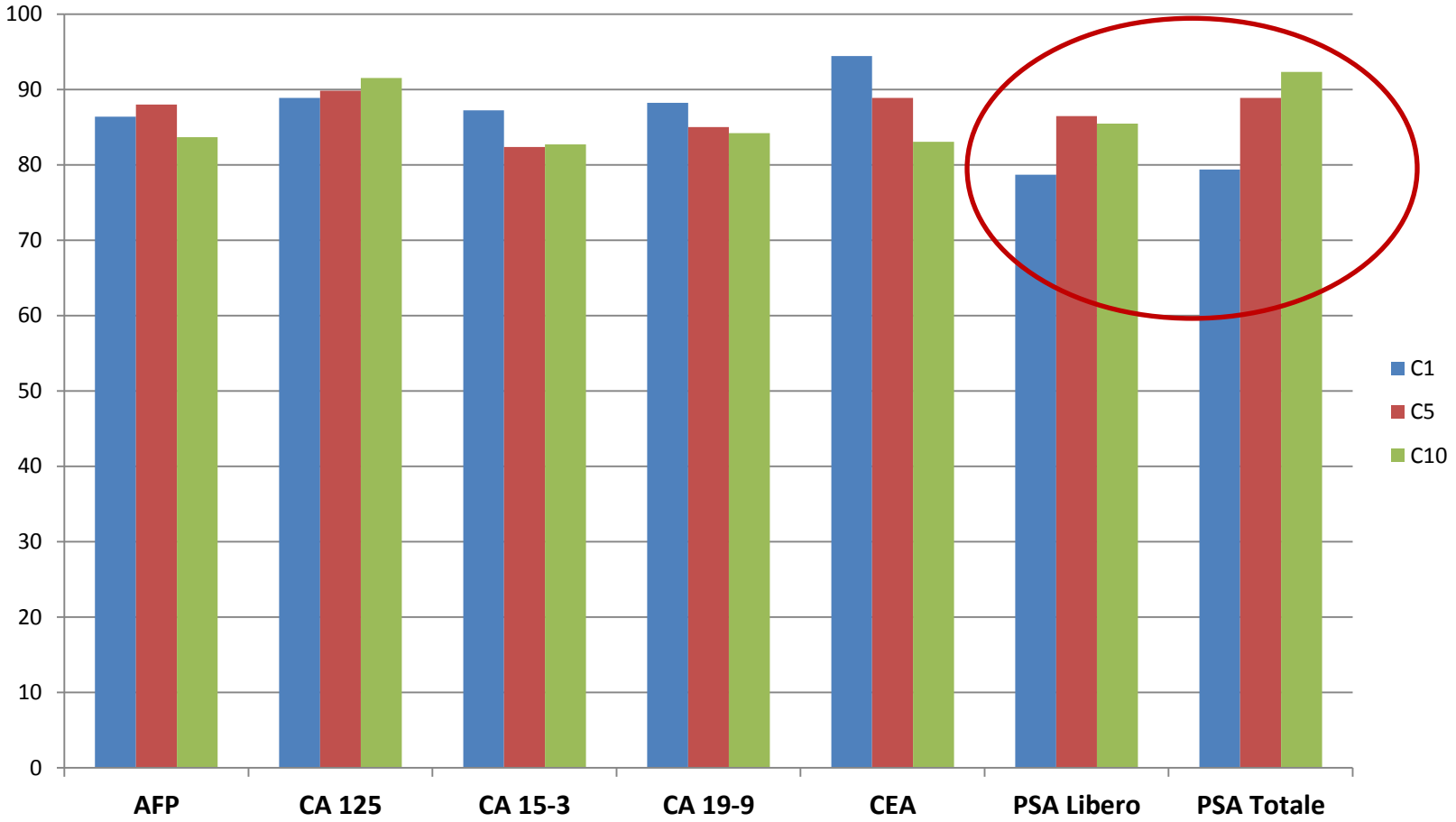
Fertilità

Valore basso 130µU/mL

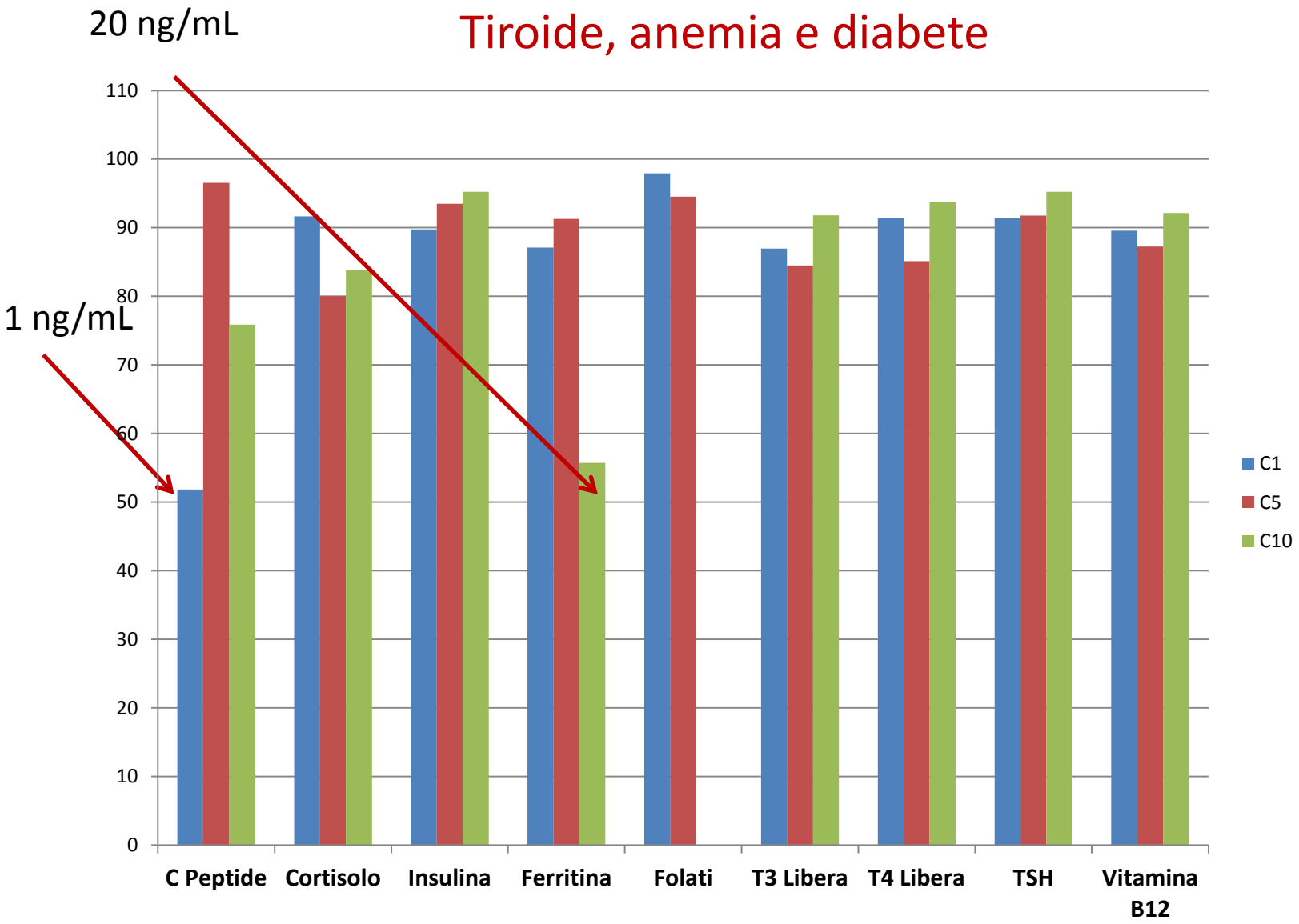


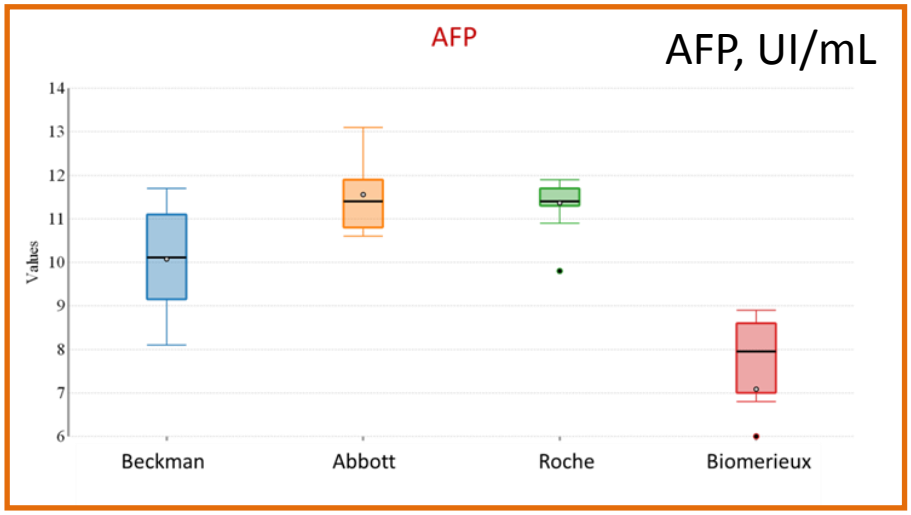
Marcatori Tumorali

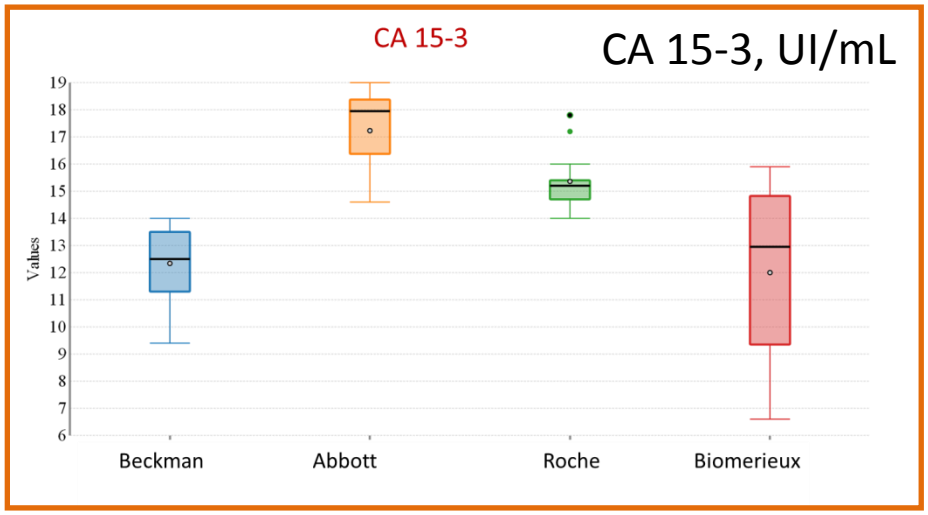
Valori alti PSA tot 9ng/mL e Psa Lib.2.5ng/mL

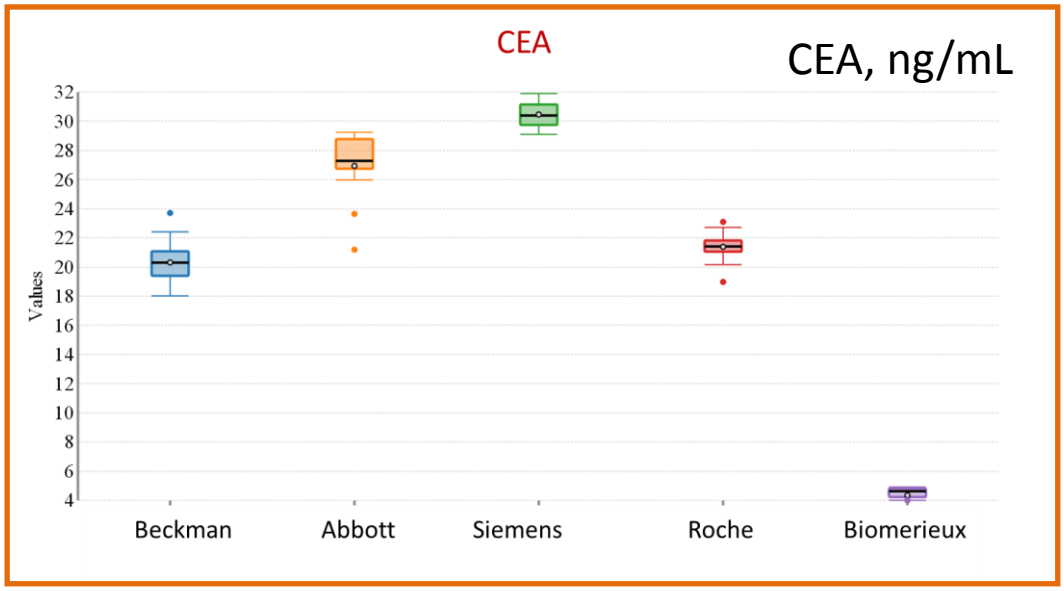


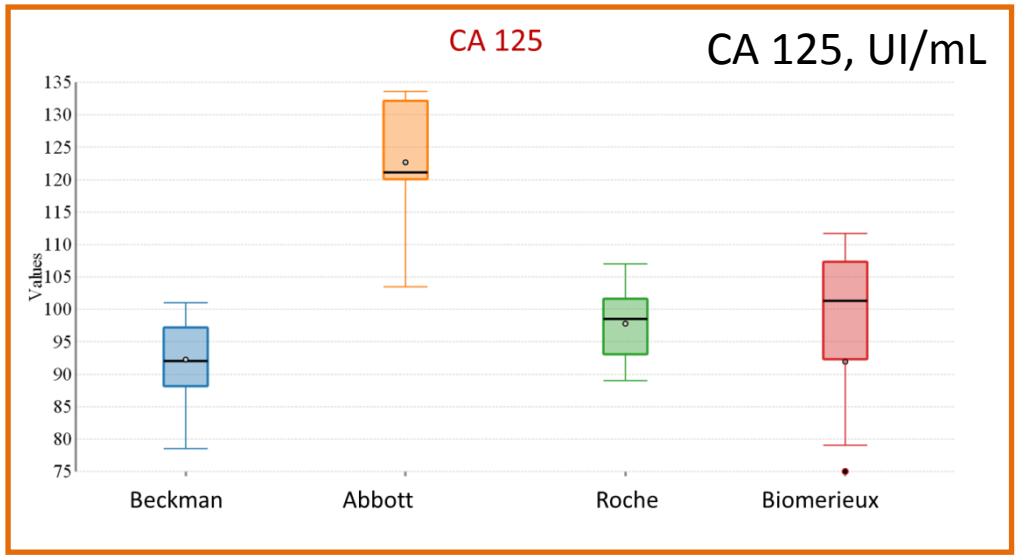
Tiroide, anemia e diabete

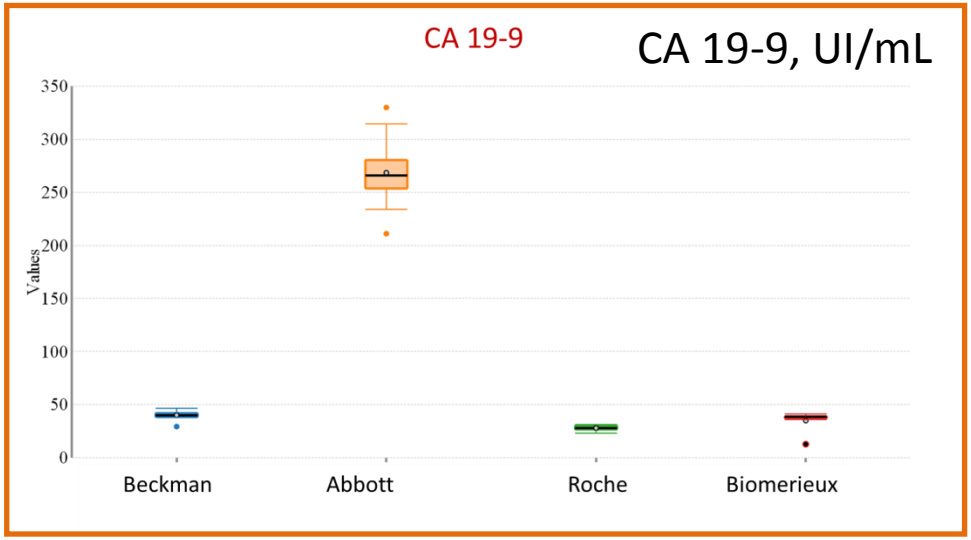



AFP
AFP, UI/mL
Values
14
13
12
11
10
9
8
7
6
Beckman
Abbott
Roche
Biomerieux

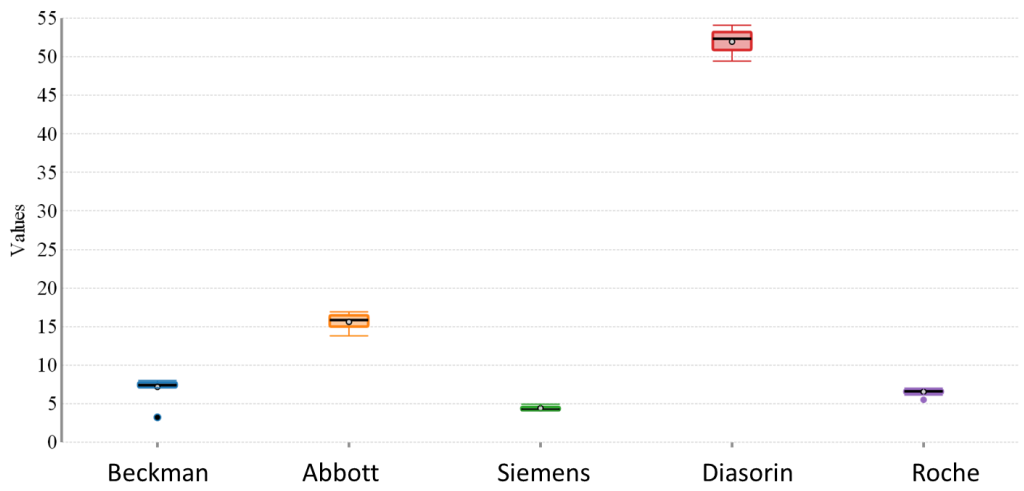

CA 15-3
CA 15-3, UI/mL
Values
19
18
17
16
15
14
13
12
11
10
9
8
7
6
Beckman
Abbott
Roche
Biomerieux


CEA
CEA, ng/mL
Values
32
30
28
26
24
22
20
18
16
14
12
10
8
6
4
Beckman
Abbott
Siemens
Roche
Biomerieux

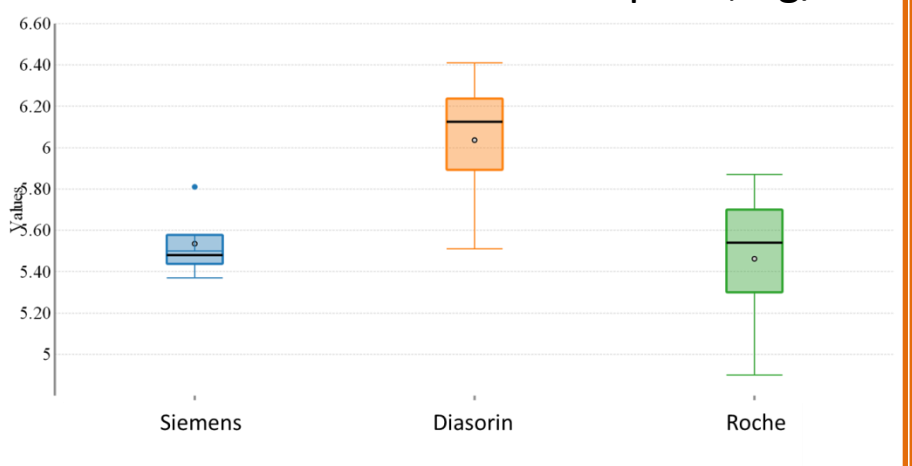

CA 125
CA 125, UI/mL
Values
135
130
125
120
115
110
105
100
95
90
85
80
75
Beckman
Abbott
Roche
Biomerieux


CA 19-9
CA 19-9, UI/mL
Values
350
300
250
200
150
100
50
0
Beckman
Abbott
Roche
Biomerieux

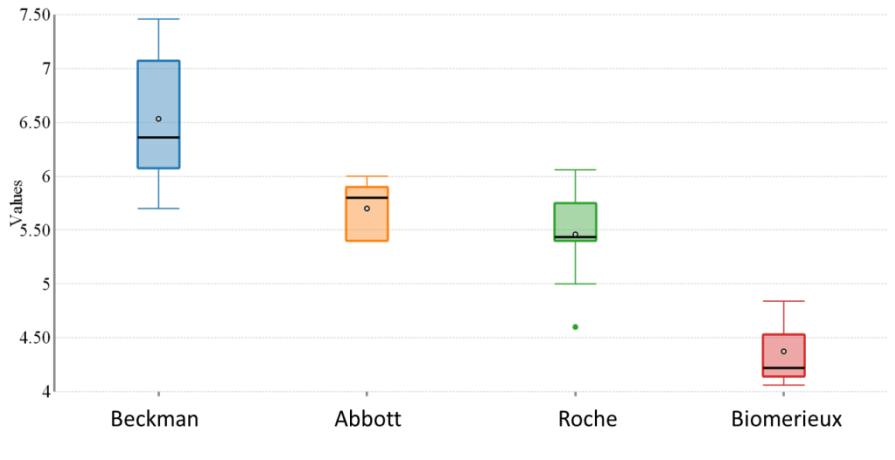
Insulina

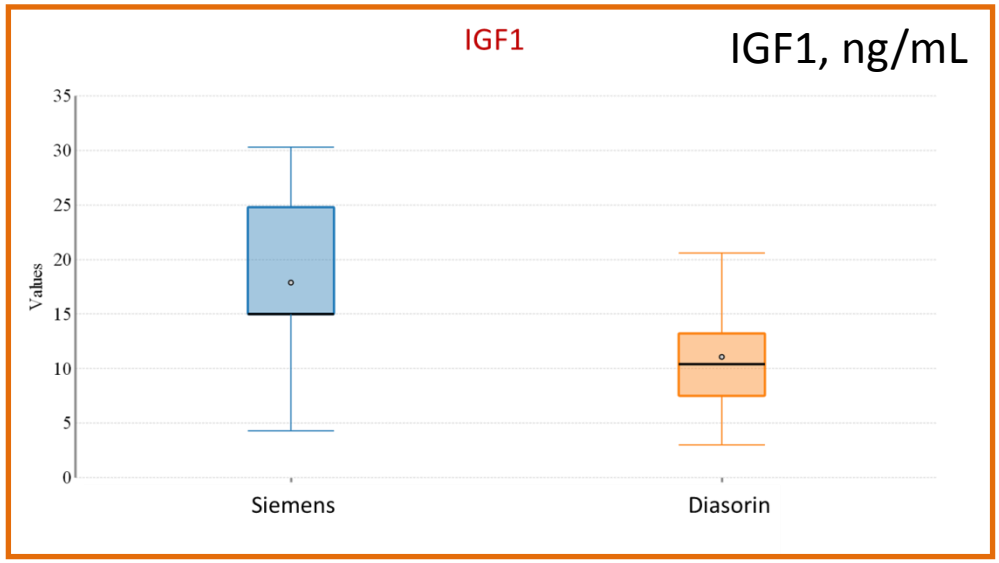


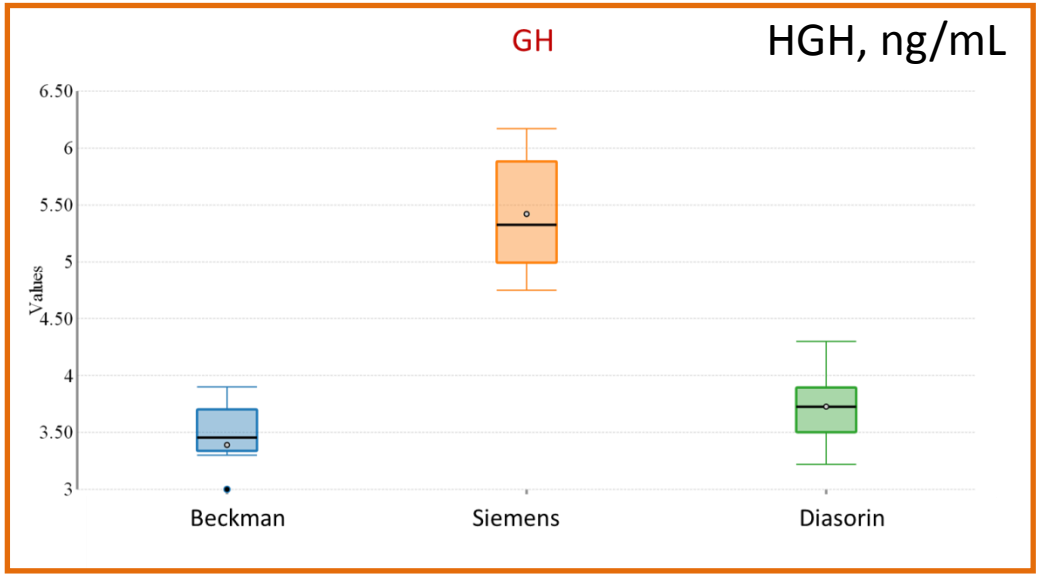
C-peptide



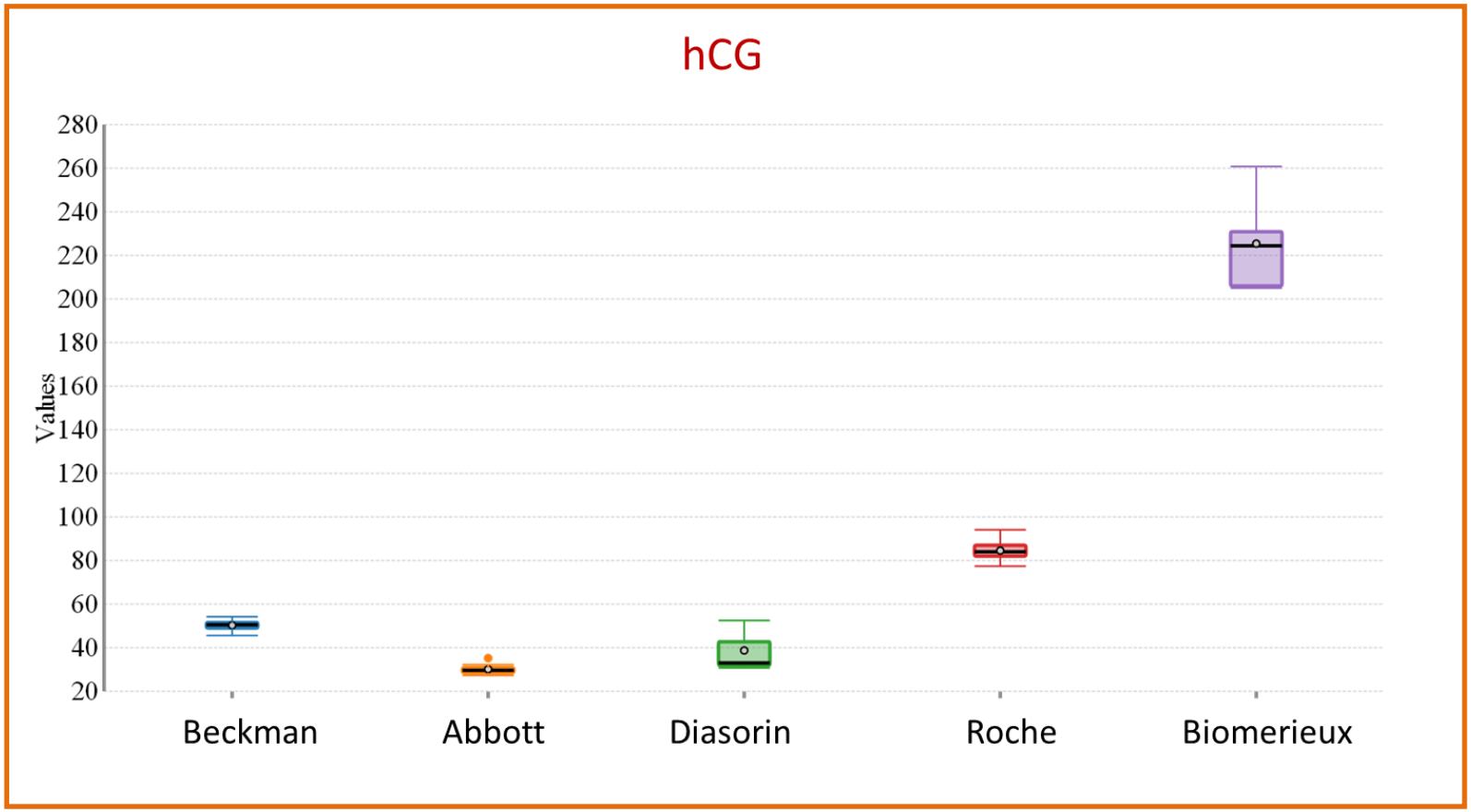
Cortisolo

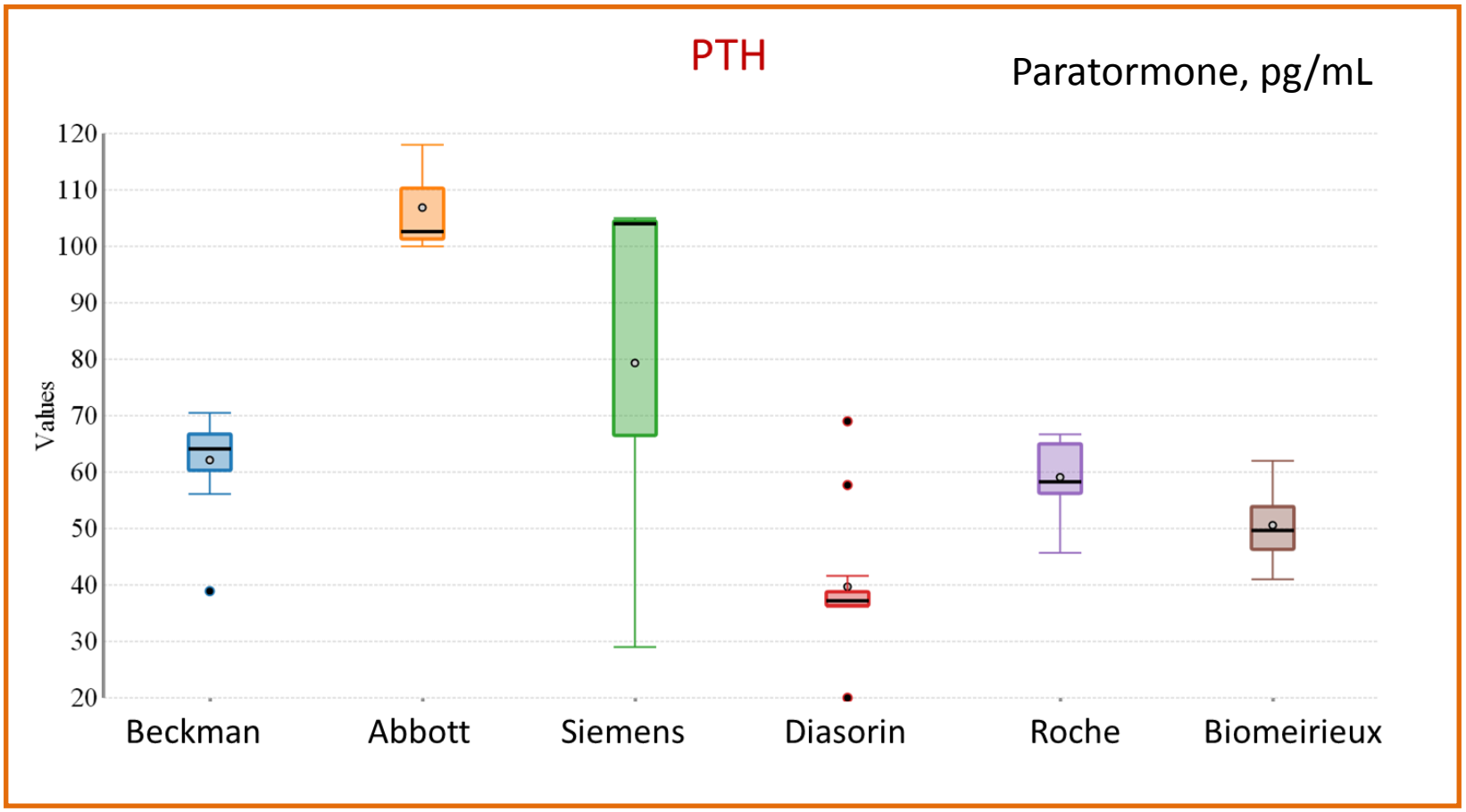



IGF1
IGF1, ng/mL
Values
35
30
25
20
15
10
5
0
Siemens
Diasorin


GH
HGH, ng/mL
Values
6.50
6
5.50
5
4.50
4
3.50
3
Beckman
Siemens
Diasorin

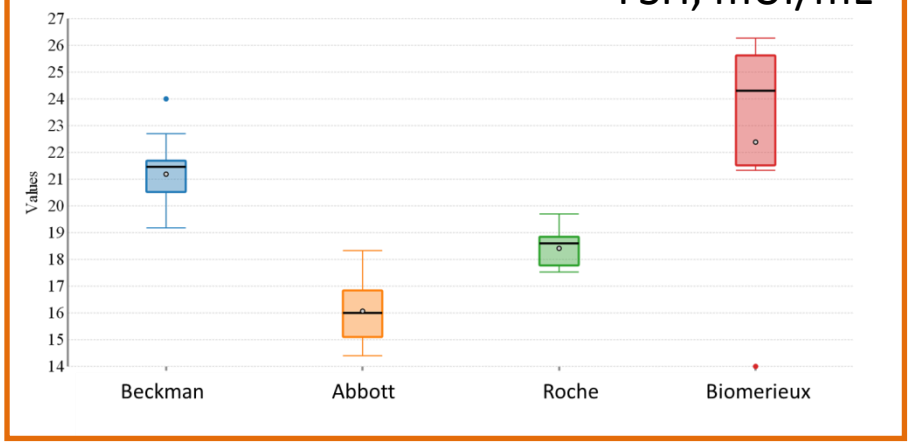
hCG, mUI/mL


hCG
Values
280
260
240
220
200
180
160
140
120
100
80
60
40
20
Beckman
Abbott
Diasorin
Roche
Biomerieux


PTH
Paratormone, pg/mL
Values
120
110
100
90
80
70
60
50
40
30
20
Beckman
Abbott
Siemens
Diasorin
Roche
Biomeirieux

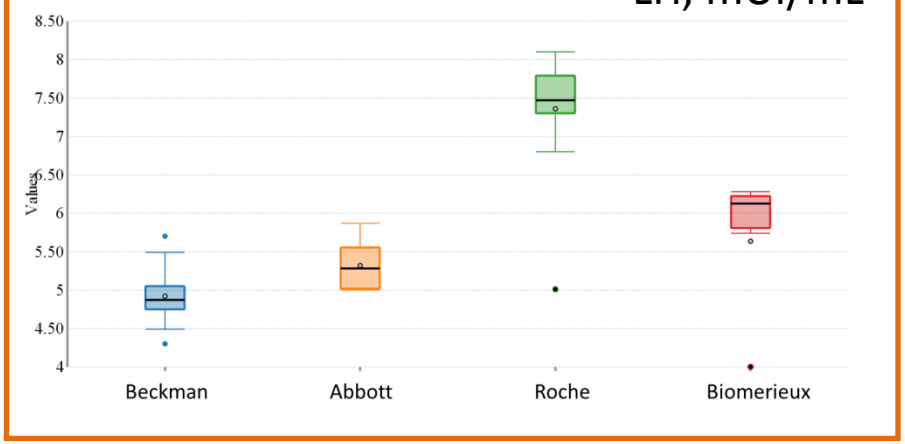
FSH

FSH, mUI/mL



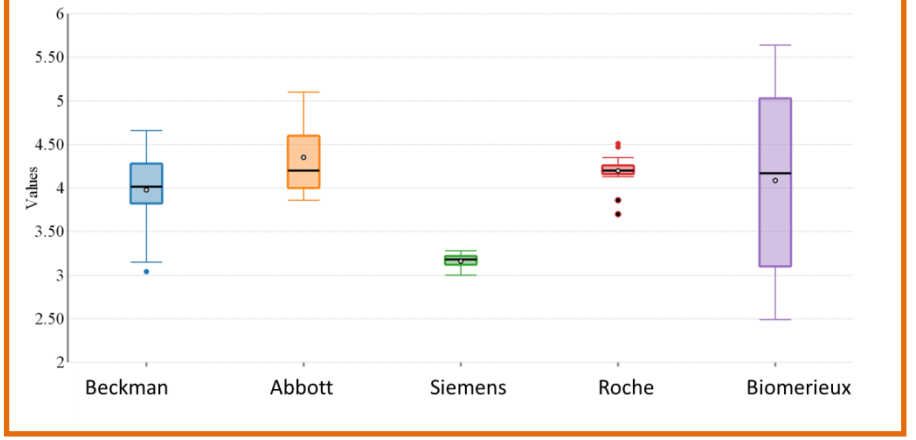
LH

LH, mUI/mL



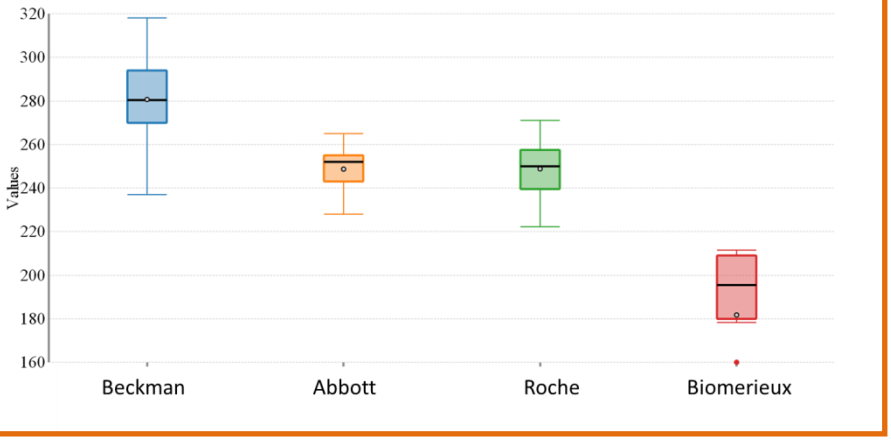
Progesterone, ng/mL

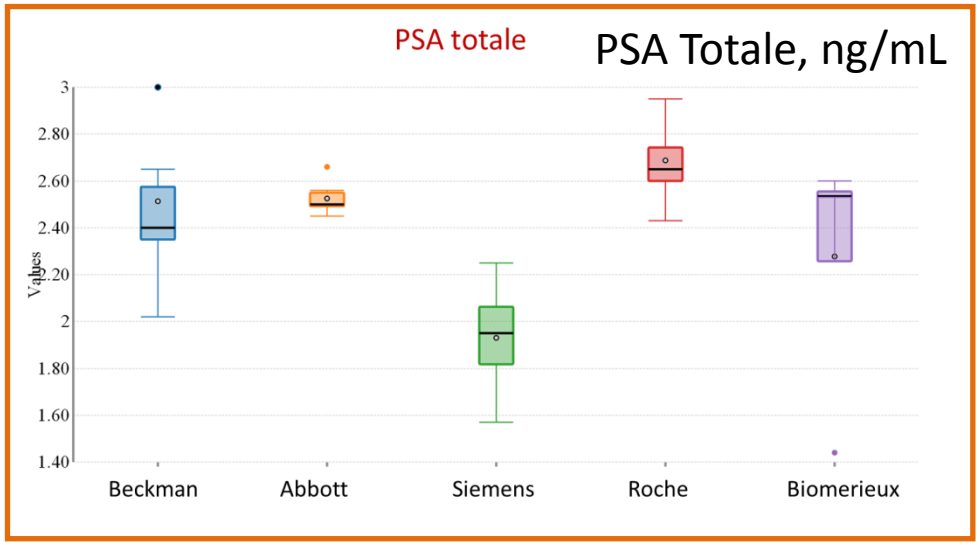
Progesterone

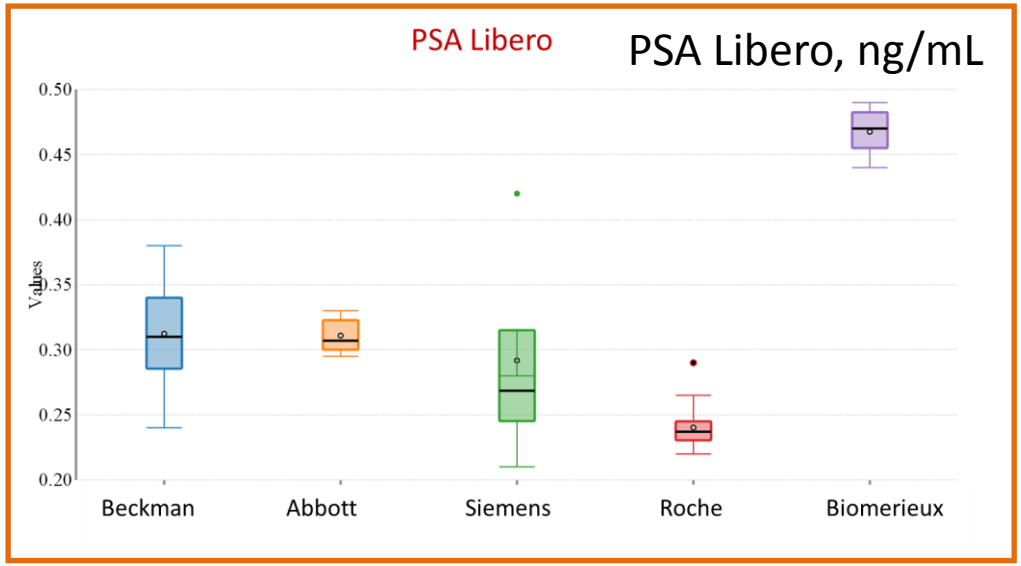


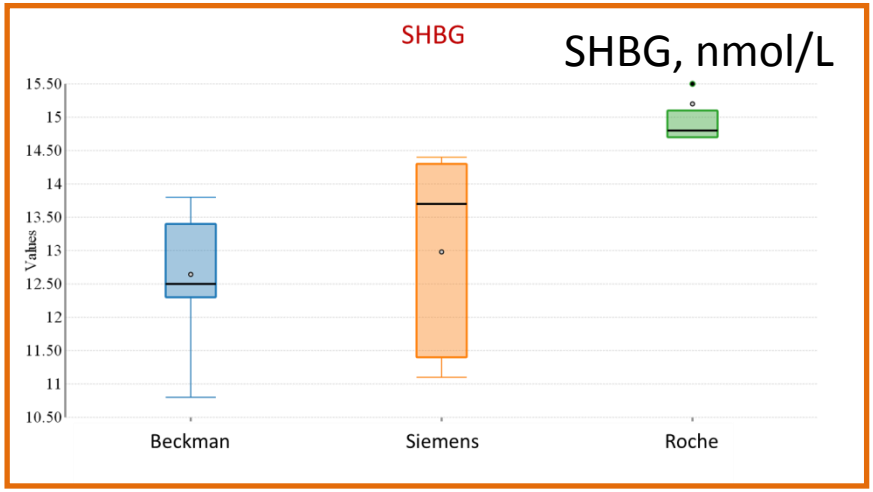
Estradiolo, pg/mL

17 beta-estradiolo

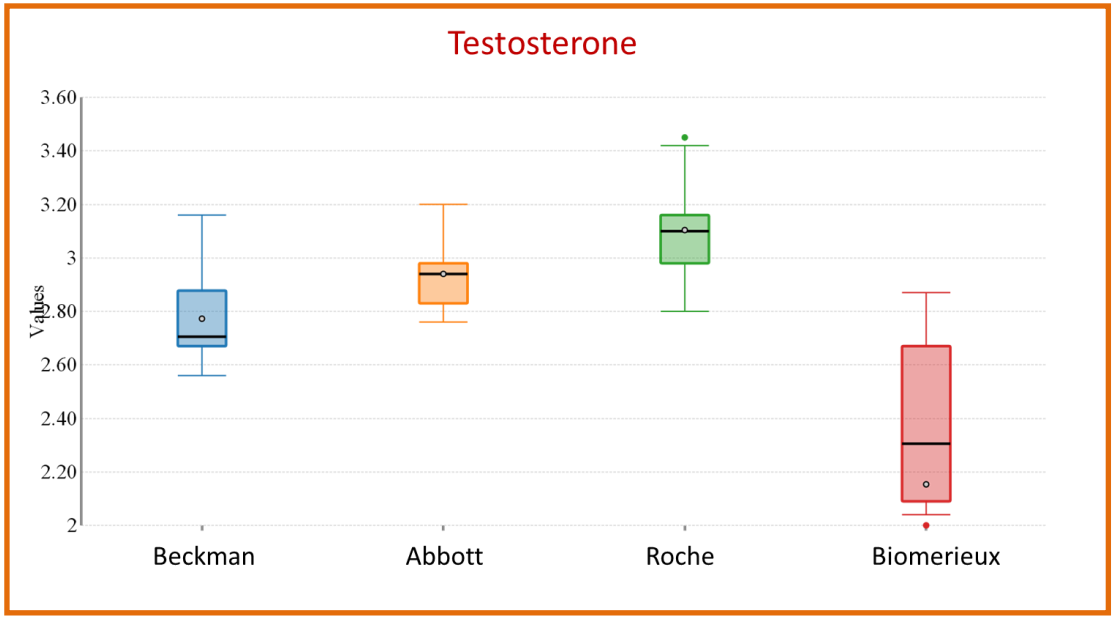


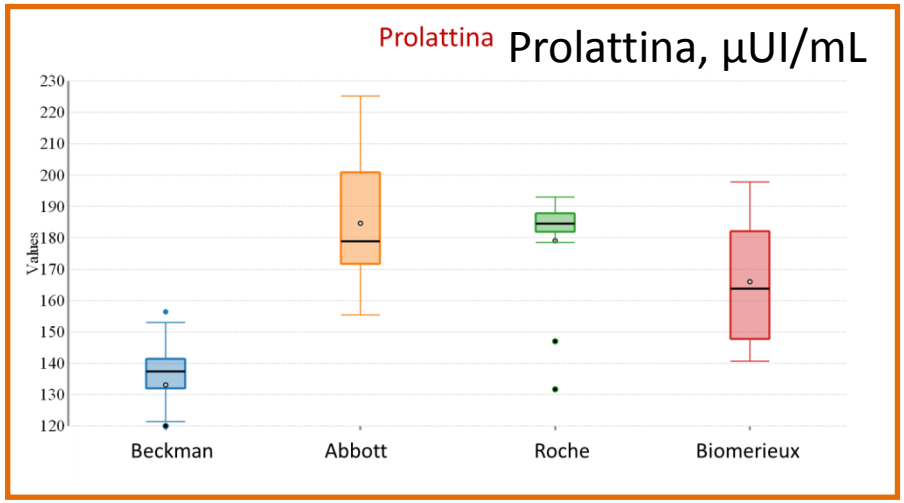

PSA totale
PSA Totale, ng/mL
Values
3
2.80
2.60
2.40
2.20
2
1.80
1.60
1.40
Beckman
Abbott
Siemens
Roche
Biomerieux

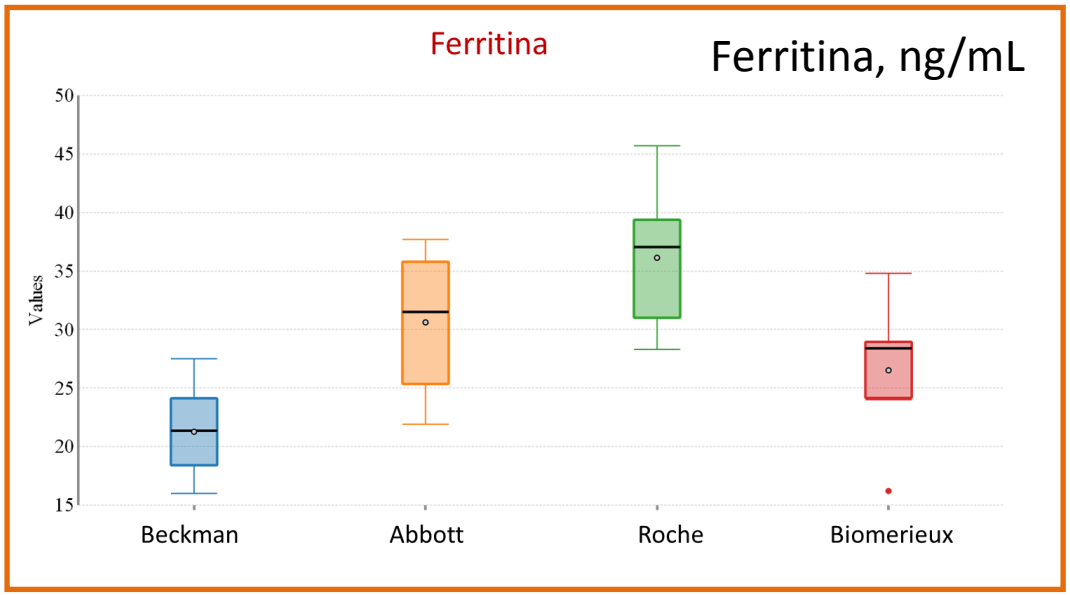

PSA Libero
PSA Libero, ng/mL
Values
0.50
0.45
0.40
0.35
0.30
0.25
0.20
Beckman
Abbott
Siemens
Roche
Biomerieux

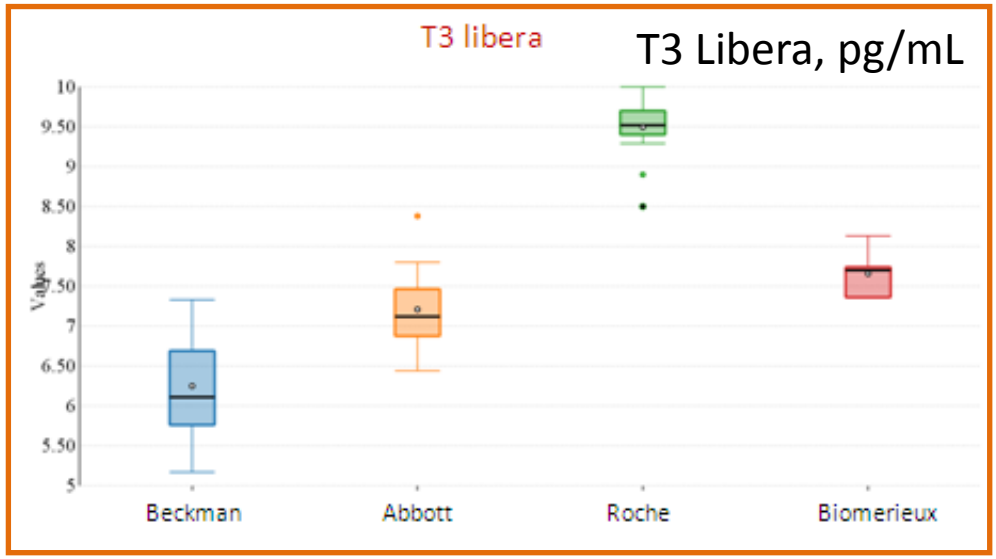


Testosterone, ng/mL



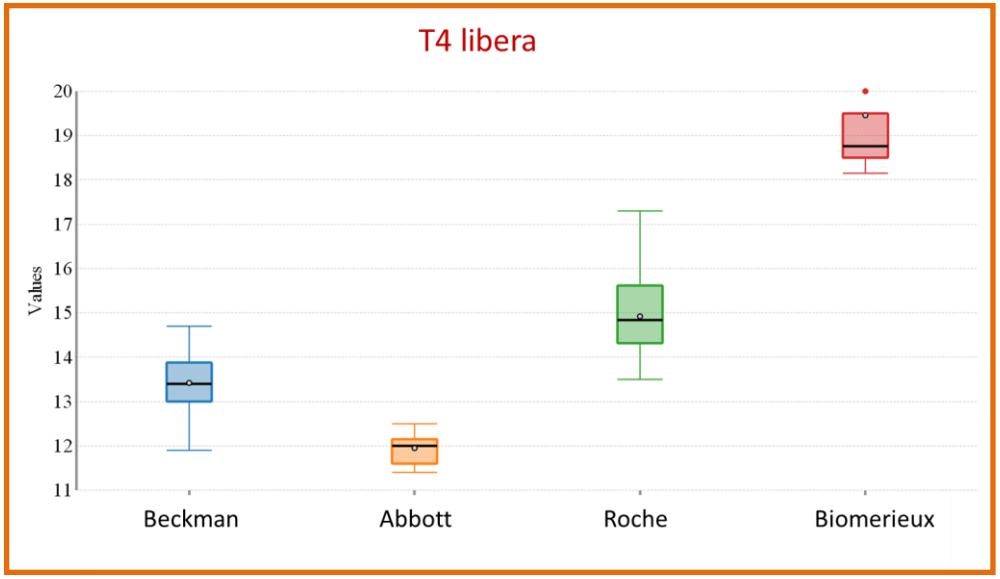

Prolattina
Prolattina, µUI/mL
Values
230
220
210
200
190
180
170
160
150
140
130
120
Beckman
Abbott
Roche
Biomerieux

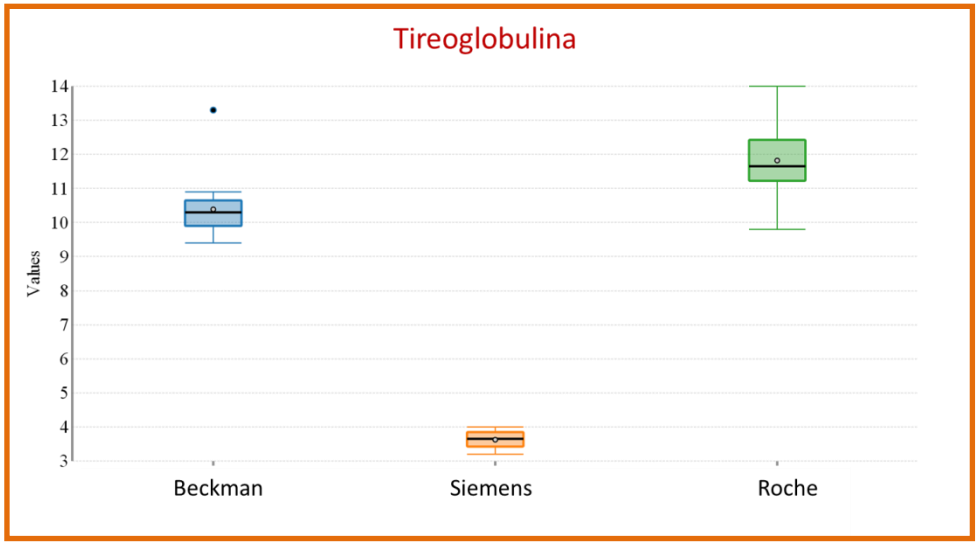

Ferritina
Ferritina, ng/mL
Values
50
45
40
35
30
25
20
15
Beckman
Abbott
Roche
Biomerieux



T3 Libera, pg/mL

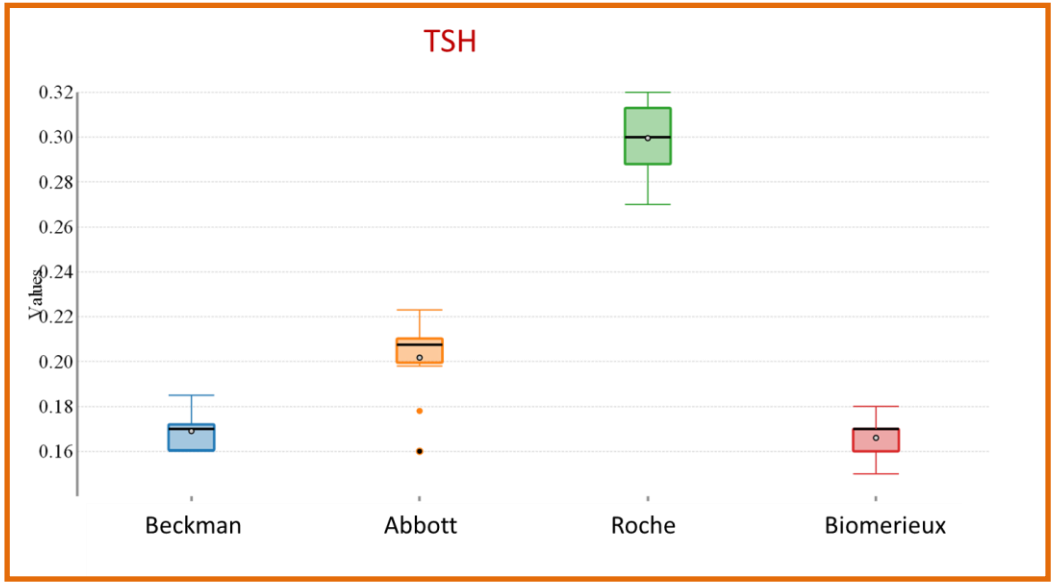
T4 Libera, pg/mL

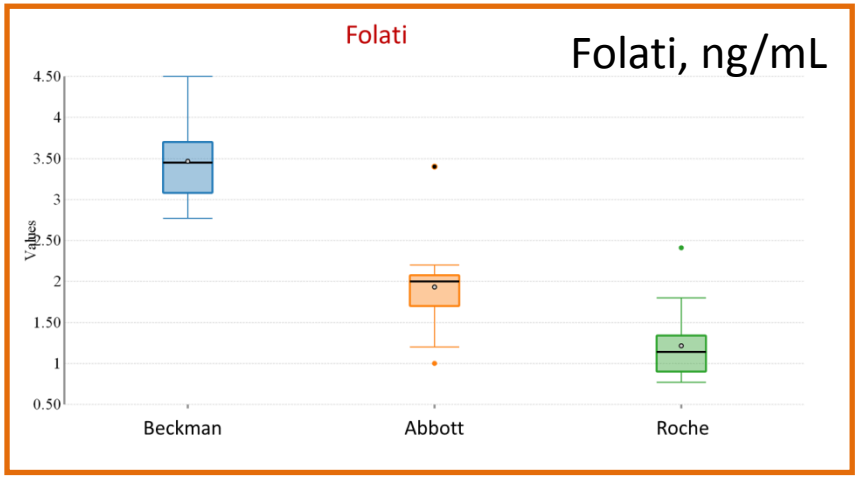


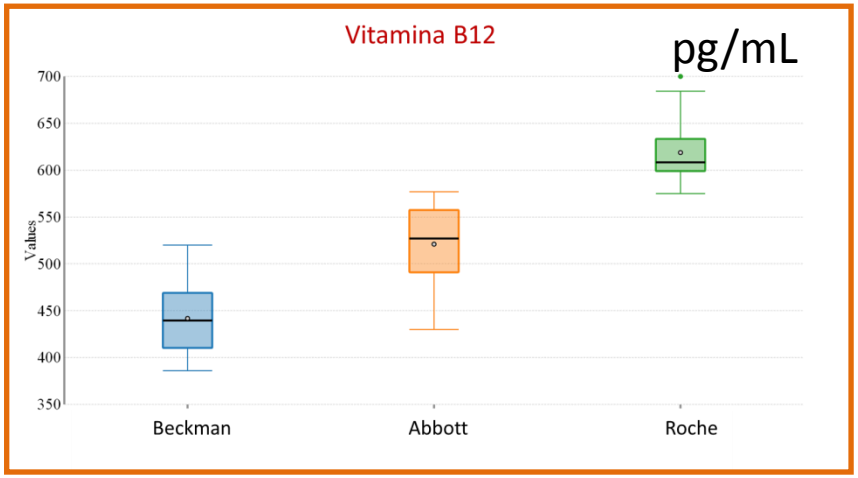


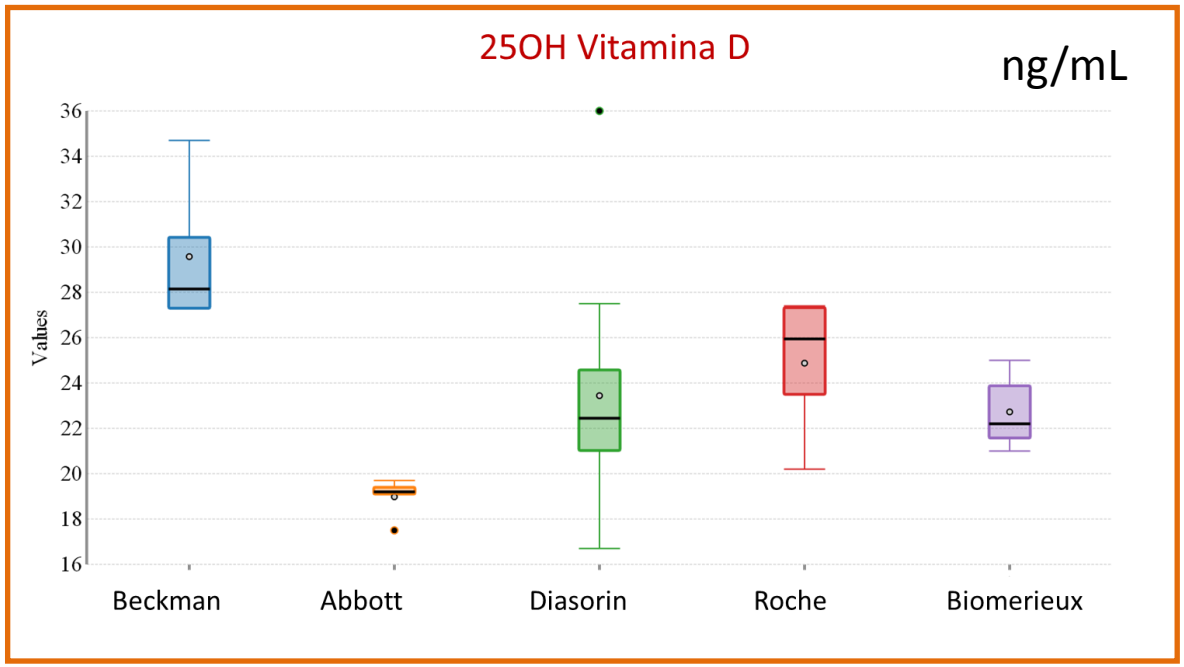
Tireoglobulina, ng/mL

TSH, µUI/mL




Folati
Folati, ng/mL
Values
4.50
4
3.50
3
2.50
2
1.50
1
0.50
Beckman
Abbott
Roche


Vitamina B12
pg/mL
Values
700
650
600
550
500
450
400
350
Beckman
Abbott
Roche


25OH Vitamina D
ng/mL
Values
36
34
32
30
28
26
24
22
20
18
16
Beckman
Abbott
Diasorin
Roche
Biomerieux

Conclusioni

1. Limiti di accettabilità calcolati in base al 95°percentile di tutti gli scostamenti
2. Alcuni Ormoni sembrano avere un errore totale maggiore a determinate concentrazioni
3. Alcune metodiche appaiono meno standardizzate di altre (anticorpi che riconoscono epitopi differenti delle molecole, problemi legati a molecole complesse)
4. L'uso di traguardi statistici per gruppi omogenei, potrebbe disincentivare l'adozione dei metodi migliori

Grazie per la vostra attenzione