

Support PK and ADA of biologics using finger prick sampling

Sanquin Diagnostic Services



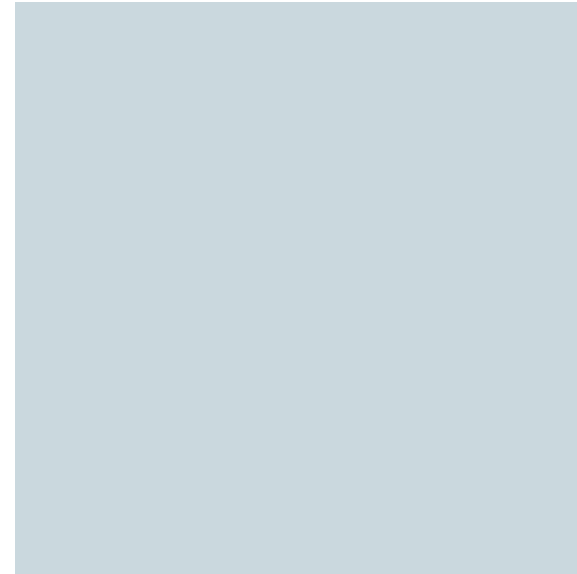
paper and scissors rock

Annick de Vries, PhD

Director Pharma and Biotech Services, Sanquin Diagnostic Services

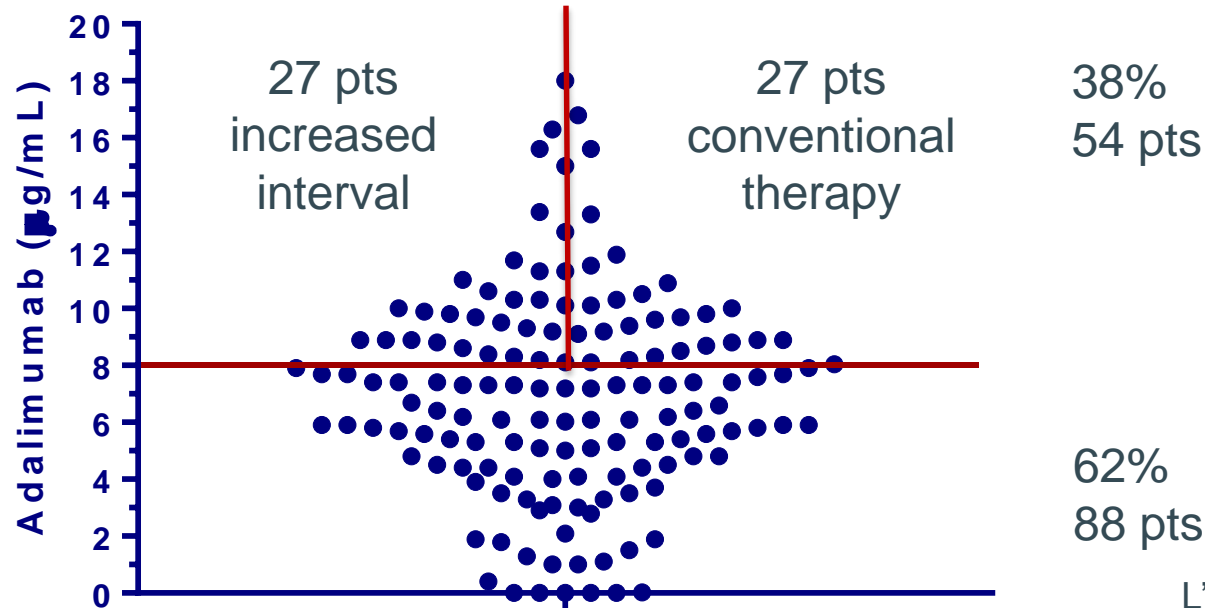
Capillary Blood sampling for biologics: A tool in Therapeutic Drug Monitoring

- Auto sampling at home
- Logistics cheap and easy
- Easy to sample frequently
- Clinician/ clinic receives serum concentration in advance
- Easy sampling to support PK studies
- Model concentration curve per patient
- Personal advice on dosing schedule



Lower dose based on serum level (note- serum concentration)

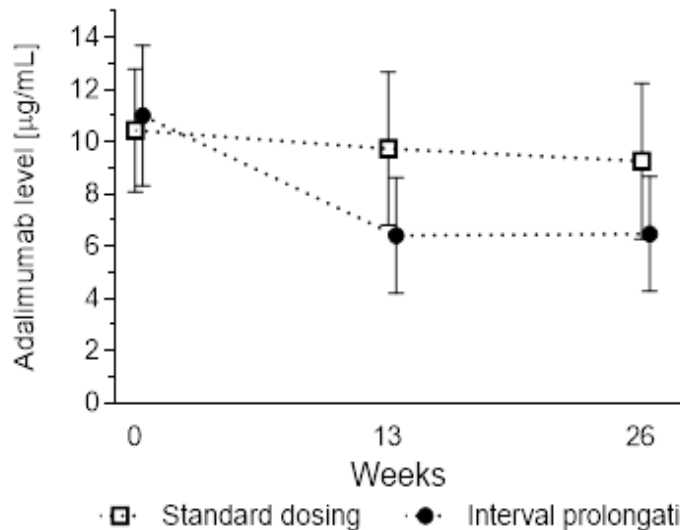
Adalimumab concentration



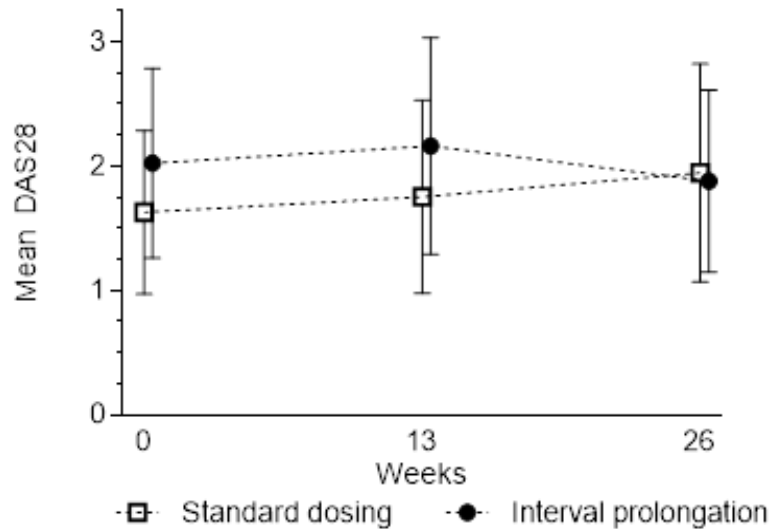
62%
88 pts

Increasing interval of administration – clinical efficacy remains

Lower serum level ADL



Clinical efficacy remains



Comparative data on venous vs. capillary blood measurement using Whatman and Mitra

Amsterdam UMC

infliximab in IBD-patients

Sophie Berends

Anne Strik

Ron Mathot



Reade Amsterdam

adalimumab in RA-patients

Eva Kneepkens

Gert-Jan Wolbink



Sanquin Diagnostic Services/Sanquin Research

Fiona Moreno

Karien Bloem

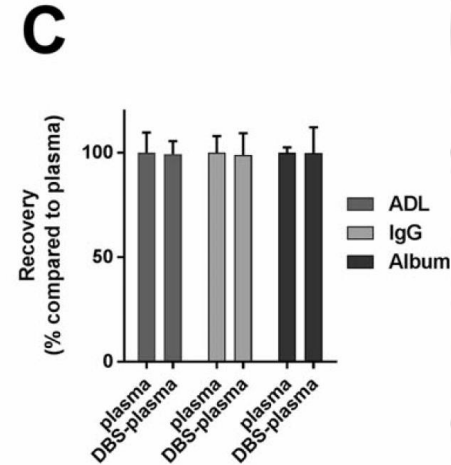
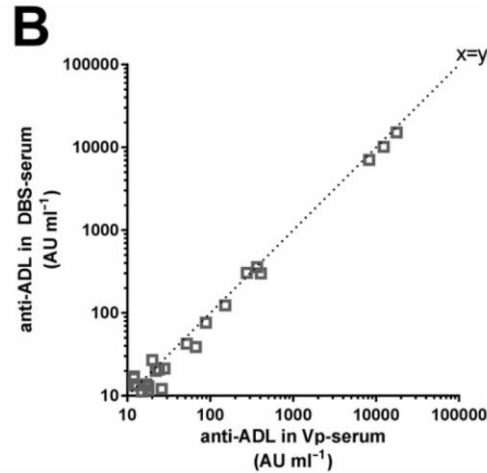
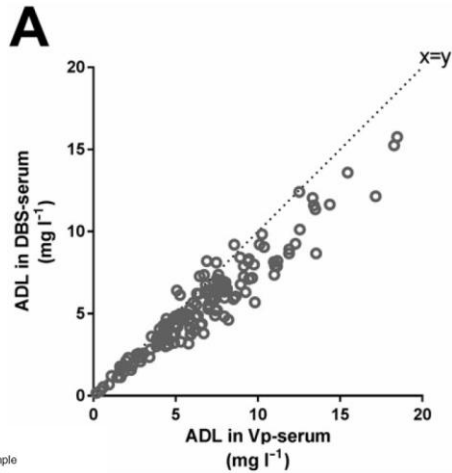
Theo Rispens

Tiny Schaap



Adalimumab in venous vs capillary blood correlates well

Whatman paper



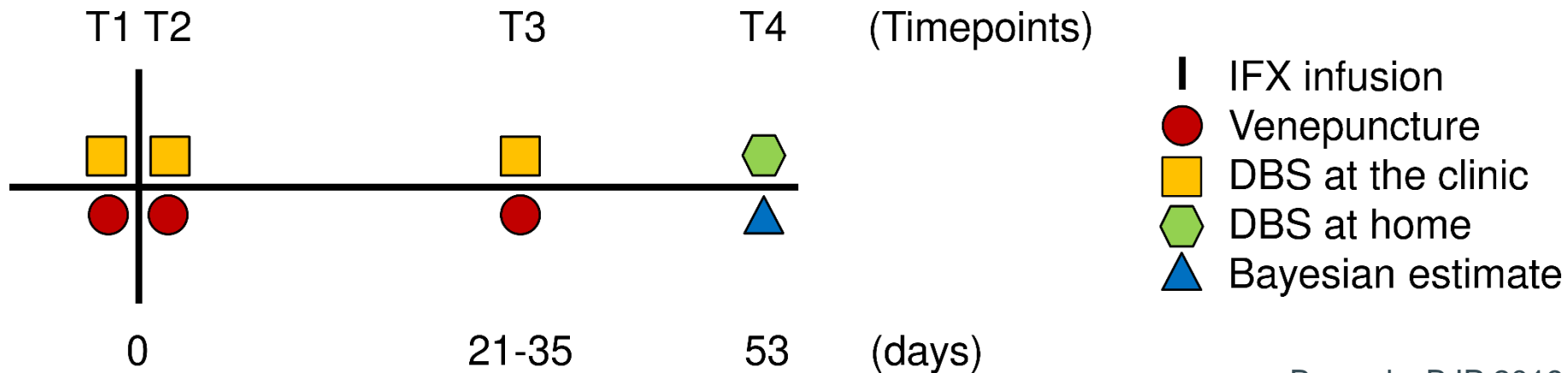
Blood sample



Hct

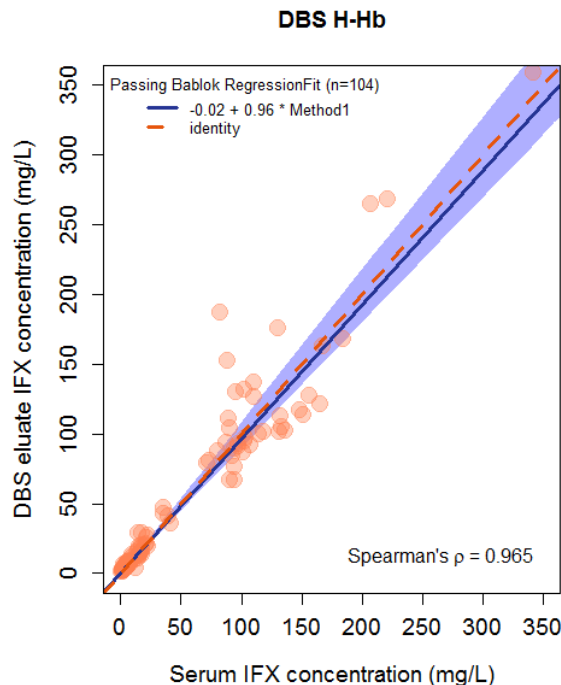
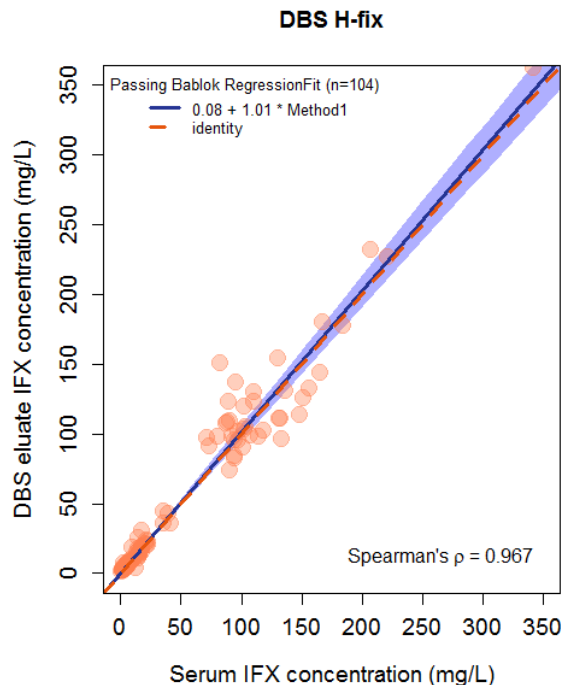
How well do concentrations derived from home-sampled DBS reflect serum concentration?

infliximab study; real-life data
 simultaneous venous/finger prick and home sampling



Good correlation between DBS and serum infliximab conc

Mitra tips- 2x 20µL

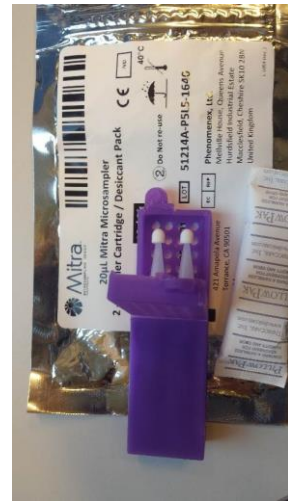
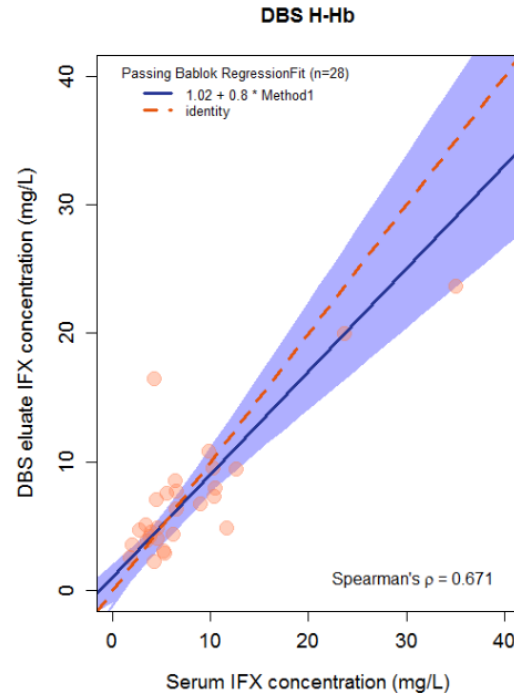
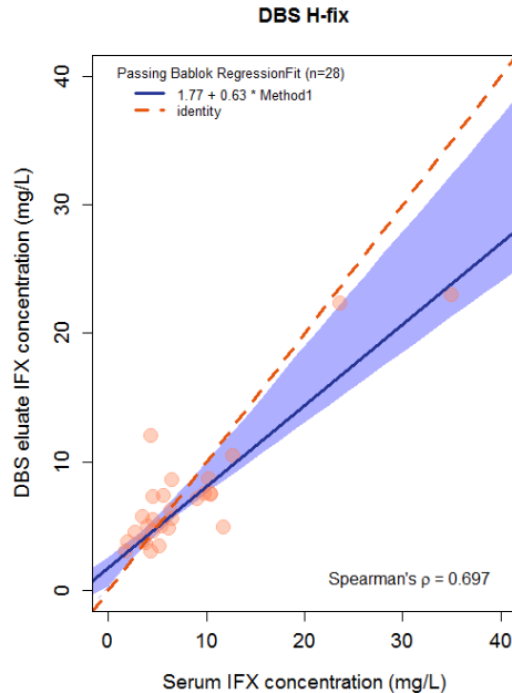


DBS H-fix: intercept: 0.08 mg L⁻¹
(95% CI -0.22-0.47 mg L⁻¹),
slope: 1.01 (95% CI 0.95-1.07)

DBS H-Hb: intercept: -0.02 mg L⁻¹
(95% CI -0.47 – 0.50 mg L⁻¹),
slope: 0.96 (95% CI 0.90 – 1.09)



Good correlation between DBS and serum infliximab conc modelled vs. home-sampling

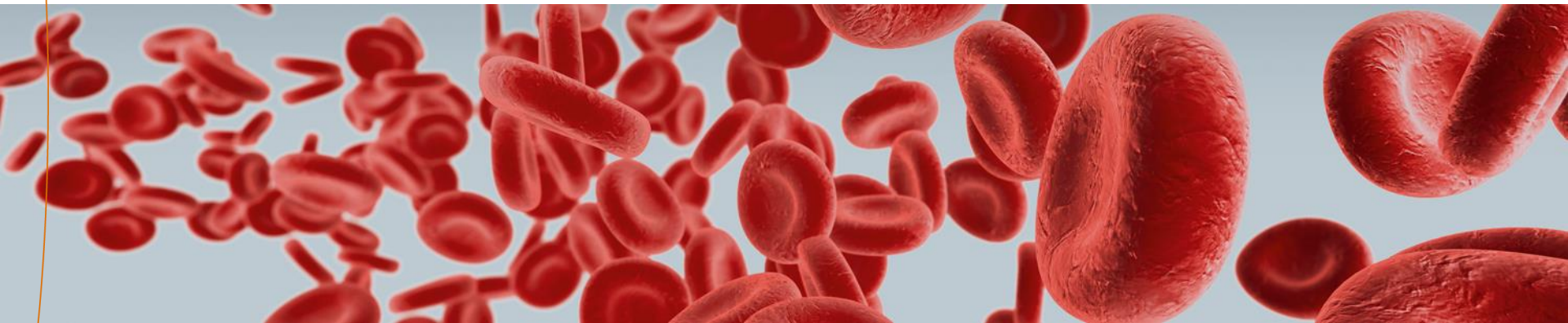


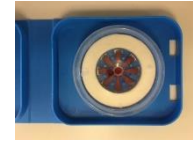
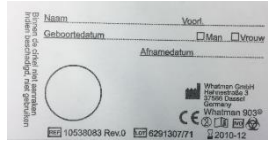
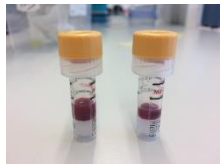
DBS H-fix; intercept: 1.77 mg L⁻¹
(95% CI 0.29 – 2.63 mg L⁻¹),
slope: 0.63 (95% CI 0.55 – 0.91)

DBS H-Hb; intercept: 1.02 mg L⁻¹
(95% CI -1.07 – 2.02 mg L⁻¹),
slope: 0.80 (95% CI 0.63 – 1.14)



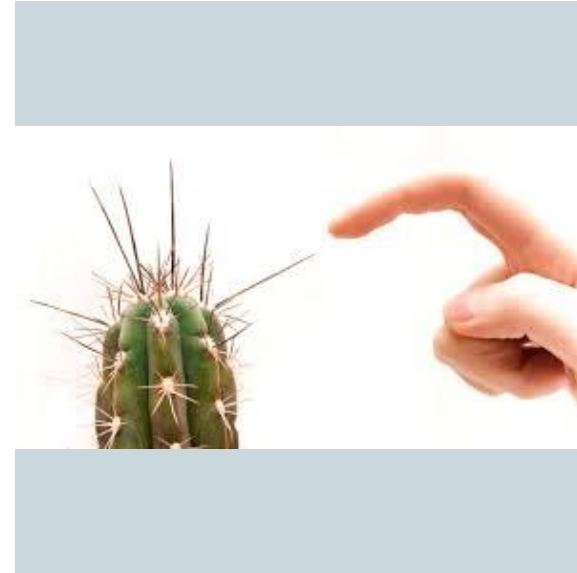
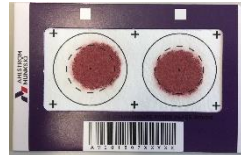
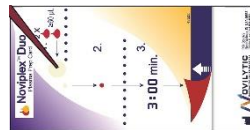
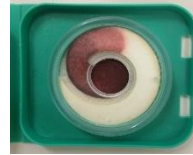
Newly tested devices





THANKS

- Fiona Moreno
- Tiny Schaap
- Theo Rispens
- Karien Bloem



Serum

MiniCollect® Z
Serum Separator
Tubes

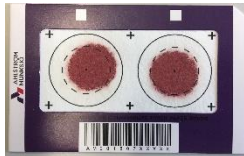
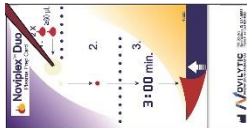
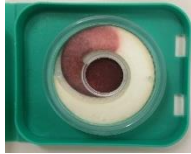
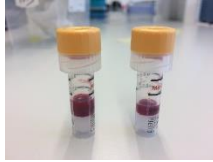
Ser-Col®

HemaSpot™-SE

PostYourLab®

Noviplex™
Plasma Prep card

HemaSep card



Whole blood

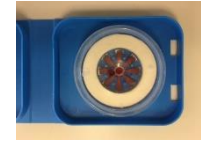
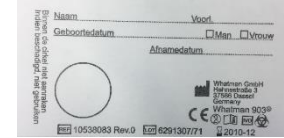
Mitra® microsampler

Whatman® 903

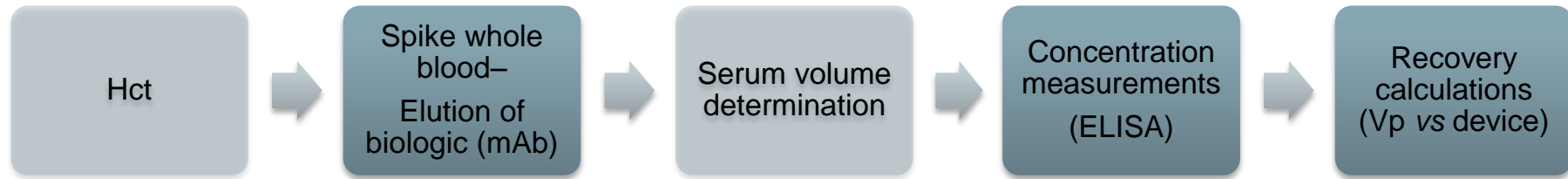
Hemaspot™-HF

HemaXis™ DB10

hemaPEN®

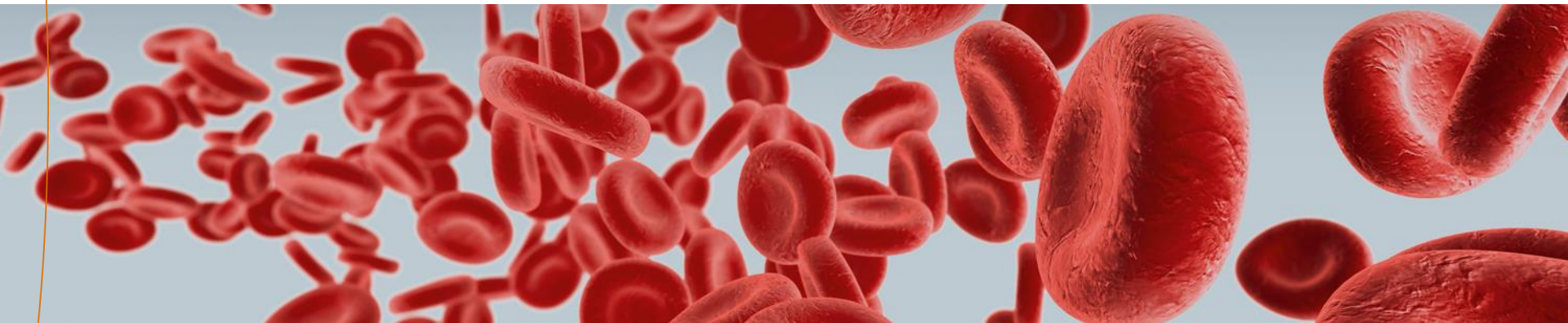


General method to test different capillary blood devices



$$\text{Recovery} = [\text{biologic}]_{\text{eluate}} / [\text{biologic}]_{\text{spiked blood control}} * 100$$

Whole blood devices



HemaXis™

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HemaPEN®

Disregarded as volume too low for our purposes

- around 6 µL of serum

Whole blood

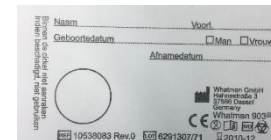
Mitra® microsampler

Whatman® 903

Hemaspot™-HF

HemaXis™ DB10

hemaPEN®



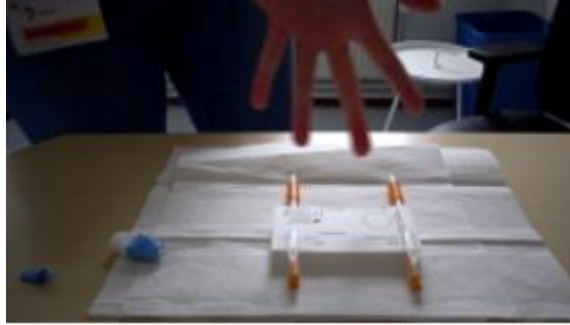
Whatman® 903

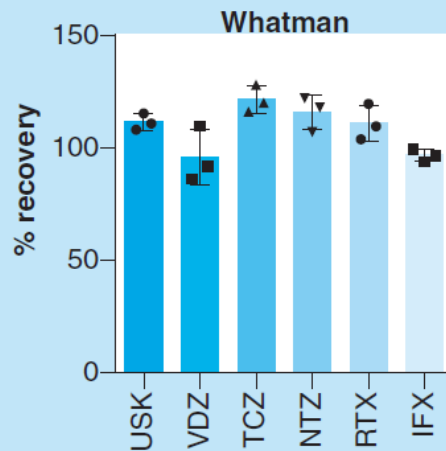
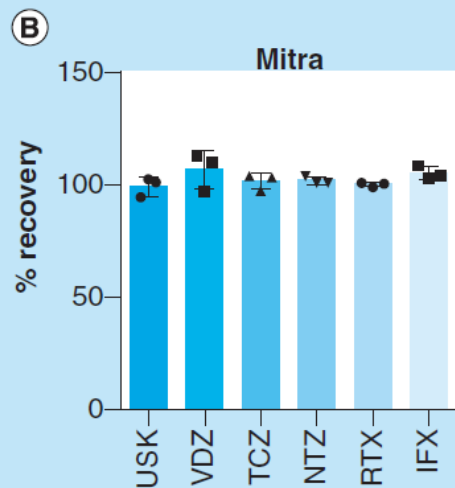
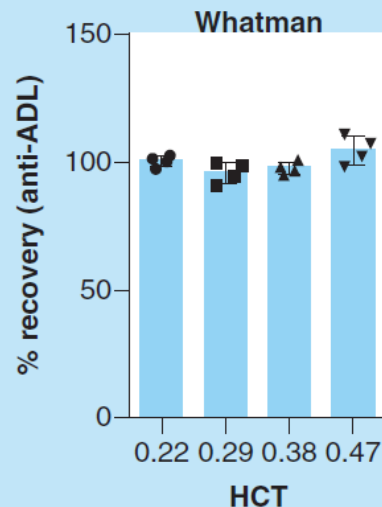
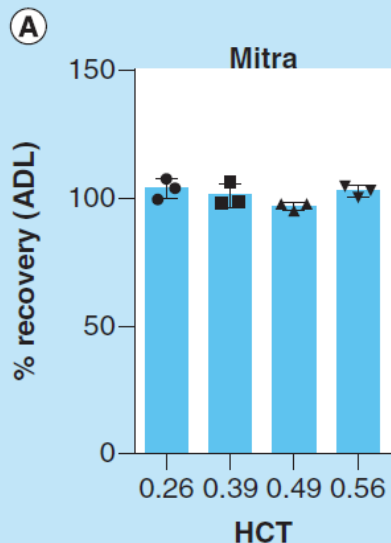
Mitra®microsampler

Naam: _____
 Gebodertum: _____
 Algemeen: _____
 Voet: _____
 Clen: ☐ Dvewer: ☐

Ervare de chent met geproven
 indien bescreid met geproven

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 2016-12



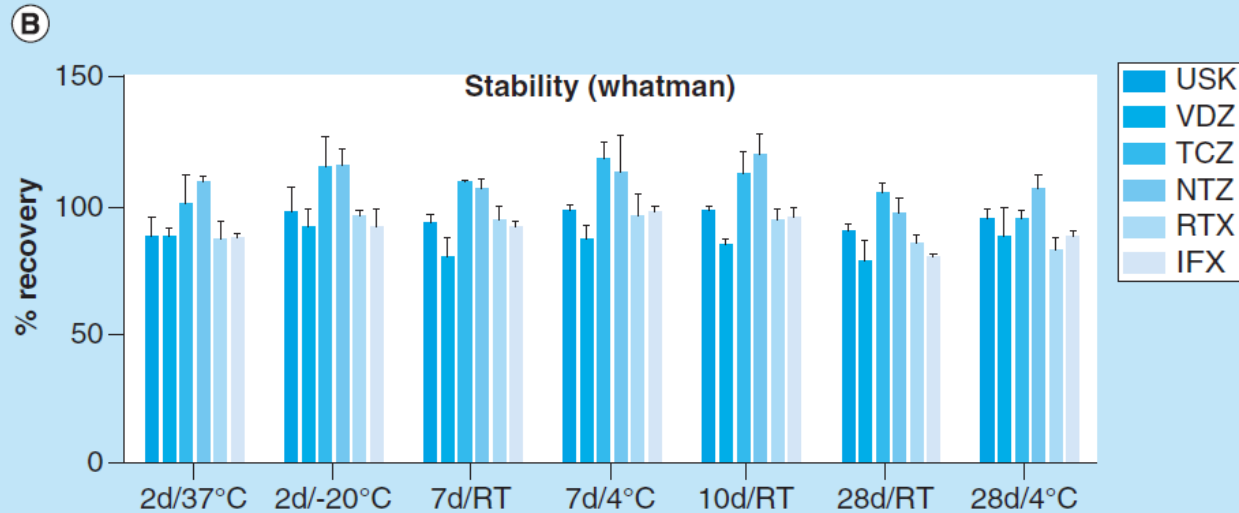
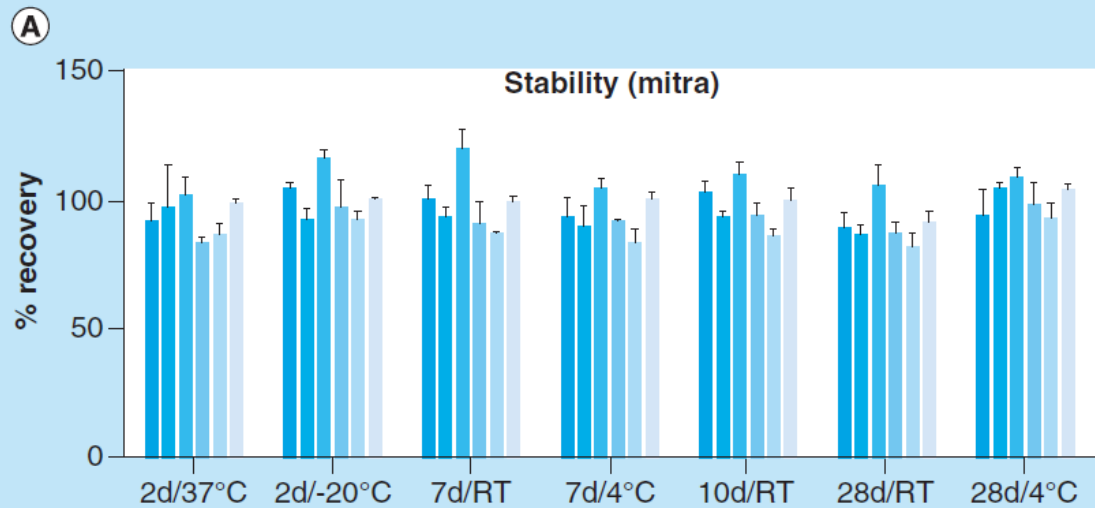


Recovery of several biologics

Shown 5 μ g/mL adalimumab
Similar 0.5—30 μ g/mL

Similar results for
Hct 0.26 and 0.56 l/l

2 μ g/ml ustekinumab
10 μ g/ml vedolizumab
5 μ g/ml tocilizumab
25 μ g/ml natalizumab
5 μ g/ml rituximab
7 μ g/ml infliximab



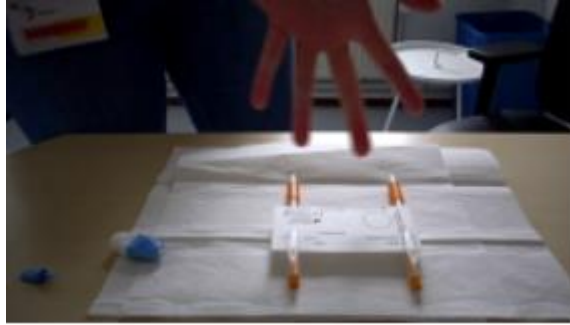
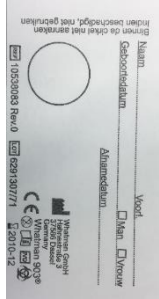
Recovery of several biologics

No effect of

- storage up to 28 days
- temperature differences -20°C-37°C

Whatman® 903

Mitra®microsampler



| | Whatman® 903 |
|-----------------|---|
| Blood retrieval | <ul style="list-style-type: none"> Drop two drops of blood on the paper |
| + | <ul style="list-style-type: none"> [biologics] recovery > 80% Two drops of blood Very cheap |
| ■ | <ul style="list-style-type: none"> Whole blood → Hct needed for serum concentration Variable volume of blood Cumbersome to handle → manually punch out/ cut the spot |

| | Mitra®microsampler |
|-----------------|---|
| Blood retrieval | <ul style="list-style-type: none"> Contact blood drop with the tips Three volumes : 10, 20 or 30µ |
| + | <ul style="list-style-type: none"> [biologics] recovery > 80% Filled in one go/ tip Fixed volume of blood Easy to analyse in the lab |
| ■ | <ul style="list-style-type: none"> Whole blood → Hct needed for serum concentration Expensive |

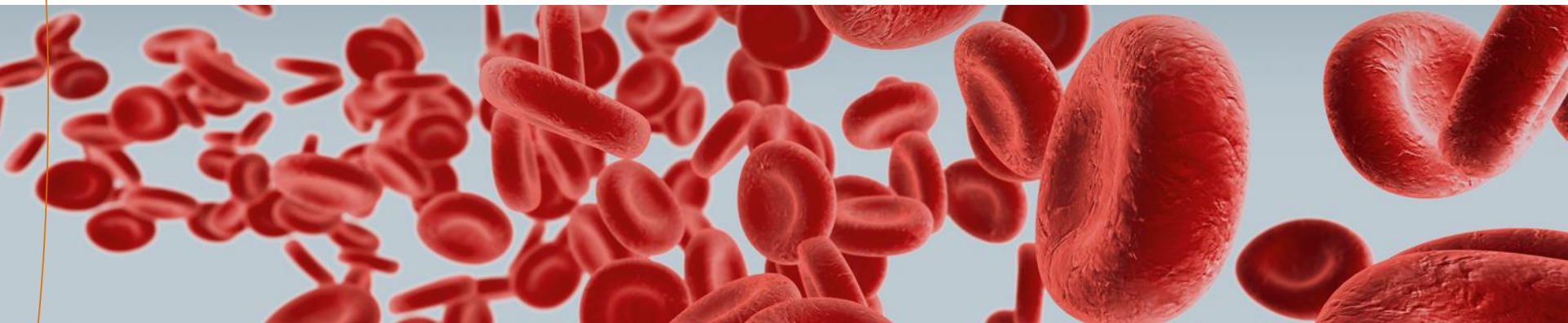
Hemaspot™-HF



Recovery of adalimumab 5 μ g/mL

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Serum devices





MiniCollect® Z
Serum Separator
Tubes



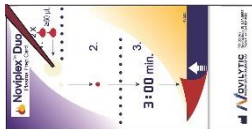
Ser-Col®



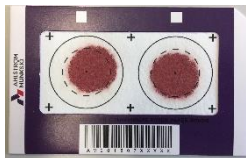
HemaSpot™-SE



PostYourLab®



Noviplex™
Plasma Prep card



HemaSep card

Ser-Col®

Removed as not published

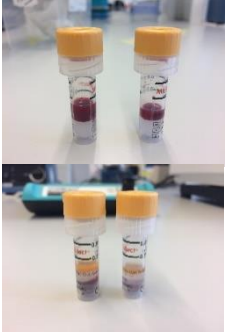
HemaSpot™-SE

Removed as not published

Noviplex™

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MiniCollect® Z Serum Separator Tubes



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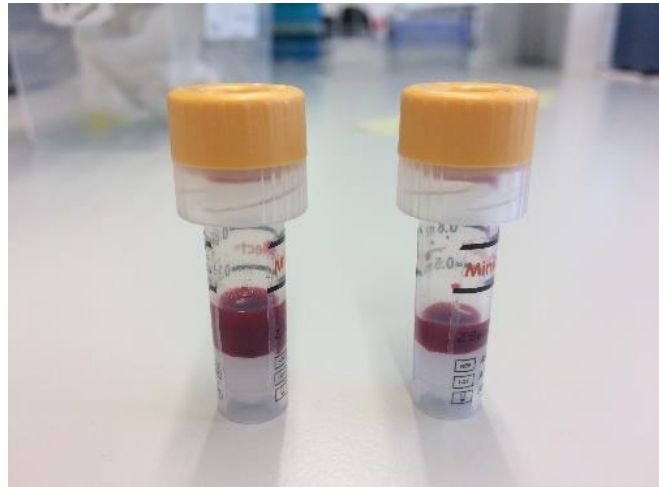


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Recovery of adalimumab

Unpublished data

Best alternative to Vp for biologics TDM to Whatmann and Mitra: MiniCollect® Z Serum Separator Tubes



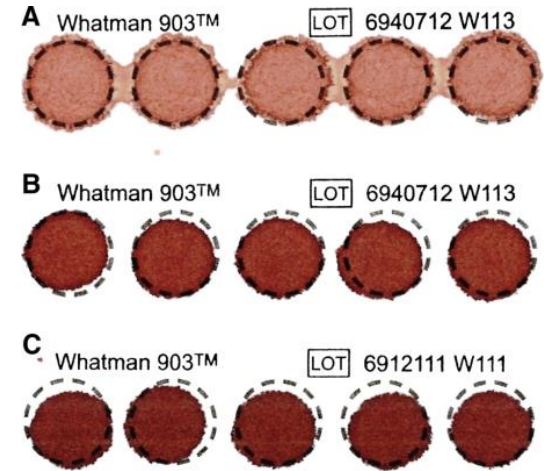
We tested a range of biologics – all work for capillary blood

| Assays | Inhibitor PK/ADA tests |
|---|--|
| TNF inhibitors | adalimumab, infliximab, <i>etanercept</i> , certolizumab, golimumab |
| B-cell and T-cell inhibitors | vedolizumab, rituximab, natalizumab, abatacept |
| Other cytokine inhibitors | ustekinumab, tocilizumab, mepolizumab, reslizumab, guselkumab, dupilumab |
| Glycoprotein Iib/IIIa receptor antagonist | abciximab |
| HER2 inhibitor | trastuzumab |
| IgE inhibitor | omalizumab |
| PD1 inhibitor | nivolumab/pembrolizumab |



Finger prick sampling paper or fixed volume sampling

- Stability:
 - Good stability
 - At room temperature
 - both eluate and filter paper
- Easy to use
 - For patient
 - For lab
- Easy to implement GxP
- Tips with fixed volume
 - Facilitates quantitative serum measurement



Questions?

Annick.deVries@sanquin.nl

www.sanquin.org



