



Nabespreking rondzendingen coeliakie 2013, 2014 en 2015

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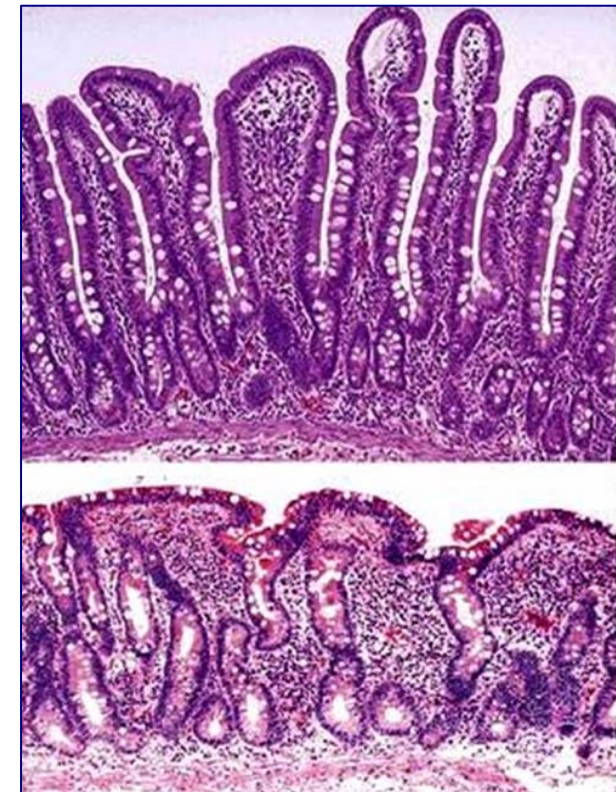
Diagnostiek van coeliakie

Richtlijnen (2008):

(Nederlandse Vereniging van Maag-Darm-Leverartsen)

- Klinische verdenking
- TGA-IgA (liefst bevestigen met EmA)
- In jonge kinderen (< 2 jr) tevens GA
- Bij IgA deficientie TGA-IgG
- Biopt (Marsh classificatie)

- Risicogroepen
- HLA-DQ typering vnl ter uitsluiting
- DQ2/8 positief: regelmatig serologisch screenen



ESPGHAN richtlijnen (2012)

Diagnose coeliakie bij kinderen (<18 jr):

- Klinische verdenking
- TGA IgA $\geq 10x$ ULN
- Bevestigd door EmA in onafhankelijk sample
- Passend HLA type (advies) (DQ2 of DQ8)

 *Diagnose coeliakie zonder biopt!*

- Screening
- TGA IgA $\geq 3x$ ULN

 *Komen juist voor biopt in aanmerking!*



Opzet coeliakie rondzending

Frequentie: 2 x per jaar (*mei en november*)

Aantal monsters: 5 monsters per keer

Verzending: per post (kamertemperatuur)

Verwerking: Qbase

Rapportage: Muse (*sinds 2013.1*)



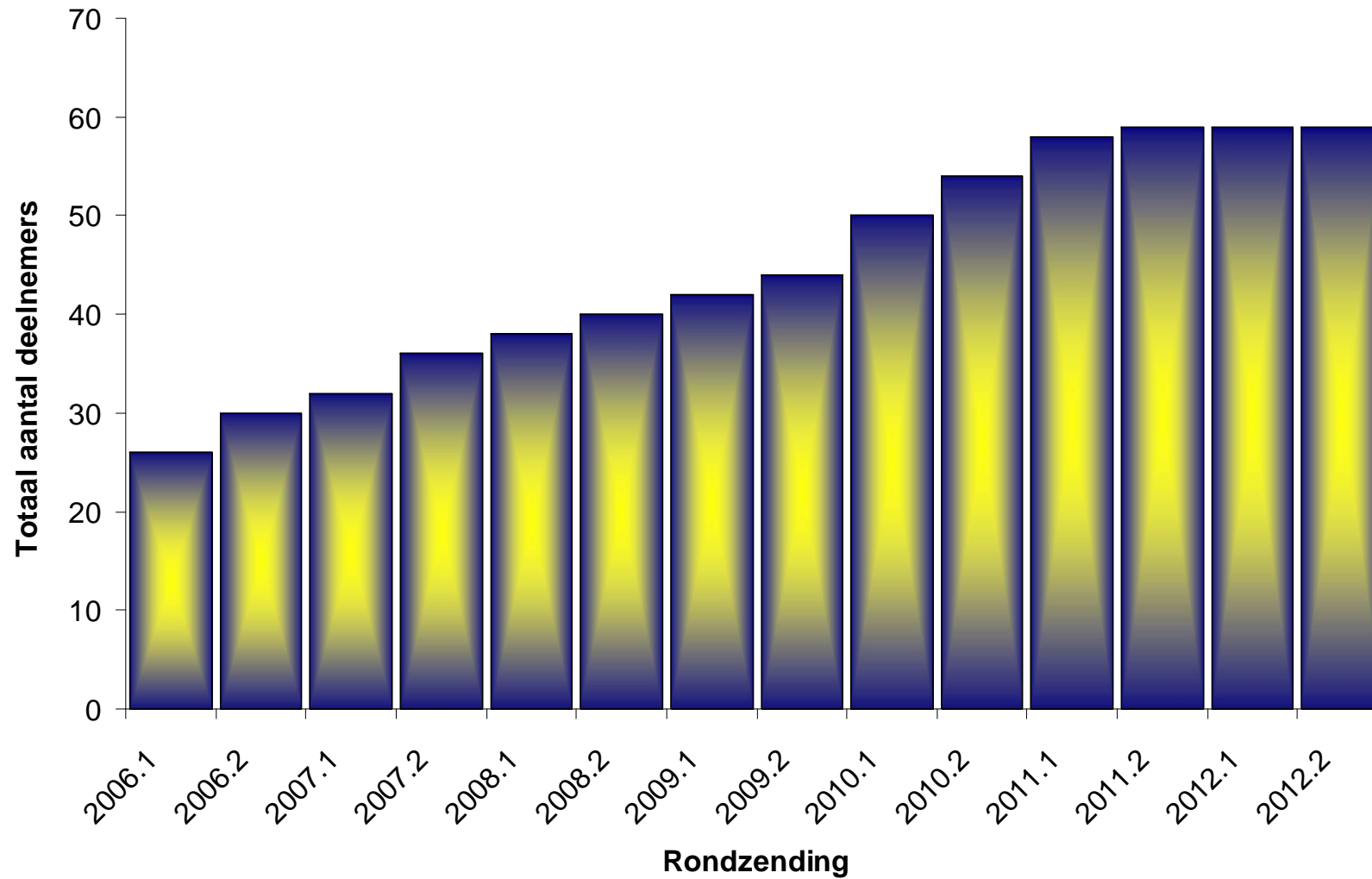
Te meten antilichamen

- ~~Gliadine antilichamen IgA~~ ~~GA-A~~
- ~~Gliadine antilichamen IgG~~ ~~GA-G~~
- **Endomysium antilichamen (IgA)** **EmA**
- **Transglutaminase antilichamen (IgA)** **TGA**
< 1x ULN < 3x ULN < 10x ULN < **ULN**
- **Gedeamideerde gliadine peptide a.l. IgA** **DGPA-A**
- **Gedeamideerde gliadine peptide a.l. IgG** **DGPA-G**
- Endomysium antilichamen (IgG) **EmA-G**
- Transglutaminase antilichamen (IgG) **TGA-G**

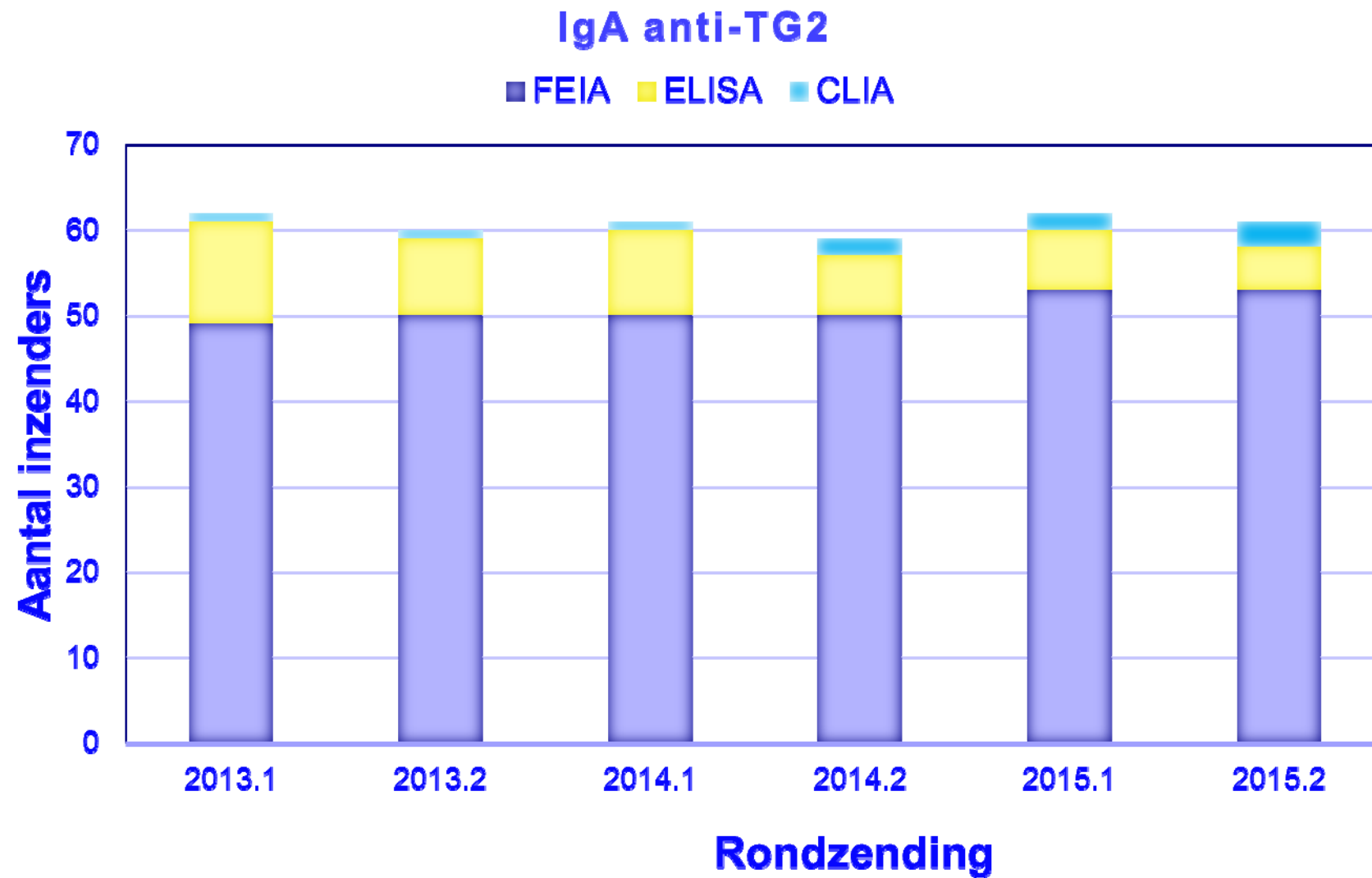
Gebruikte methoden / apparaten

<u>Methode</u>	<u>Apparaat</u>	<u>Reagentia</u>
ELISA	Alegria (Orgentec), Euroimmun Analyzer overig	Orgentec, Euroimmun Menarini
FEIA	Immunocap250 Immunocap100	TFS/Phadia Pharmacia Upjohn ?? (10x)
CLIA Luminescentie	Zenit RA, overig	Menarini, INOVA,
IIF visueel IIF software ondersteund	geen, Euroimmun Analyzer overig	ScimedX, INOVA, Menarini, Euroimmun eigen reagens, overig

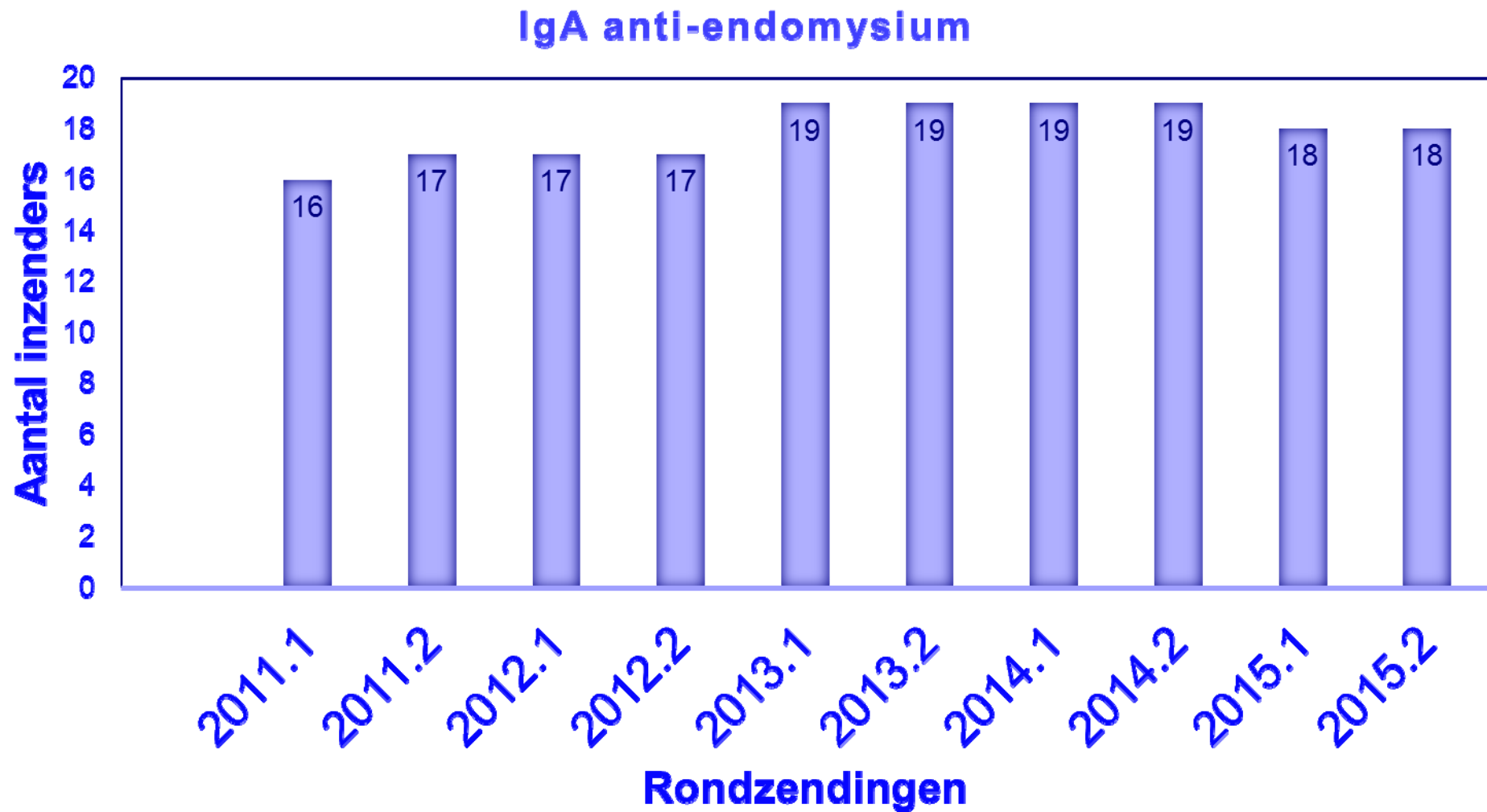
Totaal aantal deelnemers



Aantal deelnemers TGA



Aantal deelnemers EmA



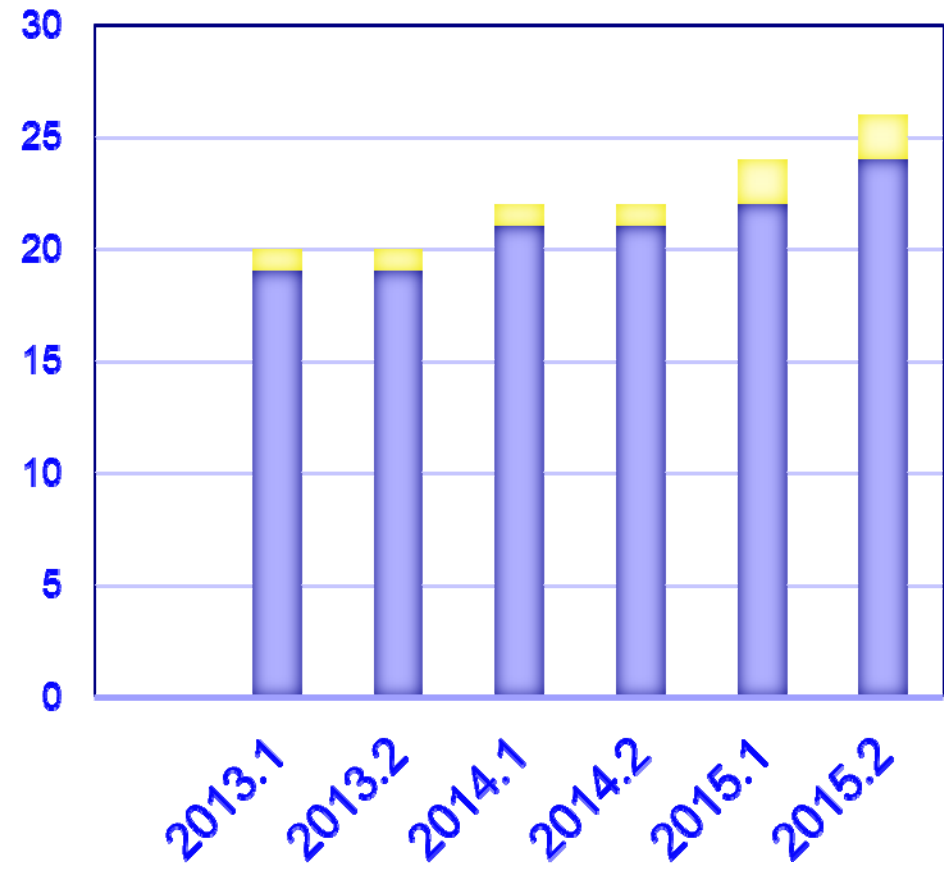
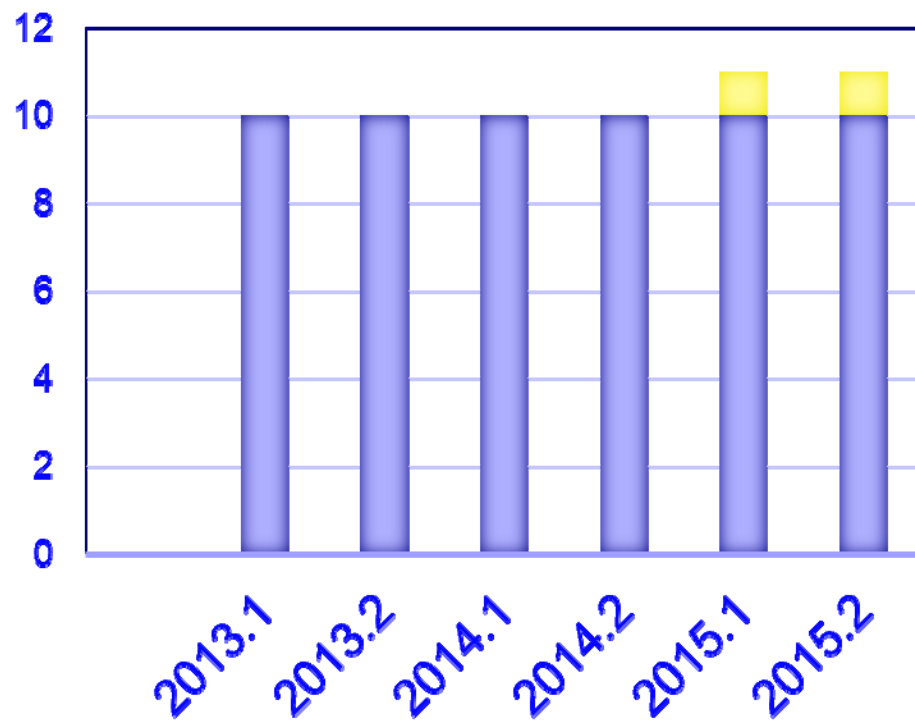
Aantal deelnemers DGPA

IgA

IgG

■ FEIA ■ ELISA

■ FEIA ■ ELISA



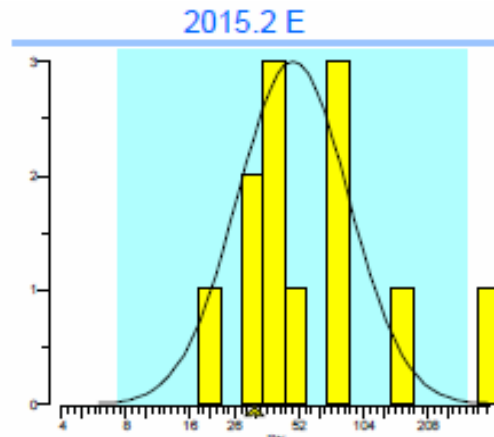
Bepalings combinaties	2013.2	2014.2	2015.2
EmA	1	1	
TGA	28	26	2
TGA + ULN			21
<i>TGA + EmA</i>	10	10	
<i>TGA + EmA + ULN</i>			10
<i>TGA + EmA + DGPA-A</i>	1	1	
<i>TGA + EmA + DGPA-A + ULN</i>			1
<i>TGA + EmA + DGPA-G</i>	3	3	
<i>TGA + EmA + DGPA-G + ULN</i>			3
<i>TGA + EmA + DGPA-A + DGPA-G</i>	4	4	
<i>TGA + EmA + DGPA-A + DGPA-G + ULN</i>			4
TGA + DGPA-G	8	10	
TGA + DGPA-G + ULN			13
TGA + DGPA-G + DGPA-A	5	5	2
TGA + DGPA-G + DGPA-A + ULN			4

Ab combinaties	2013.2	2014.2	2015.2
EmA	1	1	
TGA	28	26	2
<i>TGA + EmA</i>	10	10	
<i>TGA + EmA + DGPA-A</i>	1	1	
<i>TGA + EmA + DGPA-G</i>	3	3	
<i>TGA + EmA + DGPA-A + DGPA-G</i>	4	4	
TGA + DGPA-G	8	10	
TGA + DGPA-G + DGPA-A	5	5	2
TGA + ULN			21
<i>TGA + EmA + ULN</i>			10
<i>TGA + EmA + DGPA-A + ULN</i>			1
<i>TGA + EmA + DGPA-G + ULN</i>			3
<i>TGA + EmA + DGPA-A + DGPA-G + ULN</i>			4
TGA + DGPA-G + ULN			13
TGA + DGPA-G + DGPA-A + ULN			4

Gevraagde resultaten

- IIF kwalitatief : - +/- + ++ +++ → - +/- ++
grenswaarde /cutoff = (start)verdunning!
semikwantitatief: titer (- ; geen titer)
- ELISA/
FEIA /
CLIA kwalitatief : - +/- + ++ +++ → - +/- ++
kwantitatief: units/ml
grenswaarde /cutoff /ULN = grens dub/pos

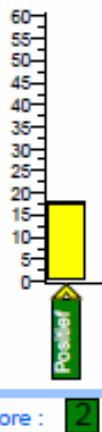
Invullen titer tbv statistiek



Startverduunningen varieert van 2 – 20:
 2 - 4 - 8 - 16 - 32 - 64 -
 20 - 40 - 80 - 160 - 320 - 640 -

	cons.	meth.	ALTM	lab
gem.	48	48	48	32
SD	40	40	40	
n	12	12	12	
nu	1	1	1	

← 12 labs titreren



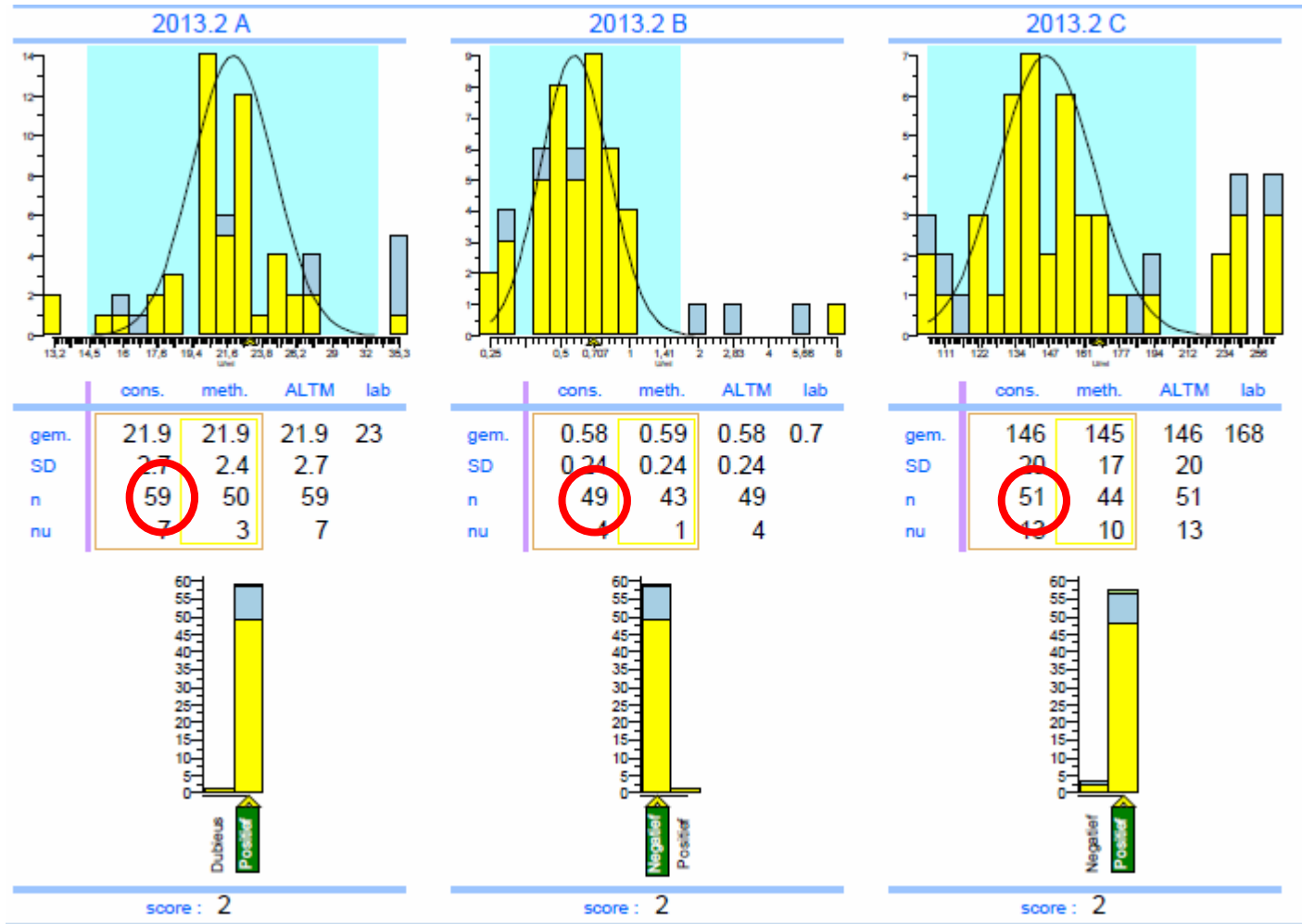
18 x EmA IIF

Legenda

	IIF vultueel		IIF software ondergrond
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Invullen concentratie tbv statistiek

TGA



In meetbereik

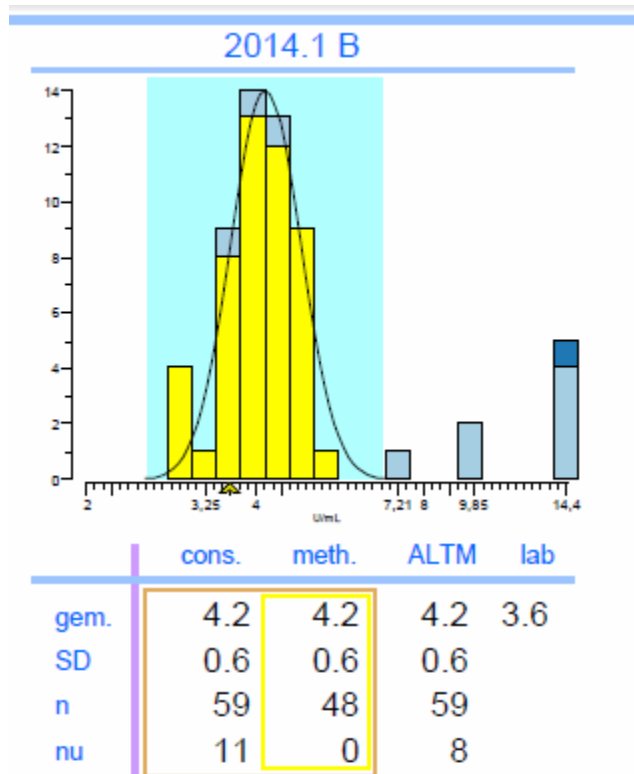
Negatief

Boven meetbereik

Verst. doorverdunnen

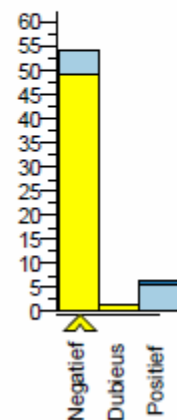


Invullen concentratie tbv statistiek



6 pos = ELISA en CLIA
 4 1-3x ULN
 2 3-10x ULN

50 FEIA met conc. **hoog** in neg. gebied



Concentraties in negatieve gebied zijn soms toch relevant

Nut van doorverdunnen

Rondzending: betrouwbaar gemiddelde
betere beoordeling eigen lab tov rest

Klinisch: Monitoring glutenvrij dieet!!
Rol DGPA? Minder vaak positief dan TGA.

date	diet	AGA-A	AGA-G	EMA	TGA-A	BIOPSY
09-06-2006	no	97	291	+++	350	
18-09-2006						Marsh IIIb
15-10-2006	GFD	7	200	+++	176	
19-11-2006	GFD	< 2	86	+++	128	
14-07-2007	GFD	< 2	< 2	+++	80	
07-06-2008	GFD	< 2	< 2	++	31	
11-02-2008	GFD	< 2	< 2	+	8	
11-07-2010	GFD	< 2	< 2	+/-	-	
11-11-2011	GFD	< 2	< 2	-	-	
02-04-2012			< 2			Marsh 0

Effect voorverdunnen door verzendlab

Monster E

	niet	1:3	1:5	1:10
EmA	+++ 1:128	++ 1:32	++ 1:16	++1:8
TGA	>+++	+++	++	++
DGPA-A	++	+	+/-	-
DGPA-G	+	+/-	-	-

Vals positieve uitslagen?

- In 2014-1 gezonde controle:

Monster A gezonde controle

1/61 TGA bepalingen is positief. Oorzaak?

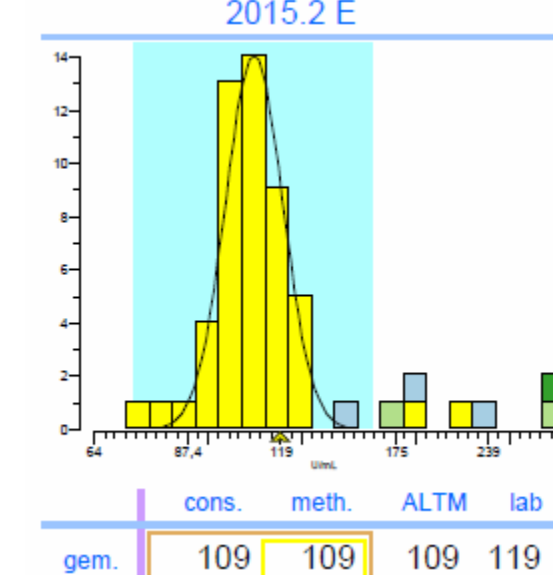
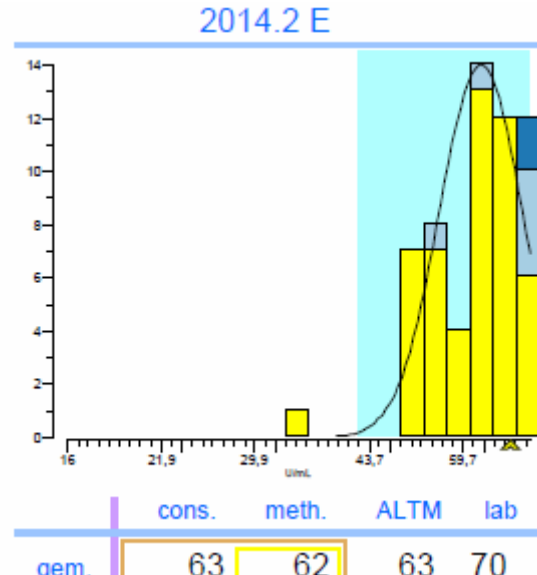
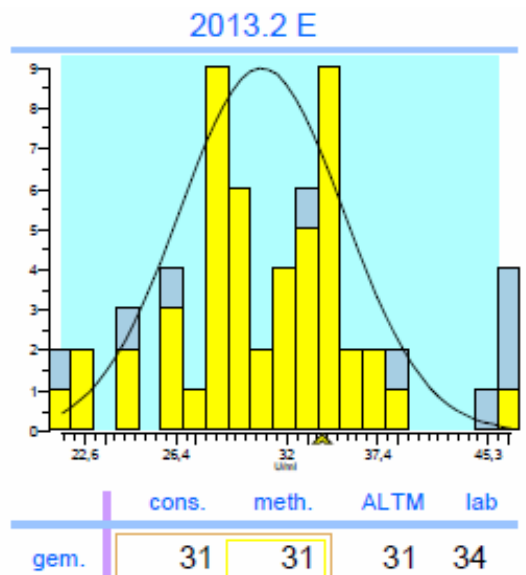
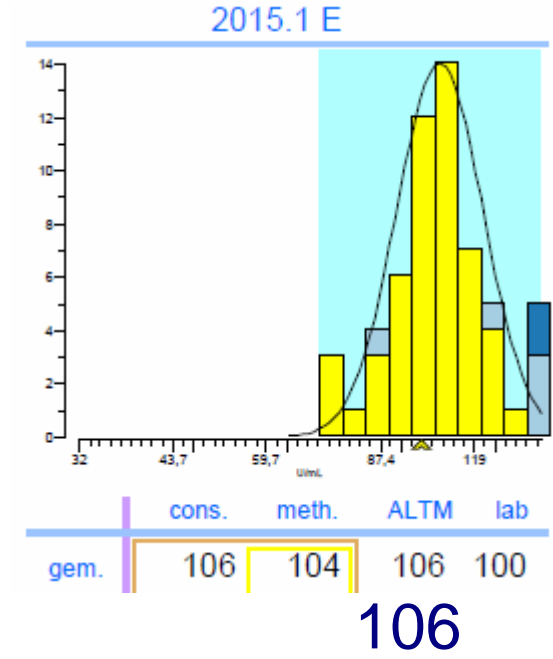
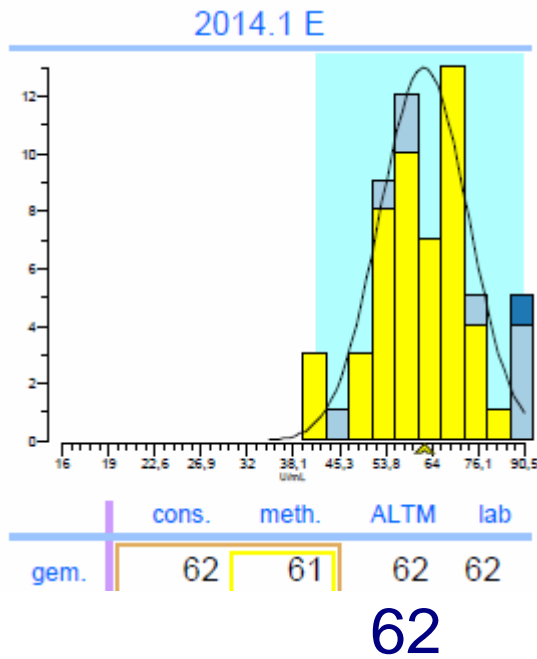
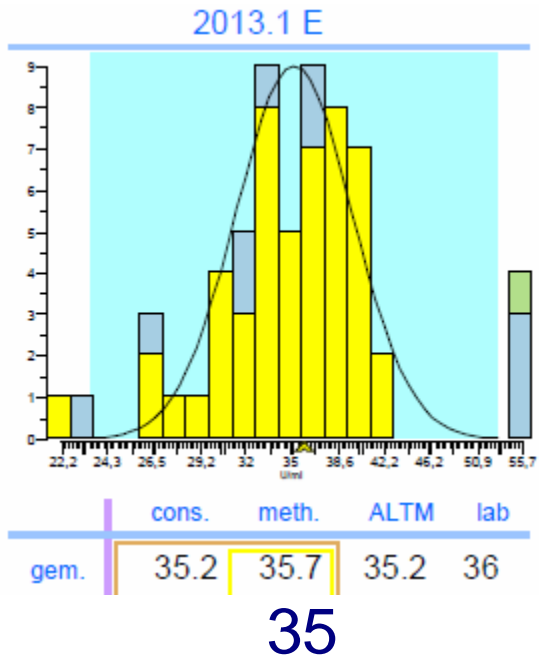
Monster C gezonde controle

1/61 TGA uitslagen is positief; lijkt verwisseling met monster D

10x verdund

5x verdund

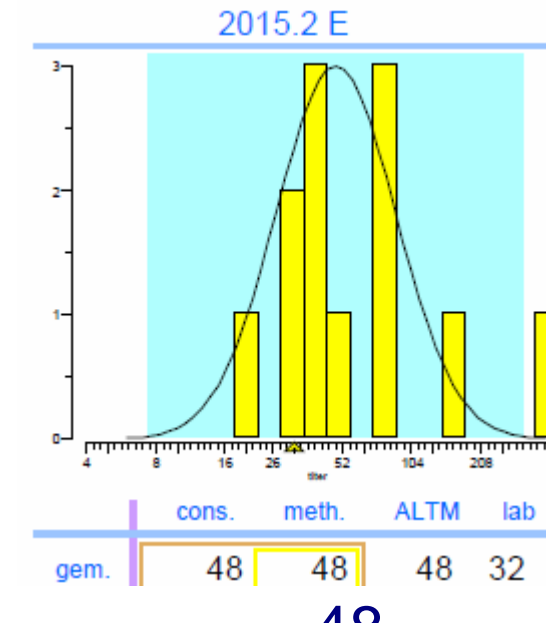
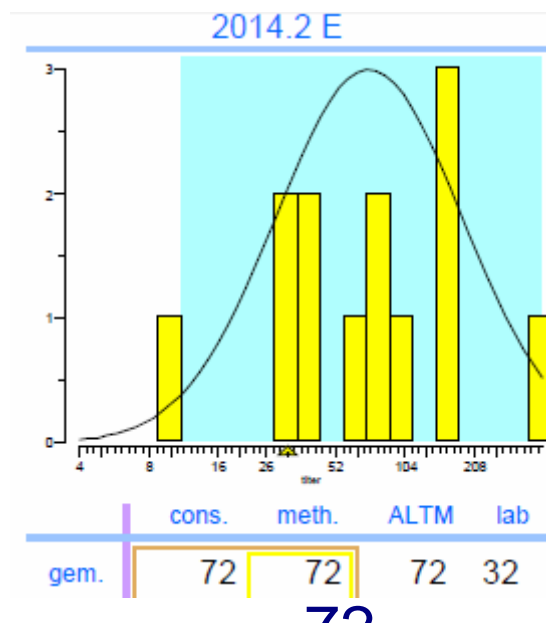
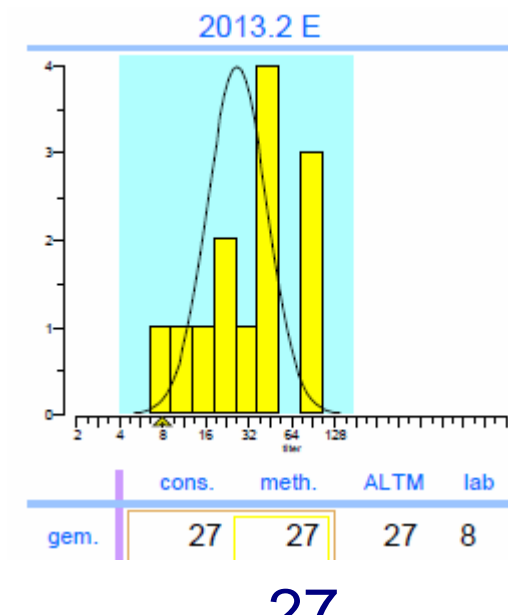
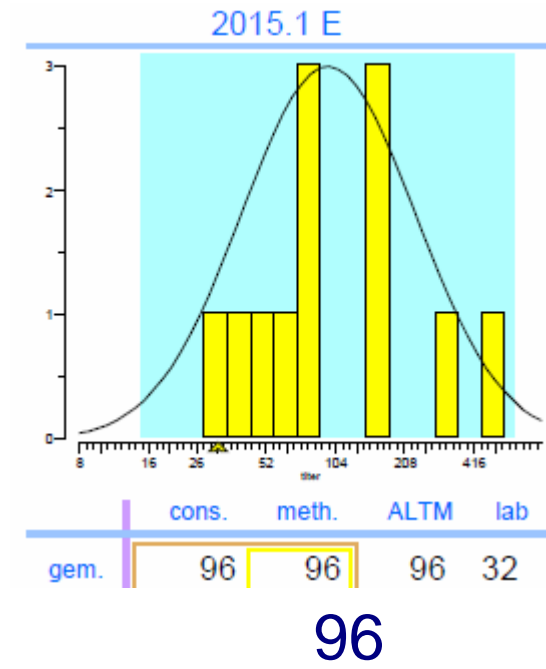
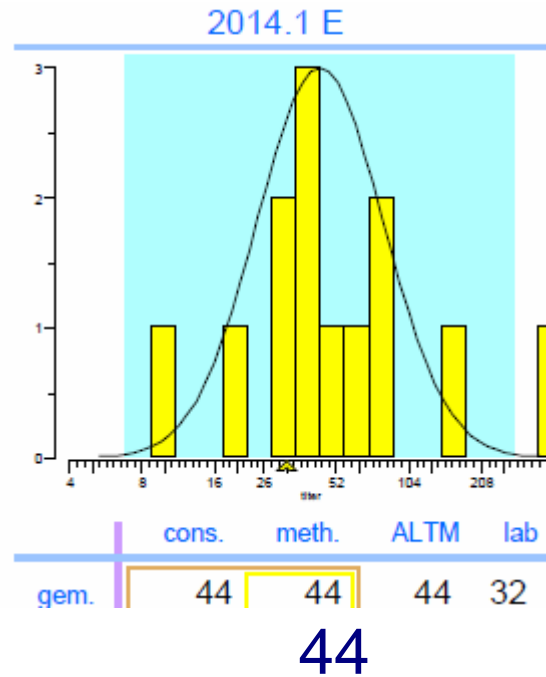
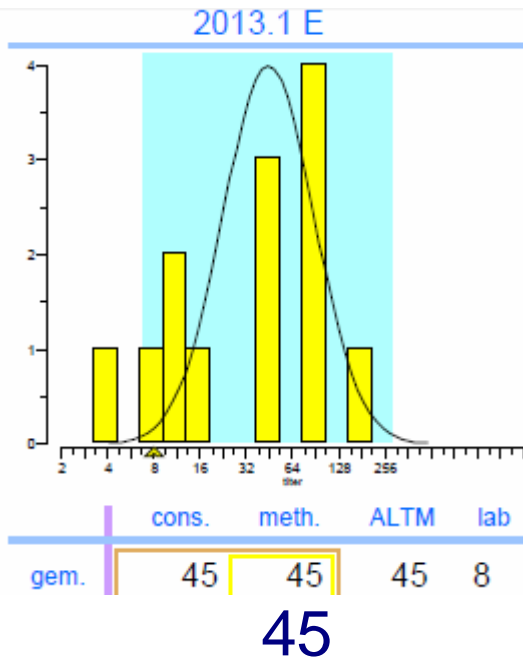
3x verdund



10x verdund

5x verdund

3x verdund



Continuïteit in de tijd (#E: DGPA-A)

10x verdund

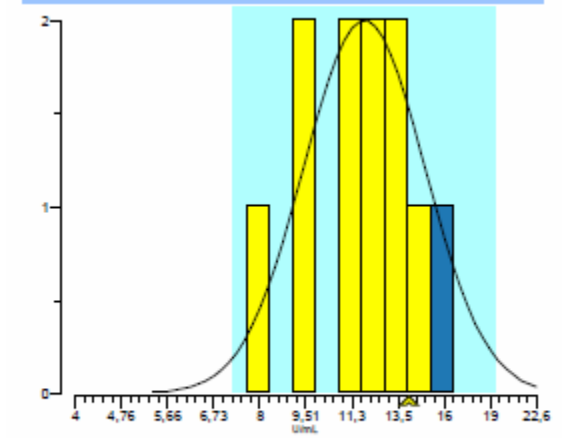
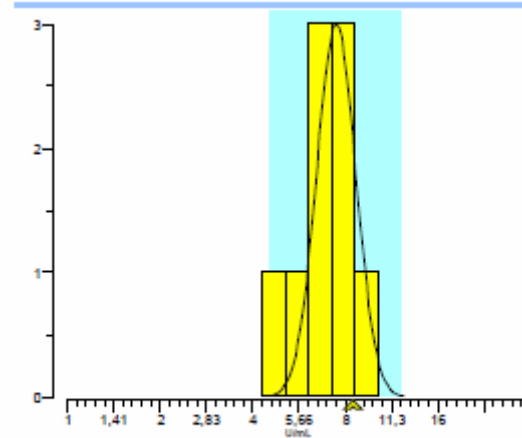
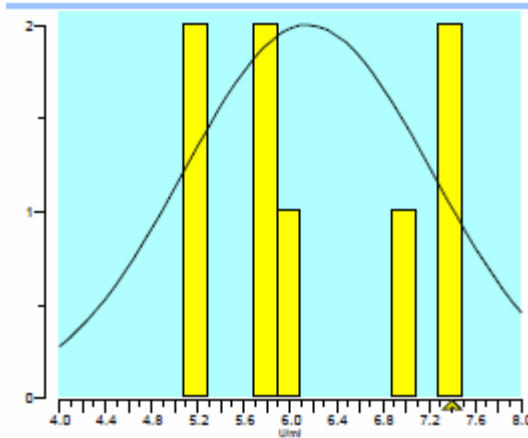
5x verdund

3x verdund

2013.1 E

2014.1 E

2015.1 E



	cons.	meth.	ALTM	lab
gem.	6.1	6.1	6.1	7.4

	cons.	meth.	ALTM	lab
gem.	7.5	7.5	7.5	8.5

	cons.	meth.	ALTM	lab
gem.	11.8	11.4	11.8	14

6

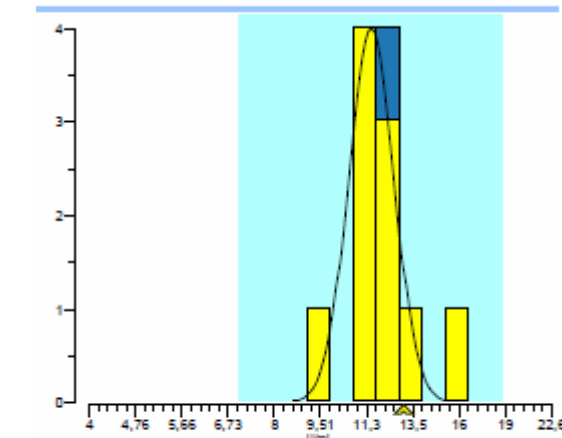
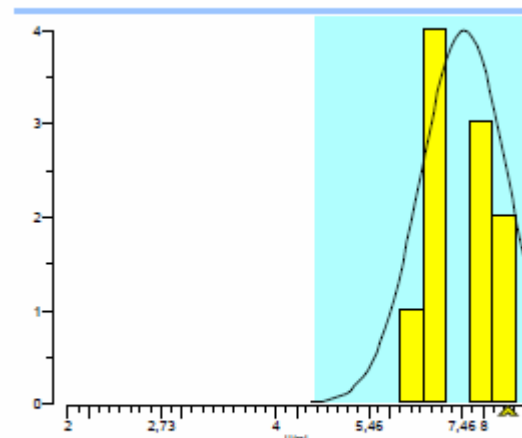
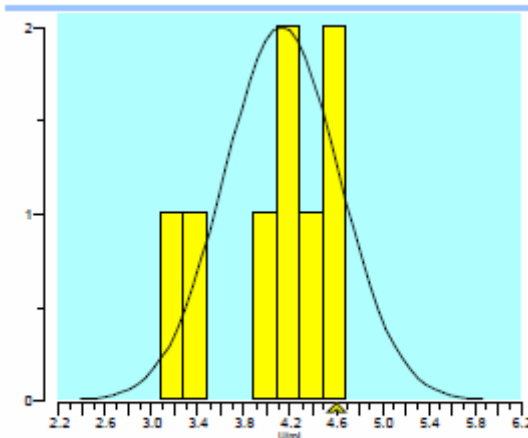
7,5

11,4

2013.2 E

2014.2 E

2015.2 E



	cons.	meth.	ALTM	lab
gem.	4.1	4.1	4.1	4.6

	cons.	meth.	ALTM	lab
gem.	7.5	7.5	7.5	8.7

	cons.	meth.	ALTM	lab
gem.	11.5	11.4	11.5	13

4

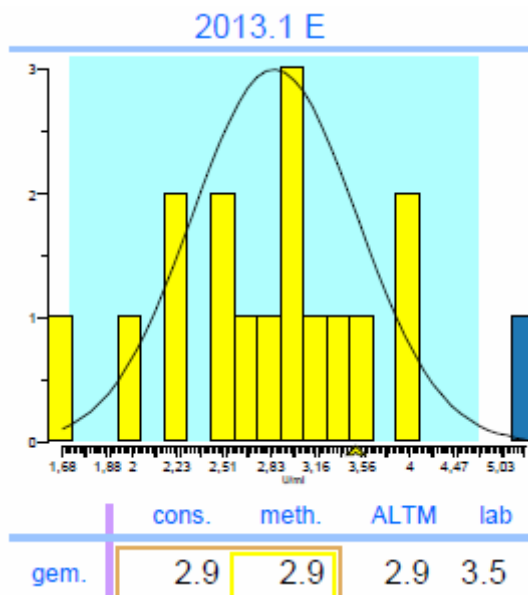
7,5

11,4

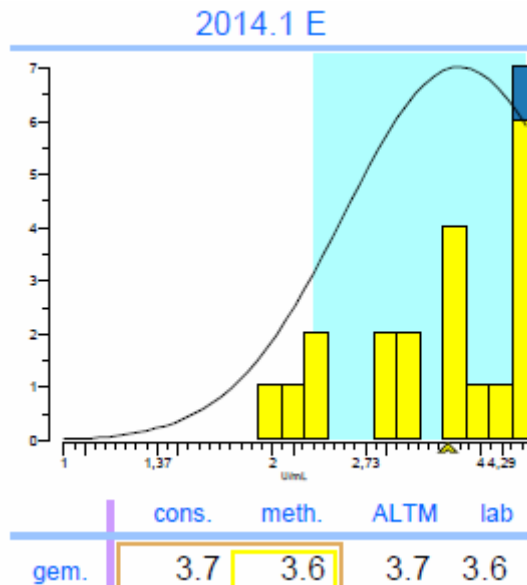
10x verdund

5x verdund

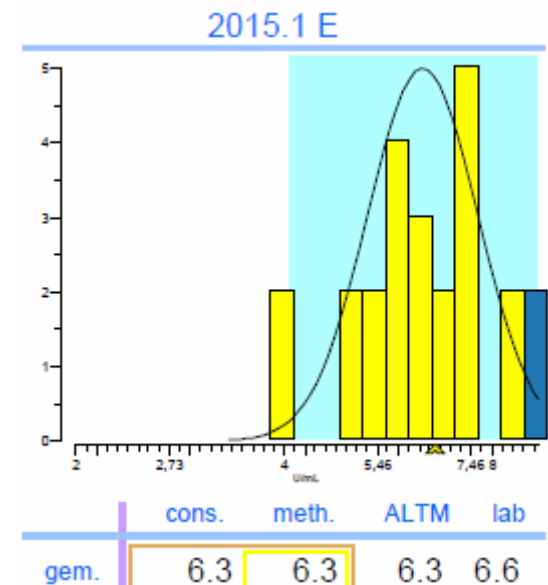
3x verdund



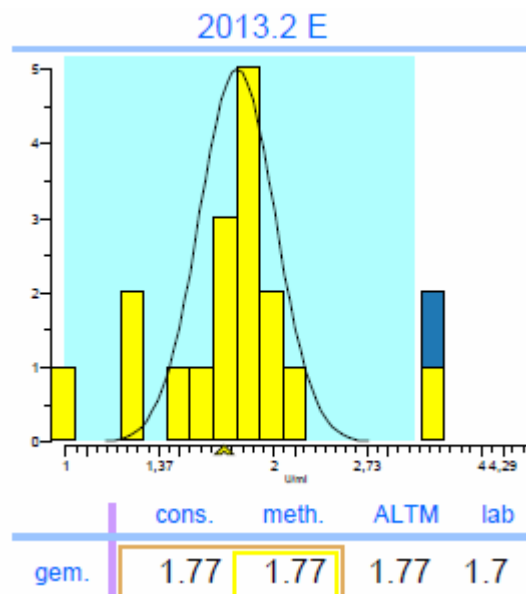
2,9



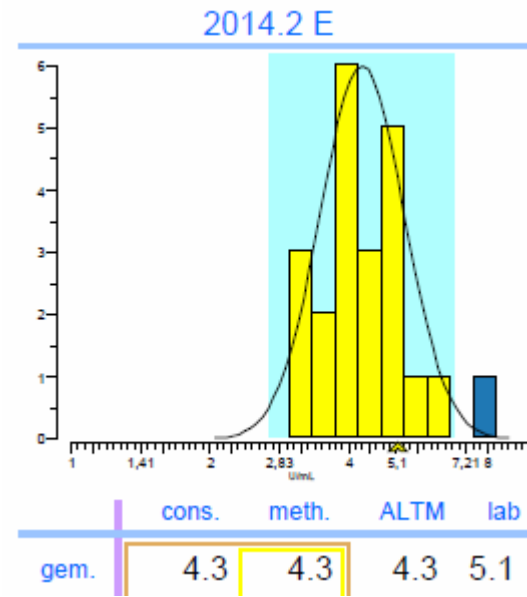
3,7



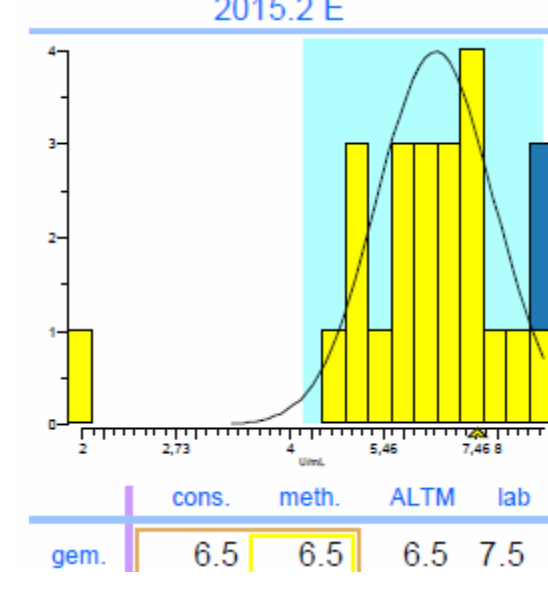
6,3



1,8

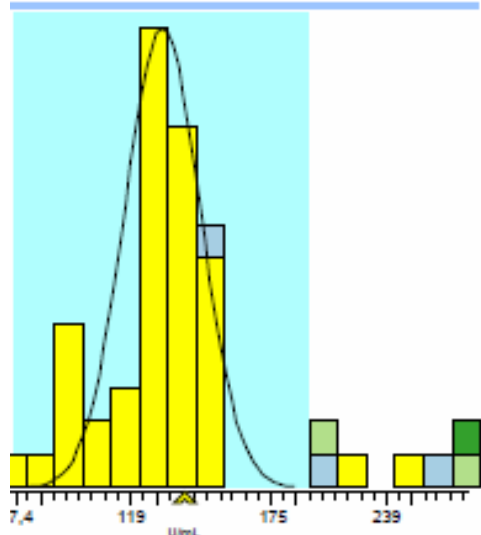


4,3



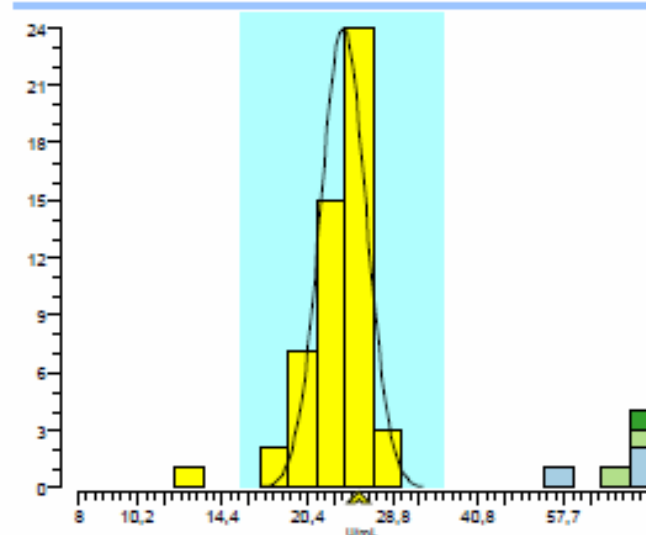
6,5

2015.2 B



cons.	meth.	ALTM	lab
130	130	132	138

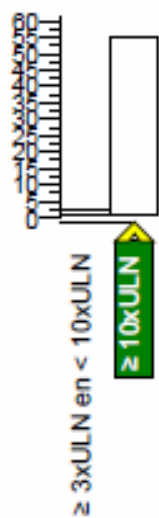
2015.2 D



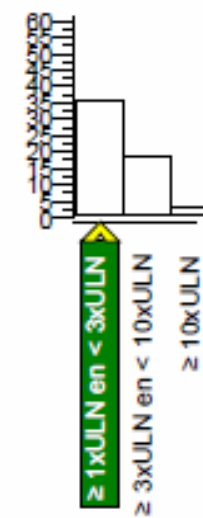
gem.	cons.	meth.	ALTM	lab
	23.5	23.5	23.5	25

Anti-TG2 ULN categorie

2015.2 B



2015.2 D



ESPGHAN richtlijnen (2012)

Diagnose coeliakie bij kinderen (<18 jr):

- Klinische verdenking
- TGA IgA $\geq 10x$ ULN
- Bevestigd door EmA in onafhankelijk sample
- Passend HLA type (advies) (DQ2 of DQ8)

 *Diagnose coeliakie zonder biopt!*

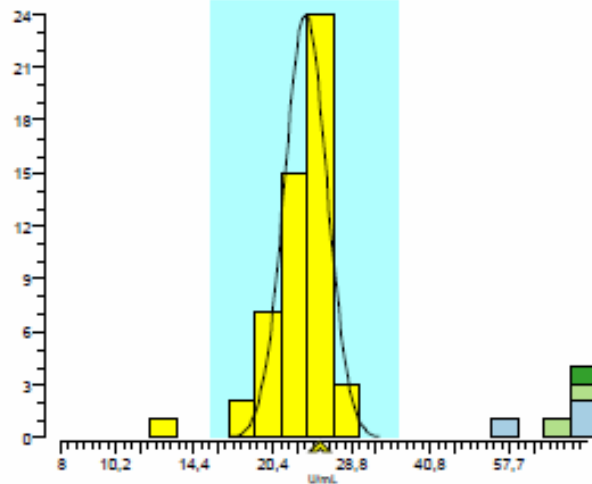
- Screening
- TGA IgA $\geq 3x$ ULN

 *Komen juist voor biopt in aanmerking!*

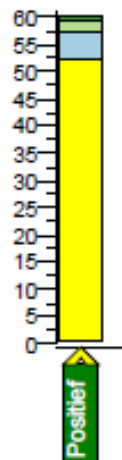


Mogelijk consequenties voor diagnostische pathway

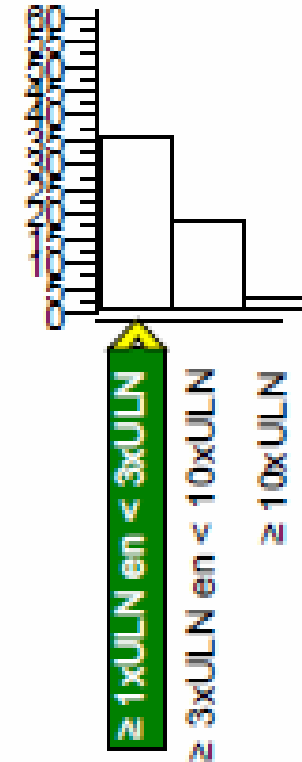
2015.2 D



	cons.	meth.	ALTM	lab
gem.	23.5	23.5	23.5	25
SD	2.3	2.3	2.3	
n	58	52	58	
nu	7	1	7	



Onderverdund serum van volwassene ttv diagnose coeliakie (M3A)



← →
Wel biopt Geen biopt

← →
Geen biopt Wel biopt

Belangrijk!

- Check altijd de Qbase instellingen; ook als er niets veranderd is in je labtechnieken.
- Gebruik de juiste benaming voor methode, techniek en reagentia, ook tbv de statistiek.
IIF visueel of IIF software ondersteund
CLIA ipv luminescentie
TFS Phadia ipv Pharmacia Upjohn
- Grenswaarde / cut-off / ULN = grens dub/pos
- Geef een getal door tbv de statistiek, dus geen bovengrens van de assay: dit betekent doorverdunnen.
(voorverdunnen tot binnen meetbereik niet altijd wenselijk)

Met dank aan Jolien Hollander
Saida Tonouh
Petra Bonnet
Janna Kruiswijk
Elise van Haastert
Martine Reijm

