Azienda Ospedaliero-Universitaria Careggi - Firenze

REGIONE TOSCANA

Centro Regionale di Riferimento per il Controllo di Qualità

VEQ Proteine Specifiche Ciclo 2017

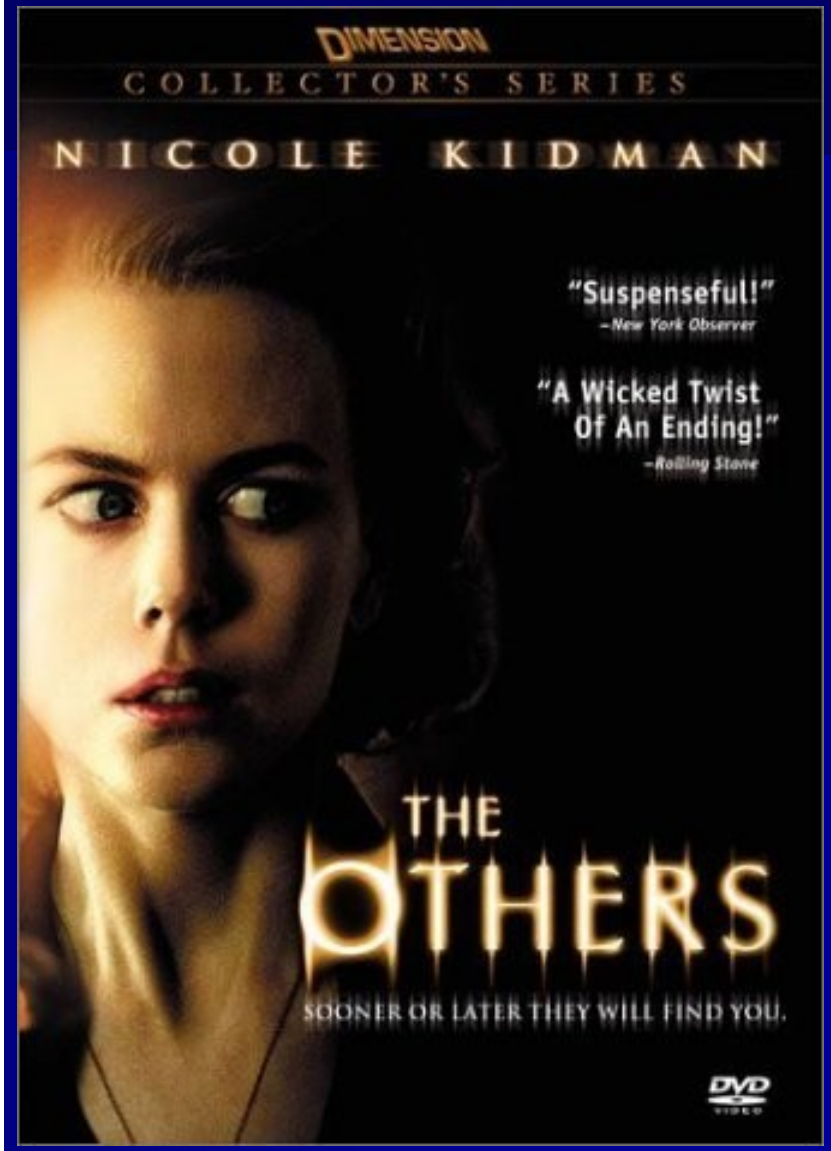
Paolo Chiarugi

U.O. Analisi Chimico-Cliniche

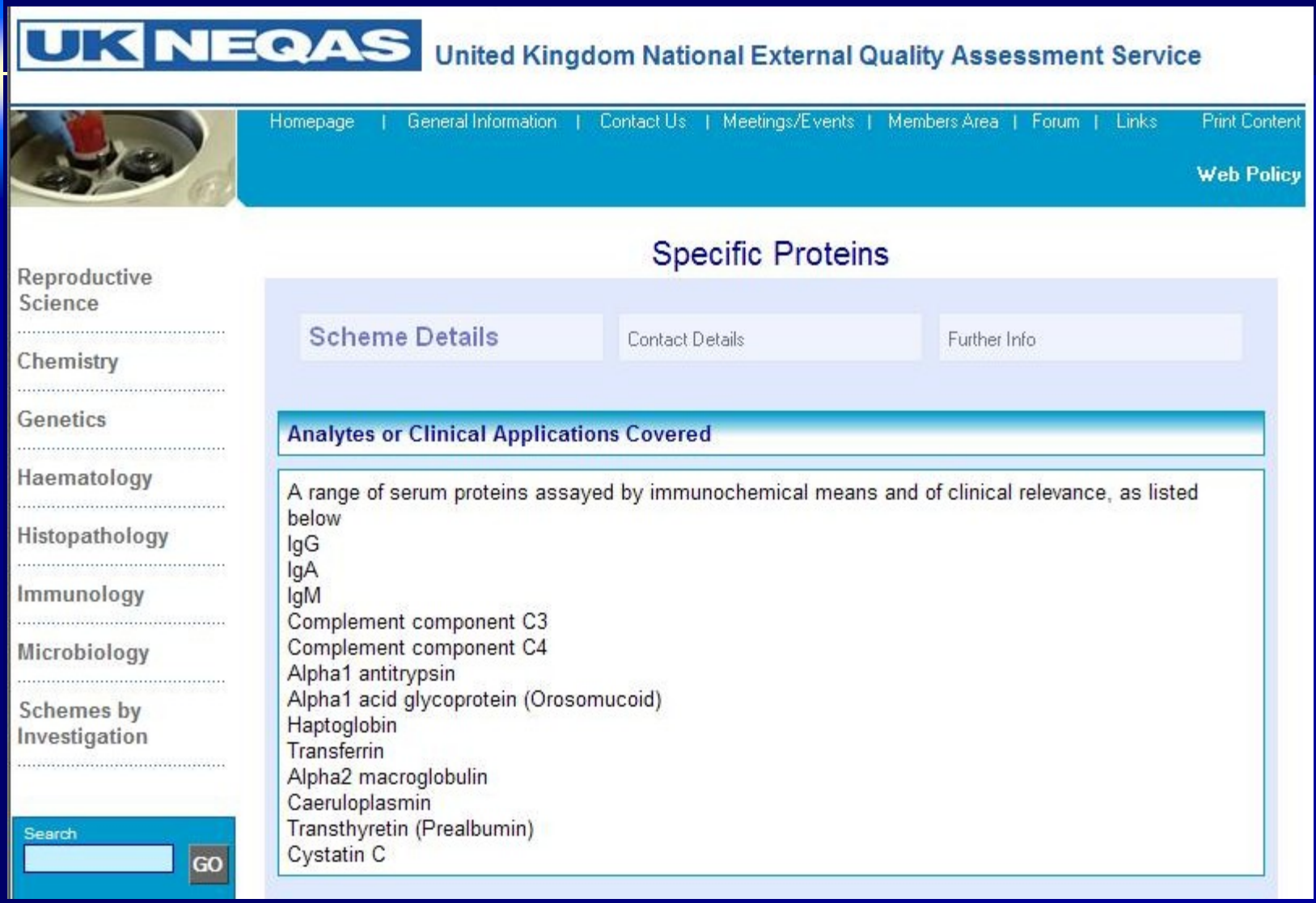
AOUP Pisa

Proteine Specifiche o Aspecifiche ?

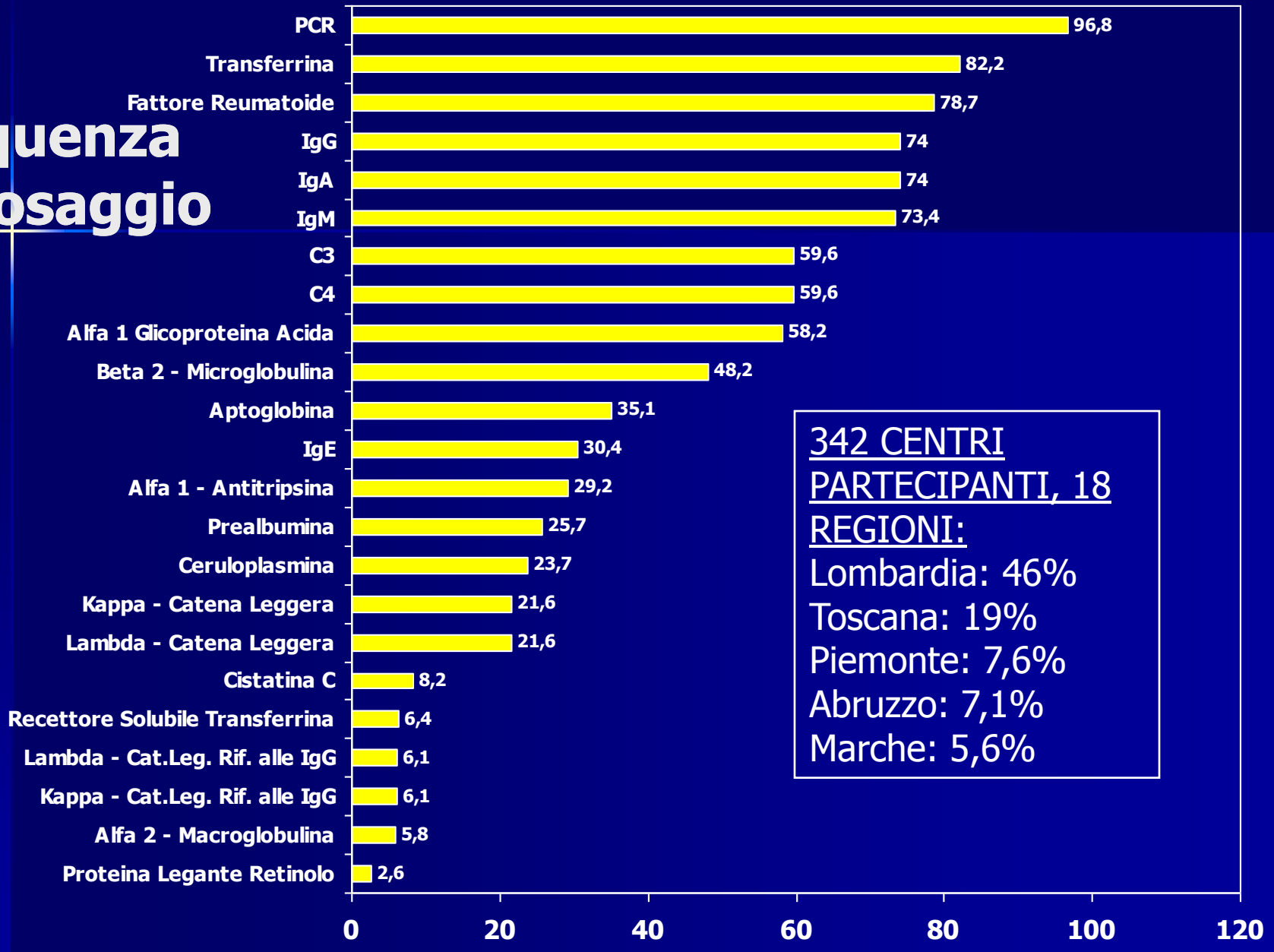
PROTEINA	Val.Rif. (g/L)	Sintesi
Alfa 1 - Antitripsina	0,9 - 2,0	Fegato
Alfa 1 Glicoproteina Acida	0,5 - 1,2	Fegato
Alfa 2 - Macroglobulina	1,3 – 3,0	Fegato
Aptoglobina	0,3 – 2,0	Fegato
Beta 2 - Microglobulina	0,0008 – 0,0025	Ubiquitaria
C3	0,9 – 1,8	Fegato
C4	0,1 – 0,4	Fegato
Ceruloplasmina	0,2 – 0,6	Fegato
Cistatina C	0,0006 – 0,0014	Ubiquitaria
Fattore Reumatoide	<10 UI/mL	S.I.
IgA	0,7 – 4,0	S.I.
IgE	<0,00043	S.I.
IgG	7 – 16	S.I.
IgM	0,4 – 2,3	S.I.
Kappa-Catena Leggera	2 - 4	S.I.
Lambda-Catena Leggera	1 – 2,4	S.I.
Proteina C Reattiva	< 0,005	Fegato
Prealbumina	0,2 – 0,4	Fegato
Proteina Legante il Retinolo	0,03 – 0,06	Fegato
Recettore Solubile Transferrina	0,0008 – 0,0018	Ubiquitaria
Transferrina	2,0 – 3,6	Fegato



VEQ Proteine Specifiche



Frequenza di dosaggio



342 CENTRI PARTECIPANTI, 18 REGIONI:
Lombardia: 46%
Toscana: 19%
Piemonte: 7,6%
Abruzzo: 7,1%
Marche: 5,6%

Metodi usati 19085 test, campioni 7 su 8

METODO	%	VARIANTI	STRUMENTO e/o REAGENTE + USATO	
AGGLUTINAZIONE	0,3	7		SIEMENS
CARD	0,1	4	I-CHROMA	BODITECH
CHEMILUM.	1,0	13	IMMULITE 2000	MEDICAL SYSTEM
COLORIMETRICO	0,03	1	CHEMACOMP 100	G.D.
DRY CHEMISTRY	0,3	4	VITROS	ORTHO
ELFA	1,13	2	VIDAS	BIOMERIEUX
IMMUNODIFF.	1,3	6		LIOFILCHEM
IMMUNOENZ.	0,15	7	CHORUS	DIESSE
IMMUNOFLUOR.	0,3	4	AIA	TOSOH
IMMUNOPREC.	0,03	1	NYCOCARD	SENTINEL
IMMUNOTURB.	64,5	167	COBAS	ROCHE
MEIA	0,02	1	AXSYM	ABBOTT
NEFELOMETRICO	29,7	34	B.N.	SIEMENS

% Metodi usati per analisi

	TURBIDIM.	NEFELOM.	RID	ALTRO
Alfa 1 - Antitripsina	40	60	0	0
Alfa 1 Glicoproteina Acida	67	30	2	1
Alfa 2 - Macroglobulina	14	86	0	0
Aptoglobina	54	46	0	0
Beta 2 - Microglobulina	49	24	0	27
C3	68	31	2	0
C4	68	31	2	0
Ceruloplasmina	35	64	1	0
Cistatina C	21	79	0	0
Fattore Reumatoide	77	19	0	4
IgA	73	24	3	0
IgE	11	23	0	66
IgG	72	25	3	0
IgM	73	24	3	0
Kappa - Cat.Leg. Rif. alle IgG	10	90	0	0
Kappa - Catena Leggera	38	62	0	0
Lambda - Cat.Leg. Rif. alle IgG	10	90	0	0
Lambda - Catena Leggera	38	62	0	0
PCR	87	9	0	5
Prealbumina	57	43	0	0
Proteina Legante Retinolo	4	96	0	0
Recettore Solubile Transferrina	3	86	0	11
Transferrina	82	16	2	0

CRM 470: la nuova era delle proteine specifiche

special report

CLIN. CHEM. 40/6, 934–938 (1994)

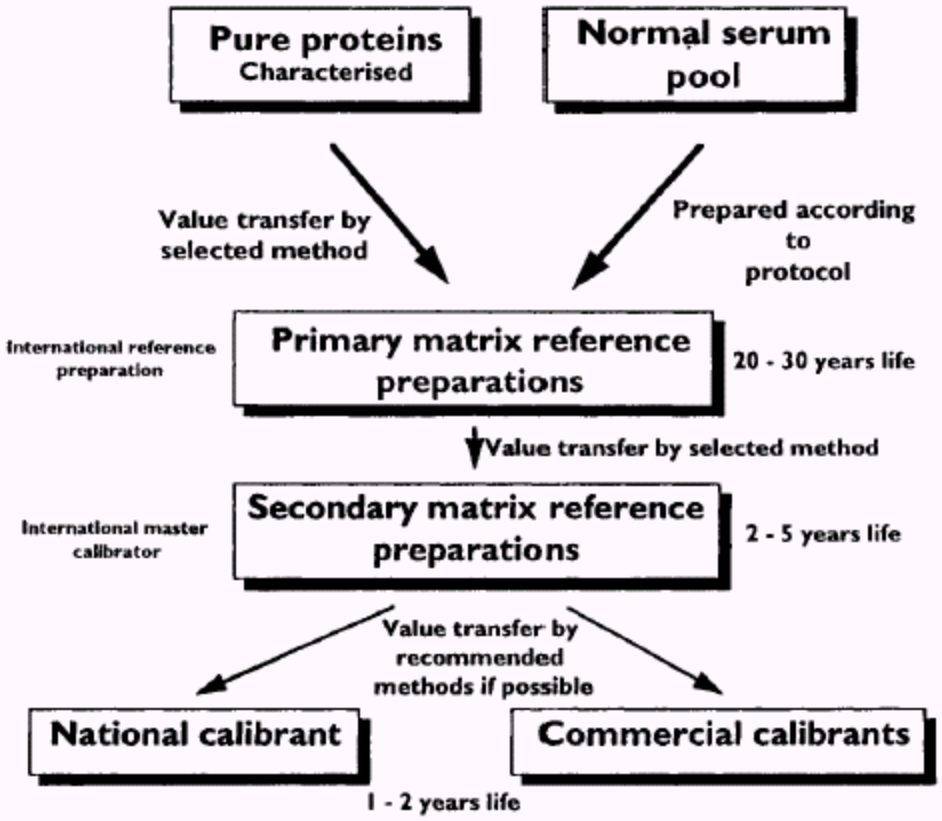
New International Reference Preparation for Proteins in Human Serum (RPPHS)

John T. Whicher,[1] Robert F. Ritchie,[2] A. Myron Johnson,[3] Siegfried Baudner,[4] Jacques Bienvenu,[5] Soren Blirup-Jensen,[6] Anders Carlstrom,[7] Francesco Dati,[4] Anthony Milford Ward,[8] and Per Just Svendsen[6]

Table 1. International reference preparations used in value assignment of the RPPHS.

Protein	USNRP, lot no. 12-0575C	Pure proteins	C-reactive protein, WHO 85/506	Complement, WHO lot no. 5/4	Immunoglobulins WHO 67/86	WHO 6HSP, lot no. 4/2
	mg/L				IU/L	
Transthyretin		●				
Albumin	●					●
α_1-Acid glycoprotein	●	●				
α_1-Antitrypsin	●	●				●
Ceruloplasmin	●					●
α_2-Macroglobulin	●					●
Haptoglobin	●					
Transferrin	●	●				●
C3/C3c	●					●
C4/C4c	●			●		
C-reactive protein			●			
IgG	●				●	
IgA	●				●	
IgM	●				●	

Preparation of CRM 470, the New International Reference Preparation for Proteins in Human Serum.



Unlike assays for ions and small molecules plasma protein measurements depend entirely on comparison of a test sample with a calibrant, known as a reference material or standard. Owing to the innate molecular heterogeneity of plasma proteins it is often impossible to ensure that the calibrator is identical in its behaviour in measurement systems to the test sample. Despite. these fundamental limitations it is clear that internationally agreed calibrants are the only way to improve consistancy of reporting of protein values in biological fluids between methods and laboratories. Unfortunately, only international units are not subject to contention and the use of mass values which are not internationally agreed, and are re-ascribed during the life of a standard, has jeopardised the value of international calibrants. If mass values are used it must be accepted that they are, to some extent, arbitrary.

Pure & Appl. Chem., Vol. 68, No. 10, pp. 1851–1856, 1996.
Printed in Great Britain.

Cause d'inaccuratezza

- Trasferimento dei valori da CRM a calibratori e controlli
- Eterogeneità delle proteine
- Effetto matrice

ERM-DA470k/IFCC

Clinical Chemistry 56:12
1880–1888 (2010)

General Clinical Chemistry

Characterization of the New Serum Protein Reference Material ERM-DA470k/IFCC: Value Assignment by Immunoassay

Ingrid Zegers,[1*] Thomas Keller,[2] Wiebke Schreiber,[3] Joanna Sheldon,[4] Riccardo Albertini,[5] Søren Blirup-Jensen,[6] Myron Johnson,[7] Stefanie Trapmann,[1] Hendrik Emons,[1] Giampaolo Merlini,[5] and Heinz Schimmel[1]

CERTIFICATE OF ANALYSIS

ERM®- DA470k/IFCC

HUMAN SERUM

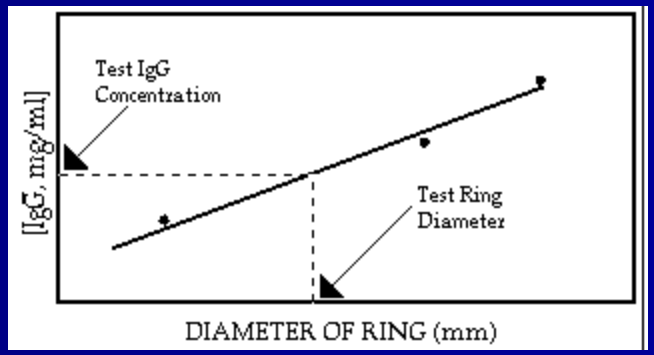
Proteins in the reconstituted material [1)]	Mass concentration	
	Certified value [2)] [g/L]	Uncertainty [3)] [g/L]
α_2 macroglobulin (A2M)	1.43 [4)]	0.06
α_1 acid glycoprotein (AAG)	0.617 [5)]	0.013
α_1 antitrypsin (AAT)	1.12 [5)]	0.03
albumin (ALB)	37.2 [4)]	1.2
β-2-microglobulin (B2M)	0.00217 [6)]	0.00007
complement 3c (C3c)	1.00 [4)]	0.04
complement 4 (C4)	0.162 [4)]	0.007
haptoglobin (HPT)	0.889 [4)]	0.021
immunoglobulin A (IgA)	1.80 [4)]	0.05
immunoglobulin G (IgG)	9.17 [4)]	0.18
immunoglobulin M (IgM)	0.723 [4)]	0.027
transferrin (TRF)	2.36 [5)]	0.08
transthyretin (TTR)	0.220 [5)]	0.018

Principali metodi usati

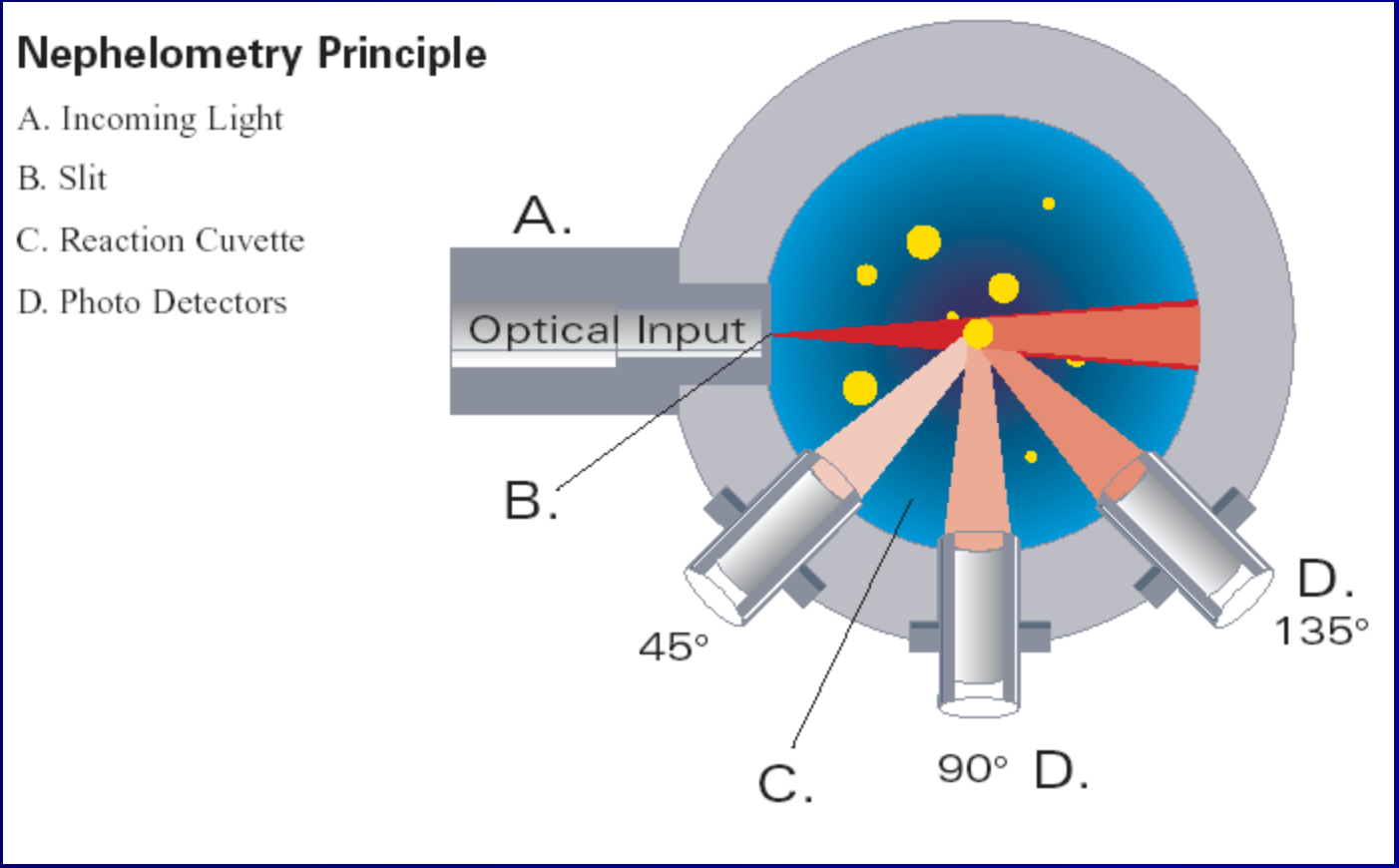
	%	VARIANTI	STRUMENTO e/o REAGENTI + USATI	
IMMUNODIFFUSIONE RADIALE	1,3	6		SIEMENS
				LIOFILCHEM
				MEDIC
				HUMATECH
				BIODEVICE
NEFELOMETRIA	29,7	34	VISTA	SIEMENS
			BN II	SIEMENS
			IMAGE	BECKMAN
			ARRAY 360	BECKMAN
TURBIDIMETRIA	64,5	167	COBAS/MODULAR	ROCHE
			ARCHITECT	ABBOTT
			ADVIA	SIEMENS
			AU, LX, CX, DX	BECKMAN
			ILAB	IL/BIOKIT
			KONELAB	SCLAVO

Immunodiffusione Radiale

In the 1960's and 1970's, as high quality antisera specific to the individual proteins became available, truly quantitative methods of assay were developed. The prototype of these was radial immunodiffusion (RID), in which a sample of serum or other fluid is placed into a well and allowed to diffuse passively into a gel (usually agar or agarose) containing antibodies to the protein of interest. The diameter of the resulting precipitin ring is proportional to the concentration of the protein of interest. This method revolutionized protein assays. However, it is slow, taking several hours to several days, and demands careful measurement of the relatively small rings.



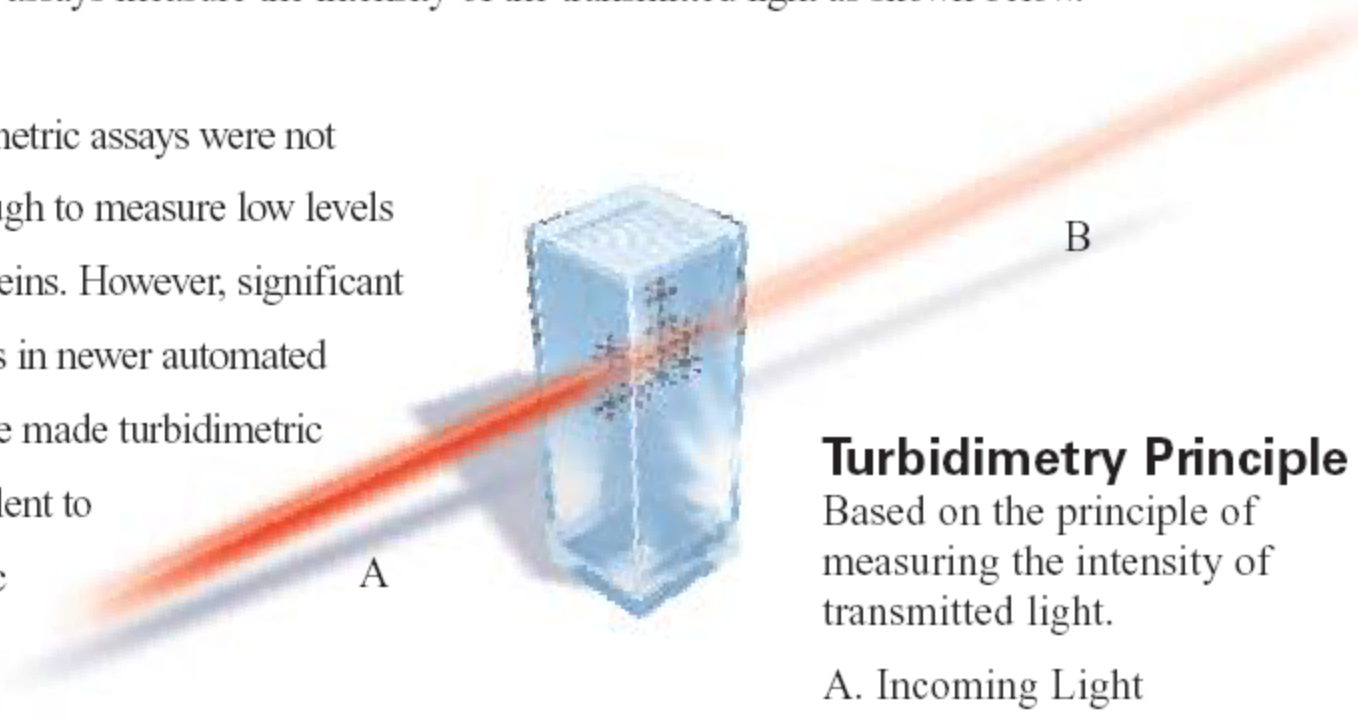
Nefelometria



Turbidimetria

Turbidimetric assays measure the intensity of the transmitted light as shown below.

Early turbidimetric assays were not sensitive enough to measure low levels of serum proteins. However, significant improvements in newer automated analyzers have made turbidimetric assays equivalent to nephelometric analysis.

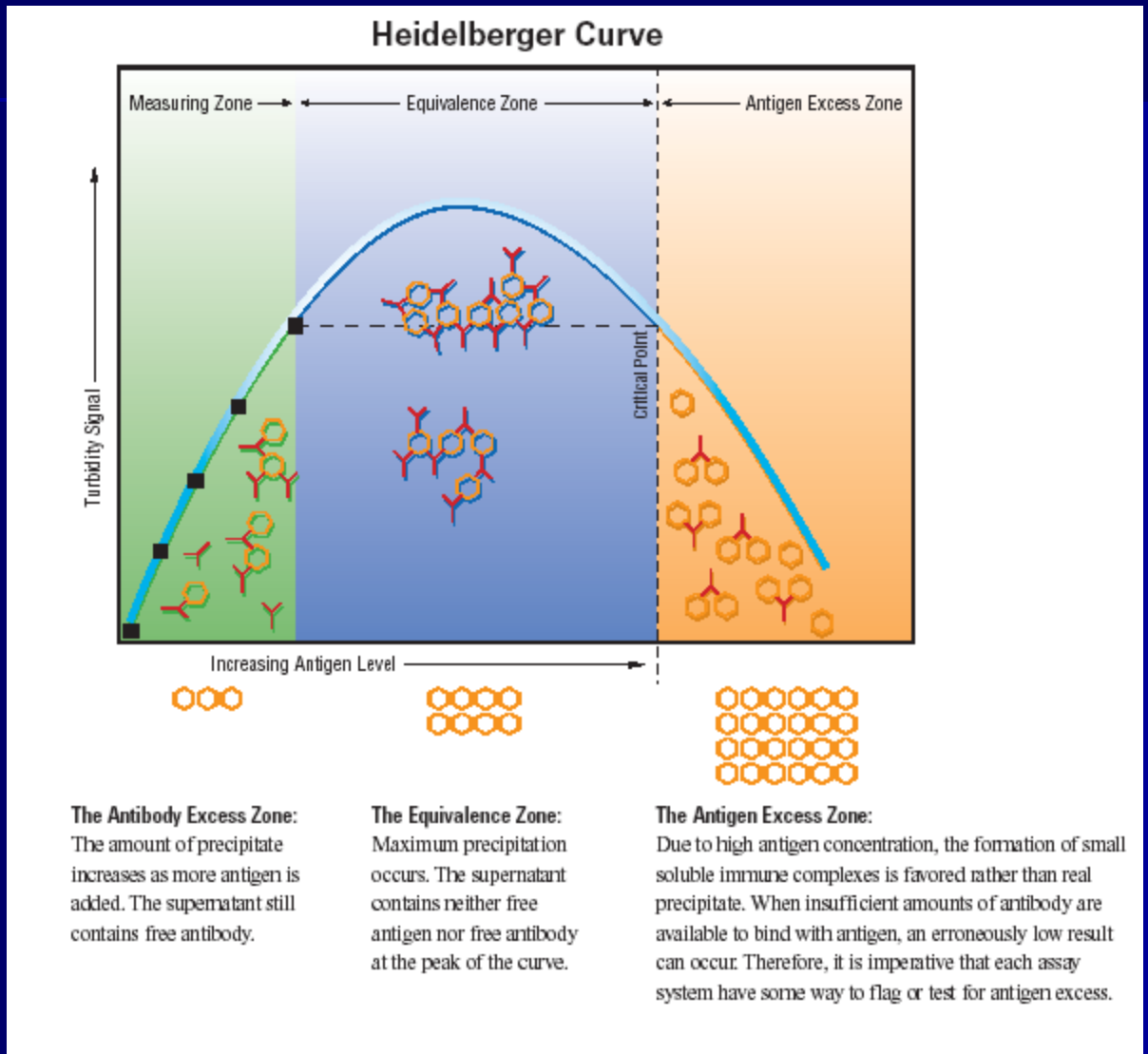


Turbidimetry Principle
Based on the principle of measuring the intensity of transmitted light.

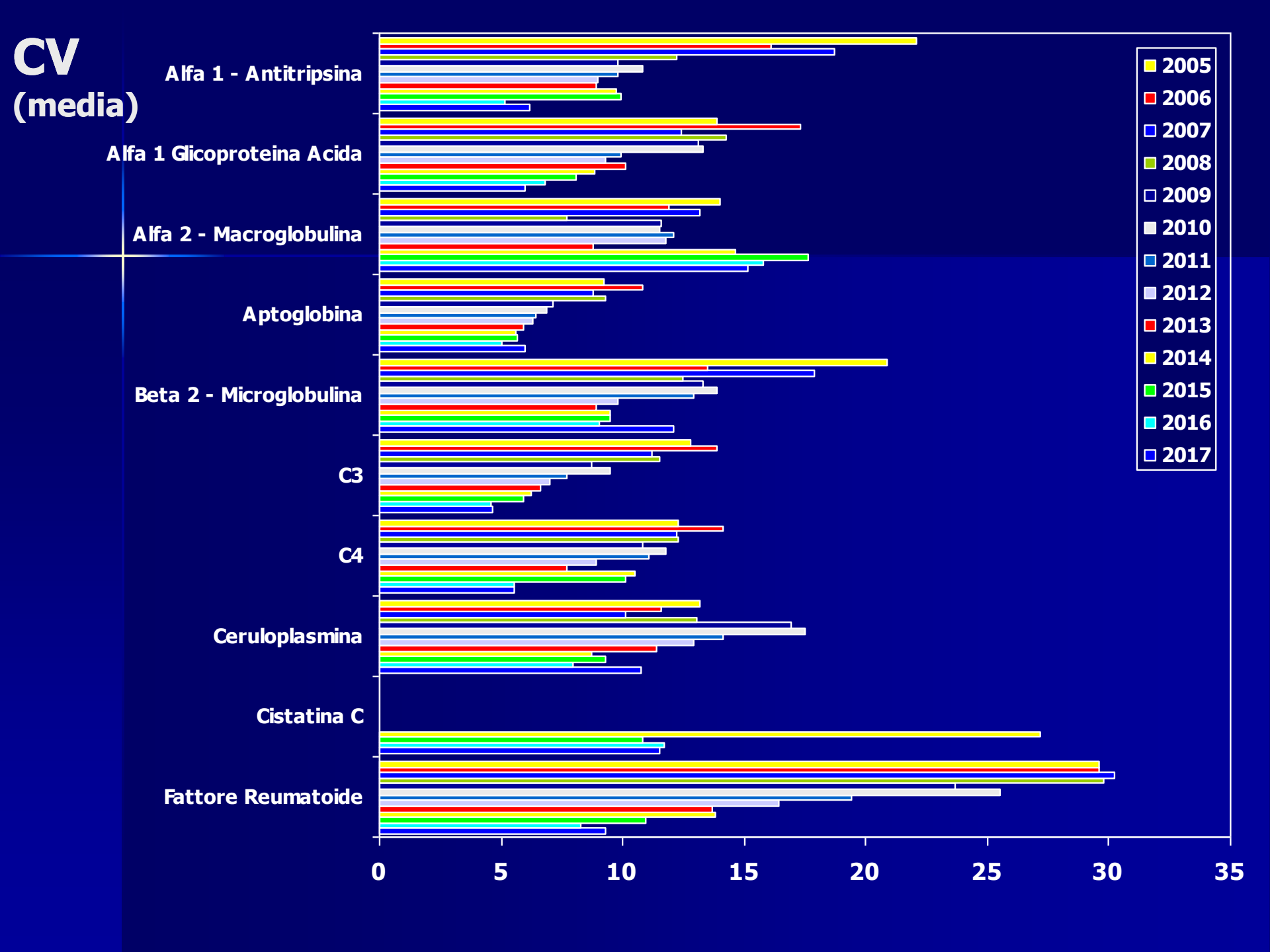
A. Incoming Light

B. Transmitted Light

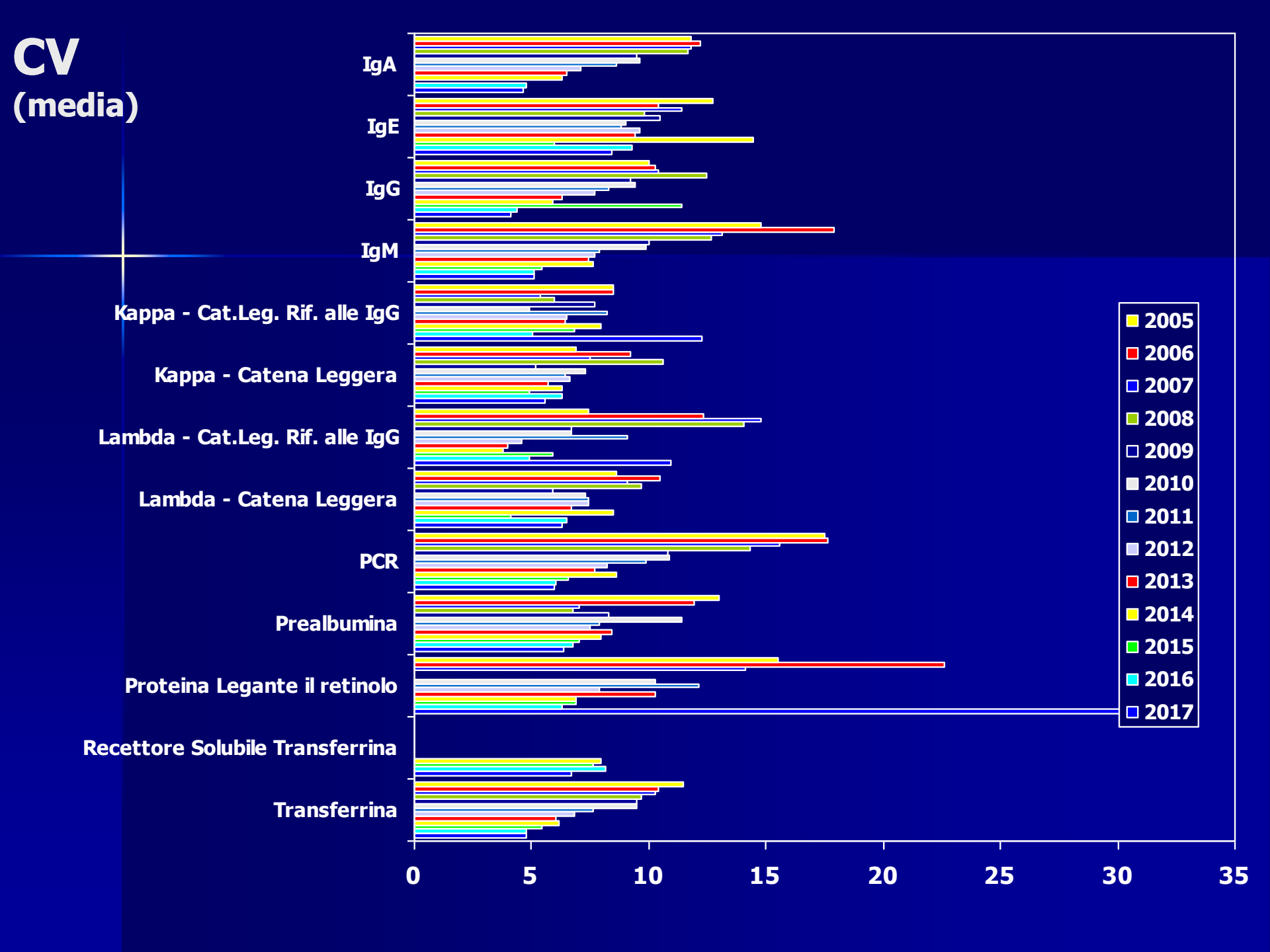
Curva di Heidelberger-Kendall



CV (media)


Alfa 1 - Antitripsina
Alfa 1 Glicoproteina Acida
Alfa 2 - Macroglobulina
Aptoglobina
Beta 2 - Microglobulina
C3
C4
Ceruloplasmina
Cistatina C
Fattore Reumatoide
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
0
5
10
15
20
25
30
35

CV (media)


IgA
IgE
IgG
IgM
Kappa - Cat.Leg. Rif. alle IgG
Kappa - Catena Leggera
Lambda - Cat.Leg. Rif. alle IgG
Lambda - Catena Leggera
PCR
Prealbumina
Proteina Legante il retinolo
Recettore Solubile Transferrina
Transferrina
0
5
10
15
20
25
30
35
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017

CV 2017

Analita	Media	Min	Max
Alfa 1 - Antitripsina	6,2	2,8	10,4
Alfa 1 Glicoproteina Acida	6,0	3,8	11,6
Alfa 2 - Macroglobulina	15,2	3,1	20,2
Aptoglobina	6,0	2,0	11,1
Beta 2 - Microglobulina	12,1	5,4	33,3
C3	4,7	2,9	12,8
C4	5,5	3,3	7,9
Ceruloplasmina	10,7	3,7	21,4
Cistatina C	11,5	8,0	14,3
Fattore Reumatoide	9,3	3,3	29,9
IgA	4,6	1,8	19,9
IgE	8,4	2,1	16,7
IgG	4,1	2,4	9,7
IgM	5,1	1,7	20,9
Kappa - Cat.Leg. Rif. alle IgG	12,2	5,1	27,7
Kappa - Catena Leggera	5,6	3,6	9,3
Lambda - Cat.Leg. Rif. alle IgG	10,9	4,3	25,9
Lambda - Catena Leggera	6,3	5,0	7,4
PCR	6,0	3,7	20,7
Prealbumina	6,4	2,5	11,4
Proteina Legante Retinolo	30,5	30,5	30,5
Recettore Solubile Transferrina	6,7	5,0	8,3
Transferrina	4,8	1,7	14,4

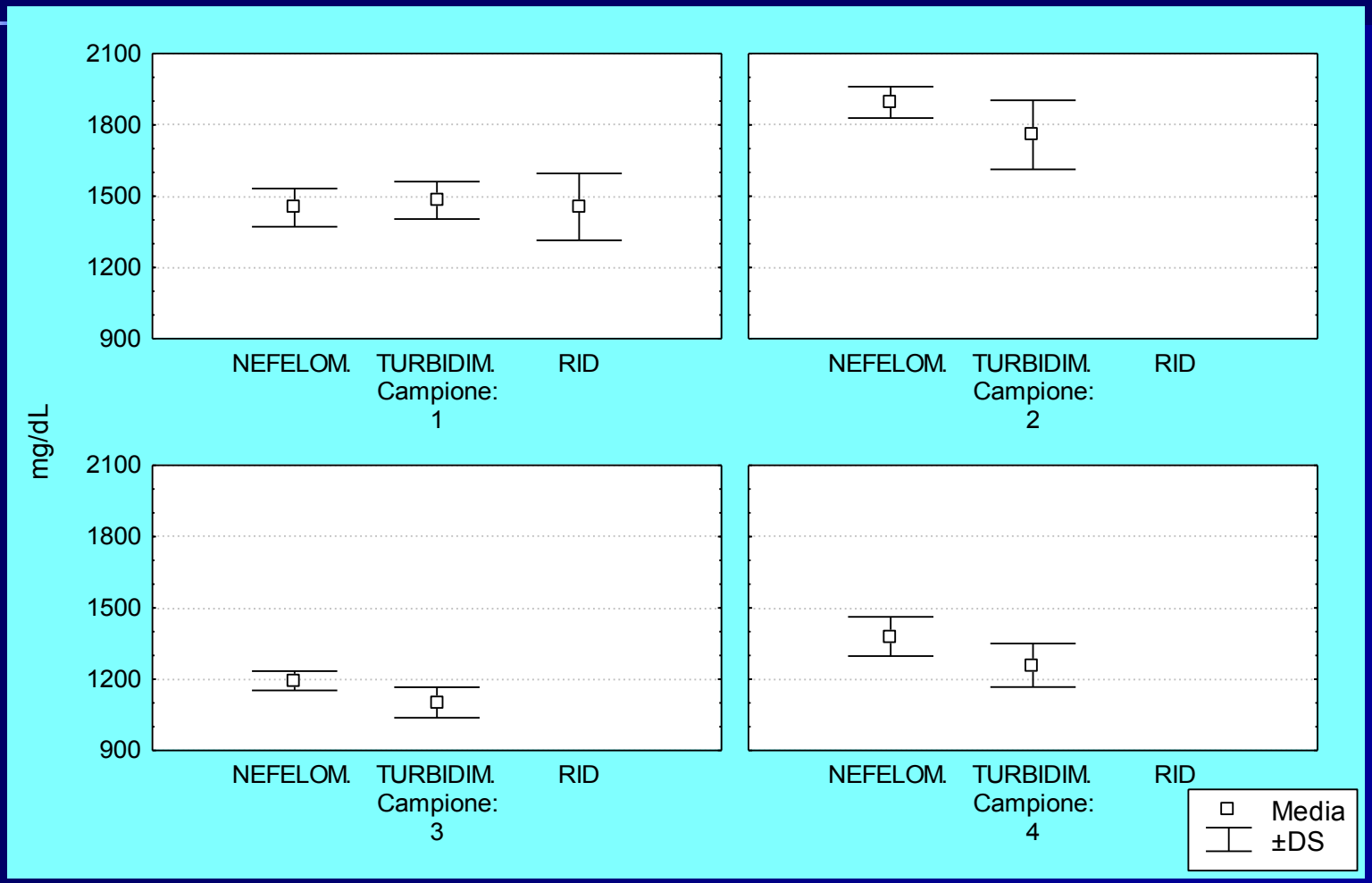
CV 2017

Metodo	Media	Min	Max
CHEMILUM.	14,3	6,7	33,3
DRY CHEMISTRY	9,9	9,9	9,9
ELETTROCHEMIL ROCHE	5,5	3,6	8,6
ELFA	10,5	6,5	15,4
IMMUNODIFF.	16,8	9,7	20,9
IMMUNOT.ROCHE COBAS 6-8000/MODULAR	4,2	2,0	14,3
IMMUNOTURB SIEMENS	6,3	3,7	20,7
IMMUNOTURB ADVIA SIEMENS	4,5	2,8	7,1
IMMUNOTURB SIEMENS	12,2	5,4	21,5
IMMUNOTURB ABBOTT ARCHITECT	4,3	3,1	6,4
IMMUNOTURB BECKMAN RF LATEX	6,9	4,7	9,5
IMMUNOTURB.	7,8	2,5	25,0
IMMUNOTURB. ABBOTT ARCHITECT	4,1	2,4	6,1
IMMUNOTURB. ADVIA SIEMENS	4,5	2,2	8,1
IMMUNOTURB. BECKMAN AU	4,7	3,2	7,9
IMMUNOTURB. BECKMAN AU	4,1	2,7	7,7
IMMUNOTURB. BECKMAN LX/CX/DX	3,2	1,8	5,2
IMMUNOTURB. I.L./BIOKIT	5,4	1,7	14,5
IMMUNOTURB. INTEGRA	9,0	6,4	11,3
IMMUNOTURB. SCLAVO	15,7	15,7	15,7
IMMUNOTURB.ABBOTT ARCHITECT	9,8	5,8	12,5
IMMUNOTURB.BECKMAN AU	3,3	2,3	3,9
IMMUNOTURB.ROCHE COBAS 6-8000/MODULAR/INTEGRA	3,4	2,8	4,2
NEFEL. BECKMAN IMAGE	5,4	4,2	6,5
NEFELOM .BECKMAN IMAGE	6,3	3,5	8,7
NEFELOM. BECKMAN	6,8	3,7	12,8
NEFELOM. BECKMAN IMAGE	4,0	3,1	4,8
NEFELOM. SIEMENS	6,0	4,1	30,5
NEFELOM. SIEMENS BN	8,5	3,0	25,3
NEFELOMET.- BECKMAN	6,3	2,8	7,7
NEFELOMETRICO	7,6	2,1	27,7
NEFELOMETRICO BECKMAN	8,6	4,4	21,4
NEFELOMETRICO/BECKMAN	14,3	7,4	29,9

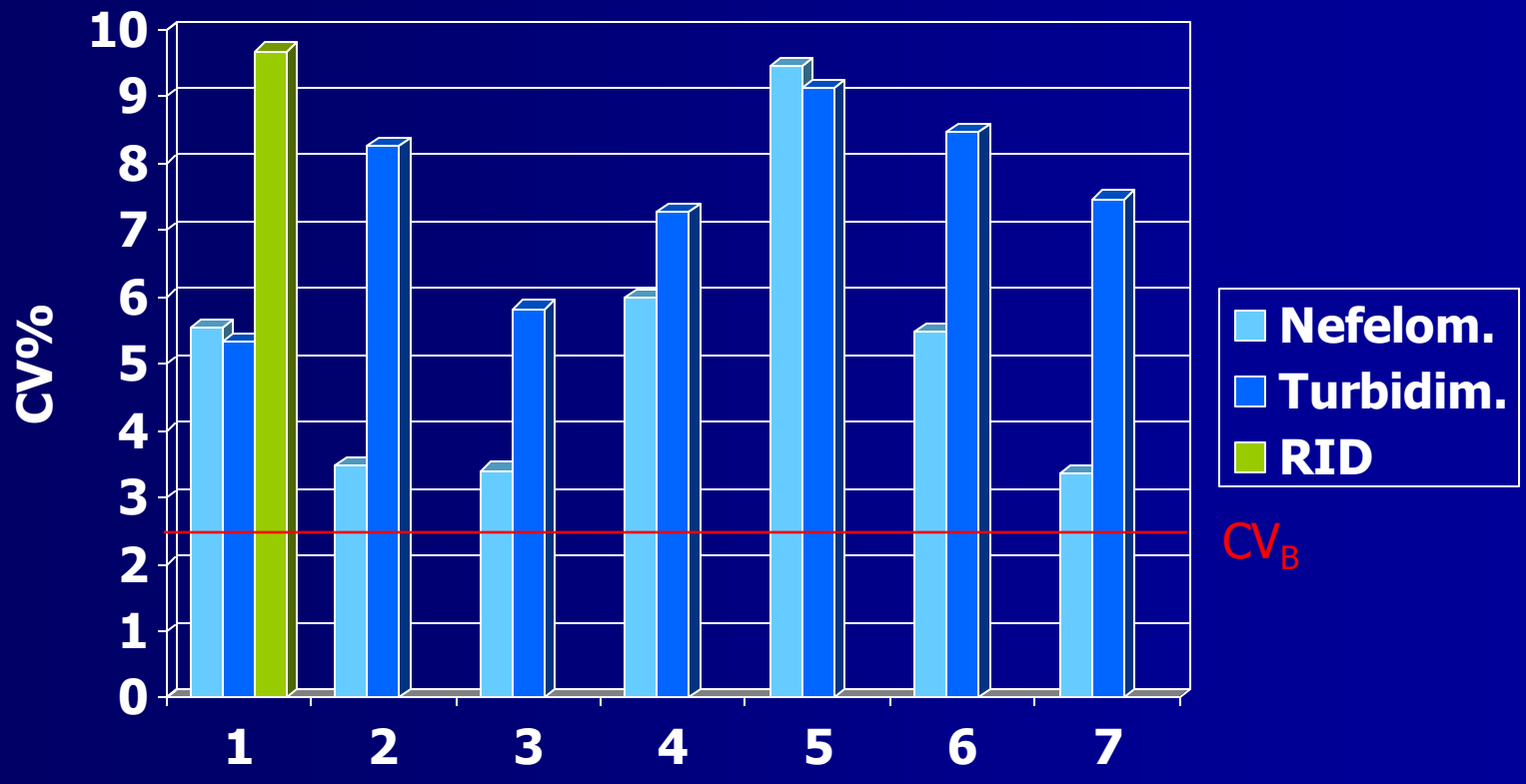
CV 2017

Prestazione	Metodo	Max
Beta 2 - Microglobulina	CHEMILUM.	33,3
Proteina Legante Retinolo	NEFELOM. SIEMENS	30,5
Fattore Reumatoide	NEFELOMETRICO/BECKMAN	29,9
Kappa - Cat.Leg. Rif. alle IgG	NEFELOMETRICO	27,7
Alfa 1 - Antitripsina (Nefelom, Siemens)	NEFELOMETRICO	26,7
Lambda - Cat.Leg. Rif. alle IgG	NEFELOMETRICO	25,9
Alfa 1 - Antitripsina (Nefelom, Siemens)	NEFELOM. SIEMENS BN	25,3
Beta 2 - Microglobulina	IMMUNOTURB.	25,0
Fattore Reumatoide	IMMUNOTURB SIEMENS	21,5
Ceruloplasmina	NEFELOMETRICO BECKMAN	21,4
IgM	IMMUNODIFF.	20,9
PCR	IMMUNOTURB SIEMENS	20,7
Alfa 2 - Macroglobulina	NEFELOM. SIEMENS BN	20,2
Beta 2 - Microglobulina	NEFELOMETRICO	20,0
IgA	IMMUNODIFF.	19,9
Fattore Reumatoide	NEFELOM. SIEMENS BN	18,6
IgE	CHEMILUM.	16,7
Beta 2 - Microglobulina	NEFELOM. SIEMENS BN	16,7
Ceruloplasmina	IMMUNOTURB.	16,6
IgM	IMMUNOTURB.	16,4

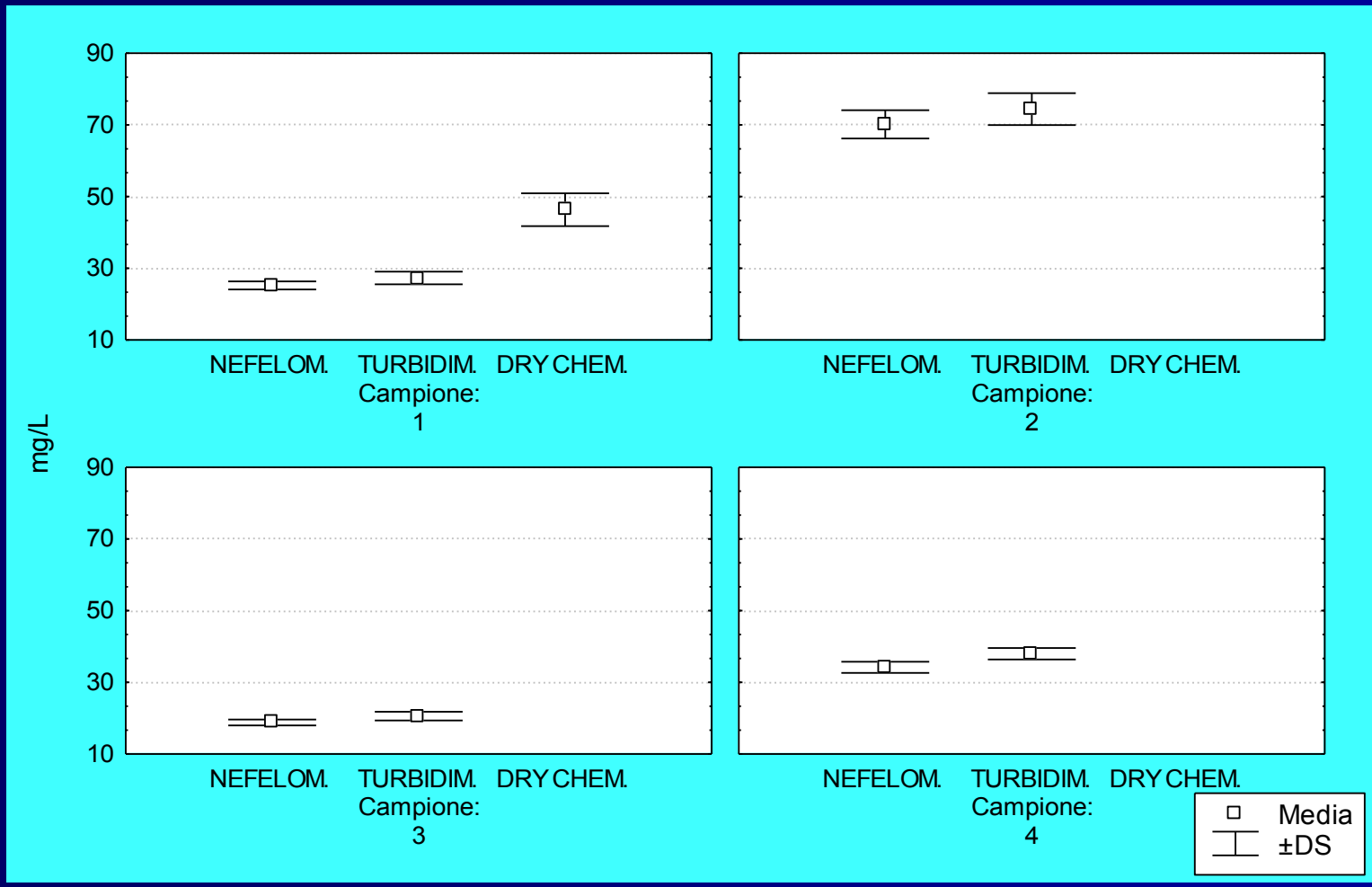
IgG


2100
1800
1500
1200
900
mg/dL
NEFELOM.
TURBIDIM.
RID
Campione:
1
2
3
4
Media
±DS

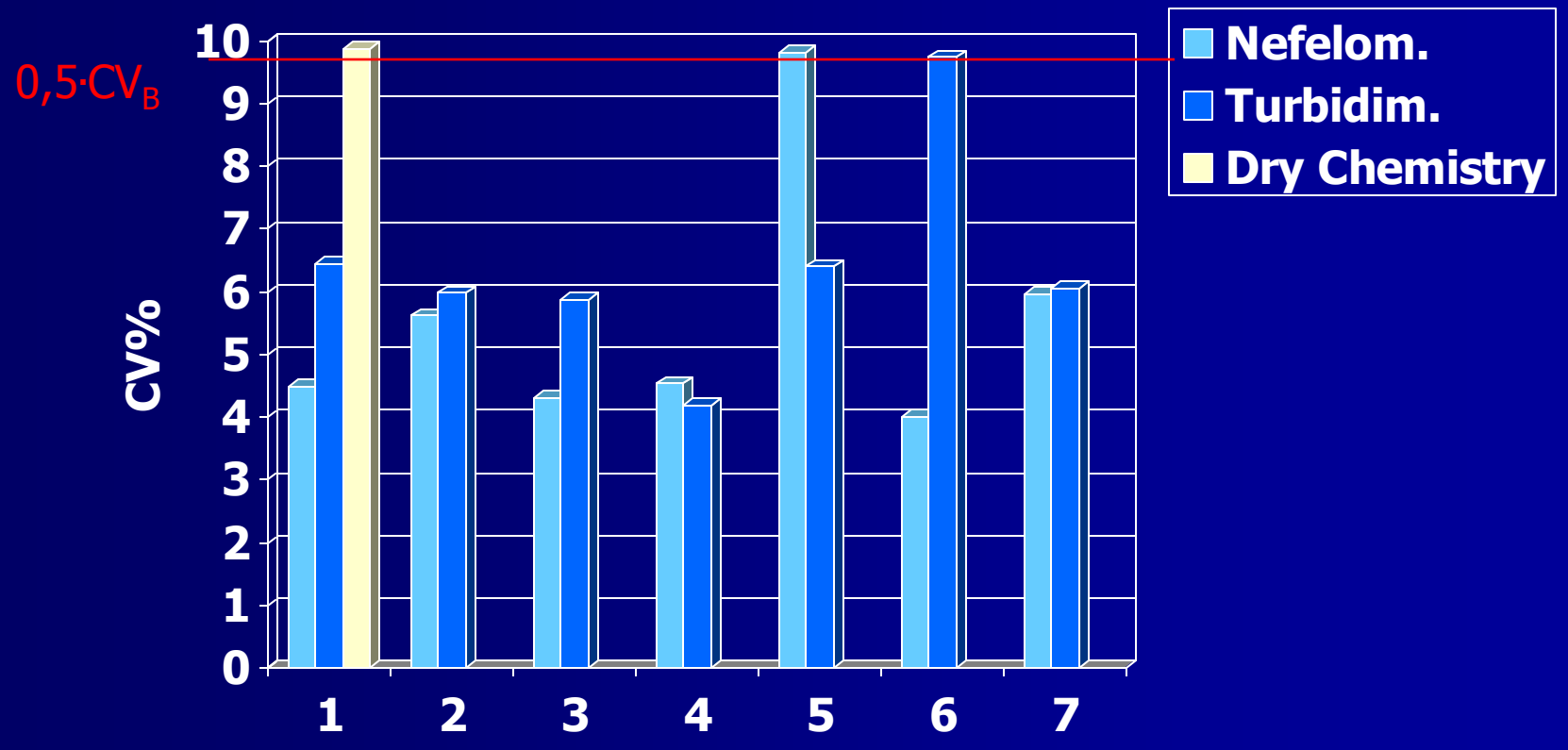
IgG



PCR


mg/L
90
70
50
30
10
NEFELOM.
TURBIDIM.
DRY CHEM.
Campione: 1
Campione: 2
Campione: 3
Campione: 4
Media
±DS

PCR


0,5·CV$_B$
CV%
10
9
8
7
6
5
4
3
2
1
0
1
2
3
4
5
6
7
Nefelom.
Turbidim.
Dry Chemistry

PCR *ultrasensibile*

UK NEQAS United Kingdom National External Quality Assessment Service

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Web Policy

Reproductive Science

Chemistry

Genetics

Haematology

Histopathology

Ultrasensitive C-Reactive Protein (CRP)

Scheme Details | Contact Details | Further Info

Analytes or Clinical Applications Covered

Prognostic indicator of cardiovascular disease and risk assessment for coronary artery disease. Monitoring of the acute phase response in neonates

Clinical Chemistry 47:3
403–411 (2001)

Review

High-Sensitivity C-Reactive Protein: A Novel and Promising Marker of Coronary Heart Disease

NADER RIFAI[1,2,4*] and PAUL M. RIDKER[2,3,5]

Table 1. RR estimates for future coronary events in men and women associated with quintiles of hs-CRP and TC:HDL-C ratio.[a]

			Quintile of hs-CRP, mg/L				
	Men	Women	1 (<0.7)	2 (0.7–1.1)	3 (1.2–1.9)	4 (2.0–3.8)	5 (3.9–15.0)
Quintile of TC:HDL-C ratio							
1	**<3.4**	**<3.4**	1	1.2	1.4	1.7	2.2
2	**3.4–4.0**	**3.4–4.1**	1.4	1.7	2.1	2.5	3
3	**4.1–4.7**	**4.2–4.7**	2	2.5	2.9	3.5	4.2
4	**4.8–5.5**	**4.8–5.8**	2.9	3.5	4.2	5.1	6
5	**>5.5**	**>5.8**	4.2	5	6	7.2	8.7

[a] RR estimates and TC:HDL-C ratio were derived from the PHS *(23)* and the WHS *(24)* databases. hs-CRP concentrations were derived from ongoing population-based surveys.

Fattore Reumatoide

Analita: *Fattore Reumatoide*	UI/mL

	N.	Out	Media	C.V.	S.D.	Med.na
Tutti	242	4	32.12	12.3	3.9	33.00
Tuo Metodo	17	1	26.28	6.7	1.8	26.10

Campione	7 *(Scad. 23/09/2016)*
Tuo risultato	26.2

	Diff. S	Diff. %
Tutti	-1.50	-18.43
Tuo Metodo	-0.04	-0.30

Valutazione errore totale							
1	2	3	4	5	6	7	8
	O	O	O	O		O	

O = Interno X = Esterno rispetto ai L.A *L.A. camp. corrente: 13.66*

N. risultati numerici	242
N. risultati semiquantitativi/qualitativi	4

Riepilogo x Metodo risultati numerici (> 7 Centri)

Metodo	N.	Out	M.	C.V.	u_x	Pos.	Neg.	Dub.
IMMUNOTURB.	56	2	33.41	10.3	0.6			
IMMUNOT.ROCHE COBAS 6-8000/MODULAR	51	1	33.86	4.5	0.3			
IMMUNOTURB.ABBOTT ARCHITECT	26	0	30.85	8.5	0.6			
IMMUNOTURB BECKMAN RF LATEX	25	1	33.91	4.8	0.4			
NEFELOM. SIEMENS BN	17	1	26.28	6.7	0.6*	1		
NEFELOMETRICO	17	0	28.46	5.3	0.5			
IMMUNOTURB. I.L./BIOKIT	15	0	33.76	6.7	0.7*	2		
NEFELOMETRICO/BECKMAN	14	0	27.22	8.7	0.8*			
IMMUNOTURB SIEMENS	11	0	37.90	5.8	0.8*			

** u_x non trascurabile*

Riepilogo x Metodo risultati qualitativi (> 3 Centri)

Metodo	Positivo	Negativo	Dubbio
AGGLUTINAZIONE	4		

Tuo Metodo
NEFELOM. SIEMENS BN

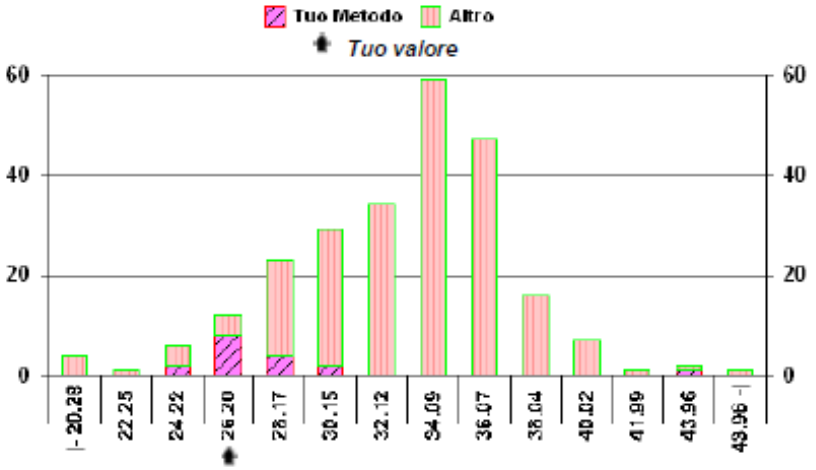
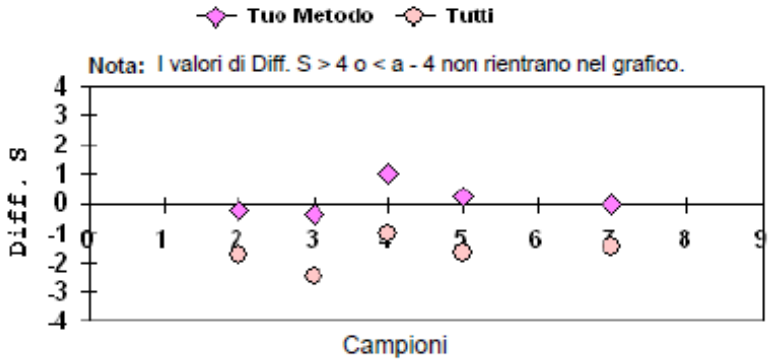
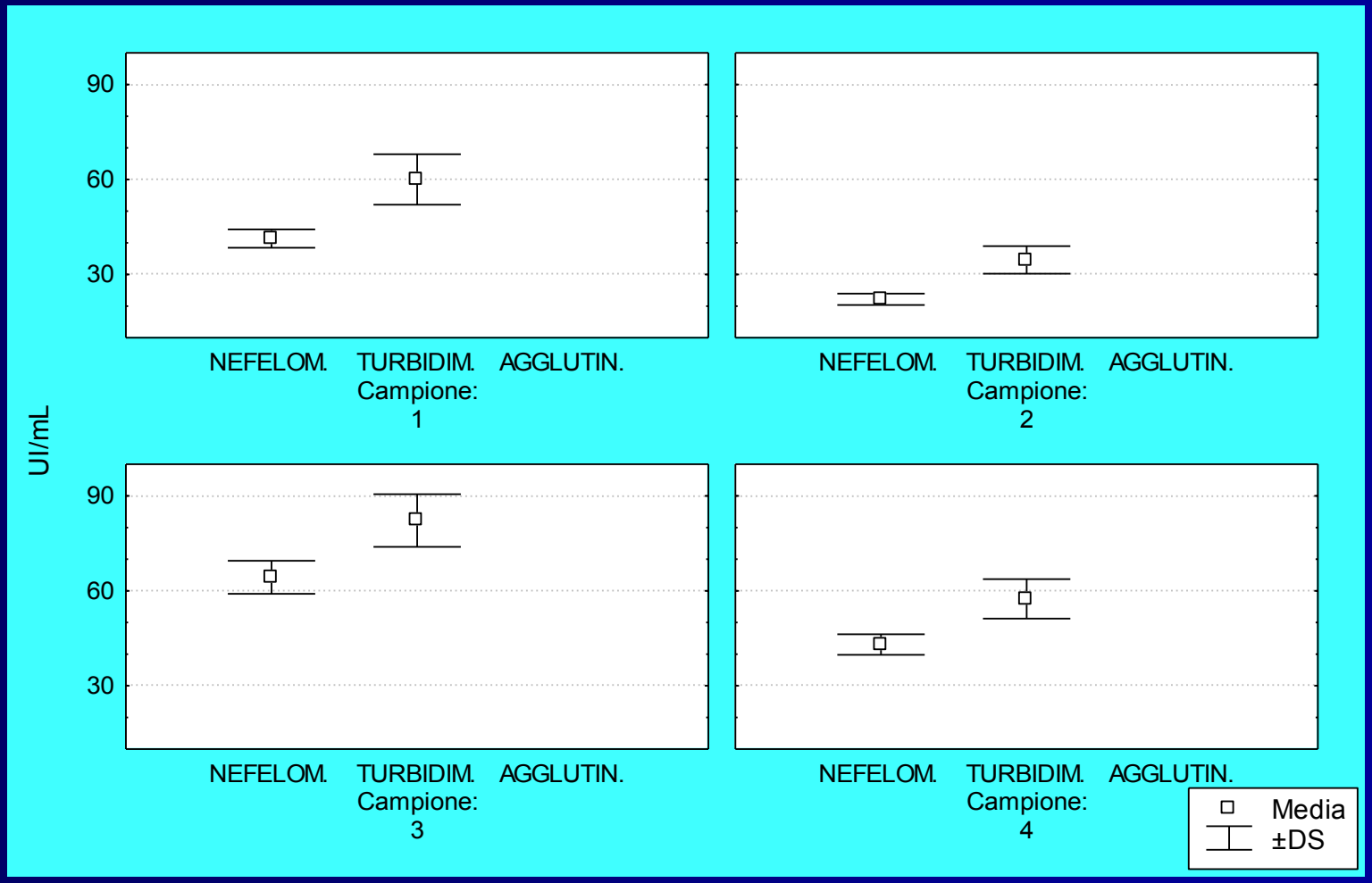


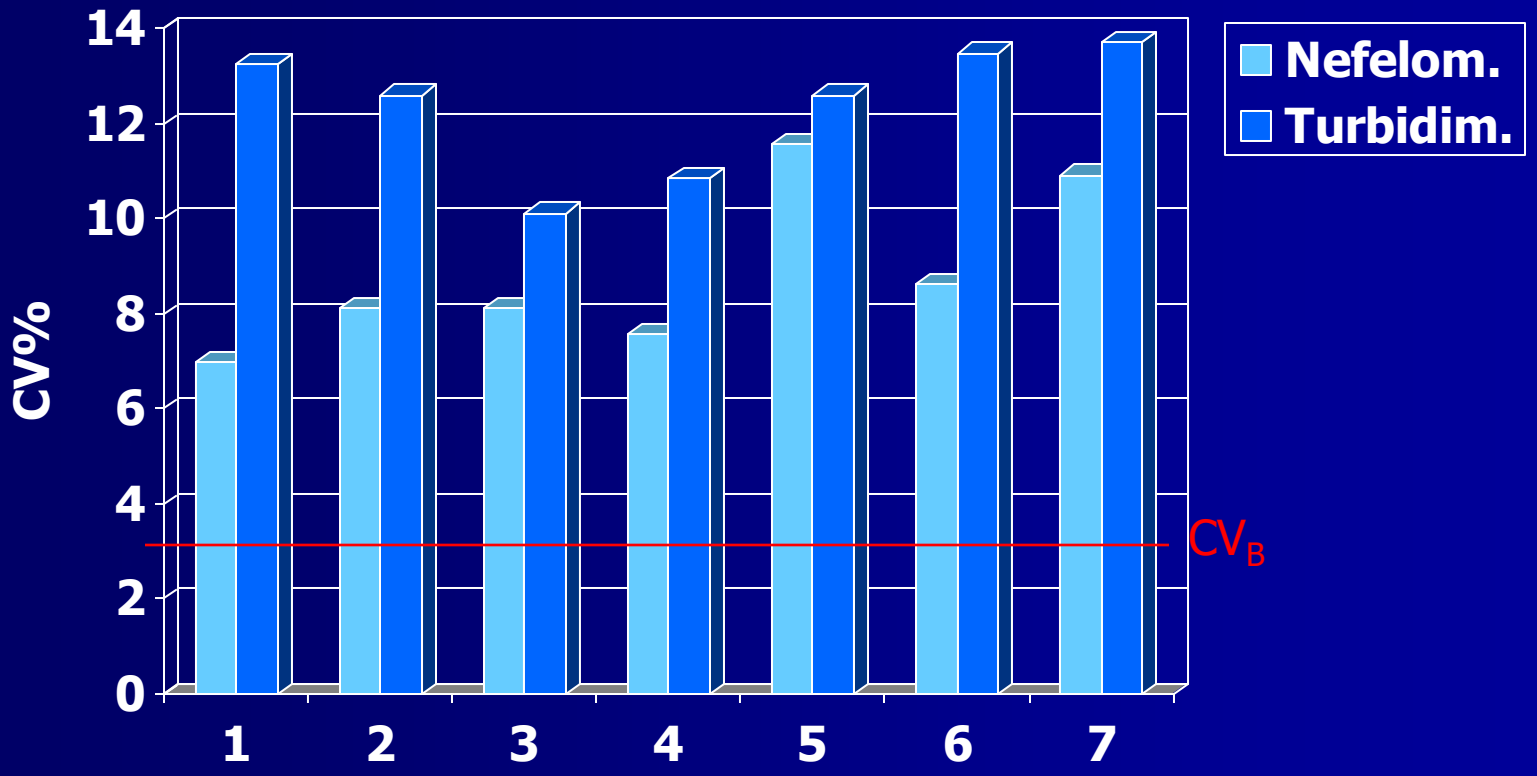
Grafico dati semiquantitativi/qualitativi	Tuo Metodo
POSITIVO	0/4



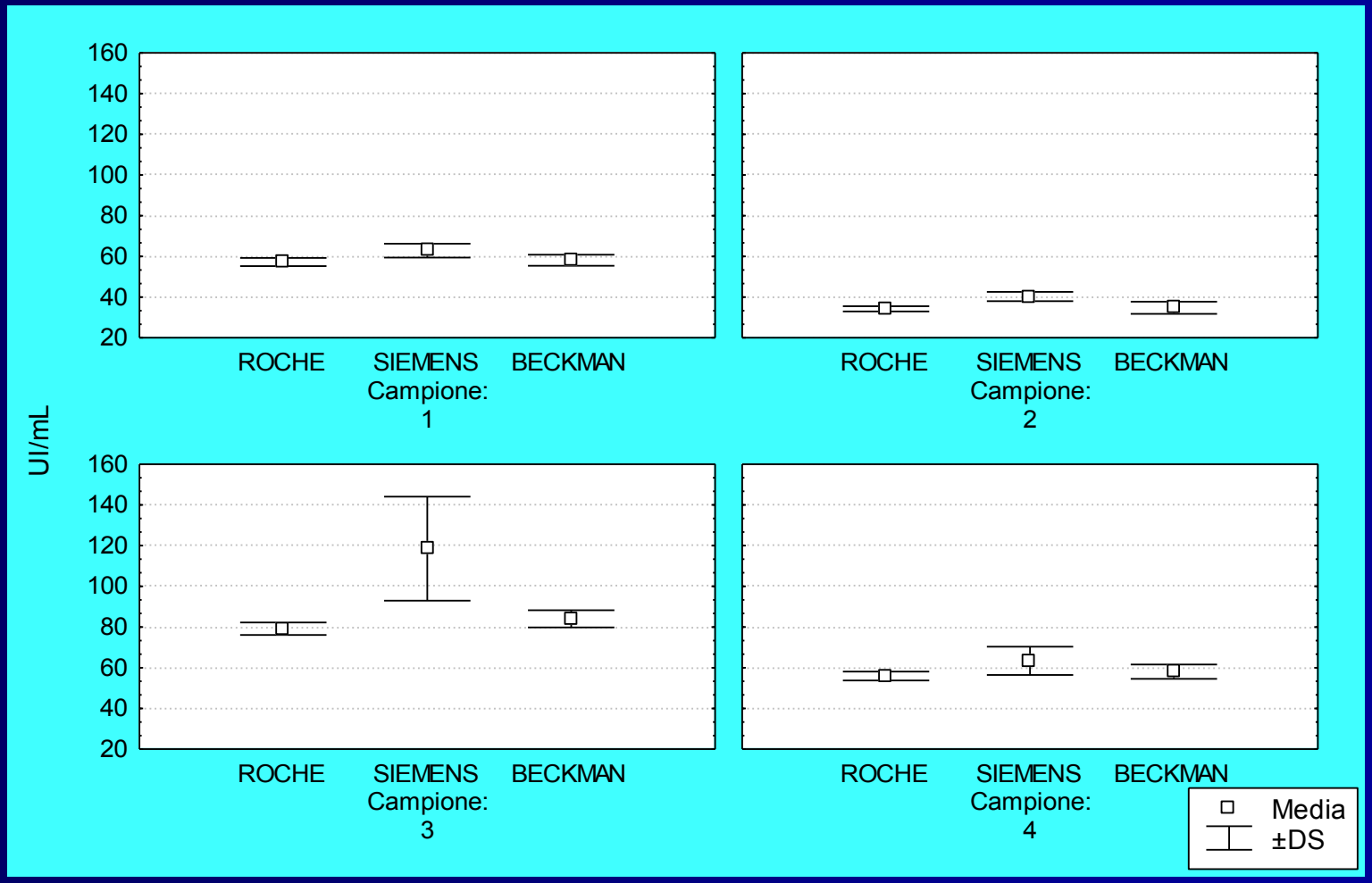
Fattore Reumatoide



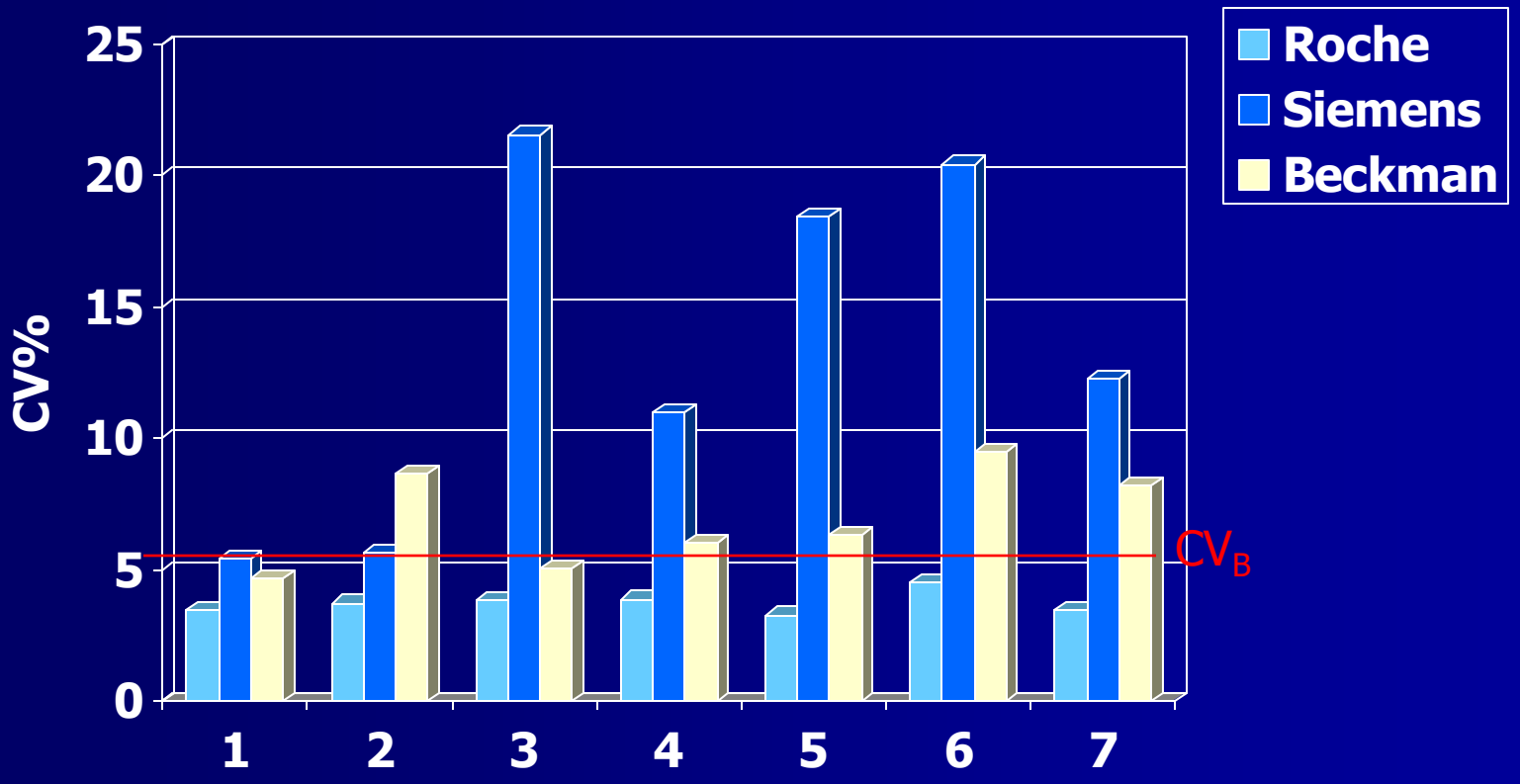
Fattore Reumatoide



Fattore Reumatoide (Turbidim.)



Fattore Reumatoide (Turbidim.)



Fattore Reumatoide

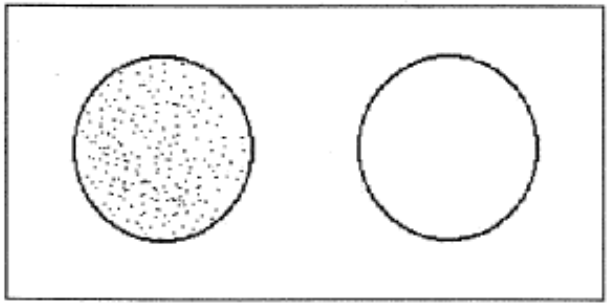
- Standardizzazione non ERM-DA470
- Non dosabile come IgM in unità di massa
- Persistenza di metodi qualitativi - semiquantitativi

Semi-quantitative Test:

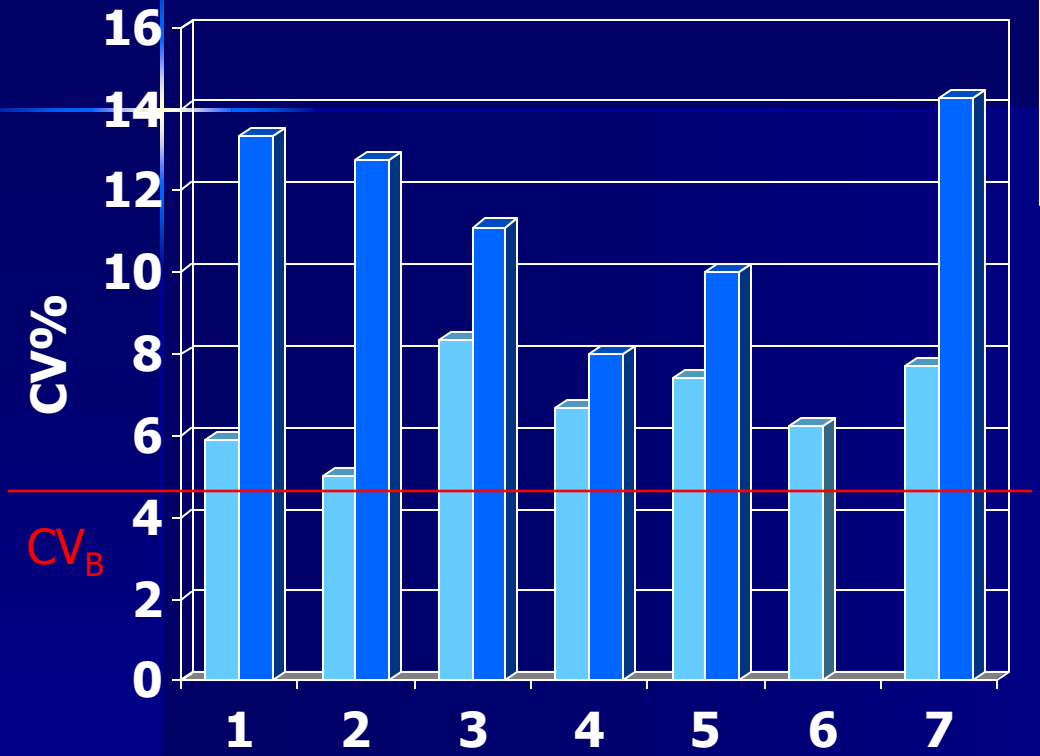
The titer of the serum is the reciprocal of the highest dilution, which exhibits a positive reaction.

An estimate of the RF concentration in the specimen can be expressed in IU/ml by using the following equation:

IU/ml of specimen = IU/ml control × specimen titer

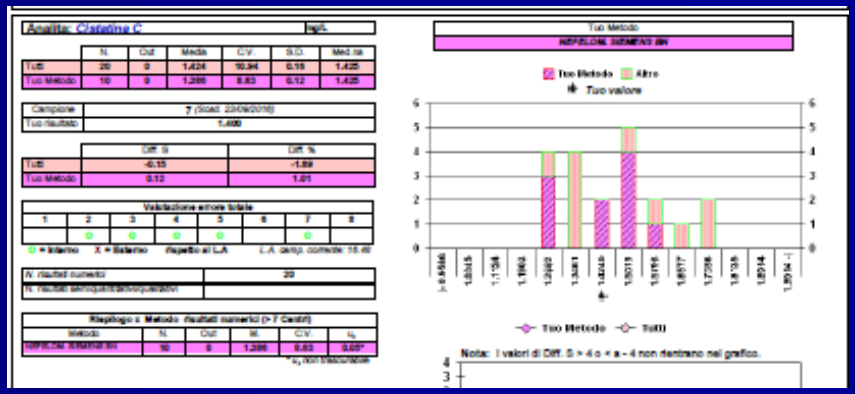


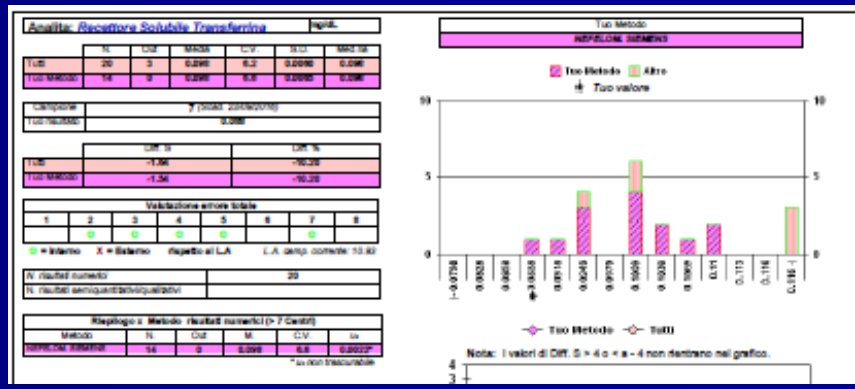
Recenti esordienti



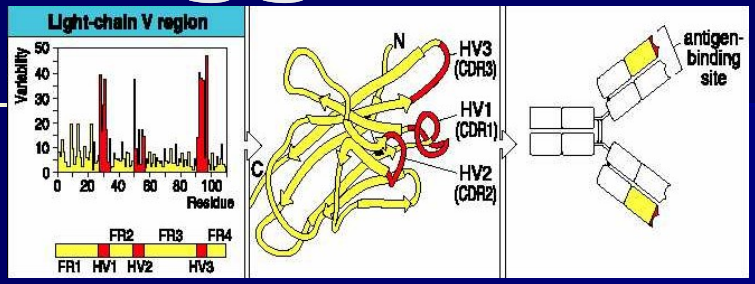
- Recettore Solubile Transferrina
- Cistatina C

NEFELOMETRICO SIEMENS





Leggere le catene leggere



CATENE LEGGERE

LEGATE
K(2-4)g/L
λ(1-2,4)g/L

- **POLICLONALI**
- **MONOCLONALI**

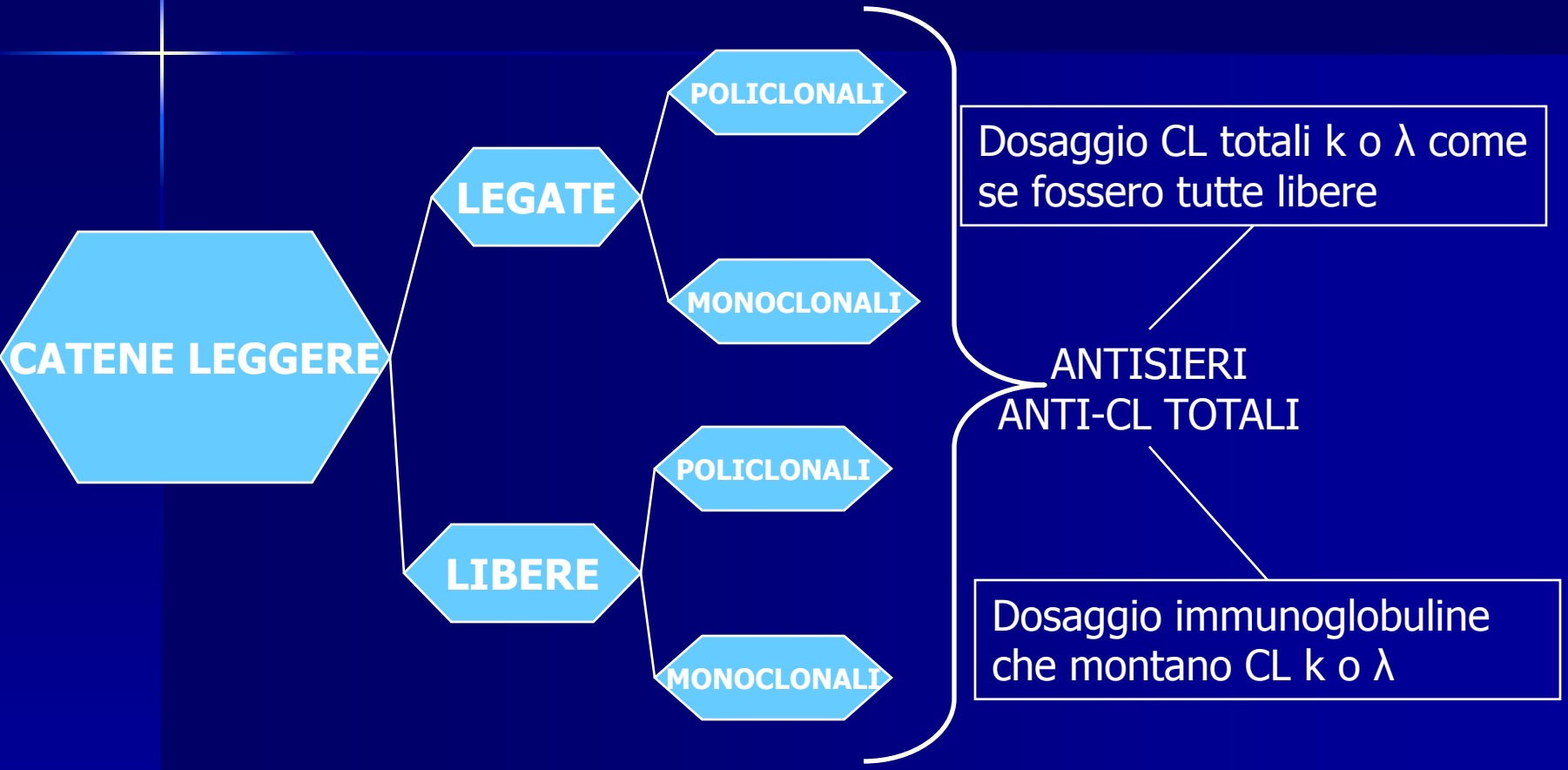
LIBERE
K(3-19)mg/L
λ(6-26)mg/L

- **POLICLONALI**
- **MONOCLONALI**

ANTISIERI
ANTI-CL TOTALI

ANTISIERI
ANTI-CL LIBERE

Leggere le catene leggere



Fattore di conversione = 150 (PM_{IgG}) / 46 ($2xPM_{CL}$) ≈ 3

Leggere le catene leggere

Analita: *Kappa - Catena Leggera*	mg/dL

	N.	Out	Media	C.V.	S.D.	Med.na
Tutti	56	1	336.7	6.8	22.9	333.0
Tuo Metodo	15	1	328.1	3.6	11.7	327.0

Campione	2 *(Scad. 25/02/2005)*
Tuo risultato	324

	Diff. S	Diff. %
Tutti	-0.55	-3.76
Tuo Metodo	-0.35	-1.25

Campioni			
1	2	3	4
O	O		

O = Interno X = Esterno rispetto ai limiti dichiarati

N. risultati quantitativi	56
N. risultati semiquantitativi/qualitativi	1

Riepilogo x Metodo risultati quantitativi (> 7 Centri)				
Metodo	N.	Out	M.	C.V.
NEFELOMETRICO	37	0	339.5	7.8
IMMUNOTURB.	15	1	328.1	3.6

Tuo Metodo
IMMUNOTURB.

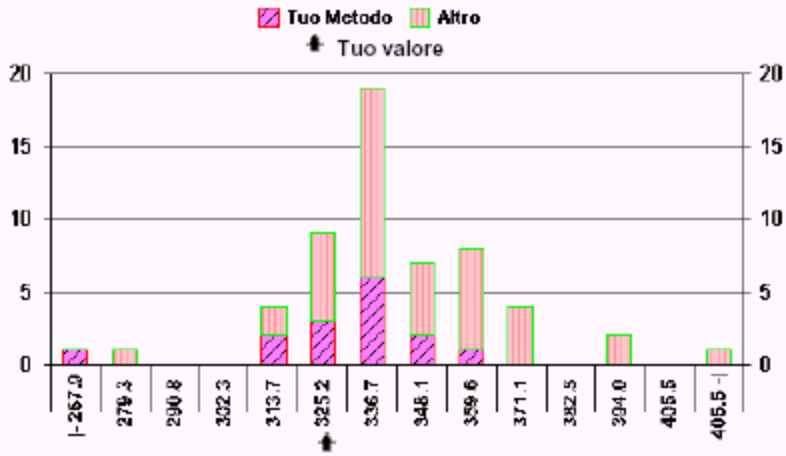
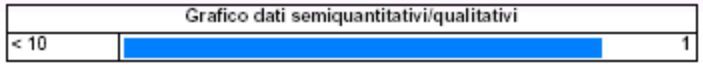


Grafico dati semiquantitativi/qualitativi



Analita: *Kappa - Cat.Leg. Rif. alle IgG*	mg/dL

	N.	Out	Media	C.V.	S.D.	Med.na
Tutti	22	0	1128.00	9.7	109.5	1140.00
Tuo Metodo	20	0	1137.60	9.6	108.8	1145.00

Campione	2 *(Scad. 25/02/2005)*
Tuo risultato	1140

	Diff. S	Diff. %
Tutti	0.11	1.06
Tuo Metodo	0.02	0.21

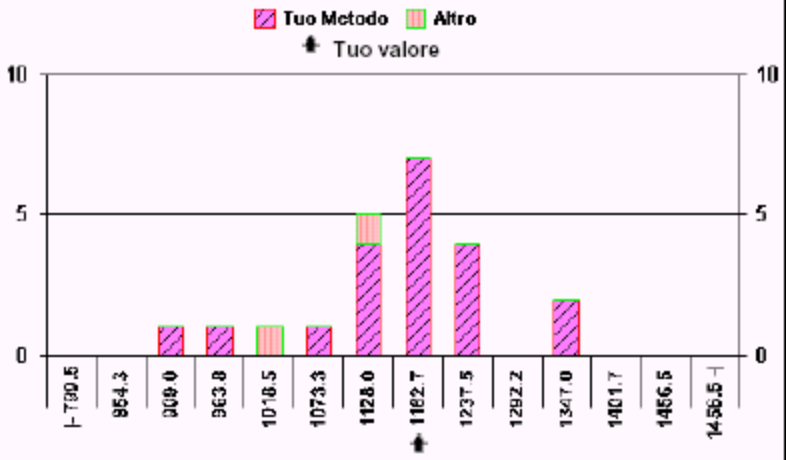
Campioni			
1	2	3	4
O	O		

O = Interno X = Esterno rispetto ai limiti dichiarati

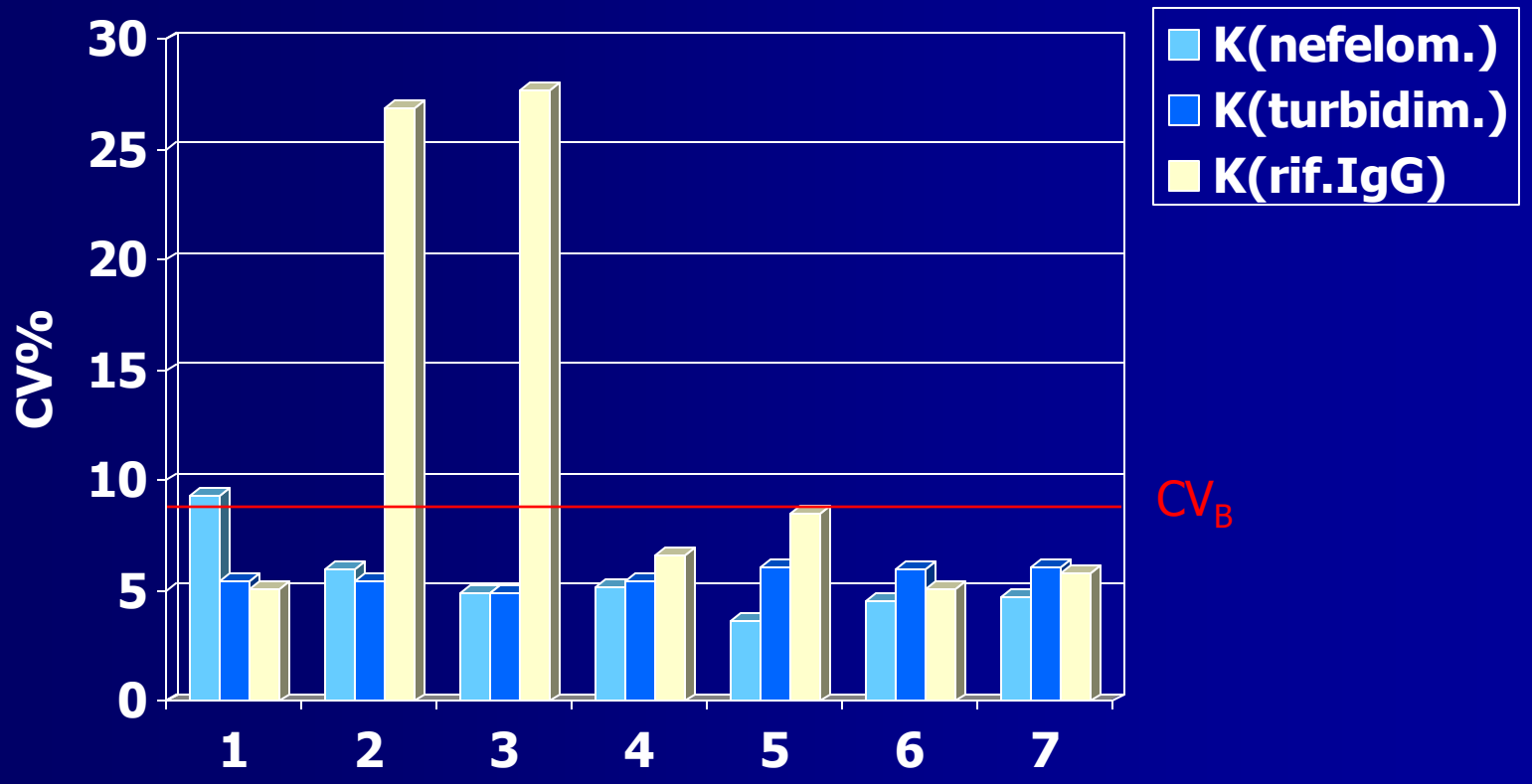
N. risultati quantitativi	22
N. risultati semiquantitativi/qualitativi	

Riepilogo x Metodo risultati quantitativi (> 7 Centri)				
Metodo	N.	Out	M.	C.V.
NEFELOMETRICO	20	0	1137.60	9.6

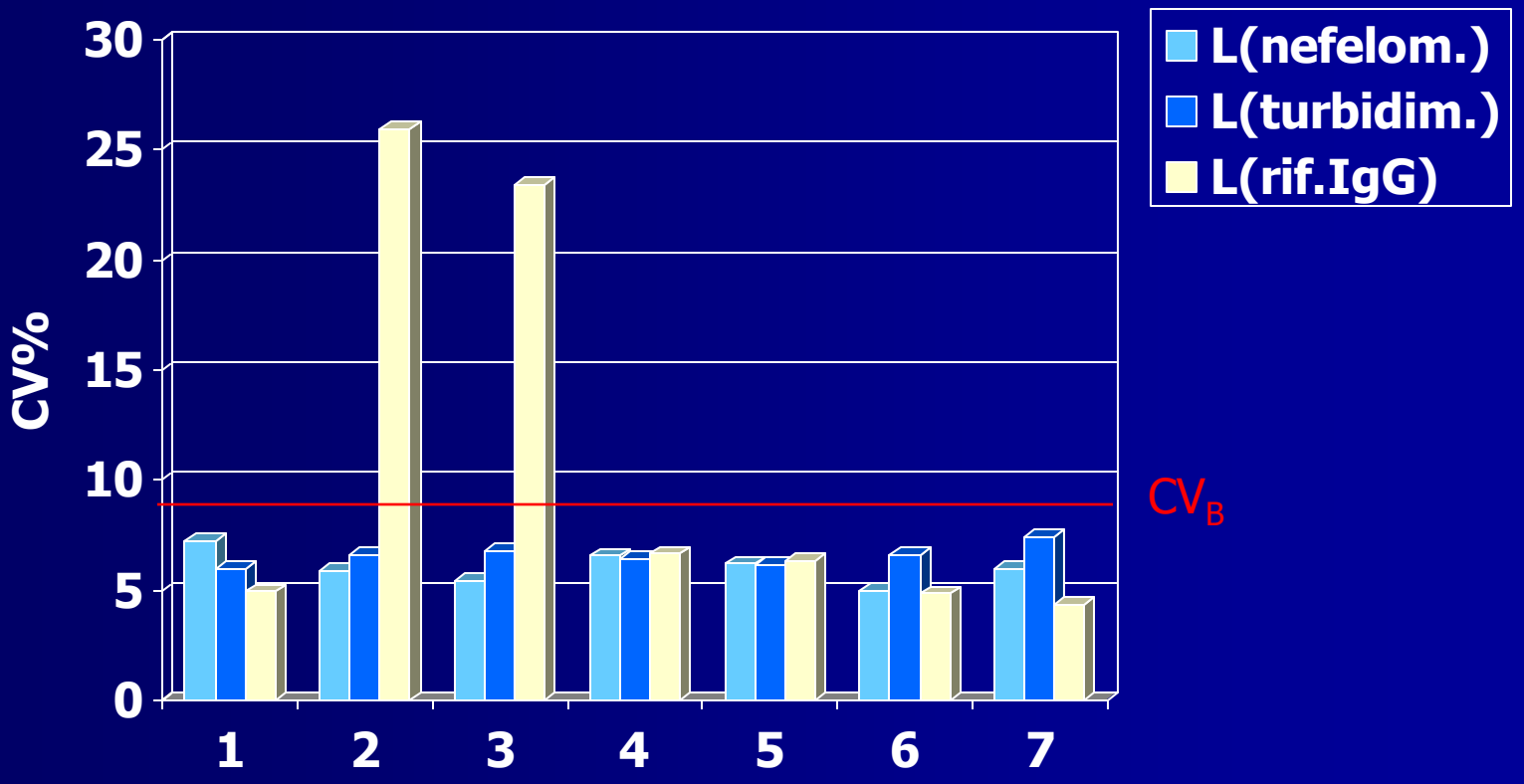
Tuo Metodo
NEFELOMETRICO



Kappa catena leggera



Lambda catena leggera



CL totali

As might be expected the values obtained from the different approaches for the certification of light chains differ markedly. For both K and L pooled monoclonal light chains provided a higher value than light chains derived from polyclonal immunoglobulins. Values in both cases differed significantly from those obtained by calculation (14) and values obtained by radial immunodiffusion differed from those of nephelometry and turbidimetry. All three sets of light chain values are incompatible with the total amount of light chains theoretically present on the basis of the ascribed values for IgG, IgA and IgM. We conclude that purified light chains, whether monoclonal or polyclonal, cannot be used to assign values for light chains bound to immunoglobulins accurately.

Pure & Appl. Chem., Vol. 68, No. 10, pp. 1851–1856, 1996.
Printed in Great Britain.

Dosaggio CL totali. Utilità clinica:

- Rapporto k/λ come indizio di monoclonalità
- Parametro di follow-up per CM già tipizzate

CLIN. CHEM. 37/11, 1917–1921 (1991)

Use of Immunoglobulin Heavy-Chain and Light-Chain Measurements in a Multicenter Trial to Investigate Monoclonal Components: I. Detection

R. G. Jones, F. Aguzzi,[1] J. Bienvenu,[2] P. Bianchi,[1] C. Gasparro,[1] M. R. Bergami,[1] A. Perinet,[2] H. Bernon,[2] G. M. Penn,[3] I. Keller,[4] and J. T. Whicher

We assessed the combined use of serum protein electrophoresis (SPE) and nephelometric measurement of immunoglobulin heavy- and light-chain components for detecting serum monoclonal immunoglobulins (monoclonal components, MC) in 4788 unselected samples from 4173 patients. MC were detected in 514 samples from 390 patients. In 356 these were detected by SPE; the other 34 had a normal SPE pattern but an abnormal kappa:lambda light-chain ratio (KLR). Only 208 of the 356 (58%) samples with bands by SPE had abnormal KLRs. Samples with MC concentrations >5 g/L had a higher proportion of abnormal KLRs (75%) than those with concentrations <5 g/L (42%). The KLR was abnormal in 13% of samples in which no MC were visible by SPE or immunofixation electrophoresis (IFE). Compared with quantitative measurements of immunoglobulin heavy and light chains, high-quality SPE remains the method of choice for the detection of MC. Quantitative methods, however, are able to detect additional MC, especially those containing free light chains, and in the absence of SPE and IFE will detect about 75% of MC present at >5 g/L.

CL libere

Clinical Chemistry 47:4
673–680 (2001)

Enzymes and Protein Markers

Highly Sensitive, Automated Immunoassay for Immunoglobulin Free Light Chains in Serum and Urine

Arthur R. Bradwell,[1*] Hugh D. Carr-Smith,[2] Graham P. Mead,[2] Lian X. Tang,[2] Paul J. Showell,[2] Mark T. Drayson,[1] and Roger Drew[2]

Serum free light chain ratio is an independent risk factor for progression in monoclonal gammopathy of undetermined significance

S. Vincent Rajkumar, Robert A. Kyle, Terry M. Therneau, L. Joseph Melton III, Arthur R. Bradwell, Raynell J. Clark, Dirk R. Larson, Matthew F. Plevak, Angela Dispenzieri, and Jerry A. Katzmann

We hypothesized that the presence of monoclonal free kappa or lambda immunoglobulin light chains in monoclonal gammopathy of undetermined significance (MGUS), as detected by the serum free light chain (FLC) assay increases the risk of progression to malignancy. Of 1384 patients with MGUS from Southeastern Minnesota seen at the Mayo Clinic from 1960 to 1994, baseline serum samples obtained within 30 days of diagnosis were available in 1148. At a median follow-up of 15 years, malignant progression had occurred in 87 (7.6%) patients. An abnormal FLC ratio (kappa-lambda ratio < 0.26 or > 1.65) was detected in 379 (33%) patients. The risk of progression in patients with an abnormal FLC ratio was significantly higher compared with patients with a normal ratio (hazard ratio, 3.5; 95% confidence interval [CI], 2.3-5.5; $P < .001$) and was independent of the size and type of the serum monoclonal (M) protein. Patients with an abnormal serum FLC ratio, non–immunoglobulin G (non-IgG) MGUS, and a high serum M protein level (≥ 15 g/L) had a risk of progression at 20 years of 58% (high-risk MGUS) versus 37% with any 2 of these risk factors (high-intermediate risk), 21% with one risk factor (low-intermediate risk), and 5% when none of the risk factors were present (low risk). (Blood. 2005; 106:812-817)

CL libere

Freelite™ & Hevylite™

Binding Site

Freelite™ Serum Free Light Chain Assays

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Keyword

Freelite is a major breakthrough for the detection and monitoring of Multiple Myeloma (MM) and other B-cell dyscrasia. There is now significant clinical evidence indicating the benefit of serum free light chain assays in initial screening for monoclonal gammopathies, identifying AL amyloidosis and Nonsecretory MM patients missed by conventional electrophoretic methods, as a prognostic indicator for progression in myeloma*, for risk stratification of MGUS patients* and rapid evaluation of treatment efficacy.

Freelite assays were developed by Binding Site to measure free lambda and free kappa immunoglobulin light chains. Our expertise in the manufacture of antibodies has enabled us to provide a quantifiable, highly specific, automatable free light chain assay for serum.

Review the clinical evidence for the utility of **Freelite** in detecting and monitoring plasma cell disorders and compare the results from laboratory protocols with and without **Freelite**.

*** In the USA diagnostic use of this product is restricted to those stated in the product insert**

Hevylite™ - See what the Hevylite ratio offers you.

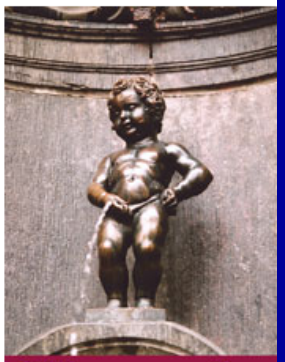
Latest News 09 April 2009

Binding Site sponsors Free Light Chain Disease workshop at Euromedlab 2009

A panel of eminent speakers from Austria, USA and the UK will discuss recent advances in the management of free light chain disease at an Industry Sponsored Workshop as part of the scientific program at the Euromedlab conference in Innsbruck this year. The workshop includes a review of clinical applications of serum free light

This site is for Healthcare Professionals only

Click here for Patient Information



Still requesting urine?

Latest News Headlines

- Binding Site sponsors Free Light Chain Disease workshop at Euromedlab 2009
  09 April 2009
- Further study indicates only serum measurements needed for MM diagnosis or exclusion
  10 February 2009
- Publication of largest Light Chain Escape – Multiple Myeloma

CL libere

Wikilite.com

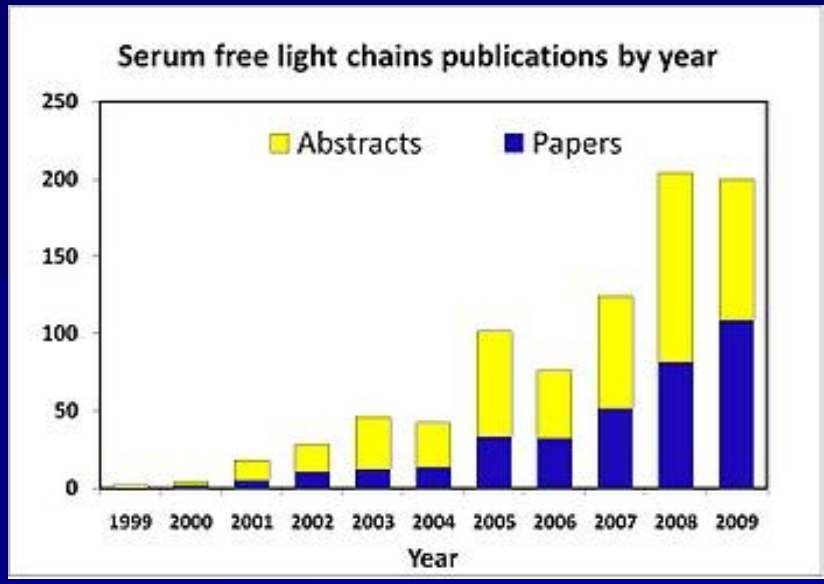
4.3. Comparison of free light chain immunoassays on different instruments

sFLC kits are made for many laboratory instruments. A complete list of those currently available is given in Chapter 27. Comparis FLC results using a Hitachi 911 and a Siemens Dade Behring BNII are shown in Figure 4.15 and the characteristics of four diff instruments are shown in Table 4.4. Comparisons of normal ranges are discussed in Chapter 5. There are no significant differe between the results on different instruments [38].

	Siemens BN™II	Beckman Coulter IMMAGE®	Roche Cobas Integra®	Binding Site SPAPLUS
Sensitivity (mg/L)	κ 0.30 (1/5): λ 0.25 (1/5)	κ 3.0 (1/5): λ 2.4 (1/5)	κ 0.6 (neat): λ 1.3 (neat)	κ 0.4 (neat): λ 0.5 (neat)
Precision (Intra-)	3.1-8.4%	2.0-8.1%	0.7-5.8%	1.6-3.4%
(CV) (Inter-)	4.7-8.4%	5.8-11.7%	0.7-2.7%	0.0-4.2%
Antigen excess	Good	Good	Good	Good
Analytical time	18 minutes	10 minutes	10 minutes	15 minutes
Time to run 20 normal/20 MM samples	52/127 minutes	40/84 minutes	33/75 minutes	33/68 minutes
Higher dilutions	Automatic	Off-line if high	Automatic & off-line if very high	Automatic & off-line if very high
Utility	Closed systems	Open system	Closed system, FLC channels on standard menu	Closed system

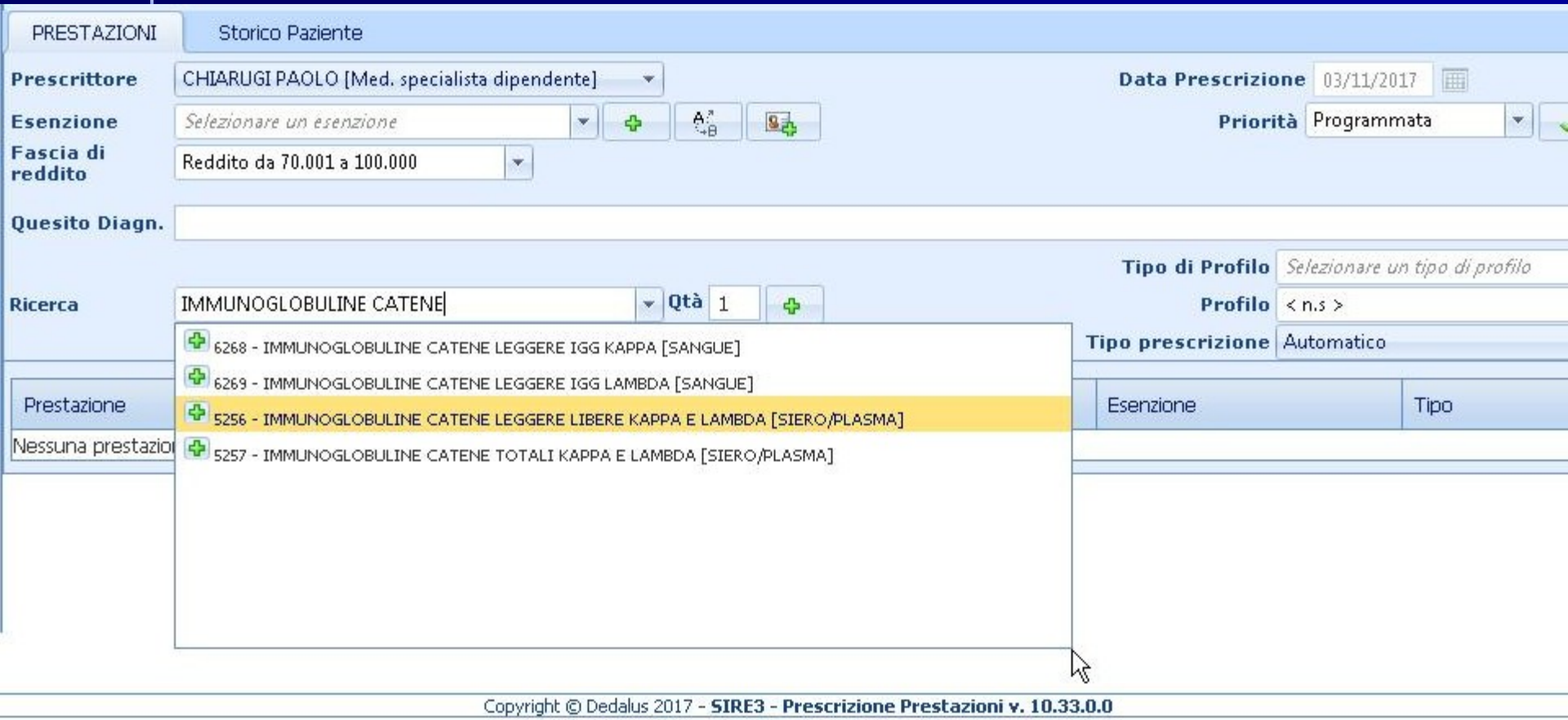
(C.V. = coefficient of variation in precision studies. Numbers in brackets refer to sample dilutions). See Chapter 27 for more details.

CL libere: discrepanza tra letteratura e pratica



Nonostante il crescente numero di pubblicazioni in materia e l'adattabilità del metodo sui principali strumenti, la maggior parte dei laboratori ignora il dosaggio delle CLL nel siero continuando ad utilizzare il dosaggio di CL totali, equivoco e destinato ad obsolescenza.

e-Prescription



CL libere: VEQ

Variabilità fra strumenti

Problema dell'eccesso di antigene

UK NEQAS United Kingdom National External Quality Assessment Service

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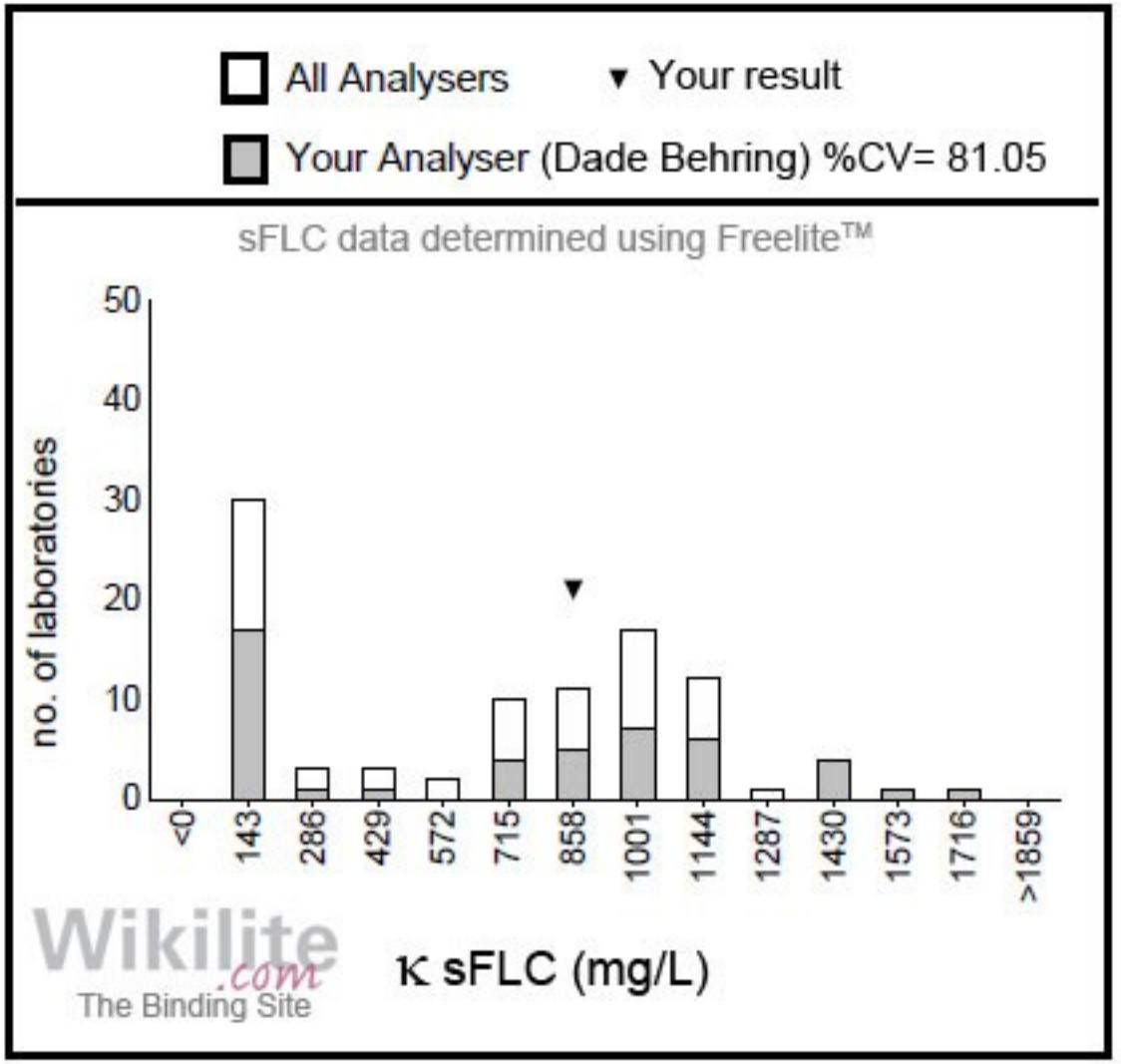
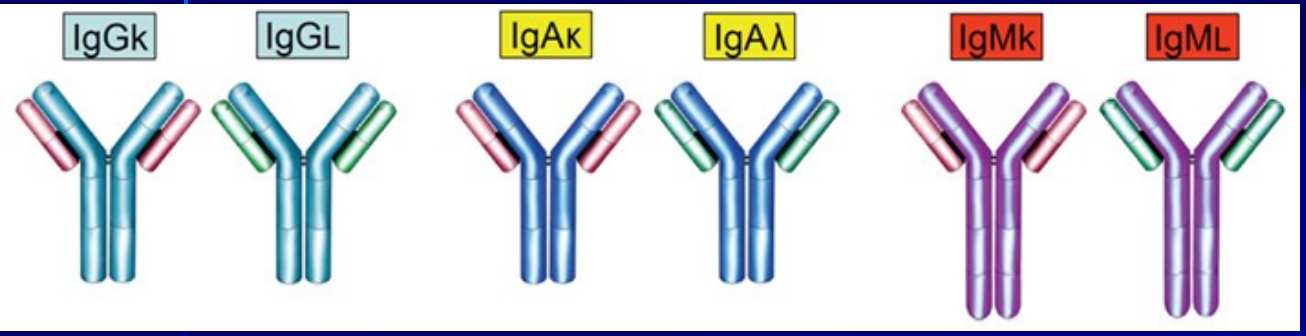
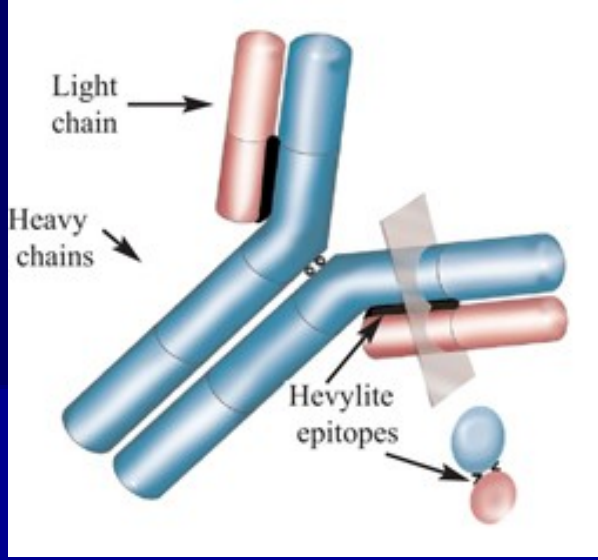
Web Polic

Monoclonal Protein Identification



Coming soon (?): Hevylite





Analysis of immunoglobulin heavy chain/light chain (HLC) pairs - Hevylite™

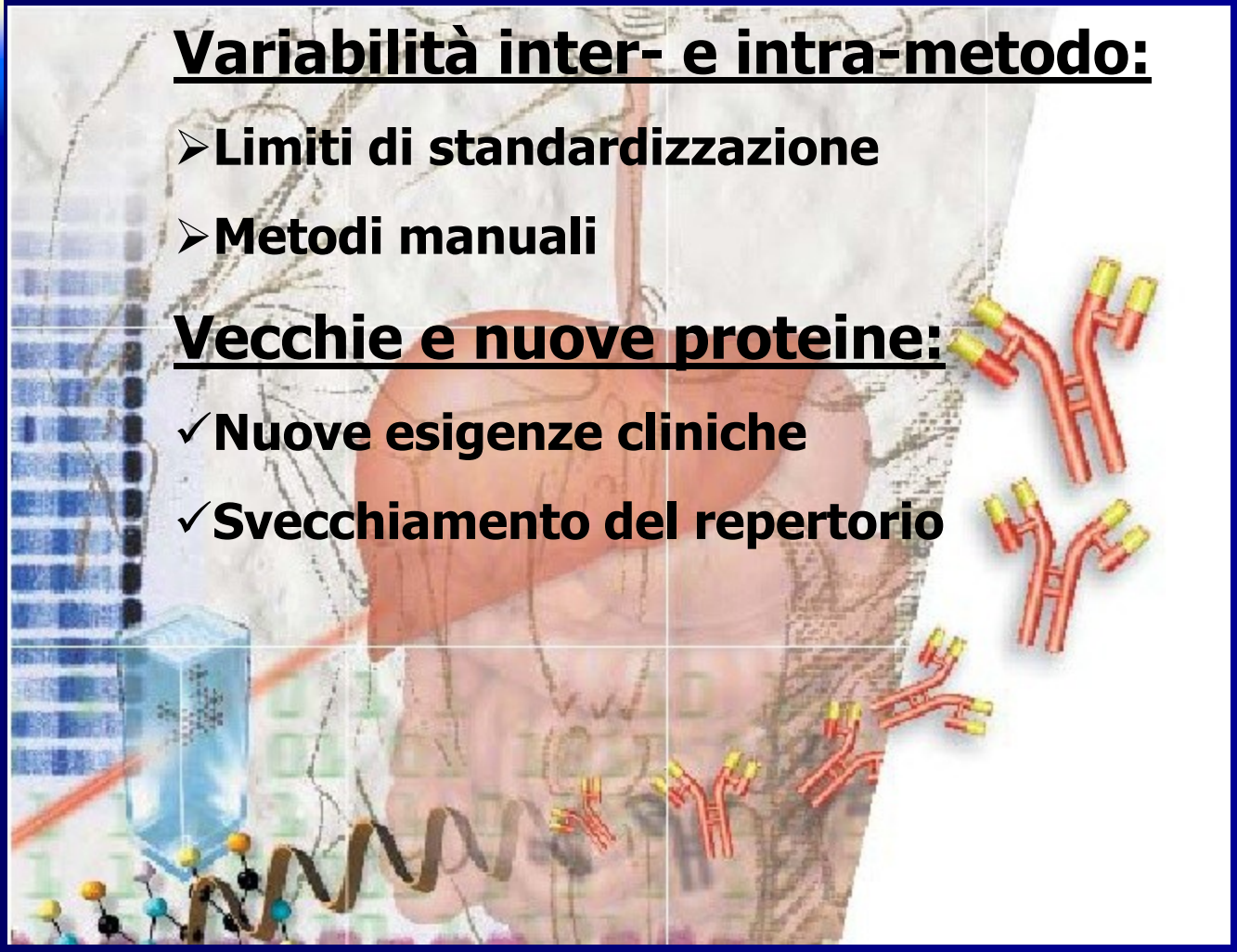
Hevylite (HLC), a new assay to be launched by Binding Site in 2009, promises to transform the way patients with B cell dyscrasia are managed, just as the **Freelite** assay has done.

Hevylite™

In summary **Hevylite** assays offer:

- higher sensitivity than serum protein electrophoresis for quantifying monoclonal immunoglobulins
- a numerical result for patients at a sensitivity as high as or better than immunofixation electrophoresis
- clinical value when monitoring patients with monoclonal gammopathies
- HLC ratios which have a greater range of changes than monoclonal immunoglobulin measurements because the non-tumour immunoglobulin allows assessment of immunosuppression
- HLC ratios which are not affected by changes in blood volume, haematocrit and variable metabolism (via FcRn receptors for IgG) that affect current assays for serum immunoglobulins
- HLC ratios that provide information about the tumour selective killing rate versus non-tumour plasma cell kill rates. The assessment of selective tumour killing rates may help with decision making regarding effective chemotherapies

Proteine specifiche: conclusioni



Variabilità inter- e intra-metodo:

- ➢ **Limiti di standardizzazione**
- ➢ **Metodi manuali**

Vecchie e nuove proteine:

- ✓ **Nuove esigenze cliniche**
- ✓ **Svecchiamento del repertorio**