ESEAP
EQALM Meeting 2022

Assessment and risk estimation of biotin interference in immunoassays

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ESEAP- Greek External Quality Assessment Scheme, Athens, GR
https://www.eseap.gr/

Main interferences in immunoassays (I)

Anti-streptavidin antibodies,
Anti-ruthenium antibodies,
Anti-alkaline phoshatase antibodies,
Hook effect,
Cross-reaction,
Macro analytes,
Heterophile antibodies,
HAAA,
RF,
Gammopathies.

BIOTIN:
COMPETITIVE ↑
SANDWICH ↓

Main interferences in immunoassays (II)

INTERFERENCES BY	ERROR TYPE
Biotin	COMPETITIVE: ↑ SANDWICH: ↓
Anti-streptavidin, anti-ruthenium, anti-alkaline phoshatase antibodies	COMPETITIVE:↑ SANDWICH:↑
Hook effect	↓
Cross-reaction	COMPETITIVE: ↑ SANDWICH: ↑OR↓
Macro analyte	↑
Heterophile antibodies, HAAA, RF	MOSTLY ↑ ↓ POSSIBLE
Gammopathy	↑ but also ↓ POSSIBLE

Biotin interference (I)

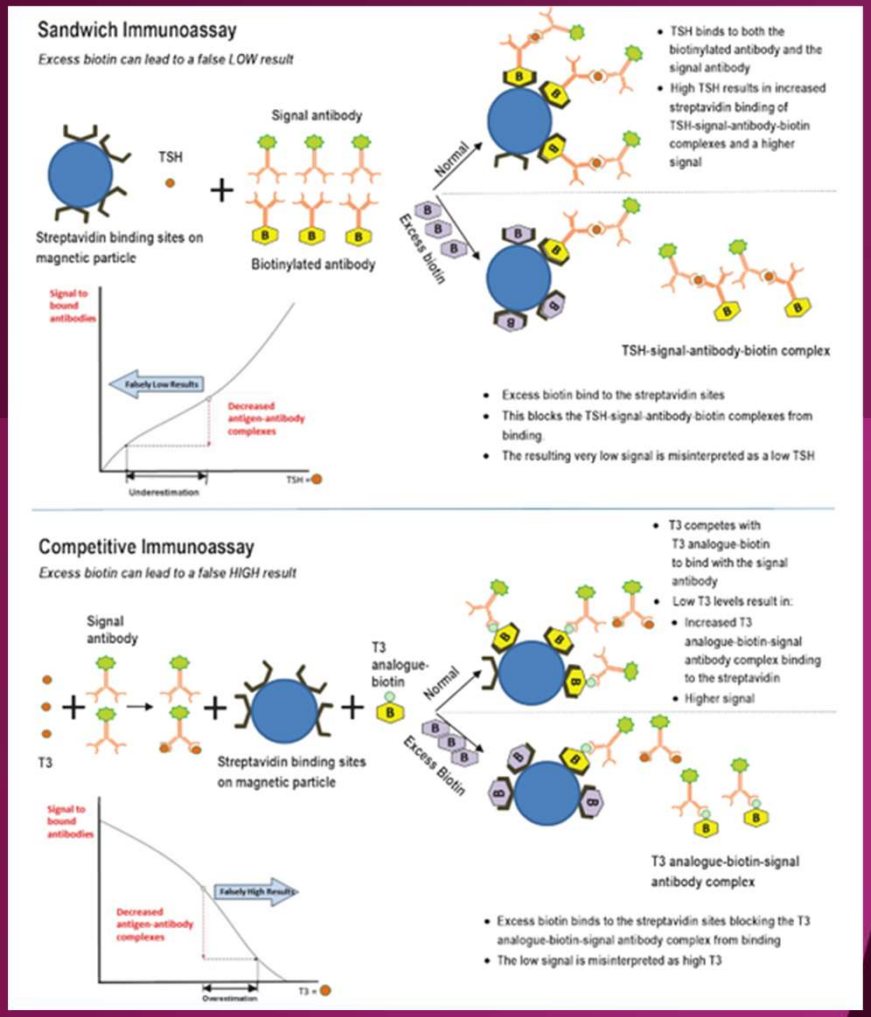
Among the most important interferences is that of biotin.

A common, usually *uncontrolled*, dietary supplement.

Excess use of biotin, mainly in nutritional supplements, creates a significant problem in laboratory results as in the majority of immunoassays the biotin-streptavidin complex is used.

The most serious incident of interference is that of the death of a patient in the ER, with symptoms of an acute myocardial infarction, from a falsely low troponin.

Biotin interference (II)



Methods

We used:

- Inserts from manufacturers,
- Bibliographic search of articles related to interferences in immunoassays,
- Communication and discussion with scientific specialists of IVD manufacturers,

in order to review the main interferences and detect automated immunoassay systems that are still affected by exogenous biotin.

Results

Platforms		Percentage of vulnerability to biotin interference **TODAY** (*mid 2022*)
Siemens	*Centaur*	20%
	Atellica	20%
Beckman Coulter (*but with* ***increased biotin threshold)***	*Access*	9%
	DxI800	9%
Abbott	*Architect*	0%
	Alinity	0%
Roche (*but with* ***increased biotin threshold)***		100%
Tosoh (*all current platforms*)		0%
SNIBE (*all platforms*)		1,2%

Conclusions

There is an increased number of reports related to biotin interference and visible efforts by IVD manufacturers to avoid it.

- Abbott's ARCHITECT & Alinity analyzers and all Tosoh and almost all SNIBE current assays are immune to biotin interference
- Access 2 and DxI 800 analyzers of Beckman Coulter have only 6 parameters measured with biotin-streptavidin assays (*threshold >10mg/day*).
- Siemens Centaur & Atellica analyzers: the percentage of vulnerability is about 20%
- Roche it is vulnerable 100% but *with low sensitivity to biotin*.

ΕΣΕΑΠ

Διοργανωτής ΣΔΙ
Αρ. πιστ. 820
ISO/IEC 17043: 2010

ISO 9001 TÜV NORD TÜV HELLAS SYSTEM CERTIFICATION
041080063-24/04/2008

Εθνικό
Σύστημα
Εξωτερικής
Αξιολόγησης
Ποιότητας

National System of External Quality Assessment

Proficiency Testing Scheme for Clinical Laboratories

https://www.eseap.gr/

Start of operation: June 1994

http://www.eseap.gr - - Microsoft Internet Explorer

ΕΚΘΕΣΗ ΑΠΟΤΕΛΕΣΜΑΤΩΝ

Γλυκόζη

Κύκλος 7 - Αποστολή 2 - 30/08/2006

Κωδικός εργ. 200

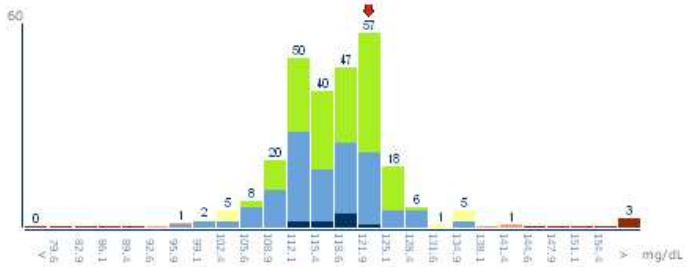
	Ορός Α Το αποτέλεσμα σας 125,00 mg/dL						
	N	N1	$\bar{x}$	SD	CV%	Δ(%)	SDI
Σύνολο εργ.	264	259	118,6	6,50	5,48	5,38 %	0,98
Η μέθοδός σας	128	126	117,8	6,73	5,71	6,08 %	1,07
Ο αναλυτής σας	9						

	Ορός Β Το αποτέλεσμα σας 184,00 mg/dL						
	N	N1	$\bar{x}$	SD	CV%	Δ(%)	SDI
Σύνολο εργ.	264	256	177,0	8,56	4,84	3,94 %	0,81
Η μέθοδός σας	128	123	176,5	9,47	5,37	4,28 %	0,80
Ο αναλυτής σας	9						

ΕΣΕΑΠ

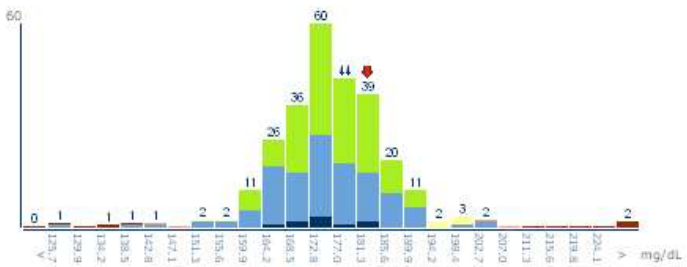
GLU

Ιστόγραμμα κατανομής ορού Α



Η μέθοδός σας
Ο αναλυτής σας
Σύνολο Μεθόδων
Οξειδάση της γλυκόζης
ROCHE - Hitachi Modular
Το αποτέλεσμά σας

Ιστόγραμμα κατανομής ορού Β



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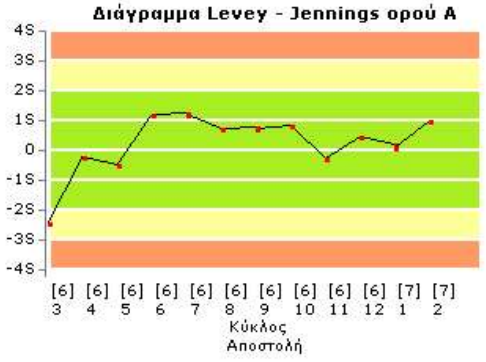
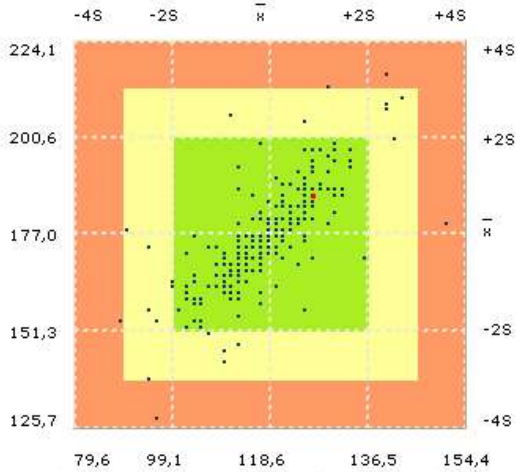
Διάγραμμα Levey - Jennings ορού Α



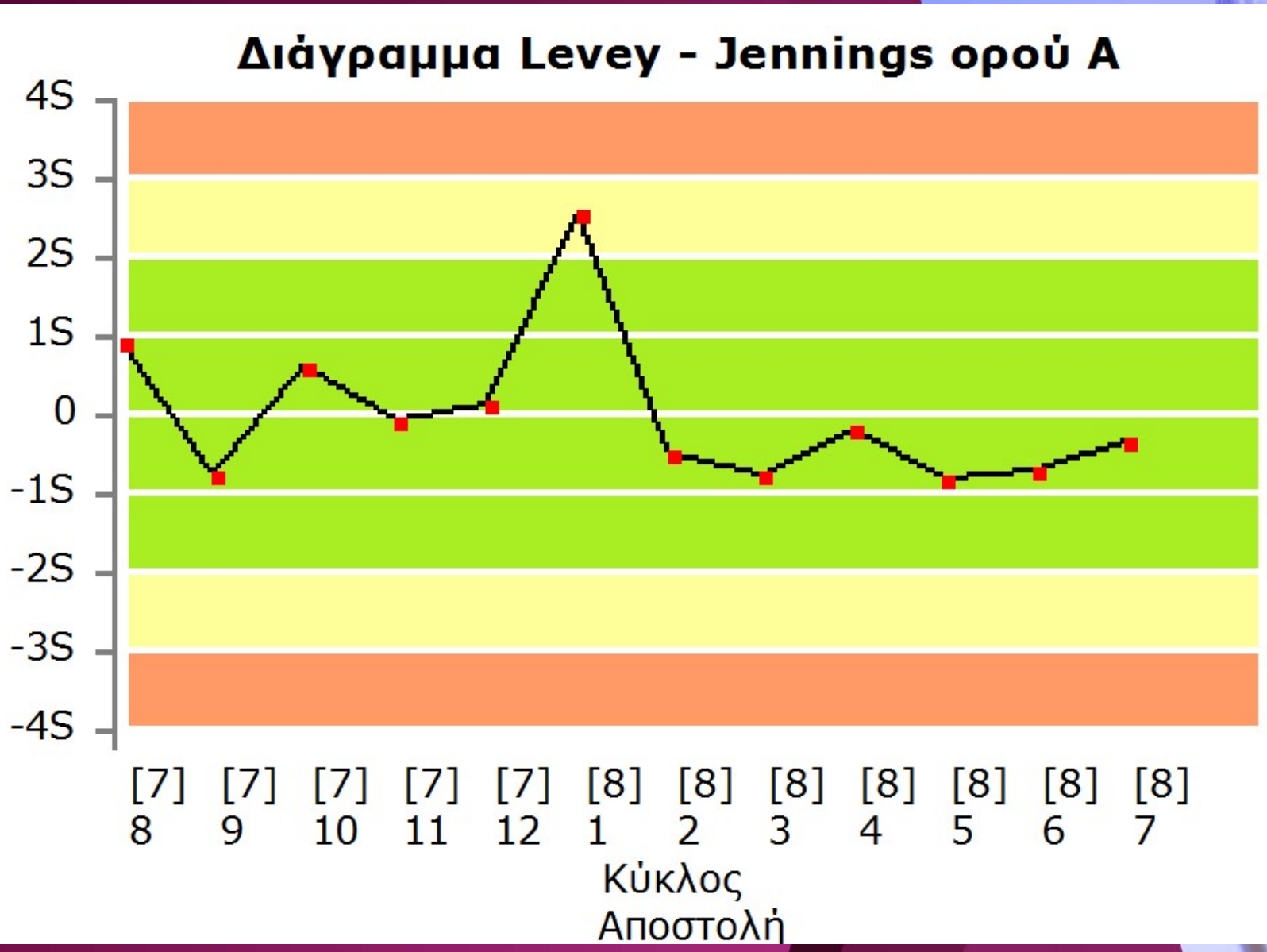
Διάγραμμα Youden



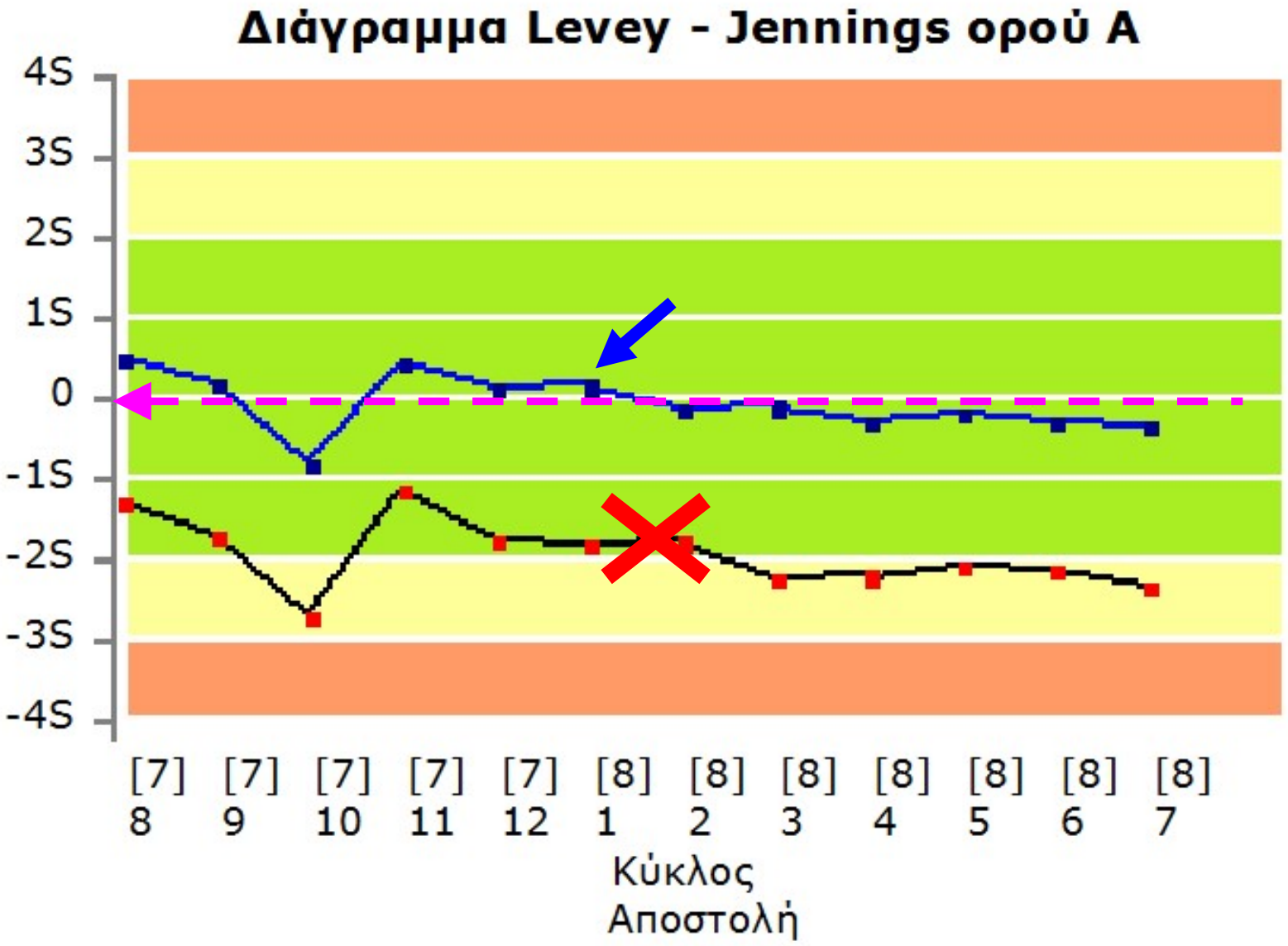
Διάγραμμα Levey - Jennings ορού Β

ΕΣΕΑΠ Εθνικό Σύστημα Εξωτερικής Αξιολόγησης Ποιότητος Αποτελεσμάτων στην Κλινική Χημεία ΕΔΡΑ: Ακαδημίας 57, 106 79 Αθήνα ΤΗΛ.: 210 7292403,210 3645751 fax: 210 7292403

Results Report of a single analyte (*Glucose*)

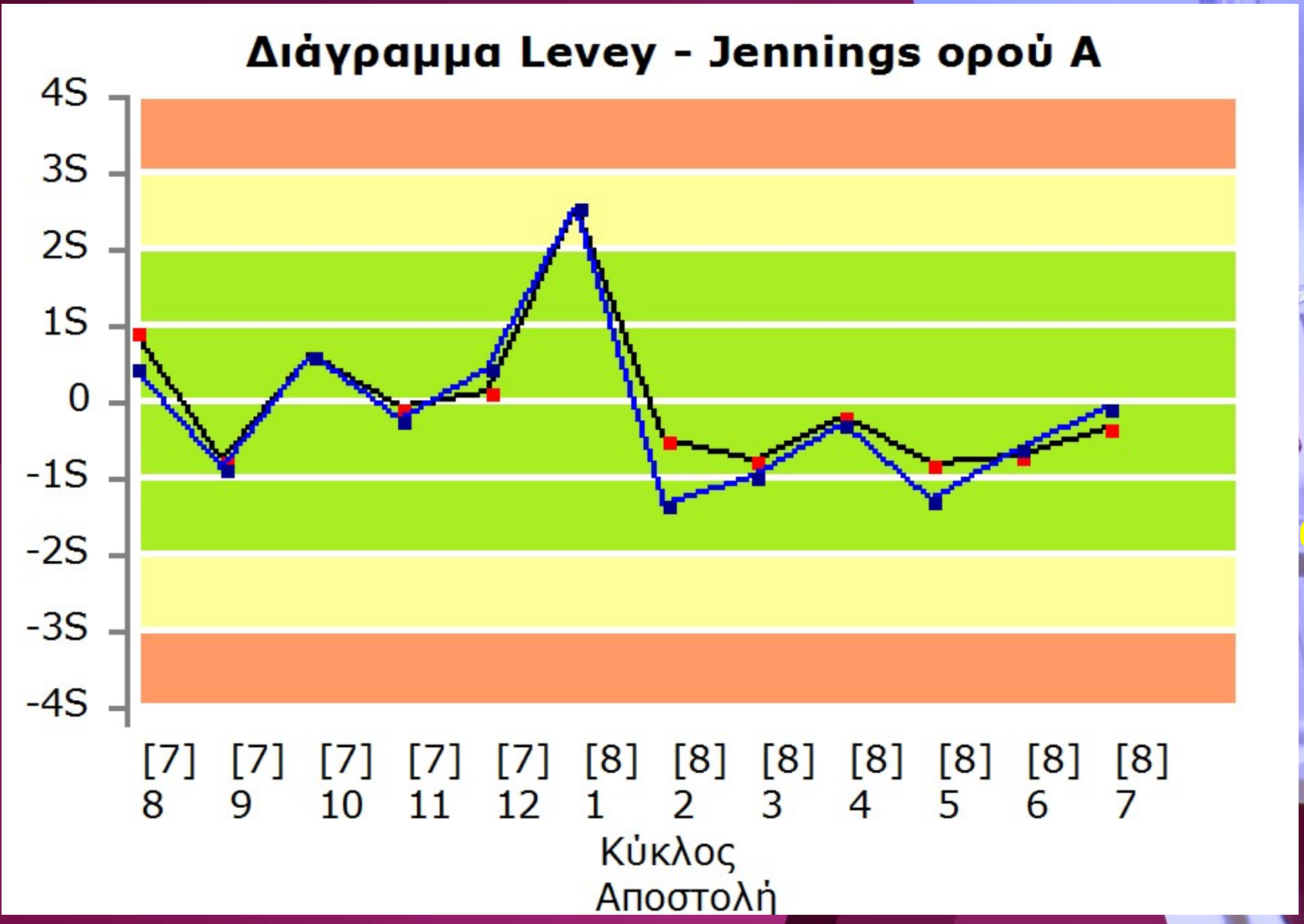


Levey-Jennings graph of a single sample



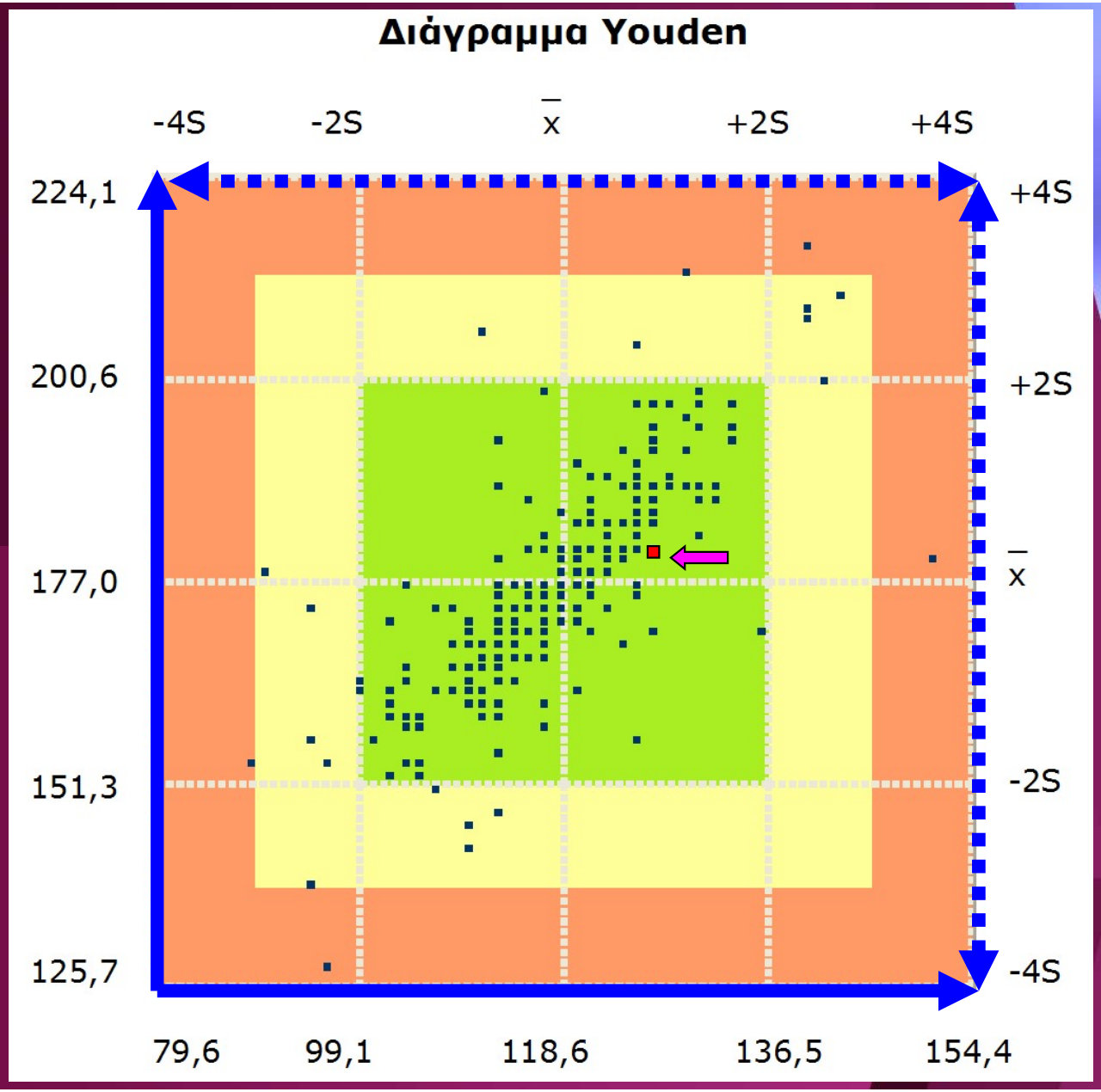
Levey-Jennings graph of a single sample

showing the *commutability* issues of control materials

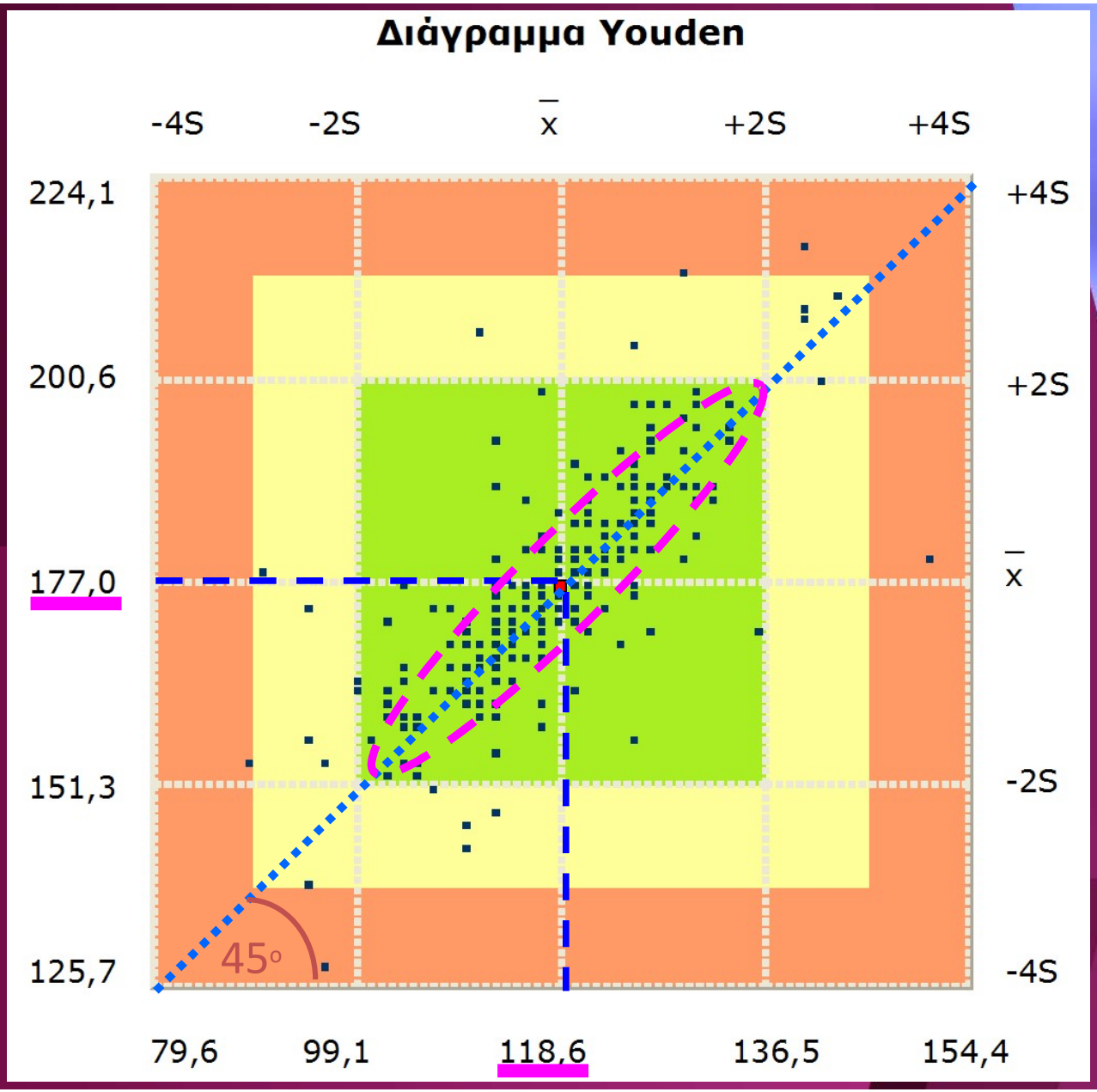


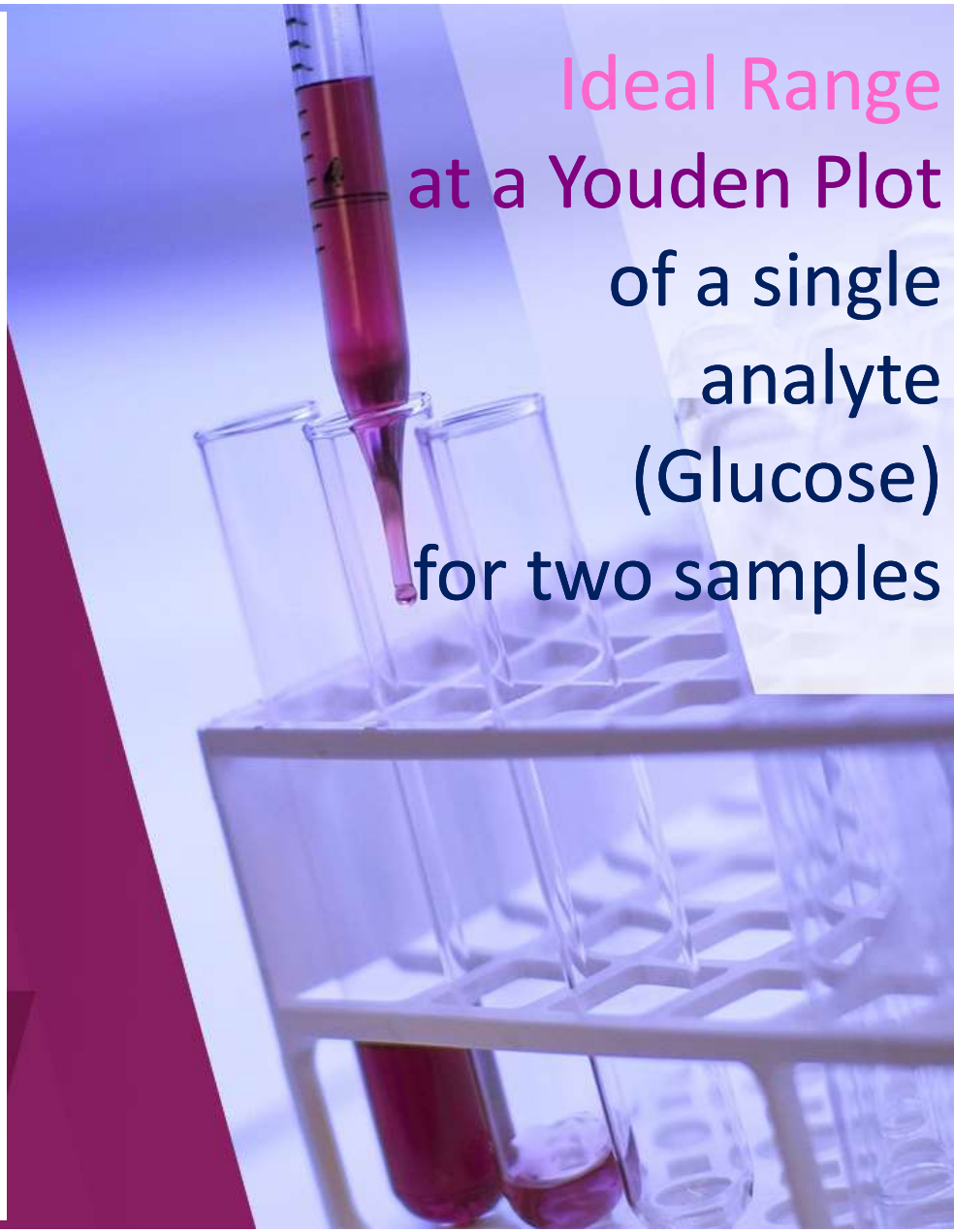
Levey-Jennings graph of a single sample

without *commutability* issues of control materials

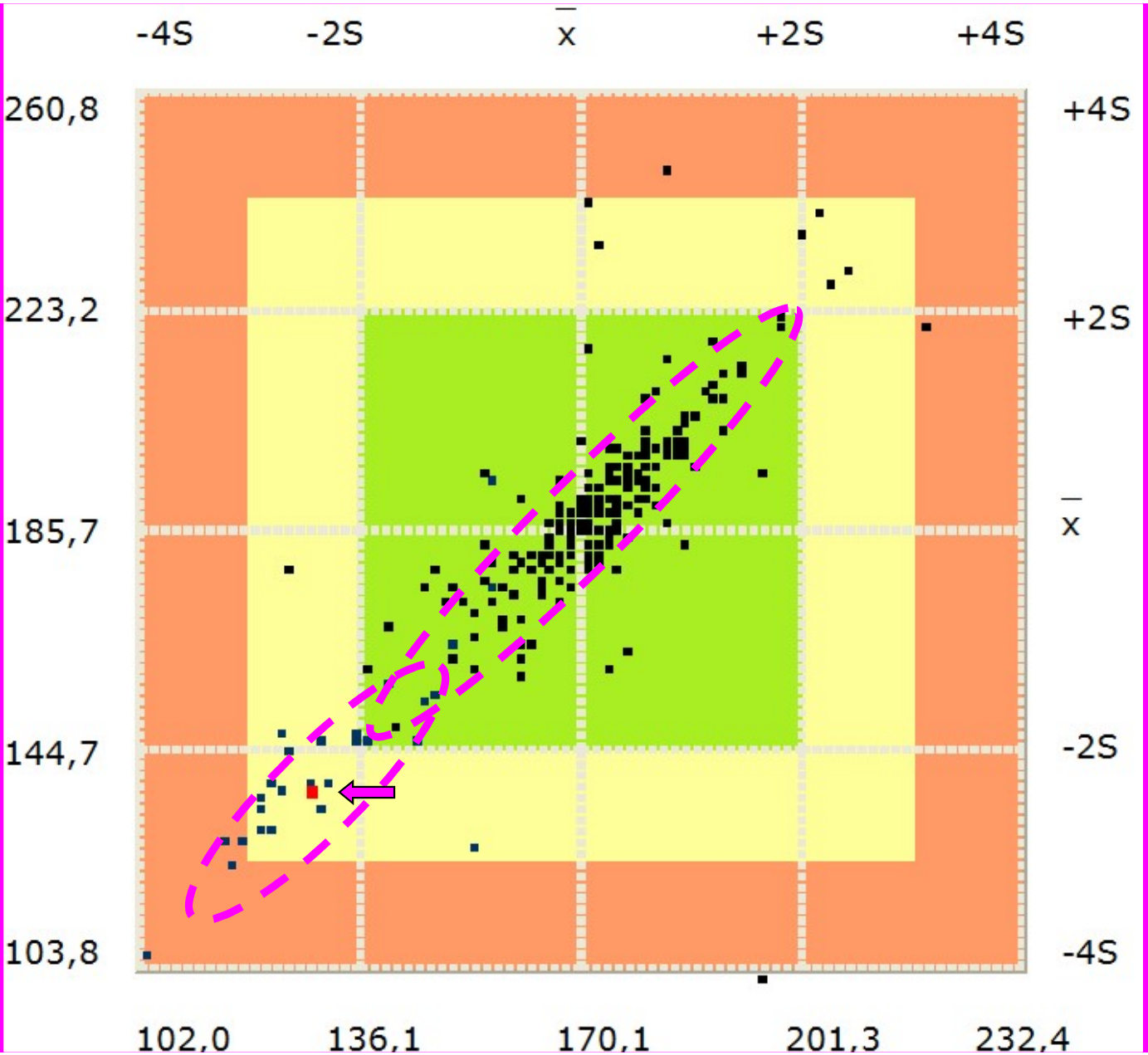


Youden Plot of a single analyte (Glucose) for two samples





Ideal Range at a Youden Plot of a single analyte (Glucose) for two samples



Ideal Ranges at a Youden Plot of a single analyte (Total Cholesterol) for two samples with commutability issues

Evaluation of Laboratories

Παράμετρος	1η	2η	3η	4η	5η	6η	7η	8η	9η	10η	11η	12η	Μ.Ο	Κατάταξη
[GLU] Γλυκόζη	9	9	9	6	9	10	8	6	10	10	10	8		
[UREA] Ουρία	10	10	10	9	8	8	10	6	10	6	9	9	**8,75**	**14/266**
[CREA] Κρεατινίνη	9	10	8	9	9	9	8	9	9	9	8	9		
[Na+] Νάτριο	9	10	8	5	-	-	-	-	-	-	-	-	**8,00**	-
[K+] Κάλιο	10	9	9	9	9	9	8	9	10	7	10	10	**9,08**	**2/239**
[T.PROT] Ολικά Λευκώματα	9	9	10	8	8	10	9	9	10	9	10	9	**9,17**	**4/260**
[ALB] Αλβουμίνη	9	8	8	10	9	10	10	10	10	10	9	10	**9,42**	**2/260**
[CHOL] Χοληστερόλη	10	10	10	10	10	8	9	9	9	9	10	9	**9,42**	**5/266**
[HDL] HDL-Χοληστερόλη	9	10	9	9	9	4	-	-	-	-	-	-	**8,33**	-
[TRIG] Τριγλυκερίδια	8	10	8	9	10	9	9	9	9	9	8	9	**8,92**	**7/265**
[URAC] Ουρικό οξύ	-	8	10	9	9	10	10	10	9	9	9	9	**9,27**	**6/266**
[TBIL] Χολερυθρίνη ολική	8	9	3	-	-	-	-	-	-	-	-	-	**6,67**	-
[Ca] Ασβέστιο	9	8	8	9	9	8	6	-	-	-	-	-	**8,14**	-
[P] Φωσφόρος	9	10	8	10	10	9	10	8	10	8	10	10	**9,33**	**2/246**
[Mg] Μαγνήσιο	10	9	8	5	-	-	-	-	-	-	-	-	**8,00**	-
[Fe] Σίδηρος	10	10	9	10	10	10	10	9	10	10	10	10	**9,83**	**1/244**
[AST] (SGOT)	9	9	7	10	10	10	8	10	9	8	-	-	**9,00**	**6/266**
[ALT] (SGPT)	10	10	8	9	10	9	10	10	9	4	-	-	**8,90**	**18/267**
[ALP] Αλκαλική Φωσφατάση	9	10	9	8	-	-	-	-	-	-	-	-	**9,00**	-
[GGT] γ-GT	10	10	10	9	10	10	10	9	10	9	8	9	**9,50**	**8/266**
[LDH] LDH	9	9	10	10	9	9	8	9	9	7	-	-	**8,90**	**9/251**
[CK] CK	9	8	9	9	10	9	9	10	10	4	-	-	**8,70**	**11/257**
[AMY] Αμυλάση	9	10	10	9	9	9	4	-	-	-	-	-	**8,57**	-
Μέσος Όρος (Μ.Ο.)	**9,23**	**9,35**	**8,61**	**8,68**	**9,32**	**8,95**	**8,67**	**8,88**	**9,56**	**8,00**	**9,25**	**9,25**	**8,80**	**8/267**

Proficiency Testing Schemes (1)

1) **Clinical Chemistry (Monthly and/or Bimonthly) from 1994**
   Glucose, Urea, Creatinine, Sodium, Potassium, Chloride, Total Protein, Albumin, Cholesterol, HDL-cholesterol, Triglycerides, Urate, Bilirubin, Direct Bilirubin, Calcium, Phosphate, Magnesium, Iron, AST/ ALT, ALP, γGT, LDH, CK, Amylase
2) **Hemoglobin A1C (HbA1c) (twice per month) from 2007** ***in cooperation with EuroRefLab***
3) **Cardiac Markers and hs-CRP from 2008**
   CK, CK-MB mass, CK-MB activity, Troponin-T, Troponin-I, high sensitivity CRP (hs-CRP), BNP, pro-BNP
4) **TDM (Therapeutic Drug Monitoring) from 2011.**
   Digoxin, Phenytoin, Valproate, Phenobarbital, Vancomycin, Acetylsalicylic acid, Paracetamol, Methotrexate
5) **Coagulation Factors from 2013**.
   Prothrombin Time (PT), Prothrombin Time INR, Partial Thromboplastin Time (PTT), Antithrombin III(AT III), Fibrinogen
6) **Thyroid Hormones from 2010**
   TSH, FT3, FT4, T3, T4, Anti-TPO, Anti-TG, Thyroglobulin

Proficiency Testing Schemes (2)

7) Reproductive Hormones & Anemia Markers from 2012
FSH, LH, Oestradiol (E2), Progesterone, Prolactin, Testosterone, Human Chorionic Gonadotropin (HCG), Alpha-fetoprotein (AFP), Cortisol, Ferritin, Vitamin B12, Folic Acid, Transferrin

8) Tumor Markers from 2012
PSA, Free PSA, CEA (Carcinoembryonic antigen), Alpha-fetoprotein (AFP), CA 125, CA 15-3, CA 19-9, β2-microglobulin, TMAB

9) Specific Proteins from 2015
ASTO, CRP, Rheumatoid factor(RF), Transferrin, Quantitative measurement of immunoglobulins (IgG, IgA, IgM, IgE), Complement components (C3, C4), Ferritin, Vitamin B12, Folic Acid

10) Immunology (2 schemes):

- Systemic autoantibodies (single donor special sample from): Antinuclear antibodies (ANA), Anti-mitochondrial antibodies (AMA), Anti-dsDNA antibodies, Anti-ENA antibodies (SS-A, SS-B, RNP, Sm), Anti–Scl-70 antibodies (Scl-70), Anti–Jo1 antibodies, Antibodies against Beta-2-Glycoprotein I (β2GPI) IgG & IgM and Cardiolipin antibodies (αCL) IgG & IgM
- Quantitative immunological parameters (sample of immunochemical parameters): Anti-TPO, Anti-TG, Quantitative measurement of immunoglobulins (IgG, IgA, IgM, IgE), Complement components (C3, C4) and Reumatoid Factor (RF)

Proficiency Testing Schemes (3)

11) Viral Markers I (TORCH) from 2017:
Toxoplasma antibodies IgG & IgM, Cytomegalovirus antibodies IgG & IgM, Rubella antibodies IgG & IgM and HSV 1 & 2 antibodies IgG & IgM

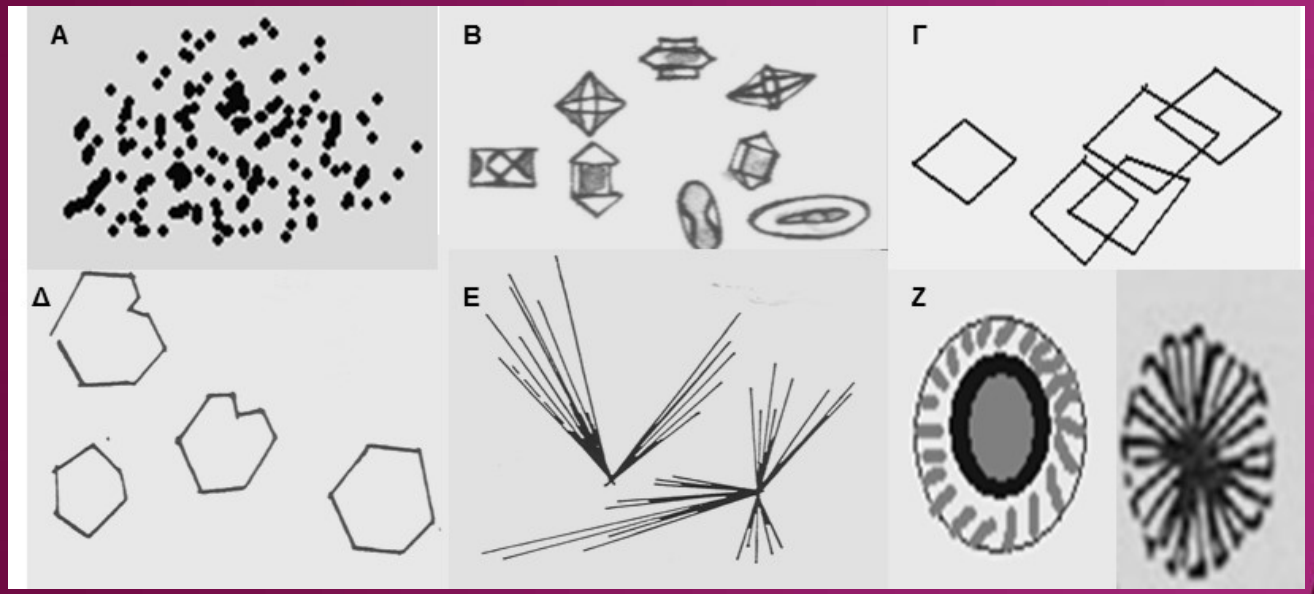
12) Viral Markers II - STDs *in cooperation with EuroRefLab* from 2017
Australian antigen (HBsAg), Anti-HBc antibodies, Anti-HBs antibodies, anti-HCV antibodies, anti-HIV & anti-HTLV antibodies, anti-Treponema pallidum antibodies

13) 25-hydroxyvitamin D (25OHD) *in cooperation with DEQAS UK* from 2015

14) Combined Clinical Chemistry (Glucose, Urea, Creatinine, Sodium, Potassium, Chloride, Total Protein, Albumin, Cholesterol, HDL-cholesterol, Triglycerides, Urate, Bilirubin, Direct Bilirubin, Calcium, Phosphate, Magnesium, Iron, AST/ ALT, ALP, γGT, LDH, CK, Amylase) along with frequent Immunochemistries (CRP, Ferritin, Folic Acid, B12, FT3, FT4, TSH, PSA, β-HCG and Oestradiol (E2)) 12 samples per year and bimonthly analysis.

Urinalysis - Pilot scheme

Urinalysis:
Will include biochemical and microscopy evaluation, in a liquid sample ready for use.
Two Samples, Bimonthly analysis.



Thank you

for your attention!!!

Questions?…