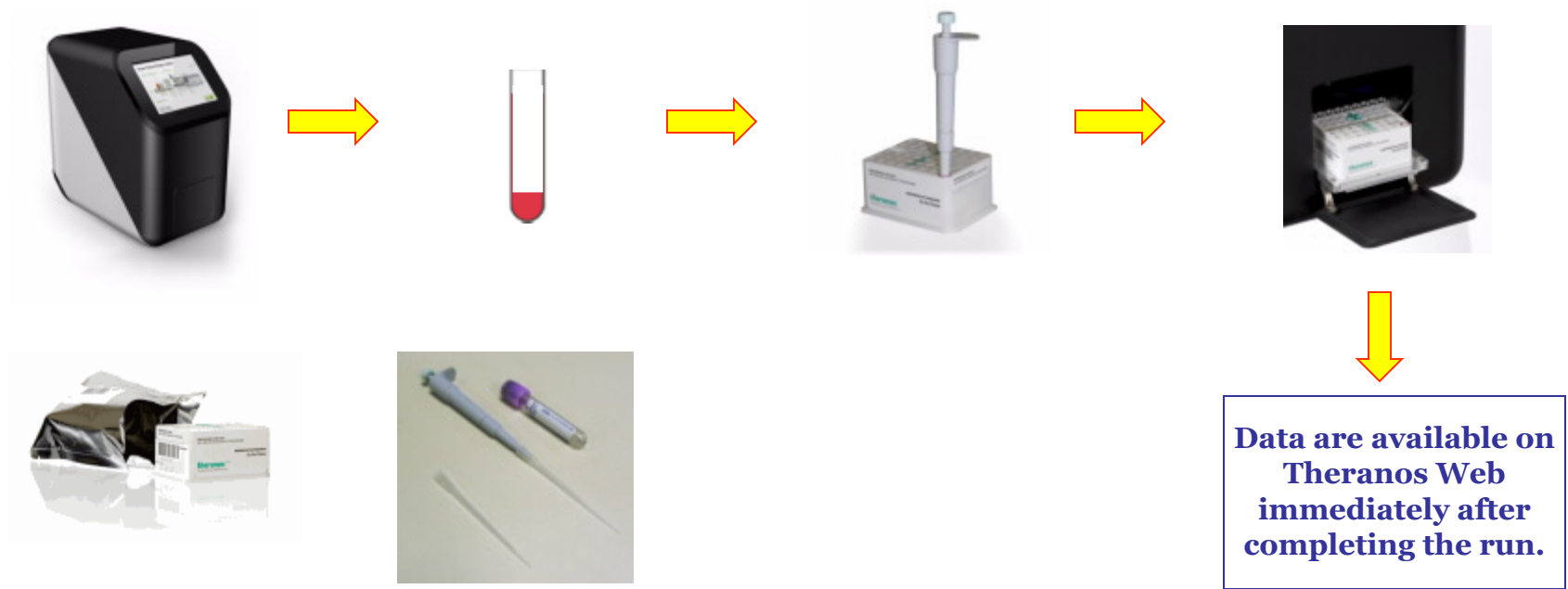
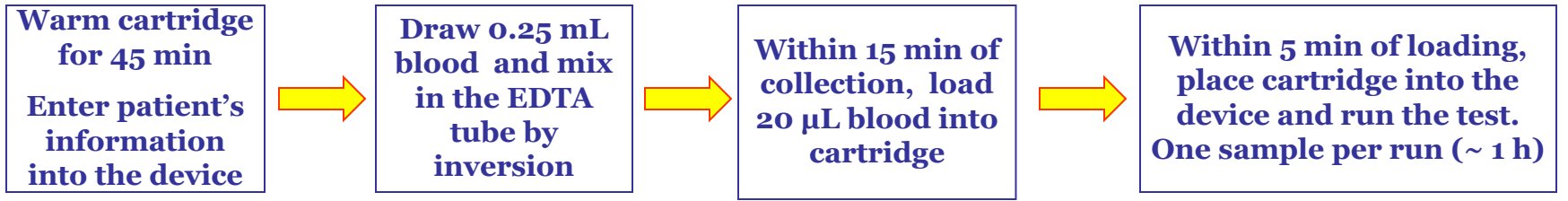




**Evaluation of Thernaos PK Assay Method
from the Clinical PK Perspective
Nianhang Chen**

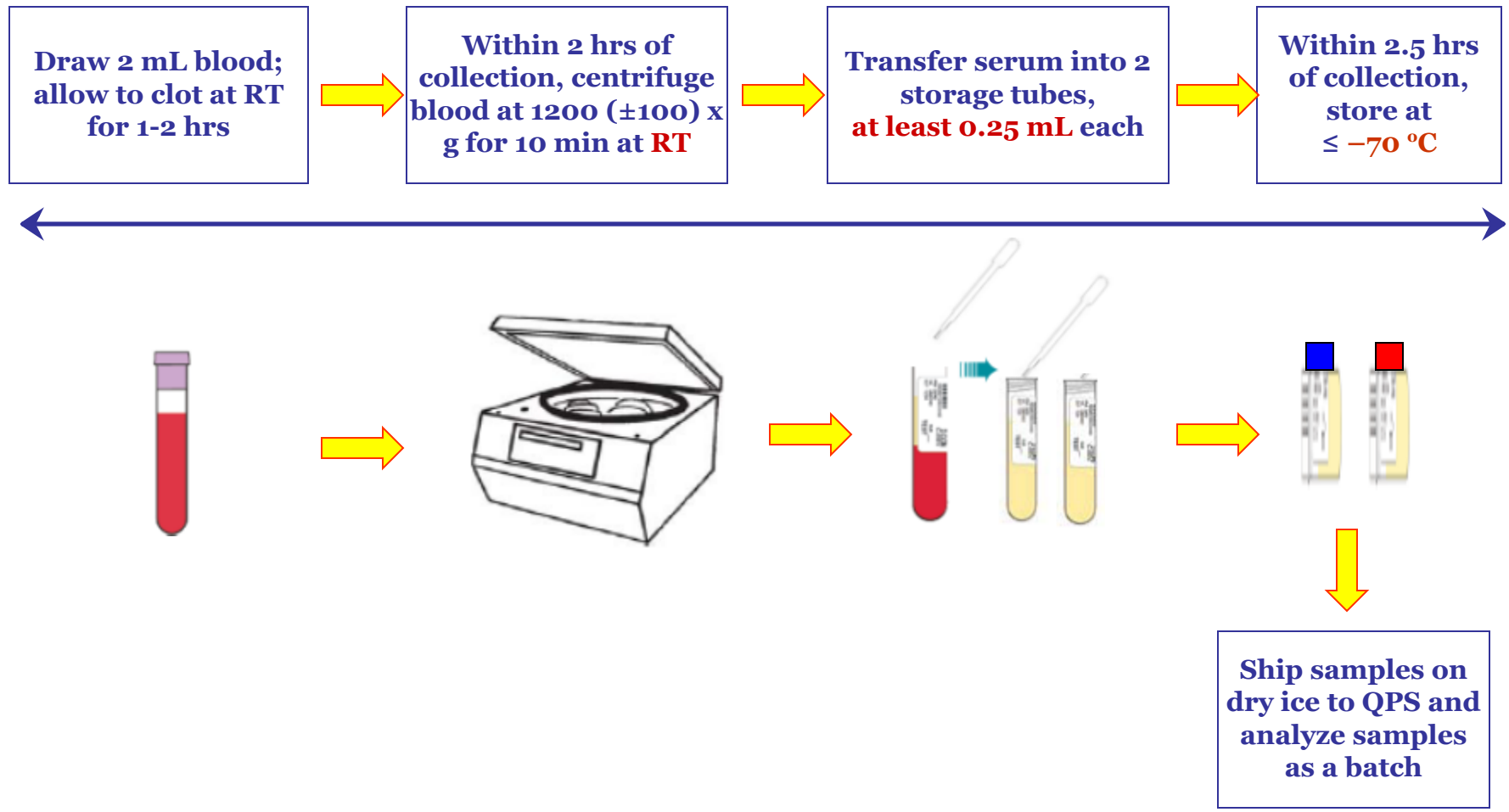


Run A PK Sample with Theranos System





Run a PK Sample with QPS System





Comparison of PK Assays: Theranos vs QPS

	Theranos	QPS
Matrix	Whole blood	Serum
Collected blood volume	0.25 mL	2 mL
Calibrations range	40 – 4000 ng/mL (insufficient!)	40-2000 ng/mL
Dilution of samples	Cannot dilute samples	10X & 20X
Ability to re-assay	No (4% NR in validation)	Yes
Incurred sample reanalysis (ISR)	Not feasible	Yes, to demonstrate data reliability and reproducibility
Sample handling	Do not need centrifuge, freezer or dry ice. Need a large space in refrigerator for cartridge storage.	Need a centrifuge, a freezer, and dry ice; errors may occur during sample handling.
Sample analysis	Assayed on-site. Multiple devices are needed for dense PK sampling. Operated by staff with limited training.	Assayed as a batch on the same device at QPS. Operated by well trained scientist.
Cartridge/PK Kits	Cartridge stability =12 weeks at 4°C	Commercial tubes (stable)
Blinded studies	Must assay both active and control samples to maintain blinding	Can analyze active samples only, without breaking blinding

Trial Exh. 0541 Page 0007

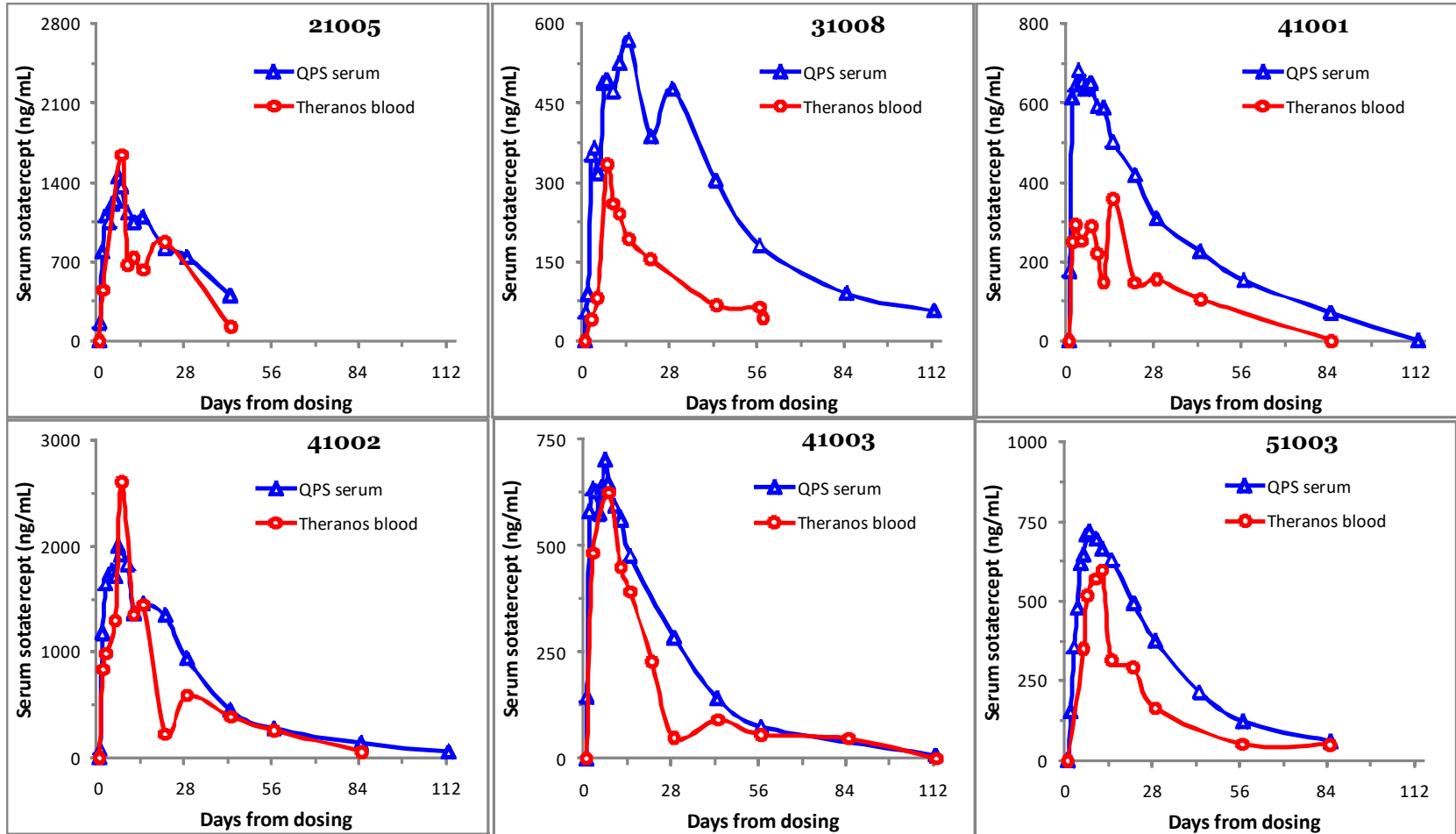


Comparison of PK Data: Theranos vs QPS (REN-001 Part 1)

	Theranos	QPS
Samples without results	14.1 %	<2%
Serum concentration	Converted from blood data with Hct. 67% data with > 25% diff. from QPS data % diff. range: -78% to +92%	Direct measurement no data manipulation
Concentration variability	Blood data: CV % = 74-100% Derived serum data: CV% = 75-100%	Serum data: CV% = 41-69%
C _{max} & AUC variability	79-90%	51-56%
Mean value of serum PK parameters	C _{max} = 1.44 µg/mL AUC _{28d} = 19.1 d*µg/mL t _{1/2} = 28 d CL/F = 4.39 mL/d/kg V _Z /F = 189 mL/kg	C _{max} = 1.02 µg/mL AUC _{28d} = 20.4 d*µg/mL t _{1/2} = 22 d CL/F = 3.29 mL/d/kg V _Z /F = 102 mL/kg



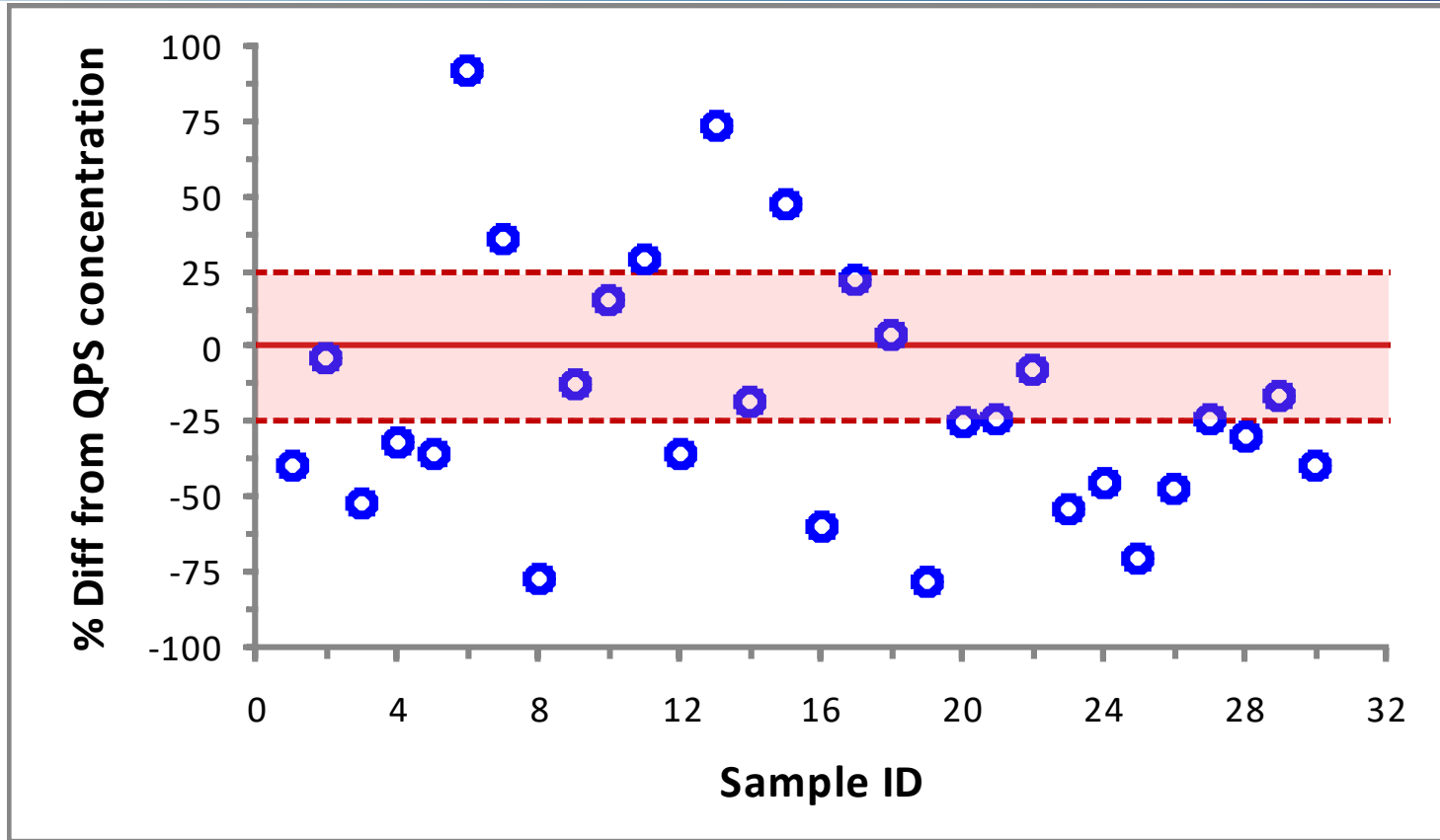
Individual Concentration Profiles Theranos Whole Blood vs QPS Serum



- There was no consistent pattern for matrix effect.
- Theranos whole blood data showed more fluctuations.



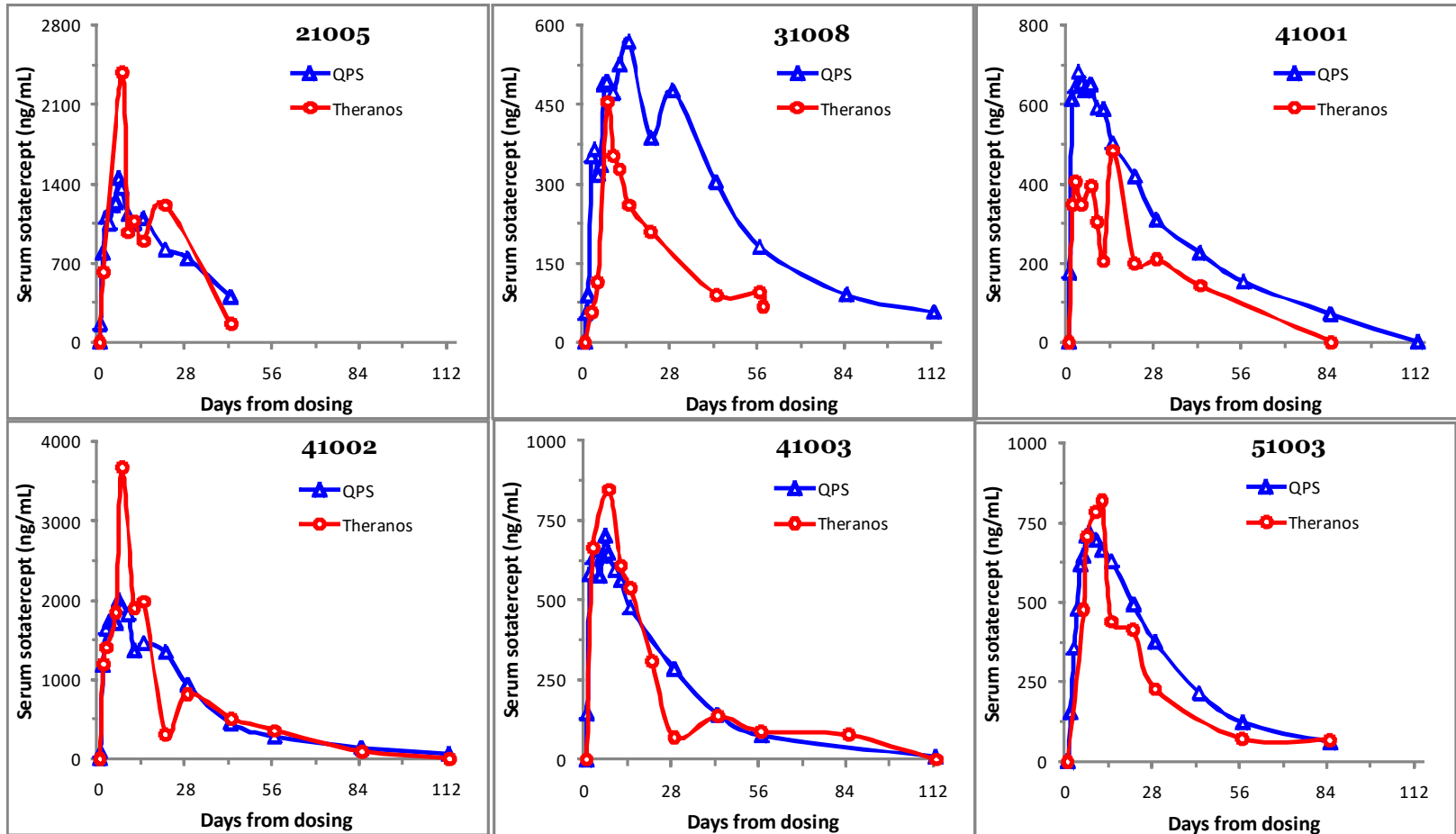
Conversion of Theranos Whole Blood Concentrations to Serum Concentrations



- **67% samples had > 25% difference in serum concentration between Theranos and QPS method**



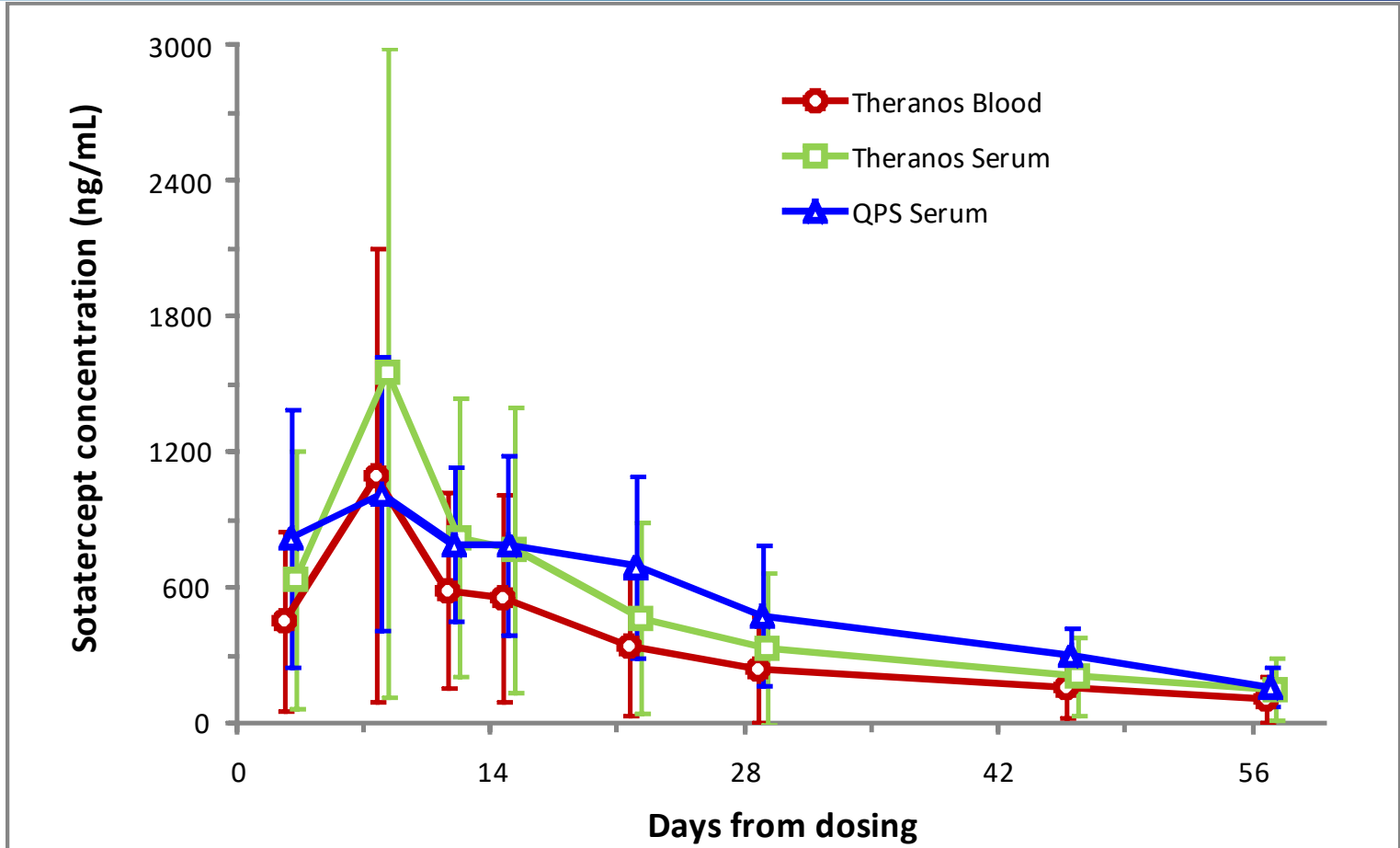
Individual Serum Concentration Profiles Theranos vs QPS



- Conversion of Theranos whole blood concentrations to serum concentrations based on Hct did not diminish the discrepancy between the two methods.
- The conversion led to unusually high level of C_{max} in 2 subjects.



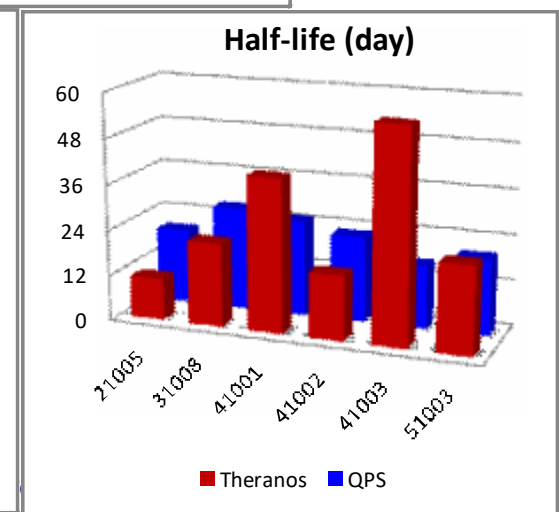
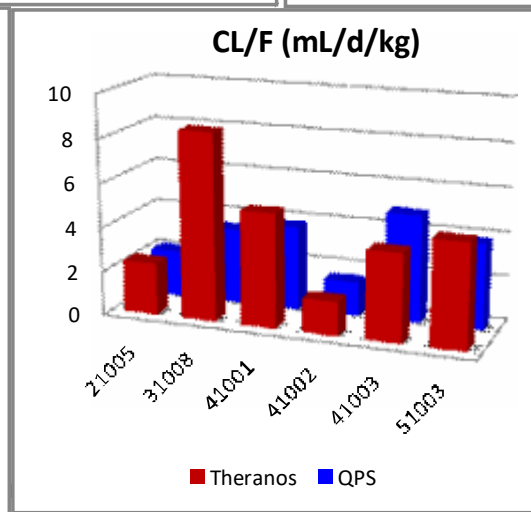
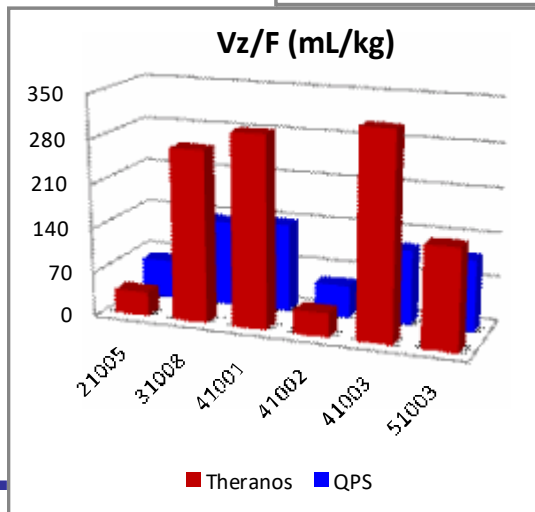
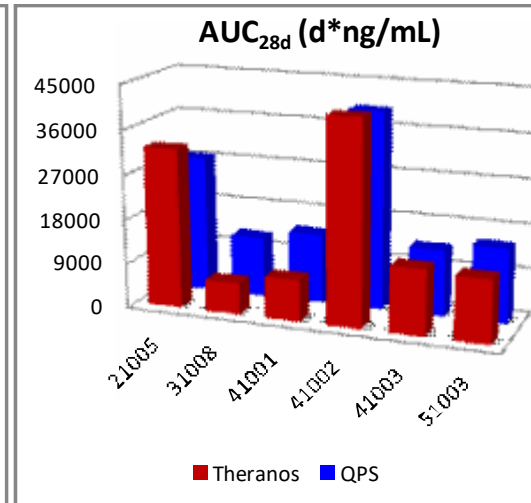
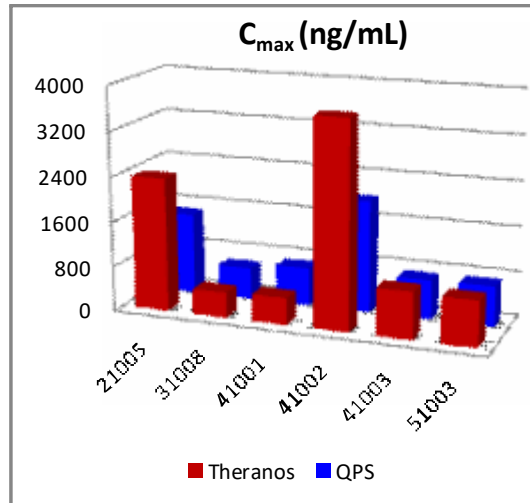
Mean (\pm SD) Concentration Profiles Theranos vs QPS



- Mean concentration profiles were not consistent between Theranos and QPS.
- Concentration variability was higher with Theranos than with QPS method.



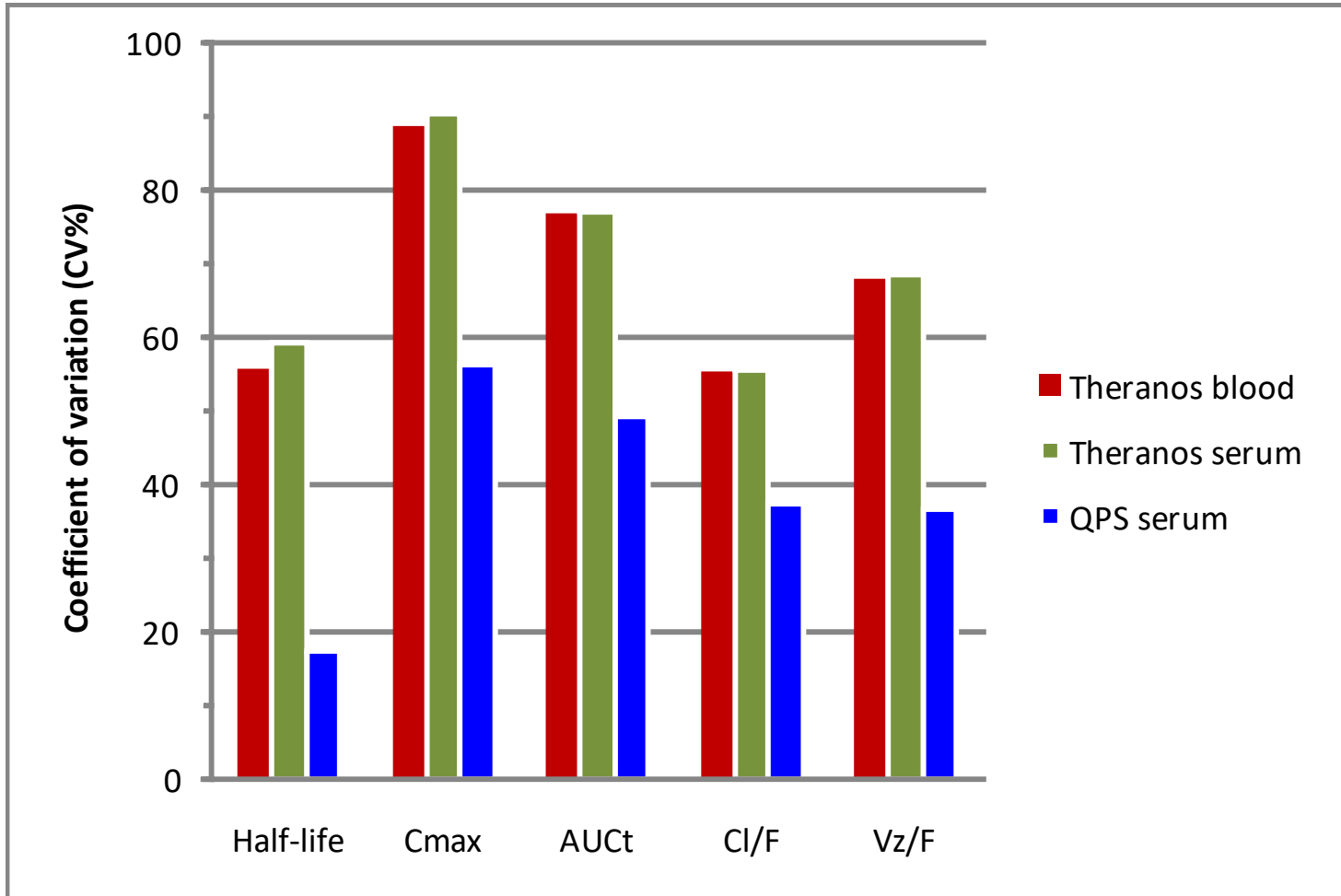
Individual Serum PK Parameters Theranos vs QPS



- >40% difference in the value between two methods occurred in at least 2 subjects (33% of subjects or higher) for each parameter.



Variability in Serum PK Parameters Theranos vs QPS



- Higher PK parameter variability with Theranos than with QPS method.

ACE-011 REN-001, Part 1

PD Endpoints: FSH, LH and estradiol

Aug. 29, 2011

Reference Values

"Normal" Range	Female	Female (PM)	Male
Estradiol (pg/ml)	20-400	<50	10.0-50.0
FSH (IU/L)	1.7-21.5	25.8-134.8	1.5-12.4
LH (IU/L)	3.0-90.0	40-104	2.0-20.0

ACM Assay Range

Estradiol	10-1000 pg/ml
FSH	0.3-200 IU/L
LH	0.07-200 IU/L

Theranos Assay Range

Estradiol	35-500 pg/ml
FSH	3-200 IU/L
LH	1-750 IU/L

Patient 21003

Female (60 yr)

Estradiol (pg/ml)	ACM	Theranos
D 1	10	Out of Range
D 15	10	Out of Range
D 29		36.4
D 113	10	46.7

FSH (IU/L)		
D 1	23.5	15.5
D 15	17.1	5
D 29	17.5	NA
D 113	11.8	NA

LH (IU/L)		
D 1	4.2	Out of Range
D 15	2.3	Out of Range
D 29	1.5	NA
D 113	0.5	NA

Patient 21005

Male (53 yr)

Estradiol (pg/ml)	ACM	Theranos
D 1	13	36.4
D 15	10.8	59.8
D 29		Out of Range
D 113		
FSH (IU/L)		
D 1	3.3	7.7
D 15	3.5	4.9
D 29	4.9	3.7
D 113		
LH (IU/L)		
D 1	2.9	Out of Range
D 15	2.8	Out of Range
D 29	5.3	Out of Range
D 113		

Patient 31008

Female (56 yr)

Estradiol (pg/ml)	ACM	Theranos
D 1	10	Out of Range
D 15	10	Out of Range
D 29	10	Out of Range
D 113	10	NA

FSH (IU/L)		
D 1	174.2	NA
D 15	172.2	129.4
D 29	175	136.5
D 113	188.3	85.6

LH (IU/L)		
D 1	112.2	NA
D 15	92.6	3
D 29	108.2	3.7
D 113	94.4	2.1

Patient 41001

Male (60 yr)

Estradiol (pg/ml)	ACM	Theranos
D 1	10	37.1
D 15	10	Out of Range
D 29	55.6	Out of Range
D 113	10	45

FSH (IU/L)		
D 1	5.7	14.5
D 15	23.5	15.5
D 29	21	14.9
D 113	27.9	8.2

LH (IU/L)		
D 1	129.4	Out of Range
D 15	117.5	2.8
D 29	125.4	3.3
D 113	105	1.8

Patient 41002

Male (49 yr)

Estradiol (pg/ml)	ACM	Theranos
D 1	10	52
D 15	10	
D 29	10	47.3
D 113	15.9	42.2

FSH (IU/L)		
D 1	8.7	4.9
D 15	7.8	
D 29	11	8.9
D 113	11	4.4

LH (IU/L)		
D 1	11.7	Out of Range
D 15	9.6	
D 29	15.6	0.7
D 113	15.9	Out of Range

Patient 41003

Male (37 yr)

Estradiol (pg/ml)	ACM	Theranos
D 1	22.7	Out of Range
D 15		67.3
D 29	32.7	47.1
D 113		50.3
FSH (IU/L)		
D 1	5.7	NA
D 15		4.4
D 29	5.2	10.8
D 113	7.1	6.3
LH (IU/L)		
D 1	13	NA
D 15		Out of Range
D 29	9.8	0.6
D 113	10.8	Out of Range

Patient 51003

Male (72 yr)

Estradiol (pg/ml)	ACM	Theranos
D 1		38.9
D 4		54.5
D 15		Out of Range
D 29		
FSH (IU/L)		
D 1	5.9	Out of Range
D 4		Out of Range
D 15		5
D 29	7.1	
LH (IU/L)		
D 1	5.3	Out of Range
D 4		Out of Range
D 15	4.5	Out of Range
D 29	4.9	