Application of GC-C-IRMS in the ABP

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Outline

- What we know so far
- Previous steps on IRMS application in doping analysis
- Longitudinal application
- Application to real passports
- Conclusions

What we know…..

- ABP needs to accumulate data before being effective
  - Difficulties on the Results Management – Interaction with APMUs
  - Delay on the final decision
  - Not fully understood by Athletes and Media

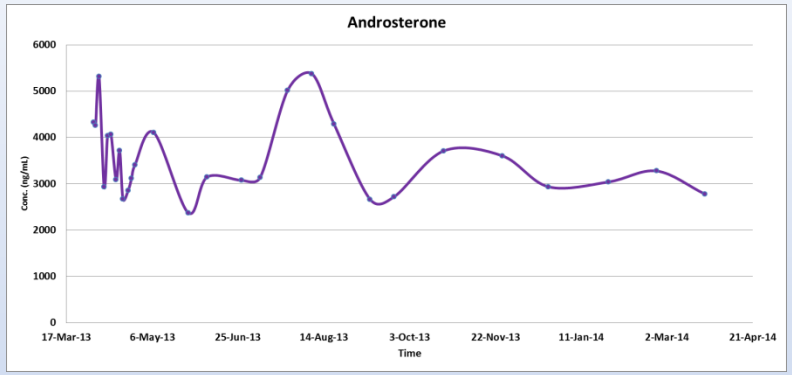
- ABP evaluation is not always effective
  - DHEA
  - T transdermal
  - Female athletes
  - Micro dosing

- The inclusion of additional parameters is not easy
  - Harmonization of new markers detection
    - ✓ Hydroxylated steroids
    - ✓ Sulphated steroids

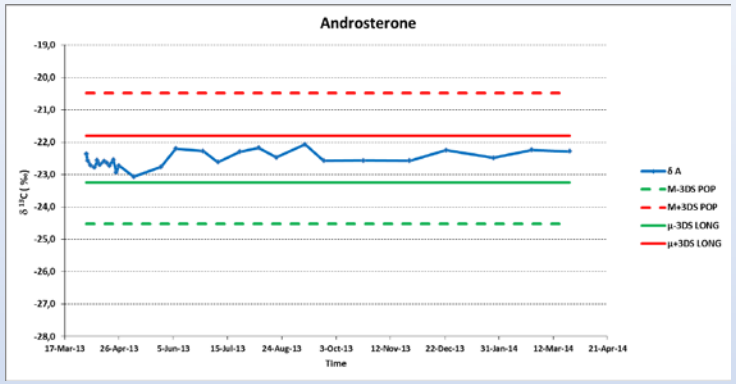
Previous steps on IRMS application in doping analysis

- IRMS Steroids data are more stable than the corresponding concentrations
- Delta values are stable in a short, mid and long term period for a given individual
- Delta and delta-delta values are normally distributed in the population and individuals
- The individual variability is much lower than the population one
- Longitudinal evaluation of the delta values extends the detection window and an equivalent approach to steroid module of the ABP is possible

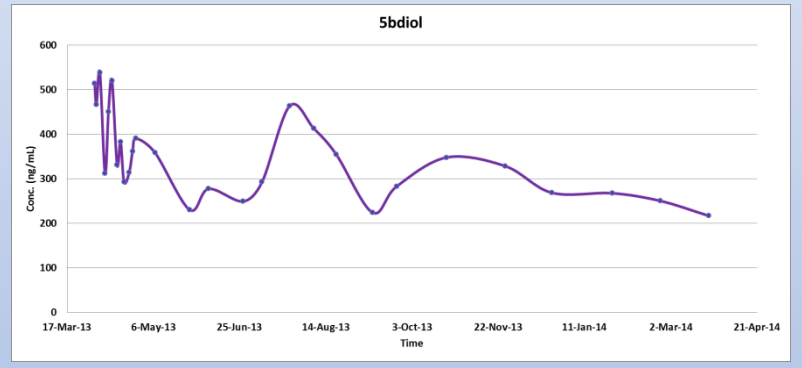
Variability Concentrations vs Delta values (Male-M1)



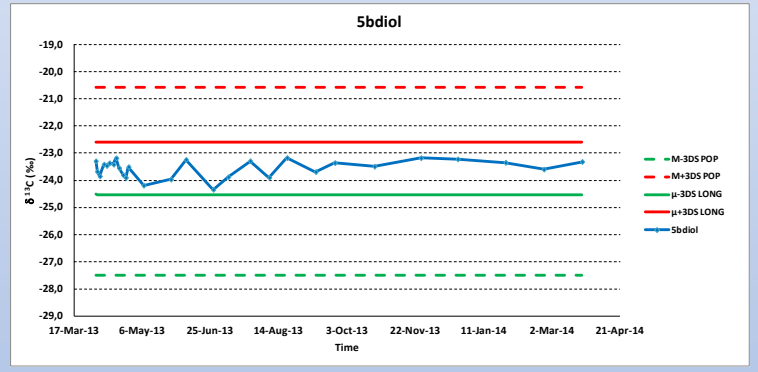
CV%=23



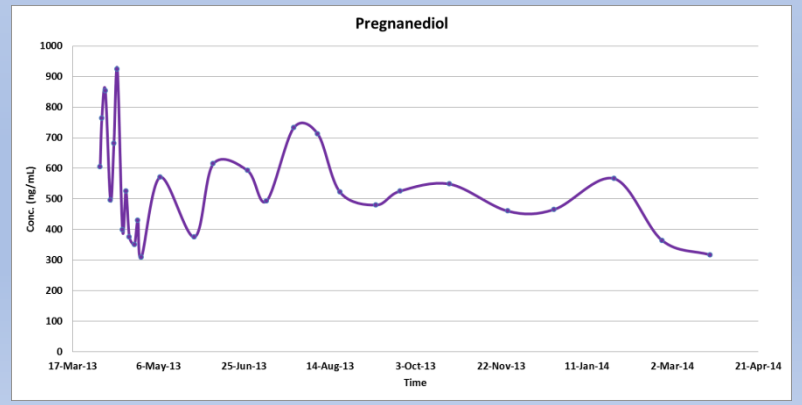
SD=0,2



CV%=27



SD=0,3



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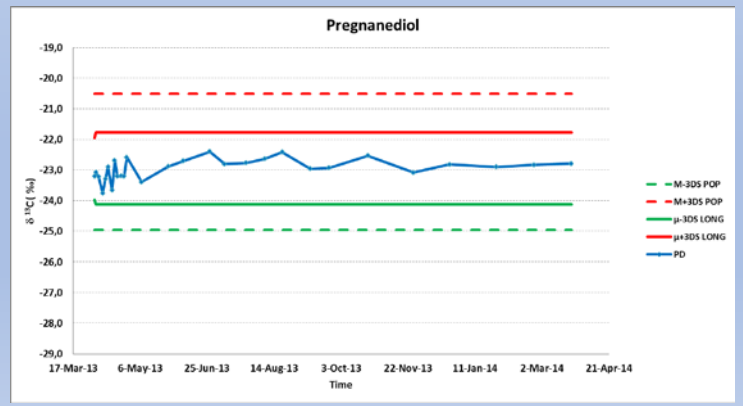
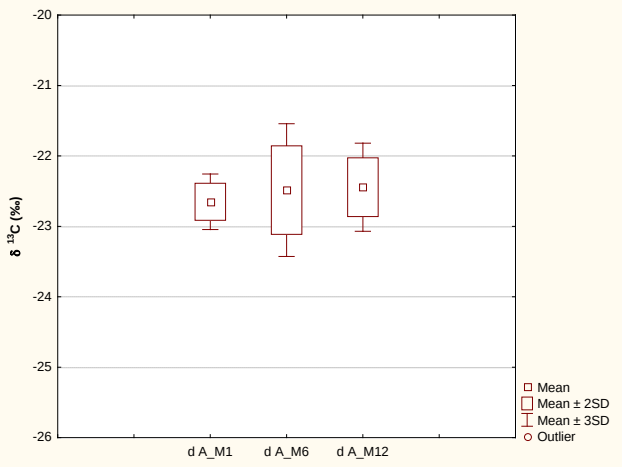


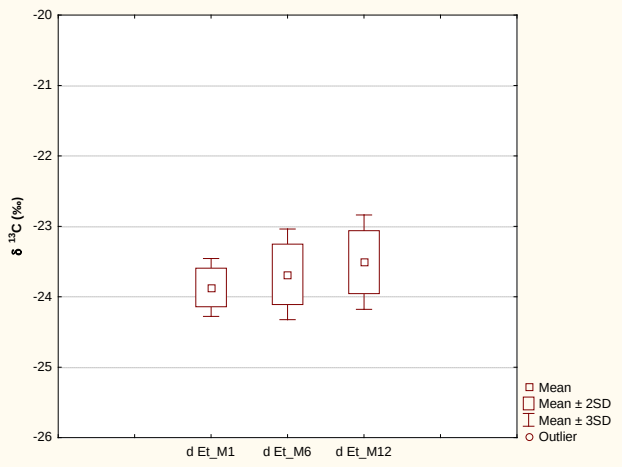
SD=0,4

Variability of $\delta^{13}C$ (‰) values (TCs)
Short, mid an long term period

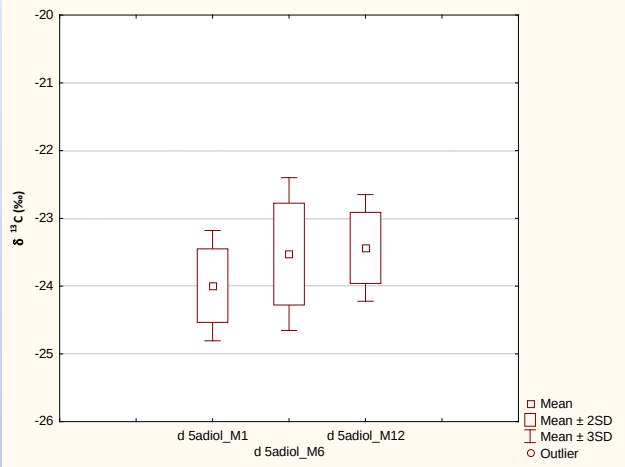
$\delta^{13}C$ (‰) A



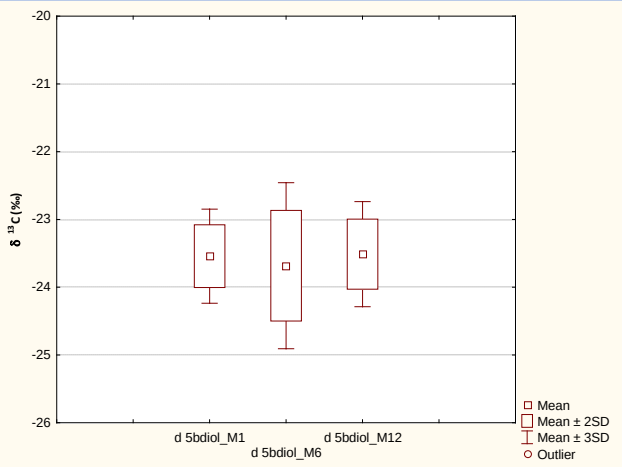
$\delta^{13}C$ (‰) Et



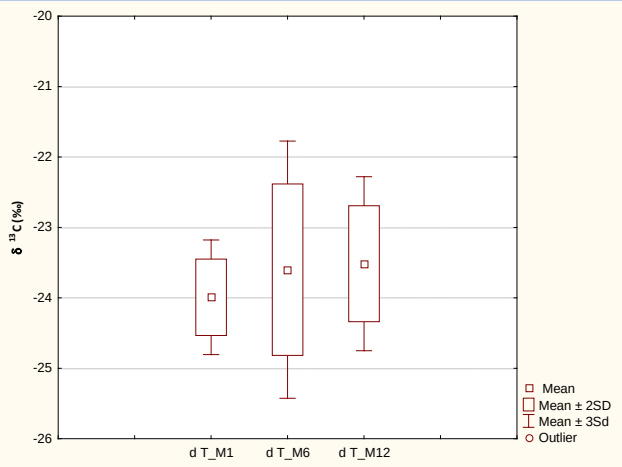
$\delta^{13}C$ (‰) 5adiol



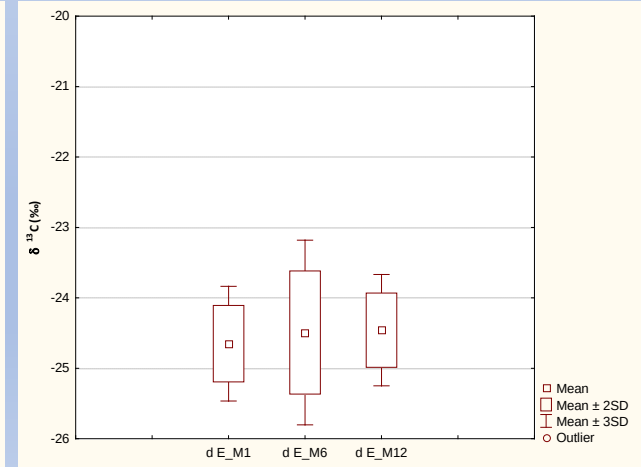
$\delta^{13}C$ (‰) 5bdiol



$\delta^{13}C$ (‰) T



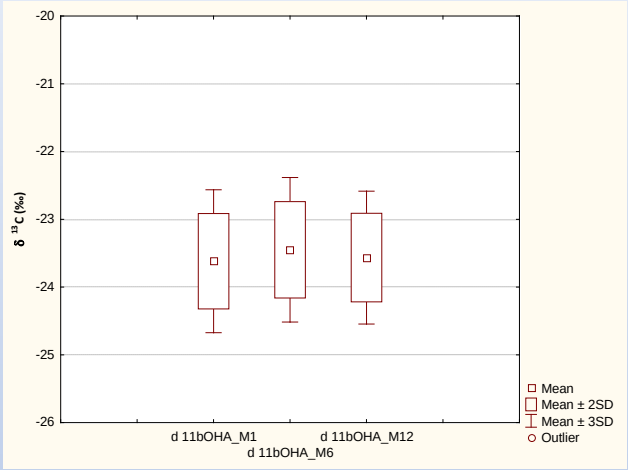
$\delta^{13}C$ (‰) E



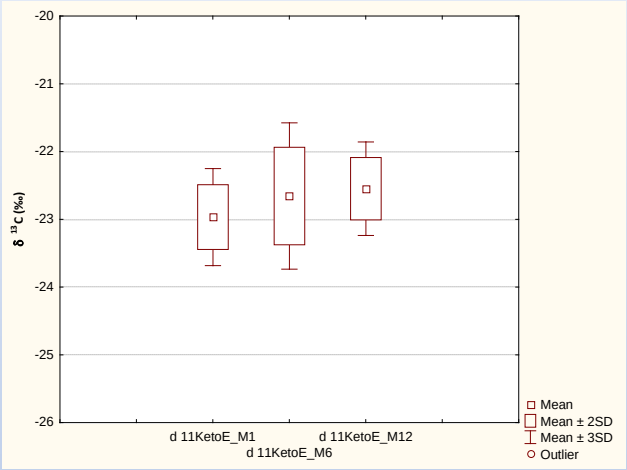
Variability of $\delta^{13}C$ (‰) values (ERCs)
Short, mid an long term period

Vol #1

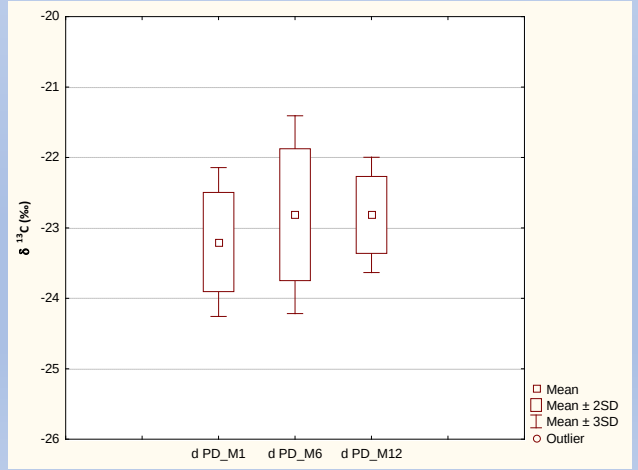
δ 13C (‰) 11OHA



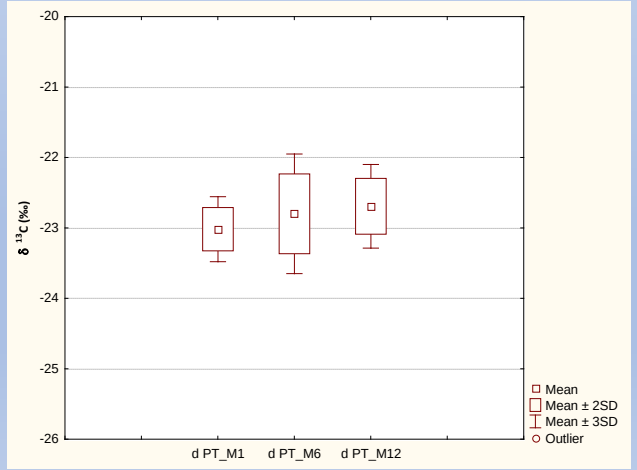
δ 13C (‰) 11KetoE



δ 13C (‰) PD



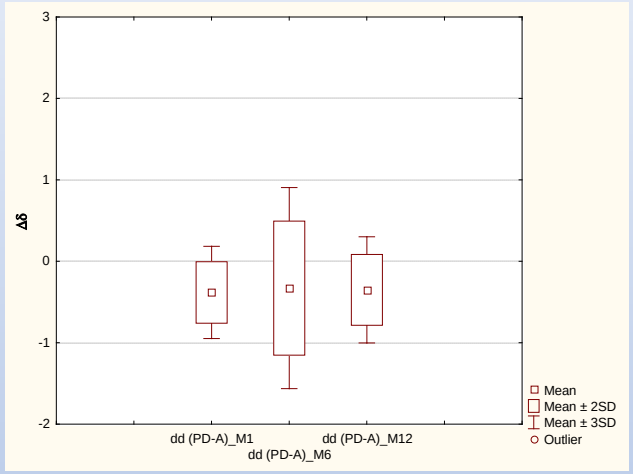
δ 13C (‰) PT



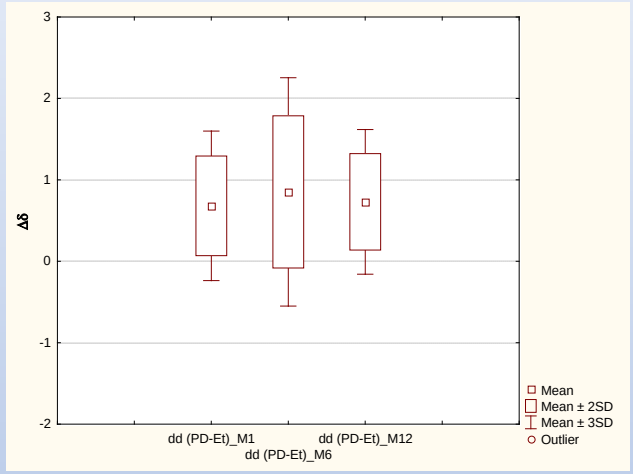
Variability of Δδ values
Short, mid an long term period

Vol #1

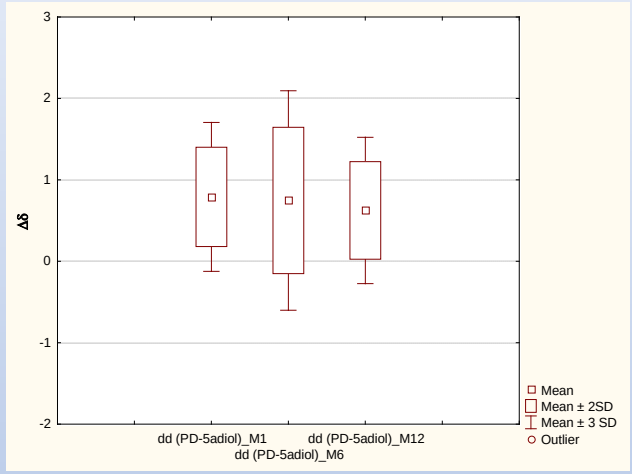
Δδ (PD-A)



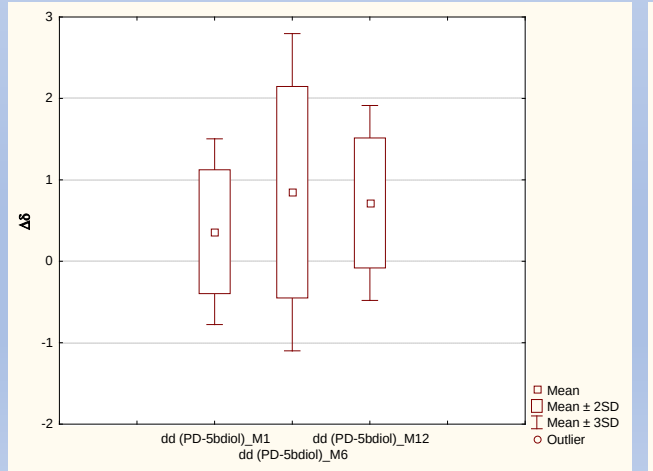
Δδ (PD-Et)



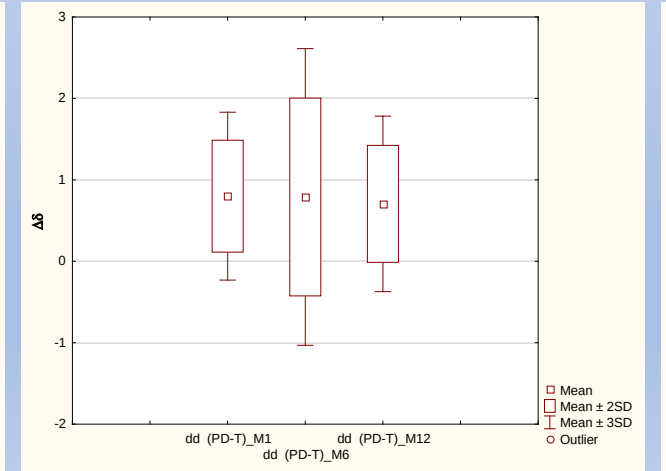
Δδ (PD-5adiol)



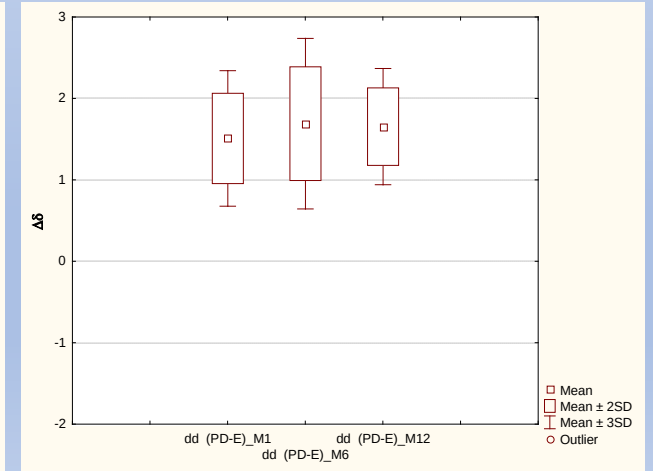
Δδ (PD-5bdiol)



Δδ (PD-T)

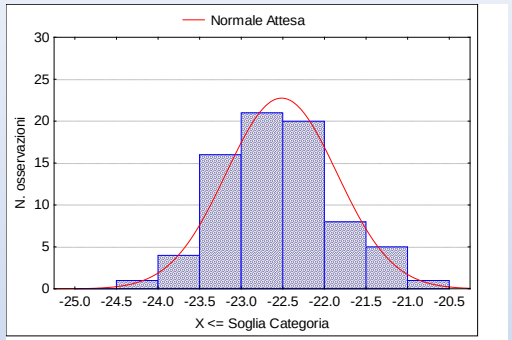


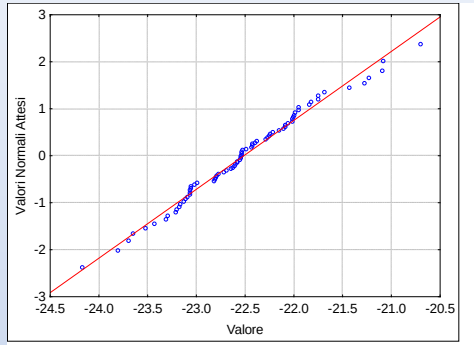
Δδ (PD-E)



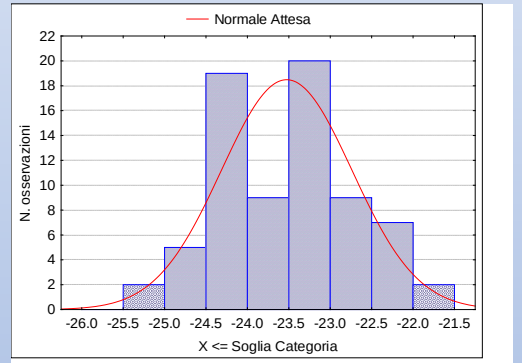
Distribution of $\delta^{13}C$ (‰) in the Population
Normal distribution and P-P plots

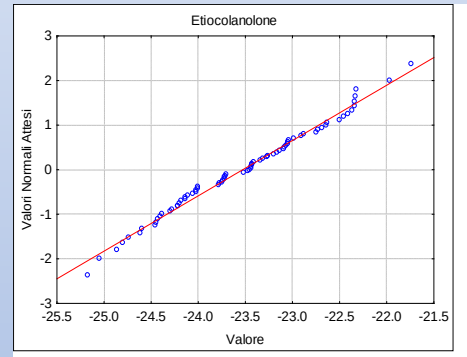
A (n=76)



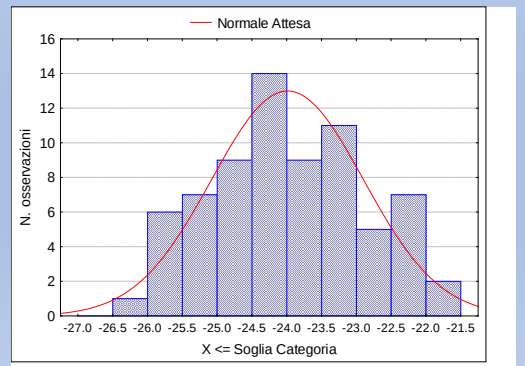


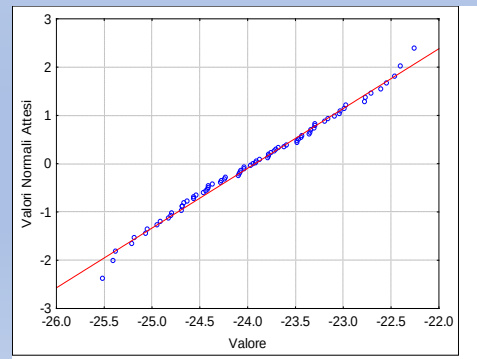
Et (n=73)





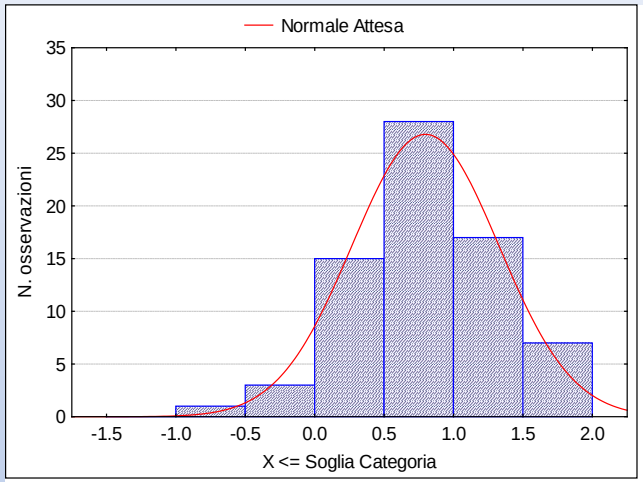
5bdiol (n=71)

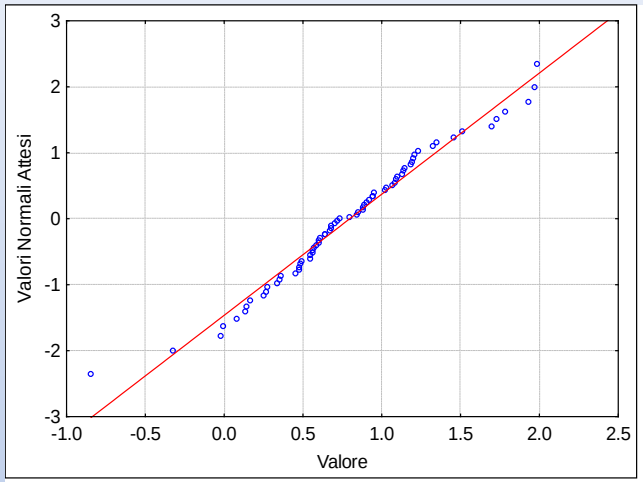




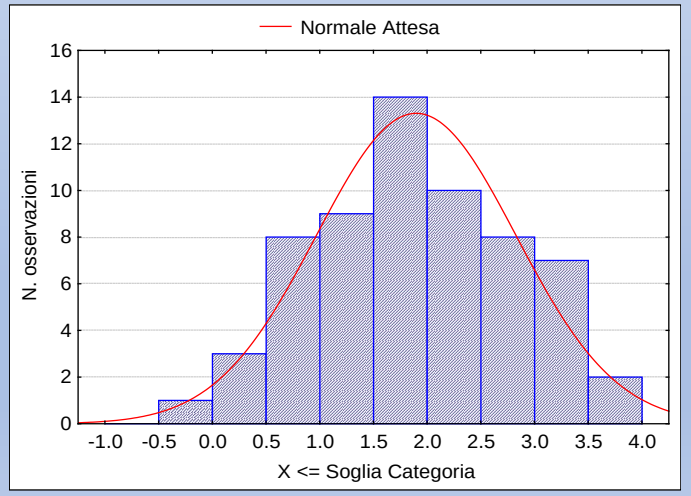
Distribution of $\Delta\delta$ in the Population
Normal distribution and P-P plots

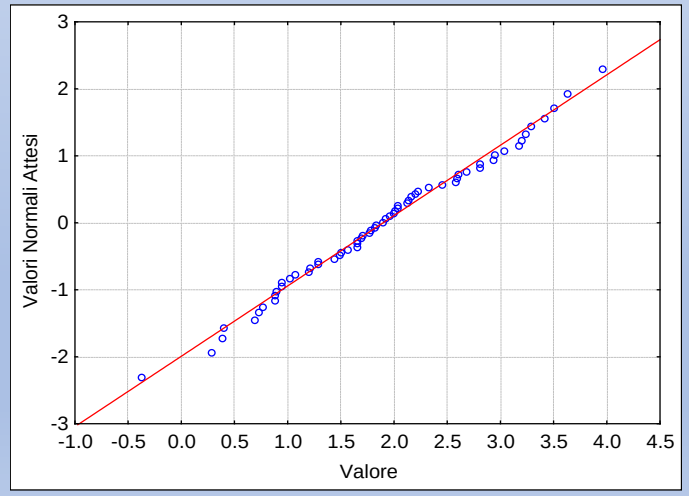
PD-Et (n=71)



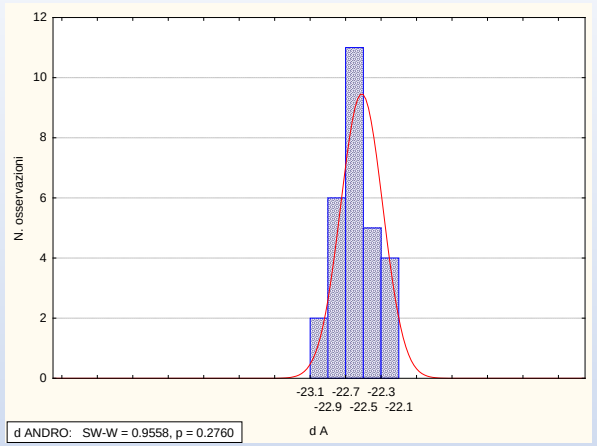


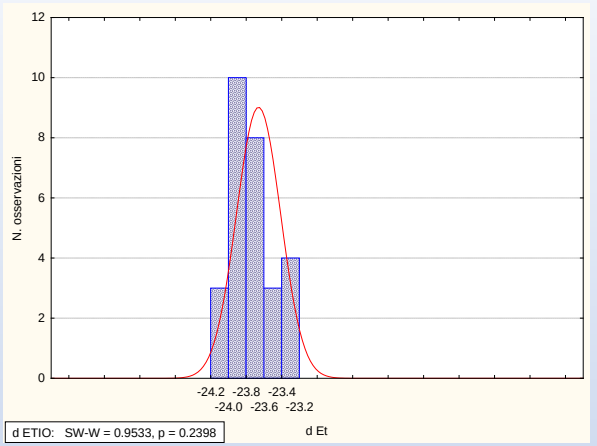
PD-E (n=62)

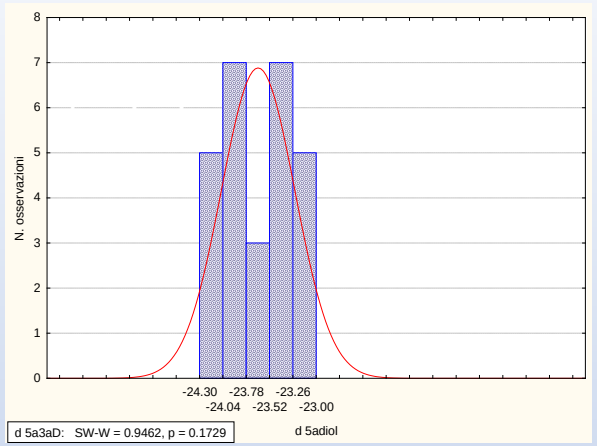


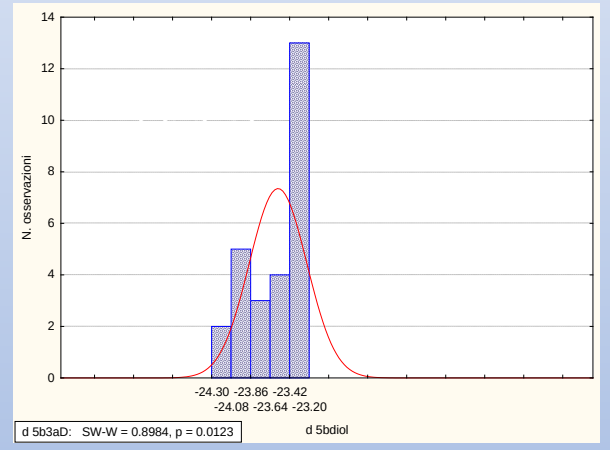


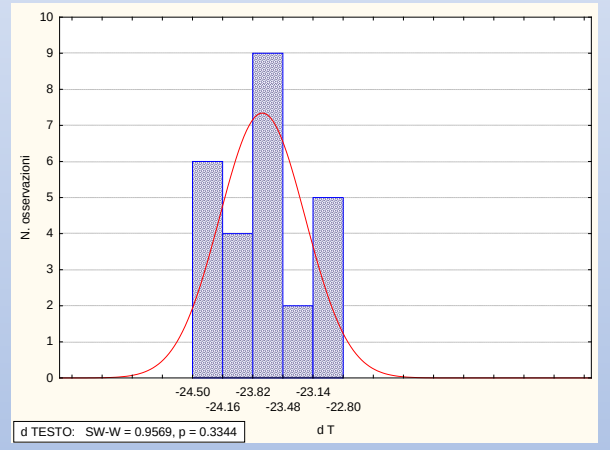
Distribution of δ ^{13}C (‰) in Vol #1 (n=28) (Shapiro Wilk Normality test; P>0,05)

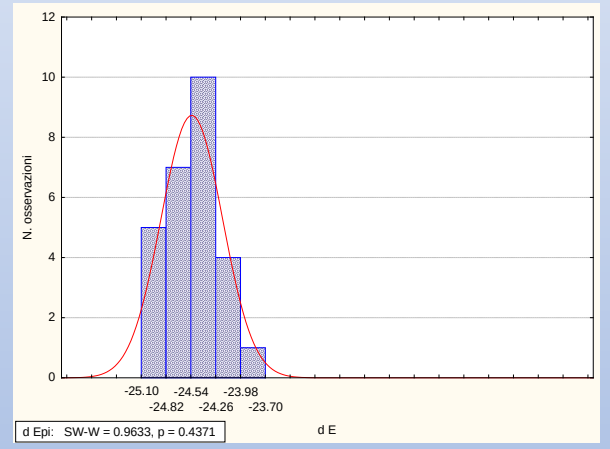


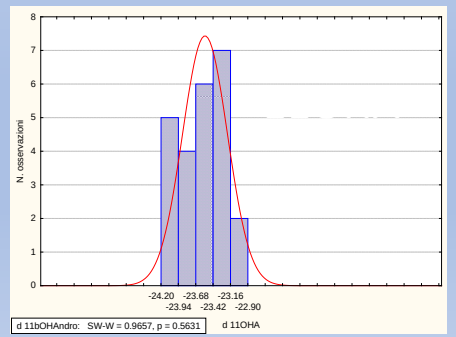


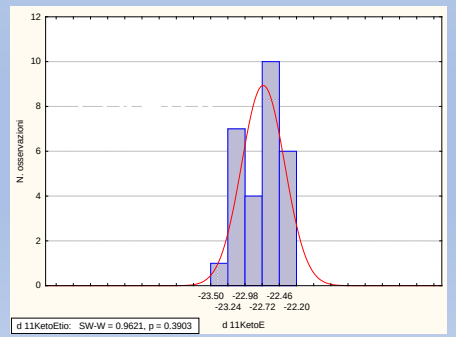


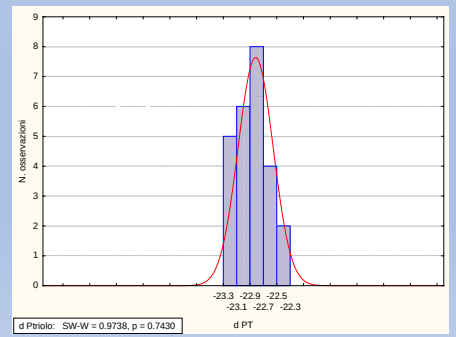


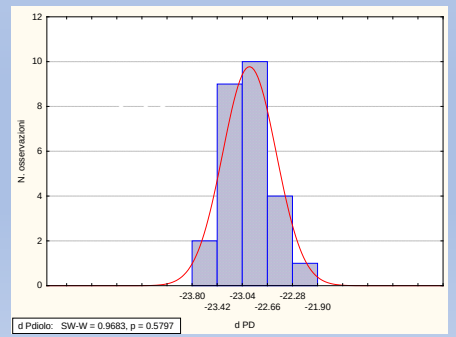






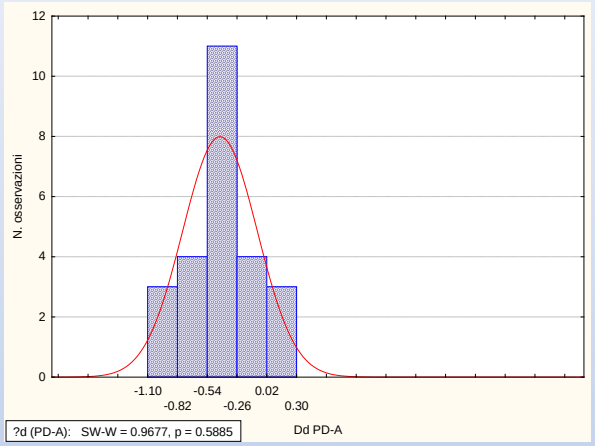




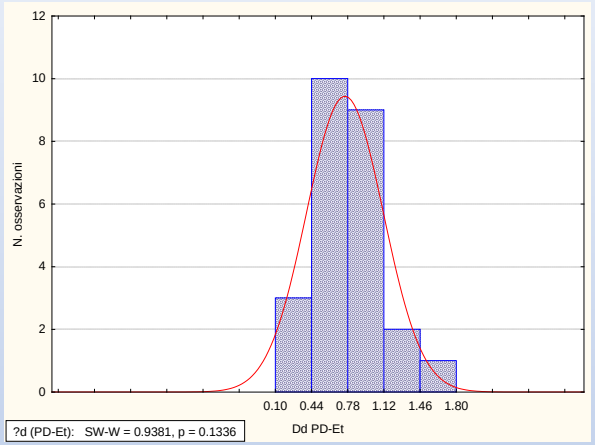


Distribution of $\Delta\delta$ (PD-TC) Vol #1 (n=28)

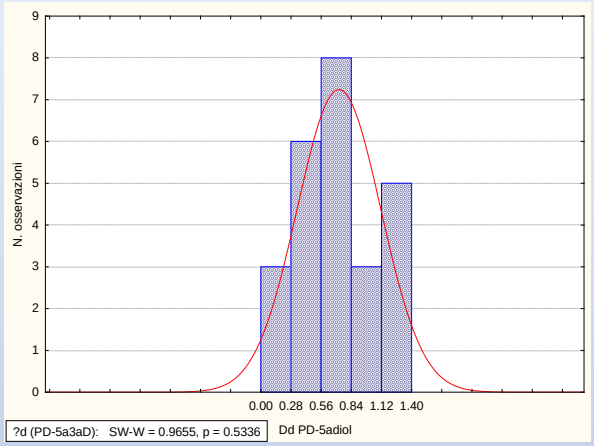
$\Delta\delta$ (PD-A)



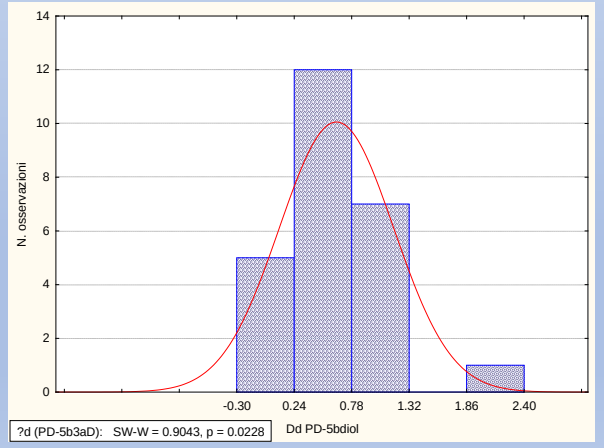
$\Delta\delta$ (PD-Et)



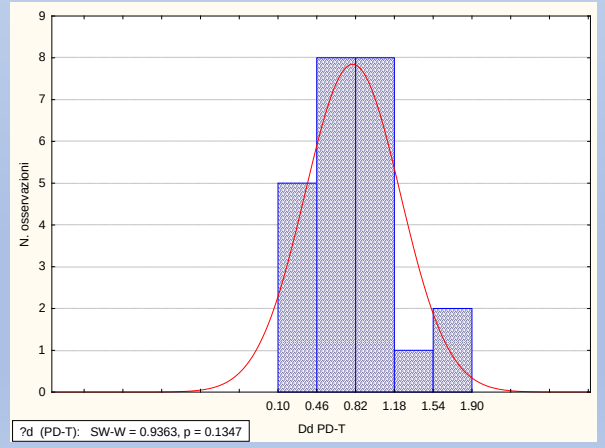
$\Delta\delta$ (PD-5adiol)



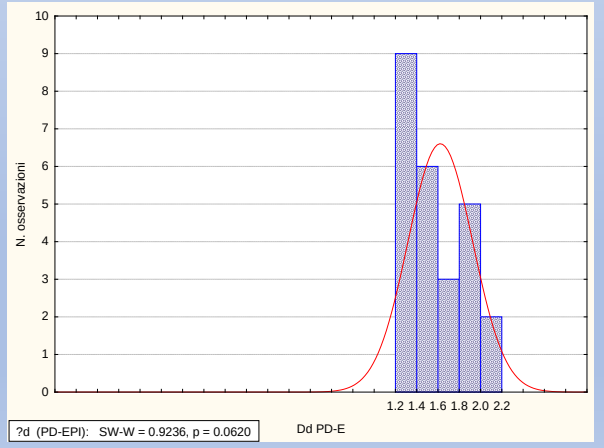
$\Delta\delta$ (PD-5bdiol)



$\Delta\delta$ (PD-T)

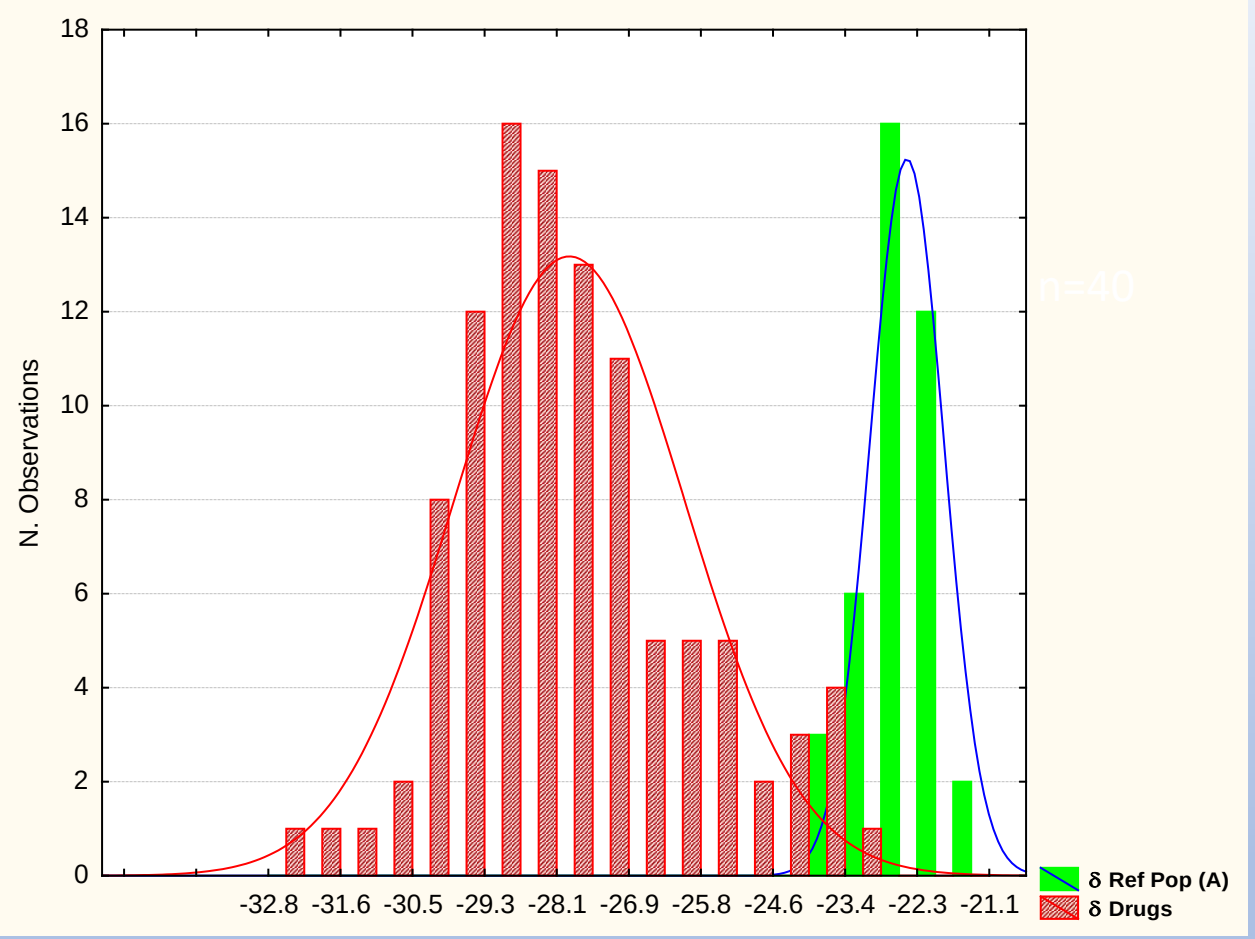


$\Delta\delta$ (PD-E)



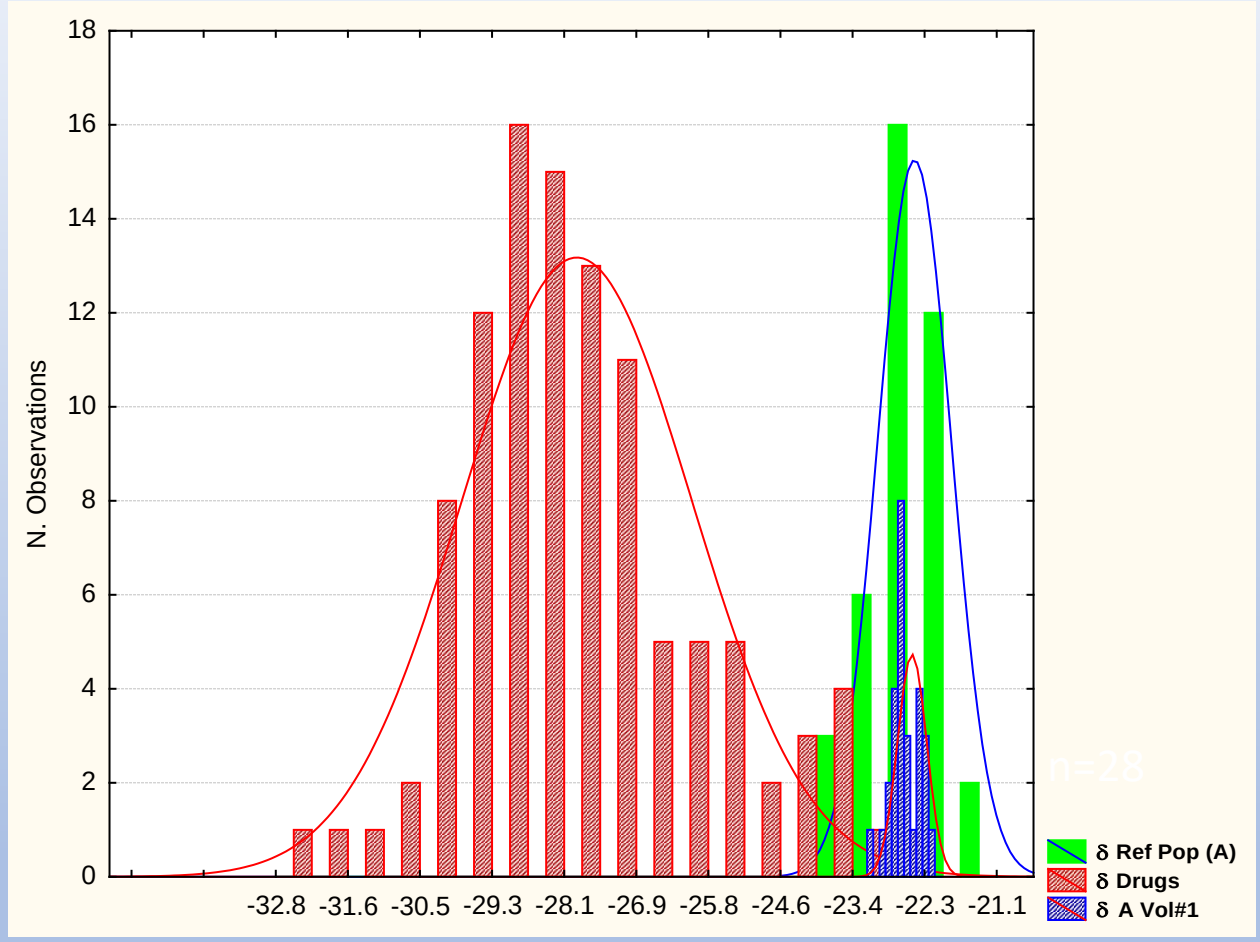
Reference Population *vs*. Pharmaceutical Preparations

N=105

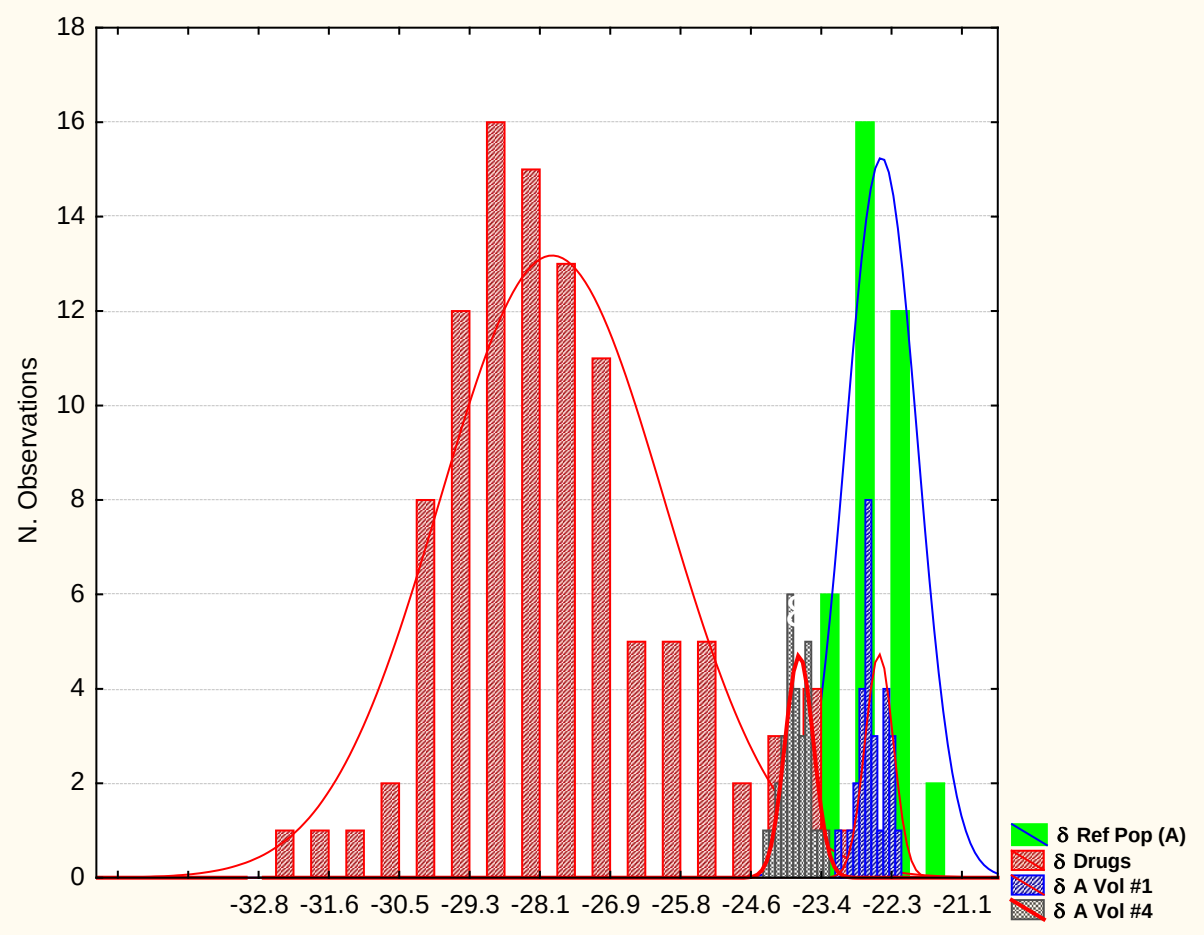


[1] Ueki M. et al. *Rapid Commun. Mass Spectrom*., **1999,** 13, 2237–2243.
[2] de la Torre X. et al. *J. Pharm. Biomed. Anal*., **2001,** 24, 645–650.
[3] Cawley A. et al. *Drug Test. Anal*., **2010**, 2, 557–567.
[4] Forsdahl G. *Drug Test. Anal*., **2011**, 3, 814–819.
[5] Brooker L. *Drug Test. Anal***., 2014**, 6, 996–1001.
[6] Pharmaceutical seized by the Carabienieri (NAS) 2014

Individual Reference *vs*. Pharmaceutical Preparations & Population



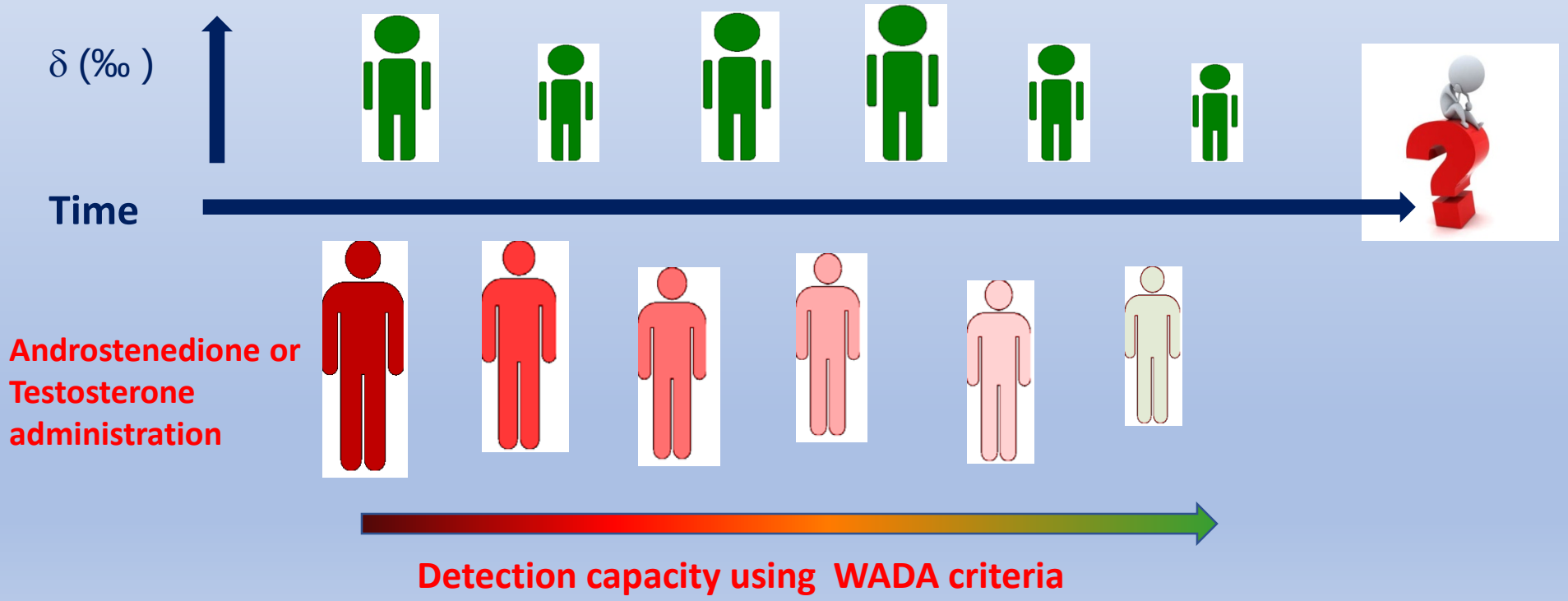
Individual Reference *vs*. Pharmaceutical Preparations & Population



Longitudinal application

Objective

To test the sensitivity of the IRMS Bayesian Model where the ABP Steroid module and the positive criteria for IRMS based on population references fail.



Experimental and Methods

SP	IRMS
Enzymatic hydrolysis, liquid-liquid extraction with TMS derivate and measure in multi-target screenings GC/MS/MS	Enzymatic hydrolysis, liquid-liquid extraction, HPLC purification and GC-C-IRMS detection

Urine samples collection, longitudinal study

3 samples/week for 1 month
2 Samples/month for 6 months
1 Sample/month for 1 year

28 samples/volunteer

Mazzarino, M. et al. Anal. Chim. Acta 683, 221–6 (2011).
de la Torre, X., et al. Anal. Chim. Acta 756, 23–29 (2012).

Administration studies

Oral Androstenedione

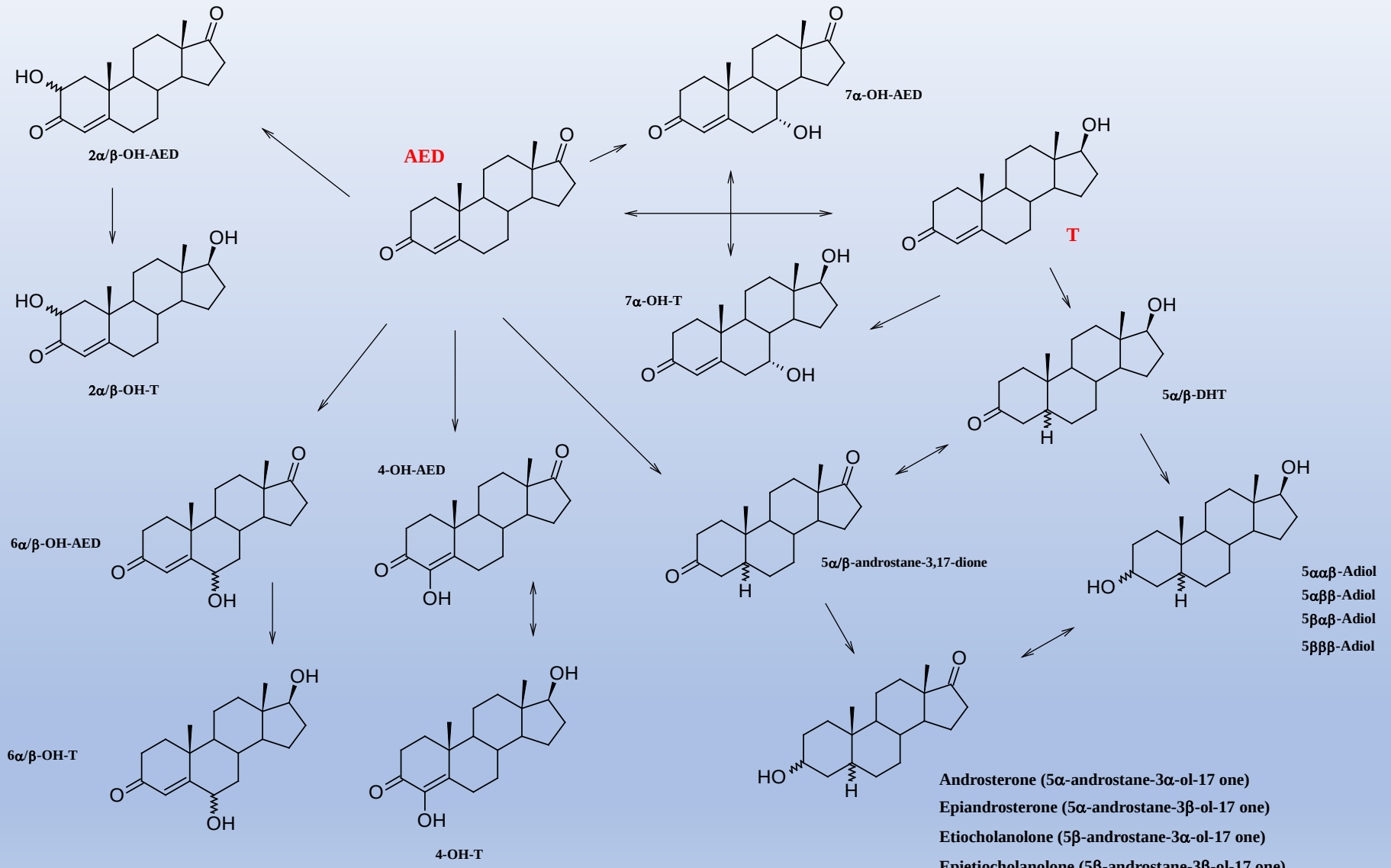
3 Male Caucasian volunteers (41 ± 8 yrs)
100 mg androstenedione (AED) p.o. (ASN Androstene 100 ™, Hood River, OR, USA)
Urine samples collected before and for 5 days after the administration
The androstenedione capsule composition was verified and the $\delta^{13}C$ (‰) value determined (-30.5 ± 0.3; n=5)

Transdermal testosterone

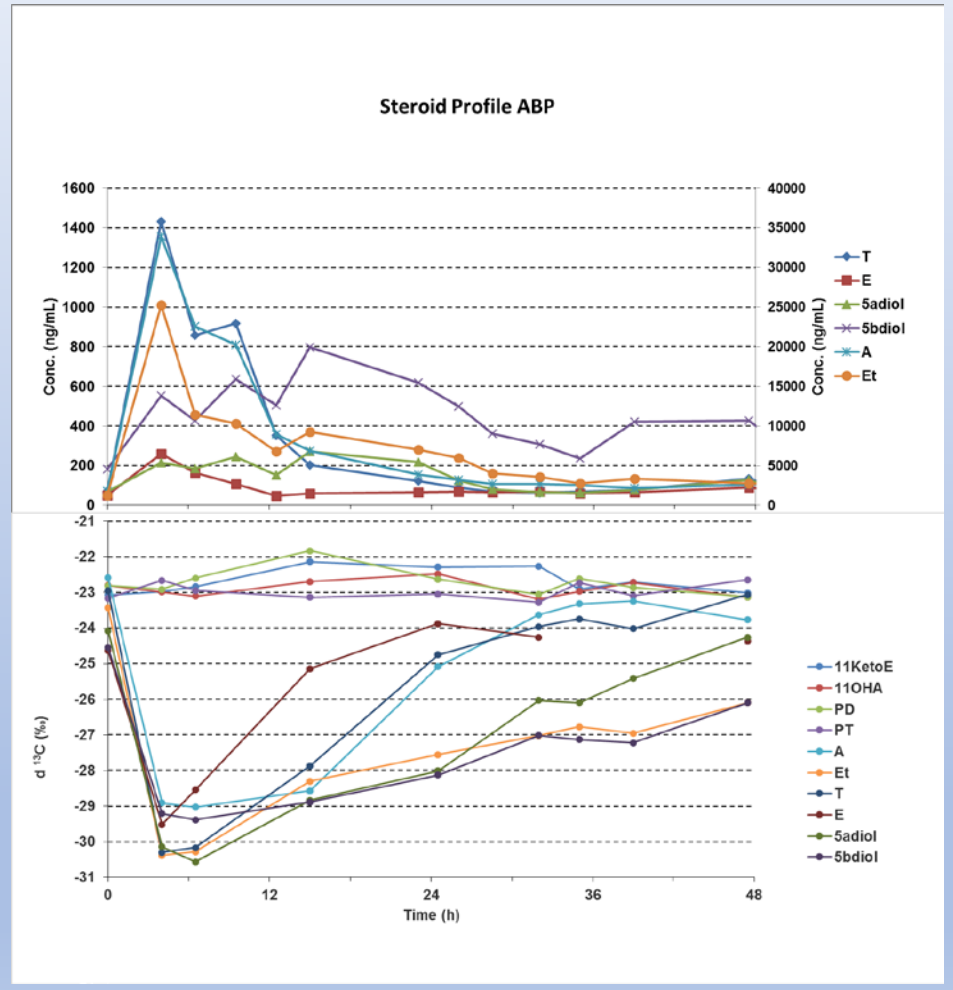
1 Male Caucasian volunteer (43 yrs)
Gel (Testogel ®, Schering) , 50 mg/day (eq. to 5 mg T), every 24 h for 4 days
Urine samples collected before and for 36 h after the last administration
The testosterone $\delta^{13}C$ (‰) value was determined (-29.6 ± 0.3; n=5)

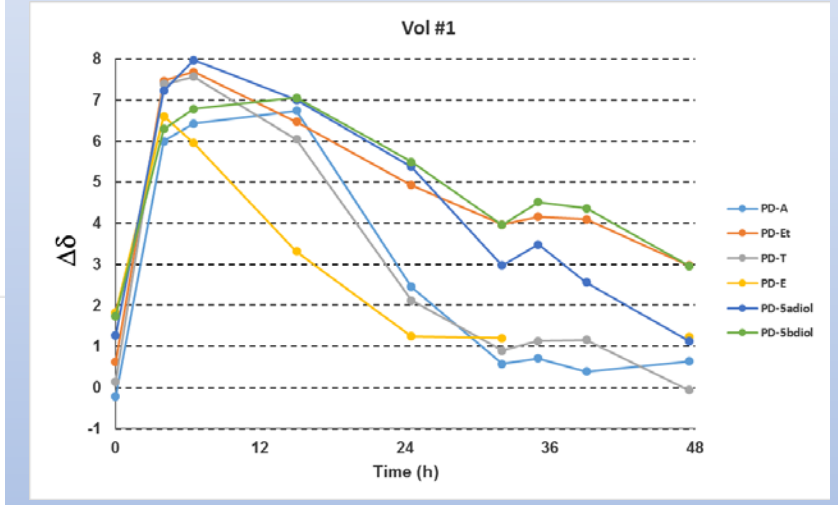
Oral Androstenedione

AED metabolism and marker



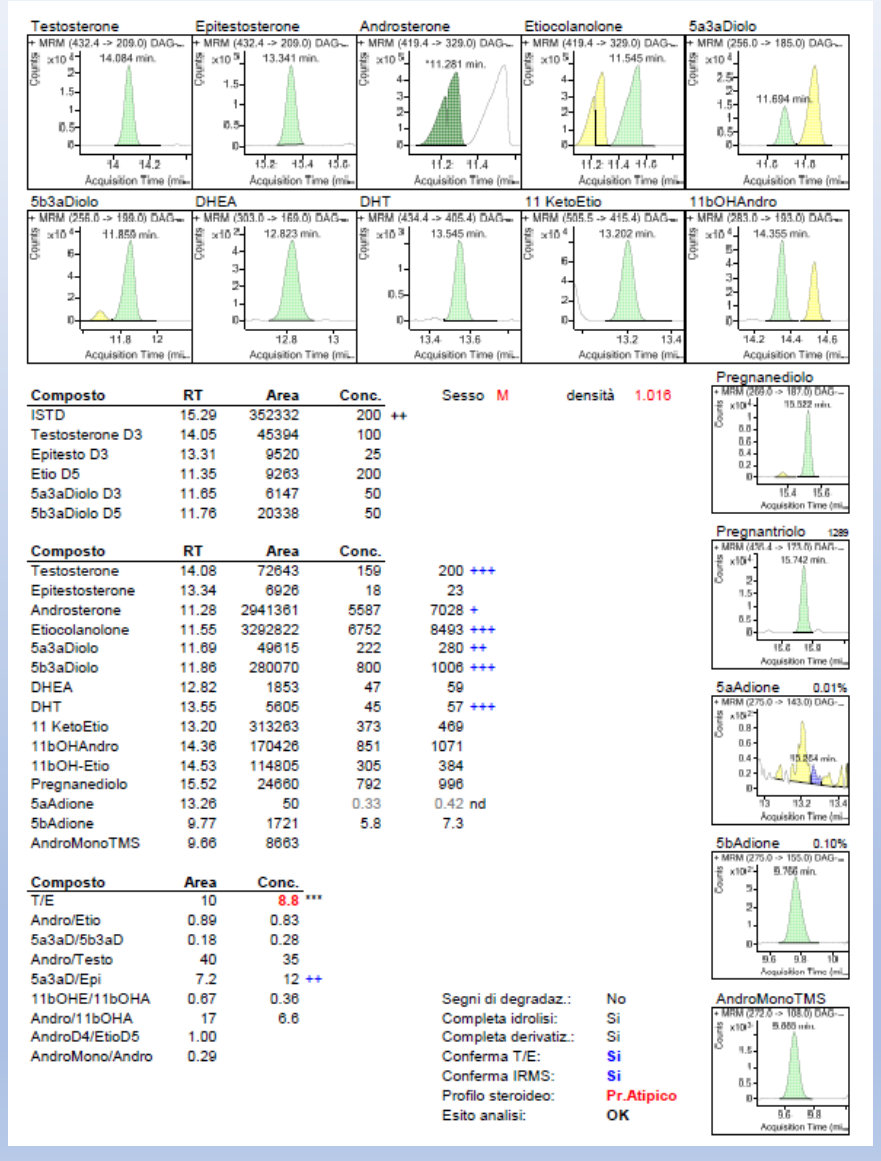
IRMS Results





Case #1 (Sample at 11.5 h)

SP ABP module

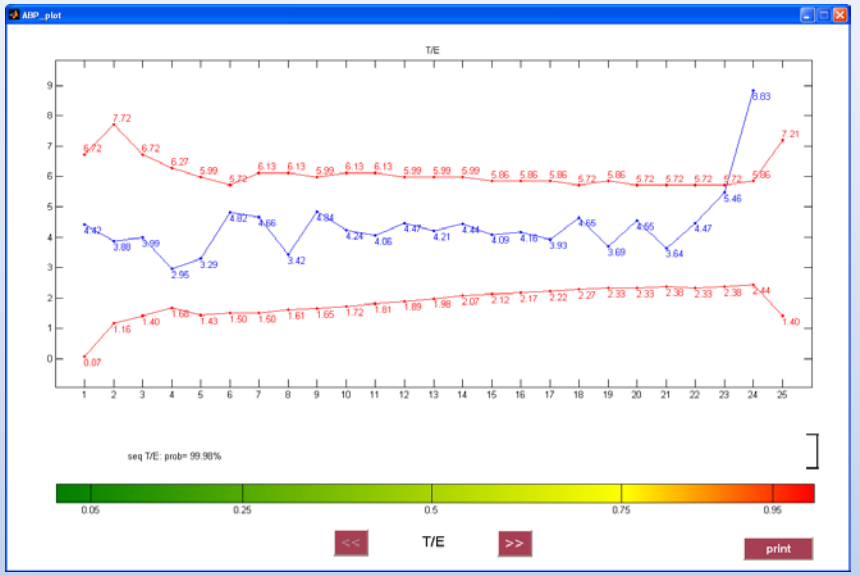


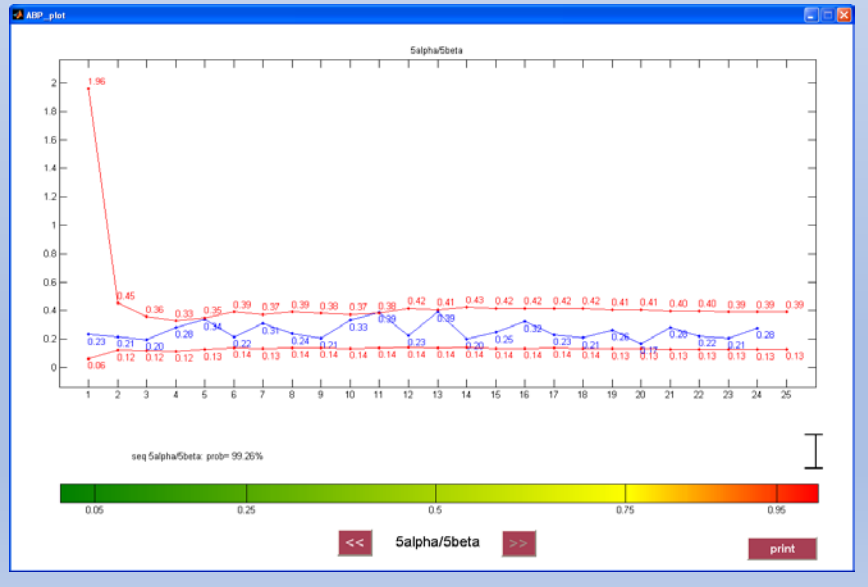
Composto	RT	Area	Conc.		Sesso M	densità 1.016
ISTD	15.29	352332	200	++		
Testosterone D3	14.05	45394	100			
Epitesto D3	13.31	9520	25			
Etio D5	11.35	9263	200			
5a3aDiolo D3	11.65	6147	50			
5b3aDiolo D5	11.76	20338	50			

Composto	RT	Area	Conc.		
Testosterone	14.08	72643	159	200	+++
Epitestosterone	13.34	6926	18	23	
Androsterone	11.28	2941361	5587	7028	+
Etiocolanolone	11.55	3292822	6752	8493	+++
5a3aDiolo	11.69	49615	222	280	++
5b3aDiolo	11.86	280070	800	1006	+++
DHEA	12.82	1853	47	59	
DHT	13.55	5605	45	57	+++
11 KetoEtio	13.20	313263	373	469	
11bOHAndro	14.36	170426	851	1071	
11bOH-Etio	14.53	114805	305	384	
Pregnanediolo	15.52	24660	792	996	
5aAdione	13.26	50	0.33	0.42	nd
5bAdione	9.77	1721	5.8	7.3	
AndroMonoTMS	9.66	8663			

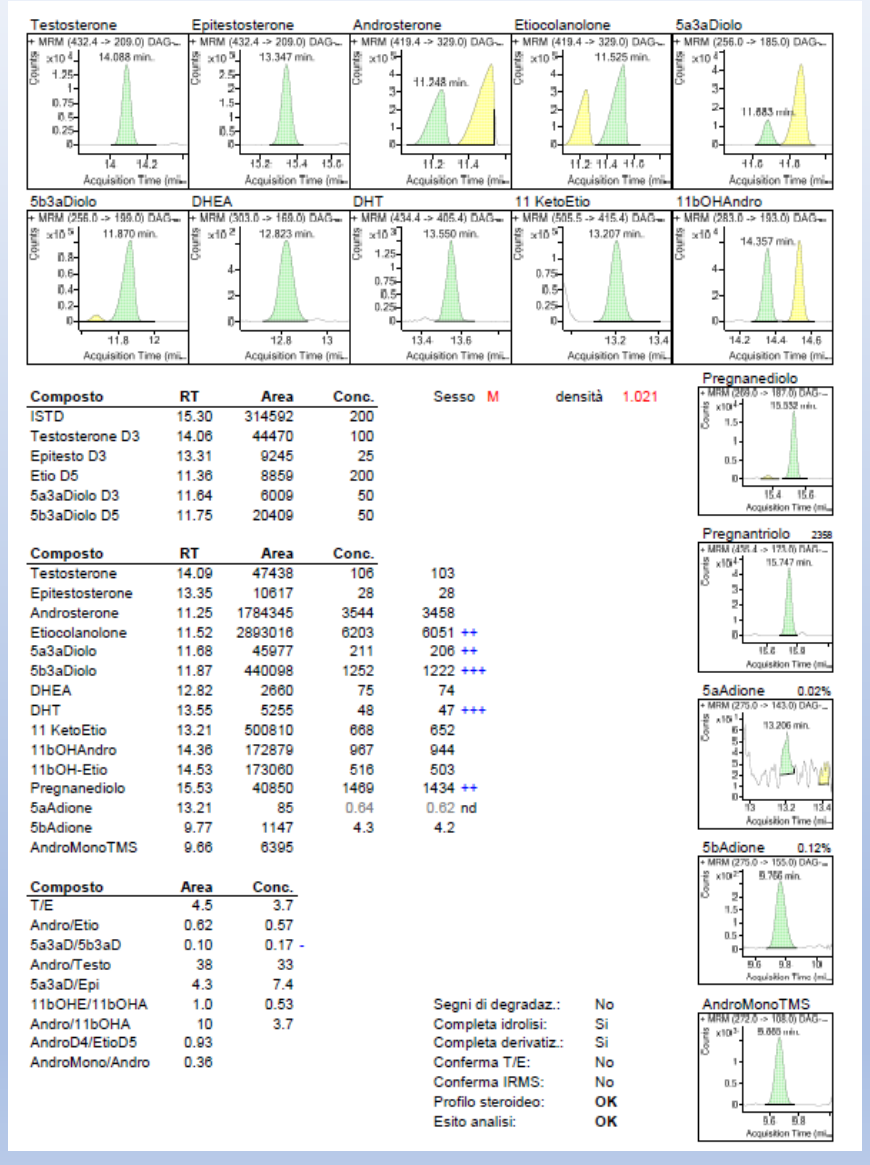
Composto	Area	Conc.	
T/E	10	8.8	***
Andro/Etio	0.89	0.83	
5a3aD/5b3aD	0.18	0.28	
Andro/Testo	40	35	
5a3aD/Epi	7.2	12	++
11bOHE/11bOHA	0.67	0.36	
Andro/11bOHA	17	6.6	
AndroD4/EtioD5	1.00		
AndroMono/Andro	0.29		

Segni di degradaz.:	No
Completa idrolisi:	Si
Completa derivatiz.:	Si
Conferma T/E:	Si
Conferma IRMS:	Si
Profilo steroideo:	Pr.Atipico
Esito analisi:	OK





Case #1 (Sample at 21.5 h)



Composto	RT	Area	Conc.
ISTD	15.30	314592	200
Testosterone D3	14.06	44470	100
Epitesto D3	13.31	9245	25
Etio D5	11.36	8859	200
5a3aDiolo D3	11.64	6009	50
5b3aDiolo D5	11.75	20409	50

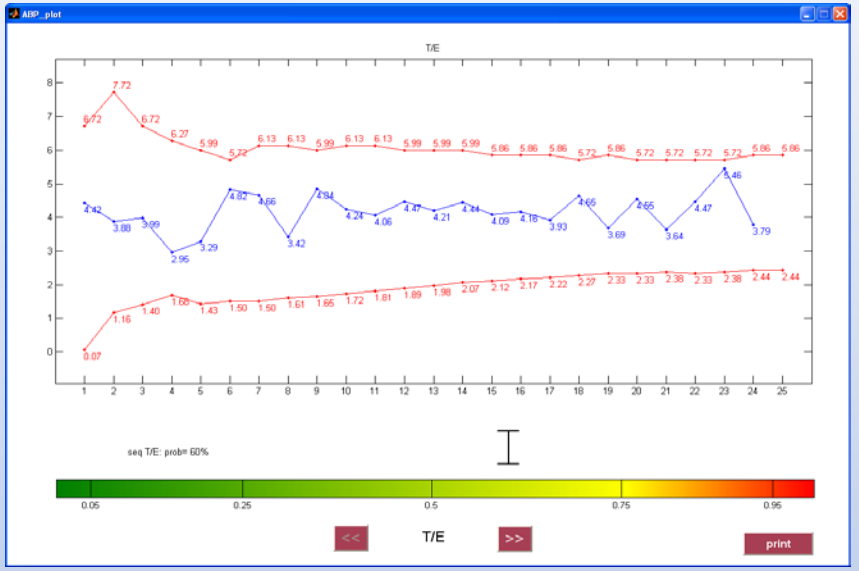
Sesso M densità 1.021

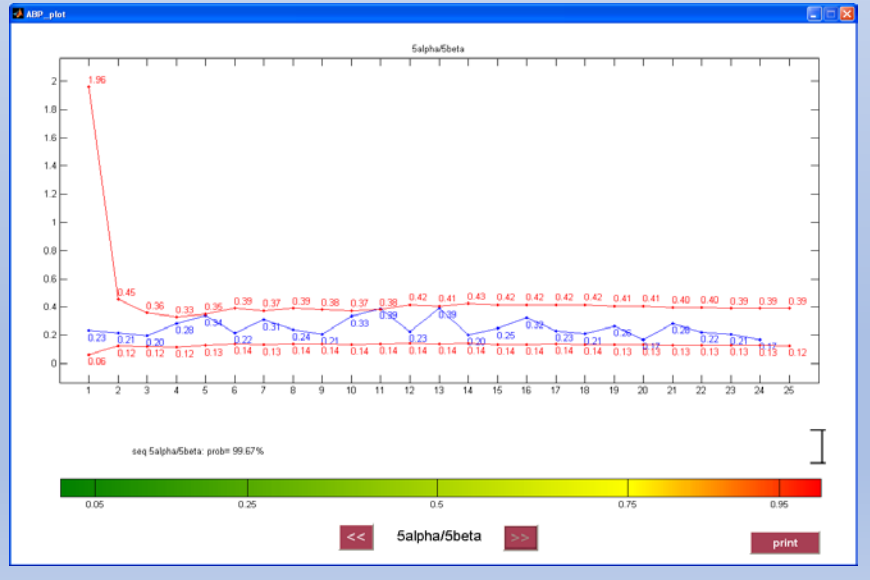
Composto	RT	Area	Conc.	
Testosterone	14.09	47438	106	103
Epitestosterone	13.35	10617	28	28
Androsterone	11.25	1784345	3544	3458
Etiocolanolone	11.52	2893016	6203	6051 ++
5a3aDiolo	11.68	45977	211	206 ++
5b3aDiolo	11.87	440098	1252	1222 +++
DHEA	12.82	2660	75	74
DHT	13.55	5255	48	47 +++
11 KetoEtio	13.21	500810	668	652
11bOHAndro	14.36	172879	967	944
11bOH-Etio	14.53	173060	516	503
Pregnanediolo	15.53	40850	1469	1434 ++
5aAdione	13.21	85	0.64	0.62 nd
5bAdione	9.77	1147	4.3	4.2
AndroMonoTMS	9.66	6395		

Composto	Area	Conc.
T/E	4.5	3.7
Andro/Etio	0.62	0.57
5a3aD/5b3aD	0.10	0.17 -
Andro/Testo	38	33
5a3aD/Epi	4.3	7.4
11bOHE/11bOHA	1.0	0.53
Andro/11bOHA	10	3.7
AndroD4/EtioD5	0.93	
AndroMono/Andro	0.36	

Segni di degradaz.:	No
Completa idrolisi:	Si
Completa derivatiz.:	Si
Conferma T/E:	No
Conferma IRMS:	No
Profilo steroideo:	OK
Esito analisi:	OK

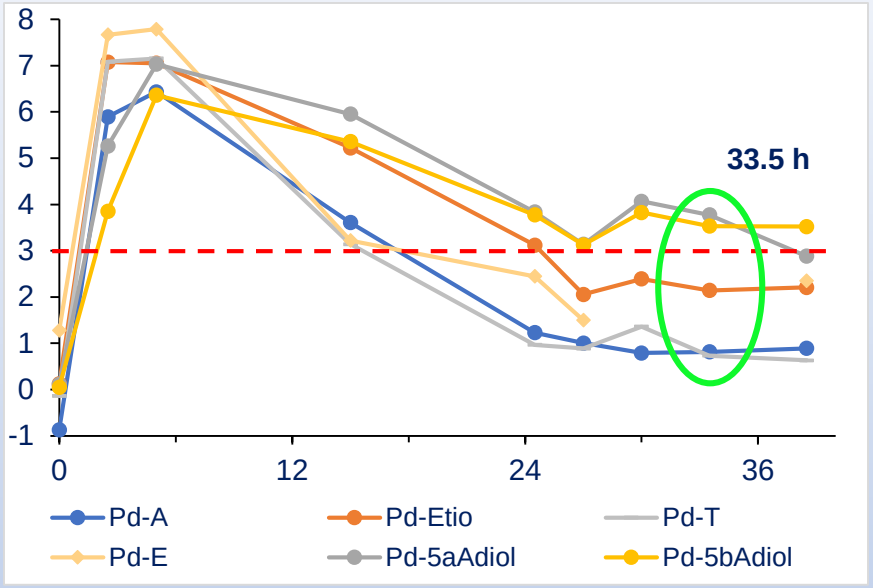
SP ABP module

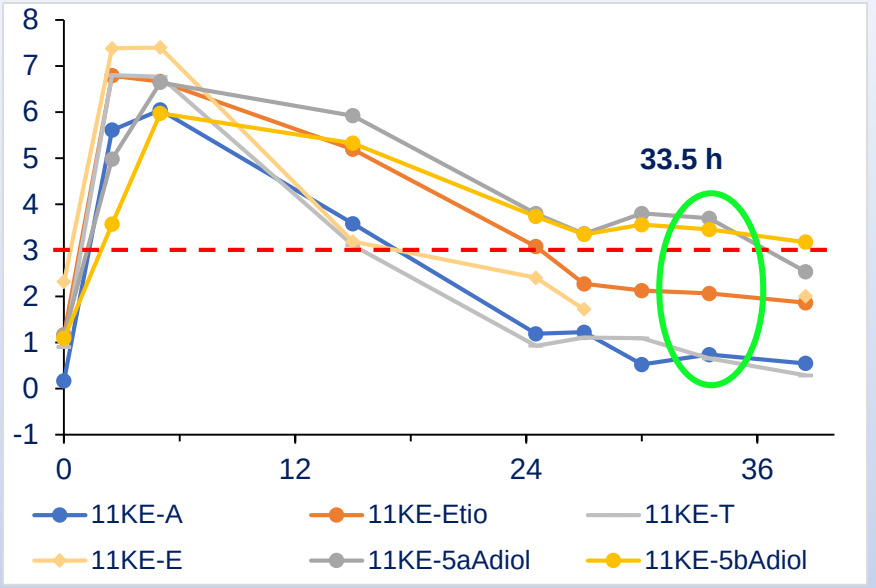


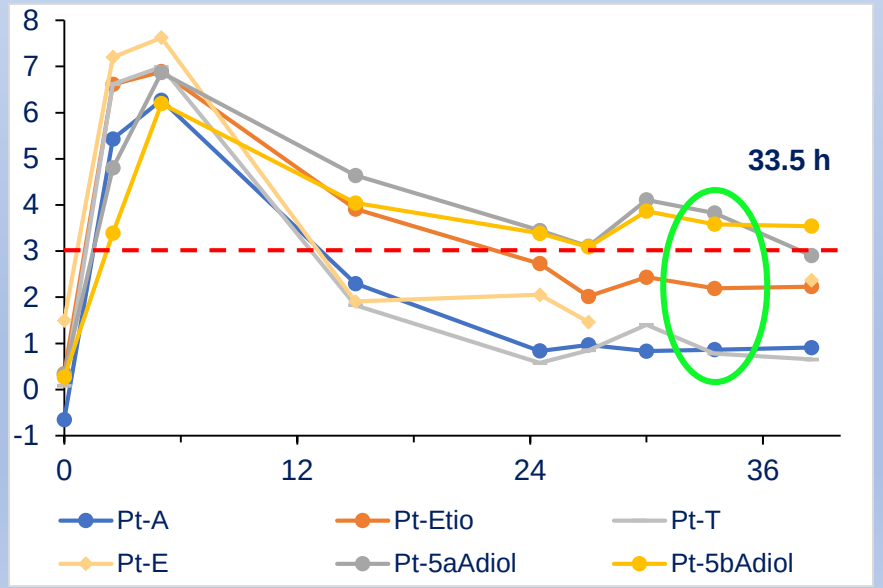


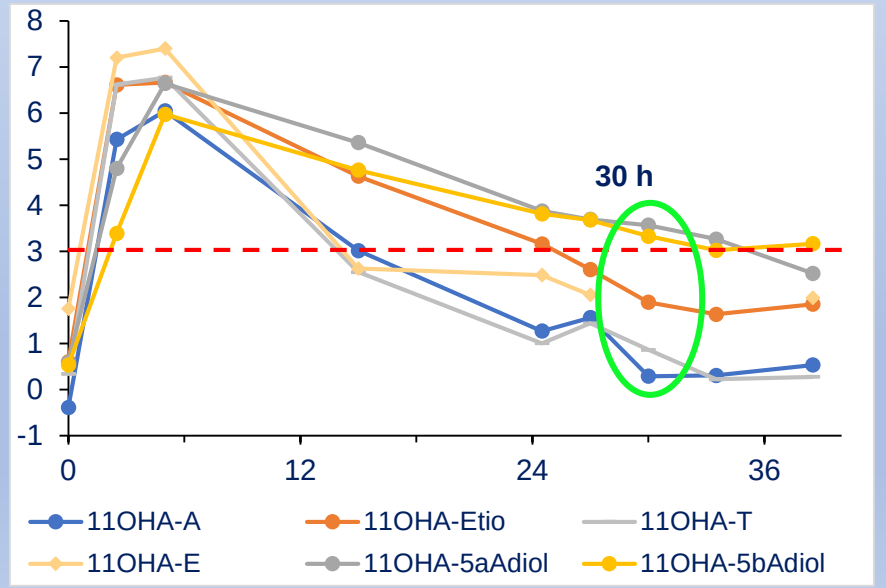
Case #1

IRMS population-based: $\Delta\delta_{ERC-TC}$(‰) vs Time (h)









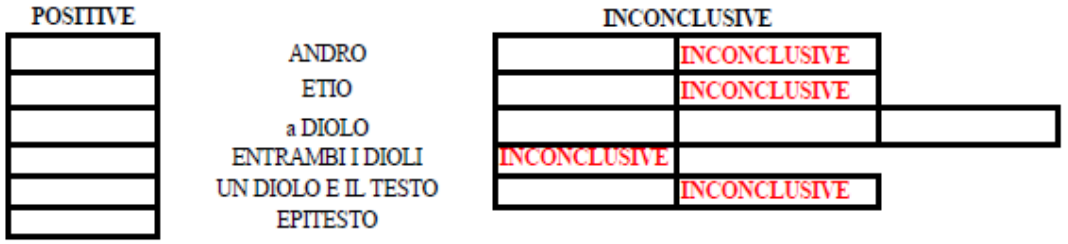
Case #1 (Sample at 38.5 h)

IRMS population-based

	11bOH-Andro	11KetoEtio	Pregnantriolo	Pregnandiolo
Andro	0,5	0,5	0,9	0,9
Etio	1,9	1,9	2,2	2,2
5a3aA	2,5	2,5	2,9	2,9
5b3aA	3,2	3,2	3,5	3,5
Testo	0,3	0,3	0,7	0,6
Epitesto	2,0	2,0	2,4	2,3
DHEA	-1,3	-1,3	-0,9	-0,9

	δ 13C/12C	u_c	Ampl 44 (mV)	Range di linerità (mV)
Frazione 1-7-8				
Etio	-25,4	0,15	2053	350-7000
Andro	-24,1	0,09	1723	350-7000
11bOH-Andro	-23,6	0,23	1202	350-7000
Frazione 2-6				
5a3aA	-26,1	0,29	2252	350-7000
11KetoEtio	-23,5	0,09	1075	350-7000
Frazione 5-9				
5b3aA	-26,7	0,24	1861	350-7000
Pregnandiolo	-23,2	0,21	2266	350-7000
Frazione 3-6pt				
Testo	-23,8	0,03	1529	350-7000
Pregnantriolo	-23,2	0,31	1052	350-7000
Frazione 4				
DHEA	-22,3	0,11	2207	350-7000
Frazione 4Epi				
Epitesto	-25,5	0,11	1054	340-7000

Inconclusive sample



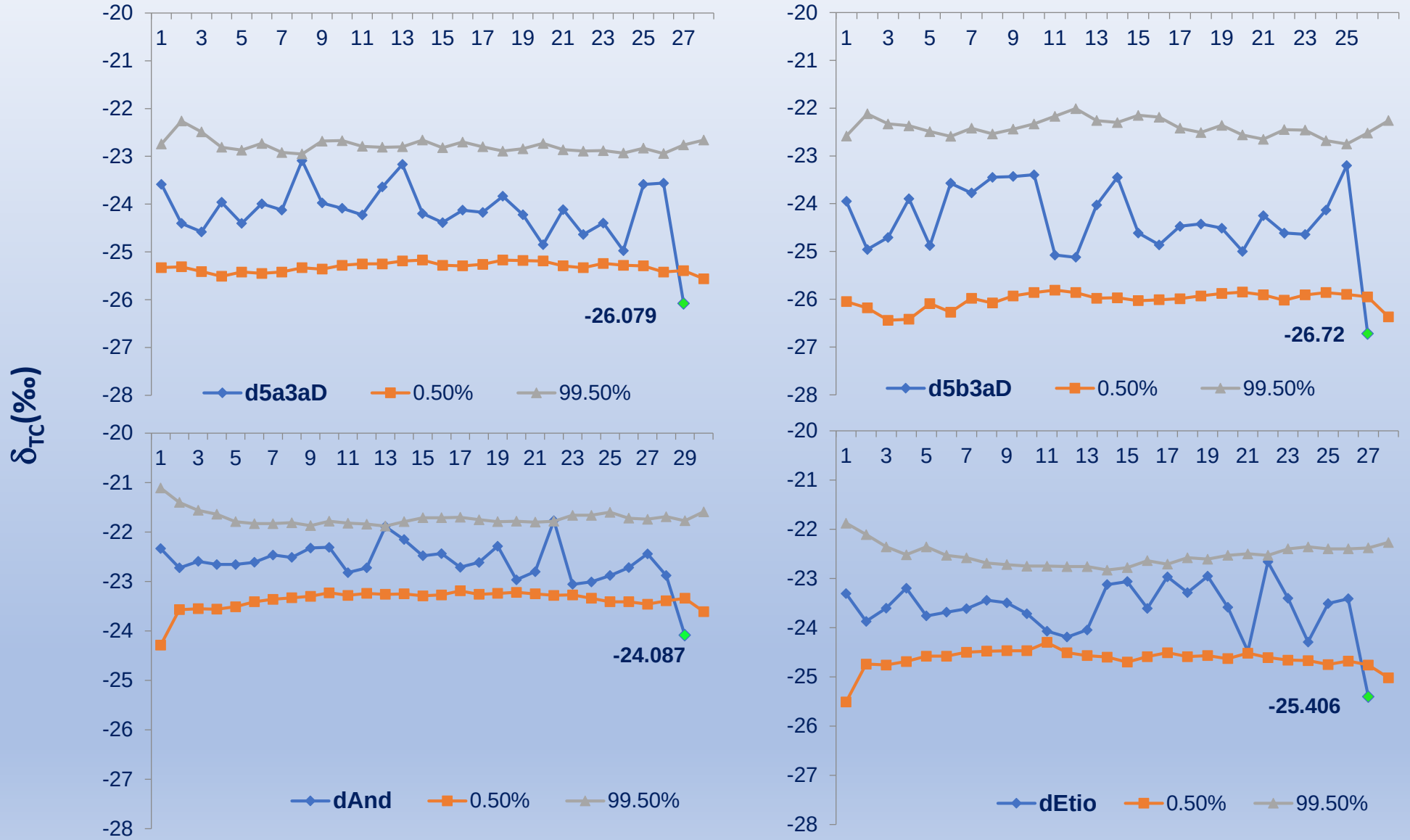
Appendix 1. Interpretation criteria for GC/C/IRMS positive test

Positive Criteria Section 2.3	Δδ ERC-TC					
	T	E#	A	Etio	5αAdiol, 5βAdiol	Formestane, Boldenone, Boldenone *Metabolites*
i.	> 3 ‰				> 3 ‰ (either Adiol)	
ii.					> 3 ‰ (both Adiols)	
iii.		> 4 ‰				
iv.			> 3 ‰			
				> 4 ‰		
v.			2-3 ‰		> 3 ‰ (either Adiol)	
				3-4 ‰	> 3 ‰ (either Adiol)	
vi.					Δδ(ERC-5α) > 4 ‰ and δ(5α) ≤ -27 ‰	
vii.						> 4 ‰

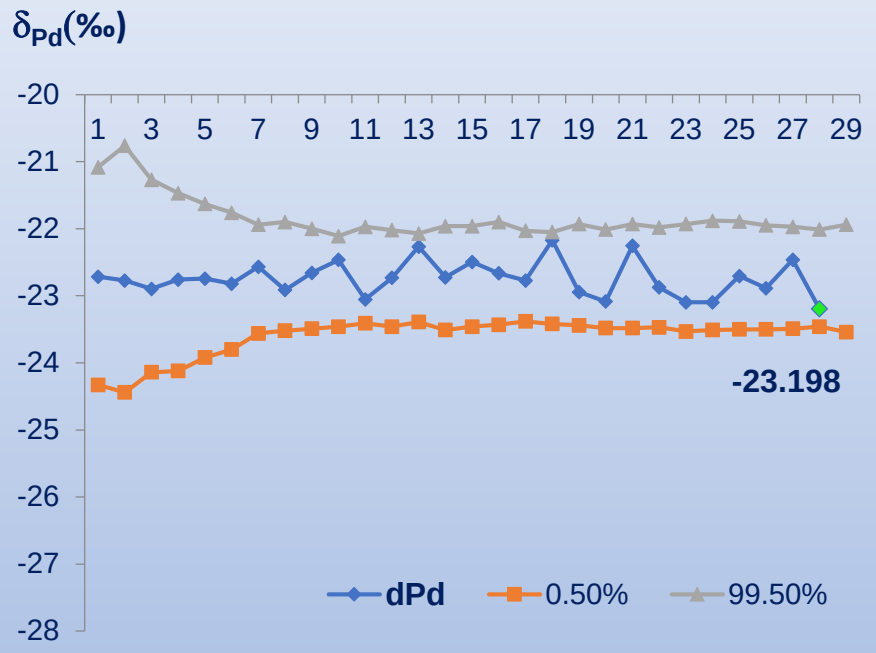
Concentration (SG-adjusted [3]) greater than 50 ng/mL in females or greater than 200 ng/mL in males.

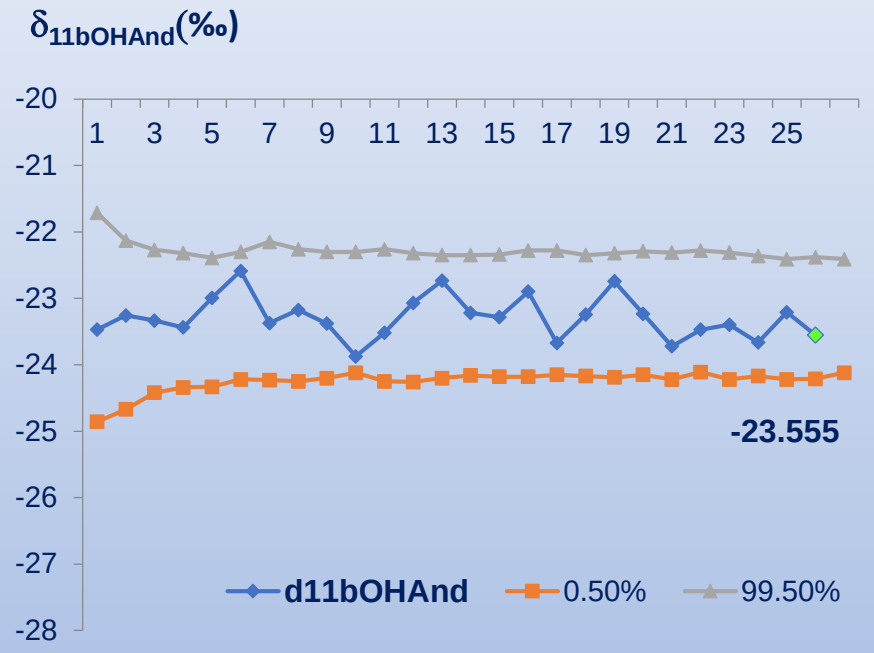
Case #1 (Sample at 38.5 h)

IRMS Bayesian approach δ_{TC}(‰)



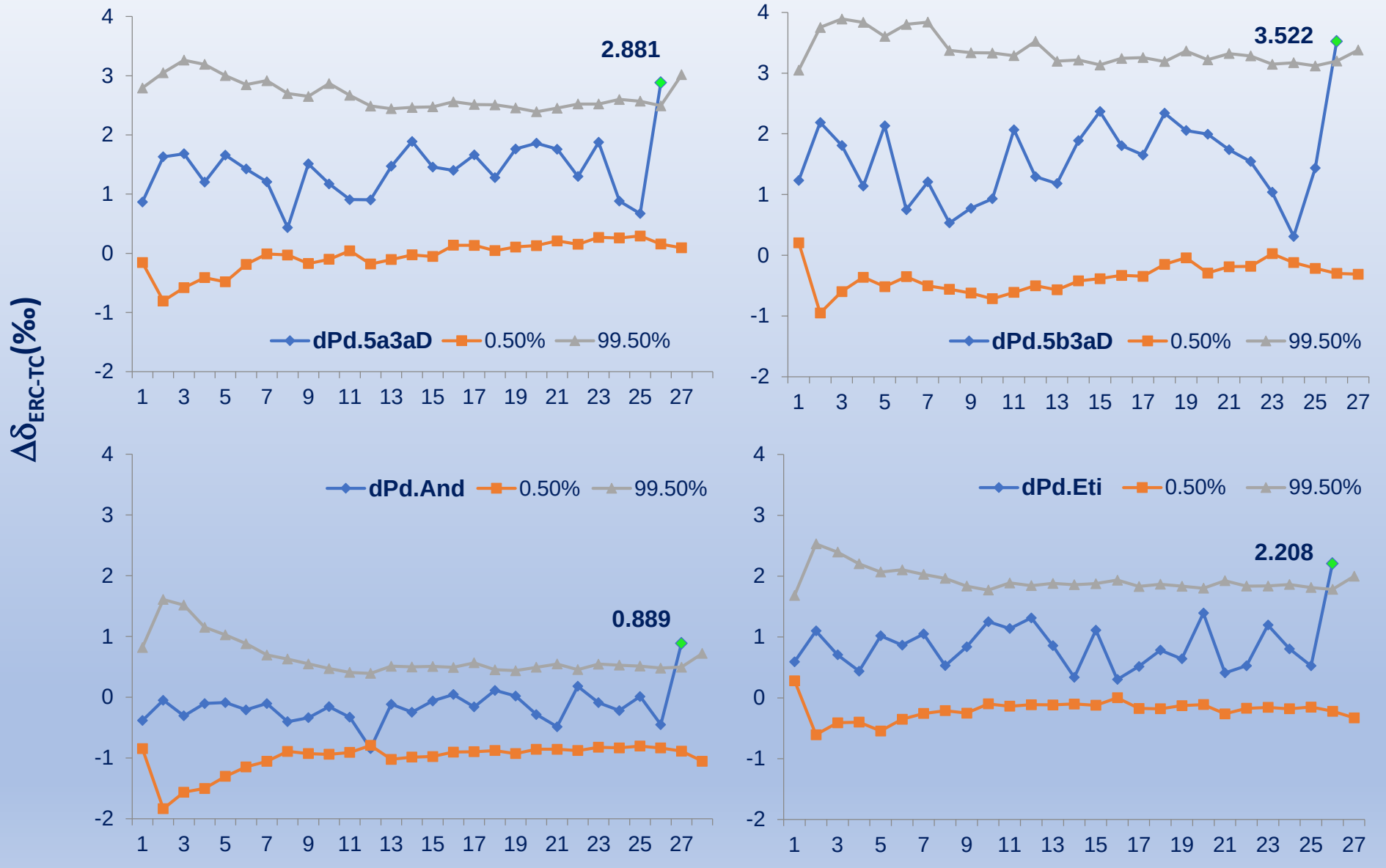
Case #1 (Sample at 38.5 h) IRMS Bayesian approach δ_{ERC}(‰)





Case #1 (Sample at 38.5 h)

IRMS Bayesian approach $\Delta\delta_{ERC-TC}$(‰)



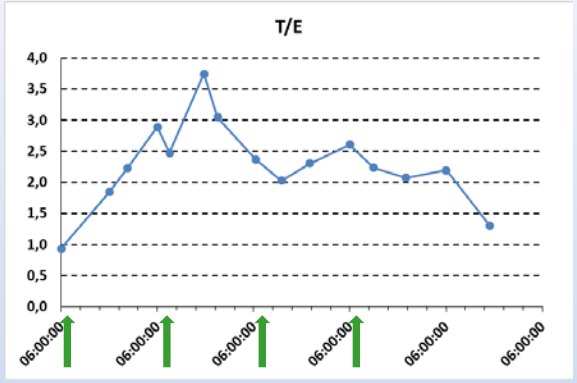
Transdermal Testosterone

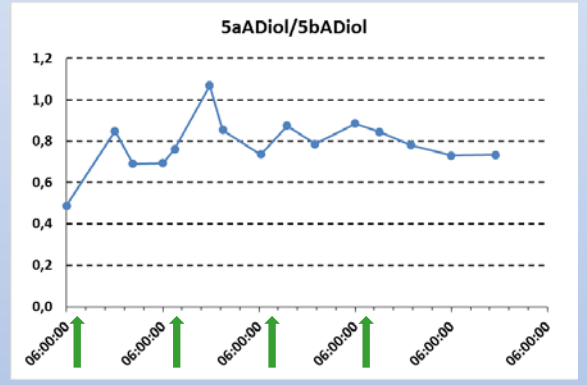
Transdermal T administration

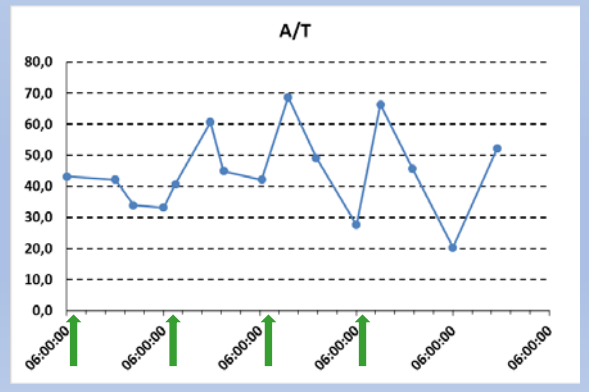
Gel (Testogel ®, Schering)

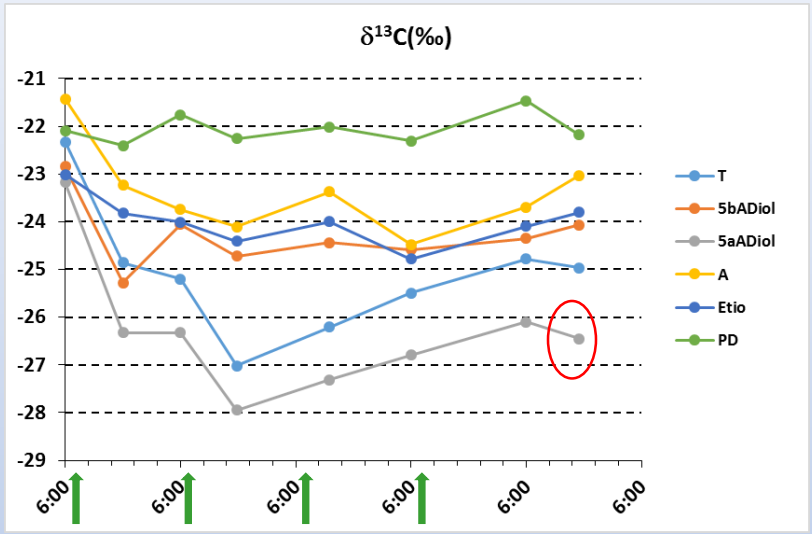
50 mg/ day (eq. to 5mg T)

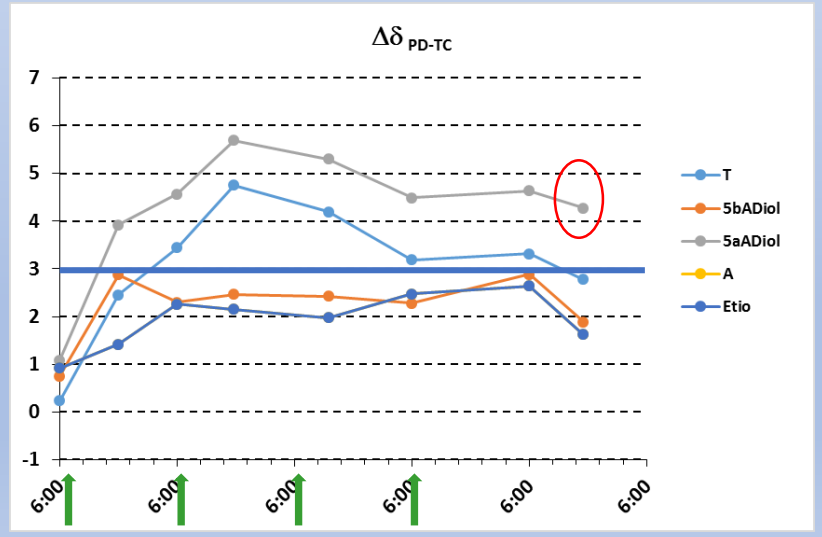
Every 24 h x 4 days











Campione n°	T-Gel 14

	11bOH-Andro	11KetoEtio	Pregnantriolo	Pregnandiolo
Andro	0,2	-0,6	0,1	0,8
Etio	1,0	0,2	0,9	1,6
5a3aA	3,6	2,9	3,6	4,3
5b3aA	1,2	0,5	1,2	1,9
Testo	2,1	1,4	2,1	2,8
Epitesto	0,9	0,1	0,9	1,6
DHEA	-0,2	-1,0	-0,3	0,5

	δ 13C/12C	u_c	Ampl 44 (mV)	Range di linerità (mV)
Frazione 1-7-8				
Etio	-23,8	0,15	3719	350-7000
Andro	-23,0	0,09	3302	350-7000
11bOH-Andro	-22,8	0,23	1259	350-7000
Frazione 2-6				
5a3aA	-26,5	0,29	2847	350-7000
11KetoEtio	-23,6	0,09	1711	350-7000
Frazione 5-9				
5b3aA	-24,1	0,24	4335	350-7000
Pregnandiolo	-22,2	0,21	7143	350-7000
Frazione 3-6pt				
Testo	-25,0	0,03	1832	350-7000
Pregnantriolo	-22,9	0,31	5158	350-7000
Frazione 4				
DHEA	-22,6	0,11	751	350-7000
Frazione 4Epi				
Epitesto	-23,8	0,11	1716	340-7000

CRITERI DI VALUTAZIONE

POSITIVE		INCONCLUSIVE		
	ANDRO	INCONCLUSIVE		
	ETIO	INCONCLUSIVE		
	a DIOLO	INCONCLUSIVE	INCONCLUSIVE!	
	ENTRAMBI I DIOLI			
	UN DIOLO E IL TESTO	INCONCLUSIVE		
	EPITESTO			

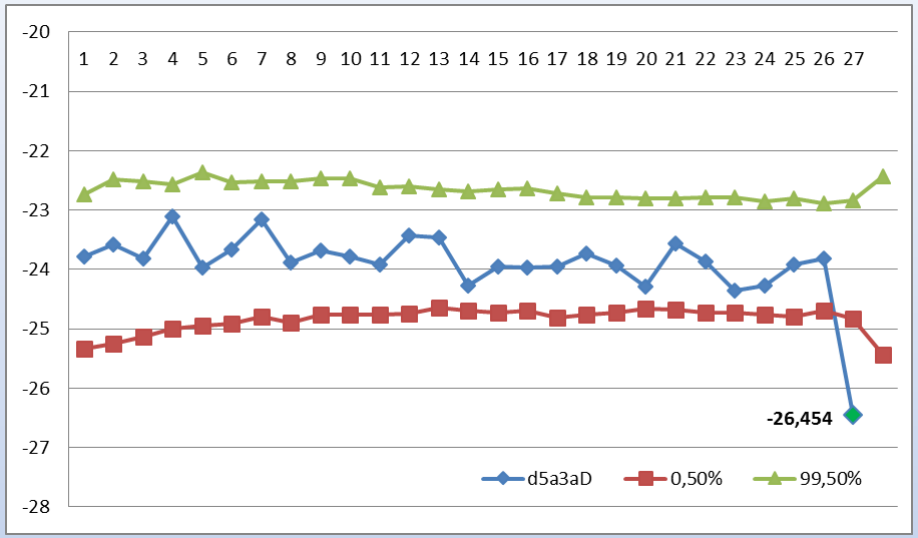
Appendix 1. Interpretation criteria for GC/C/IRMS positive test

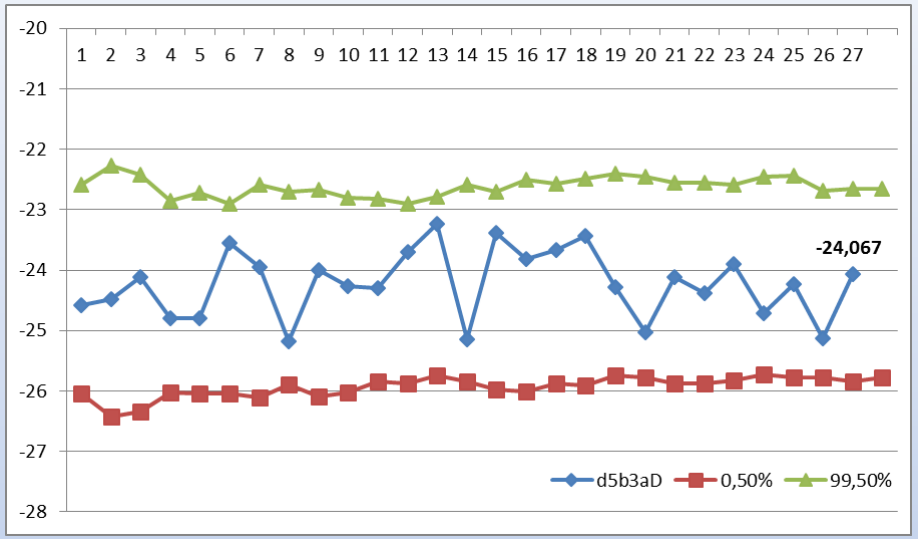
Positive Criteria Section 2.3	Δδ ERC-TC					
	T	E#	A	Etio	5αAdiol, 5βAdiol	Formestane, Boldenone, Boldenone *Metabolites*
i.	> 3 ‰				> 3 ‰ (either Adiol)	
ii.					> 3 ‰ (both Adiols)	
iii.		> 4 ‰				
iv.			> 3 ‰			
				> 4 ‰		
v.			2-3 ‰		> 3 ‰ (either Adiol)	
				3-4 ‰	> 3 ‰ (either Adiol)	
vi.					Δδ(ERC-5α) > 4 ‰ and δ(5α) ≤ -27 ‰	
vii.						> 4 ‰

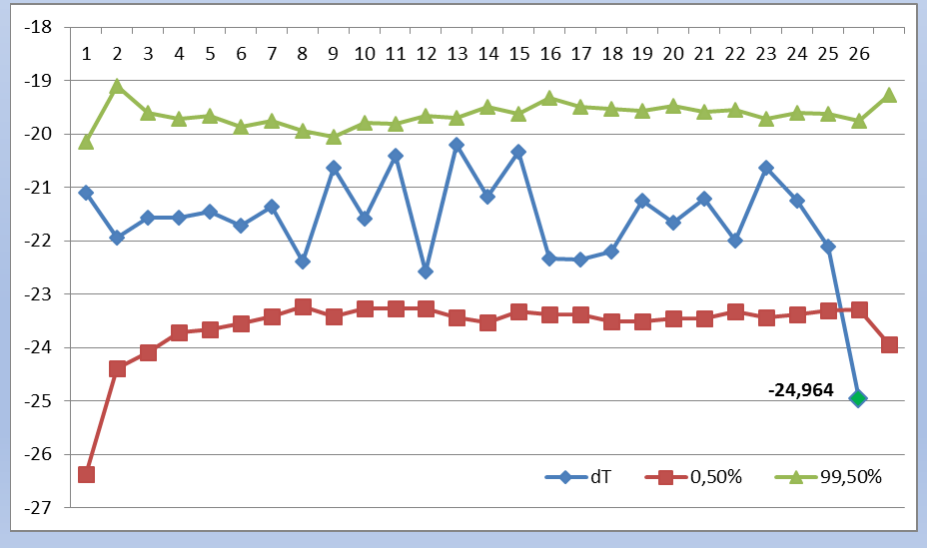
Concentration (SG-adjusted [3]) greater than 50 ng/mL in females or greater than 200 ng/mL in males.

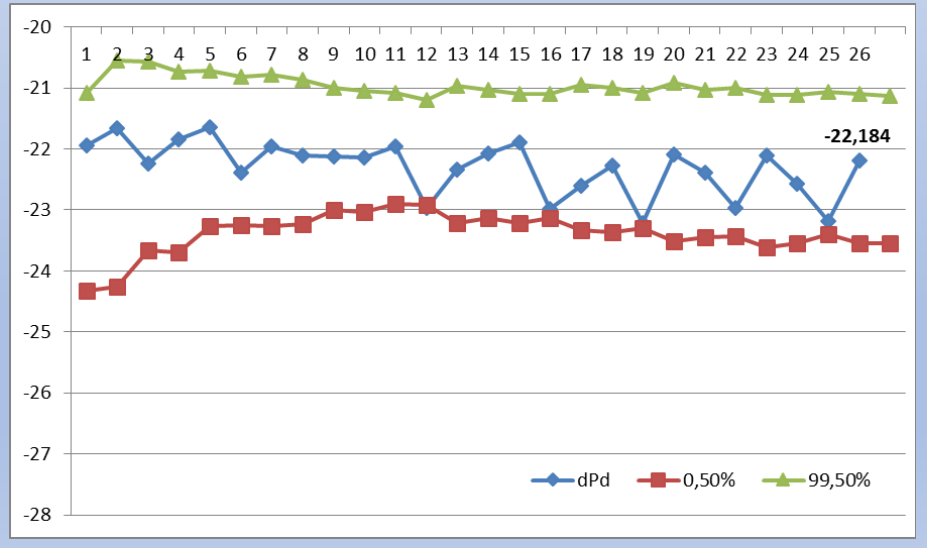
(Sample at 12 h last adm) IRMS Bayesian approach δ_{ERC}(‰)

δ_{ERC}(‰)





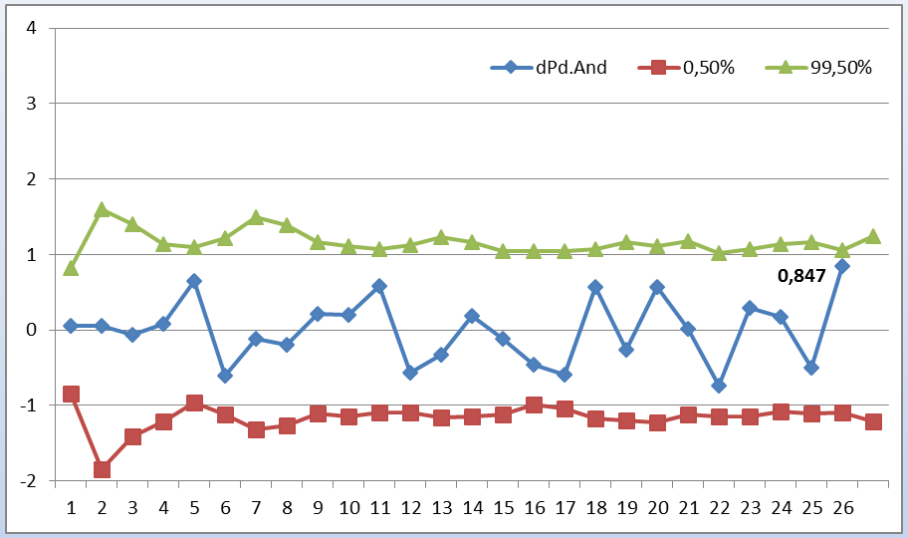


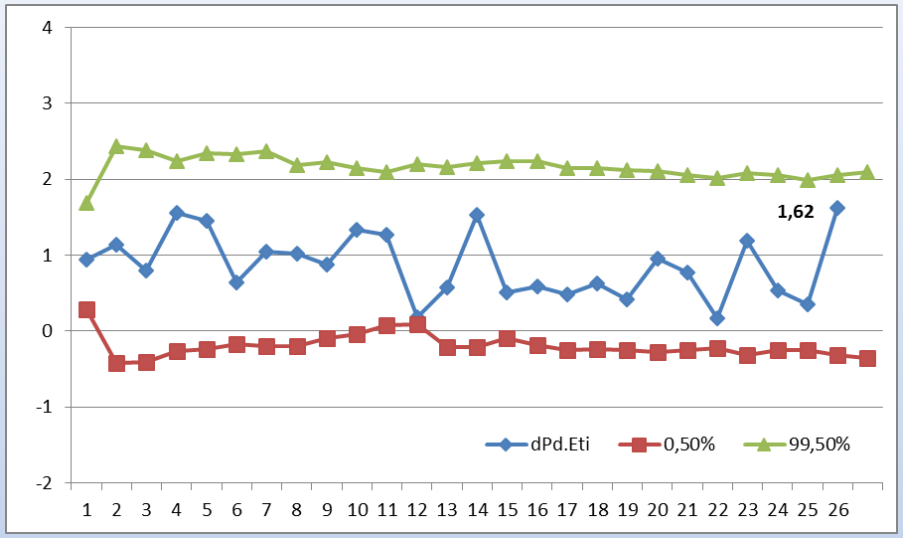


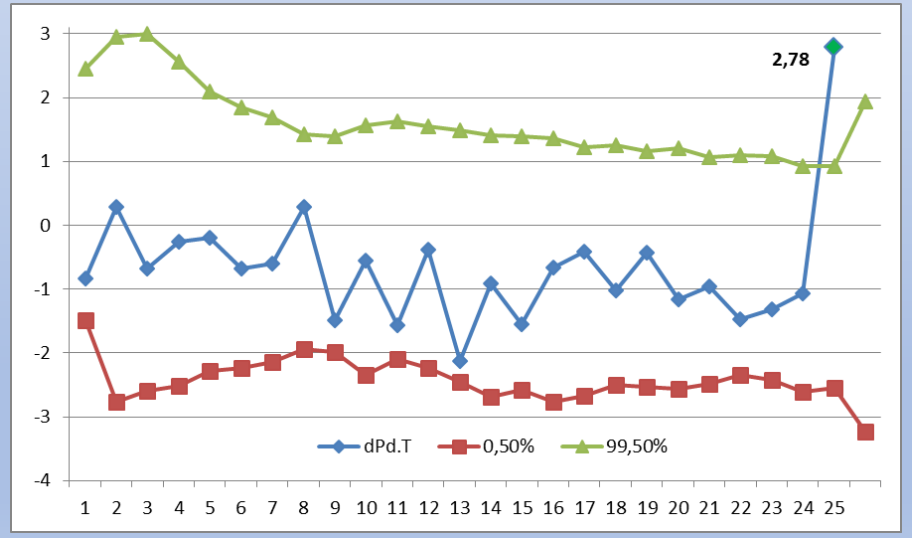
(Sample at 12 h last adm)

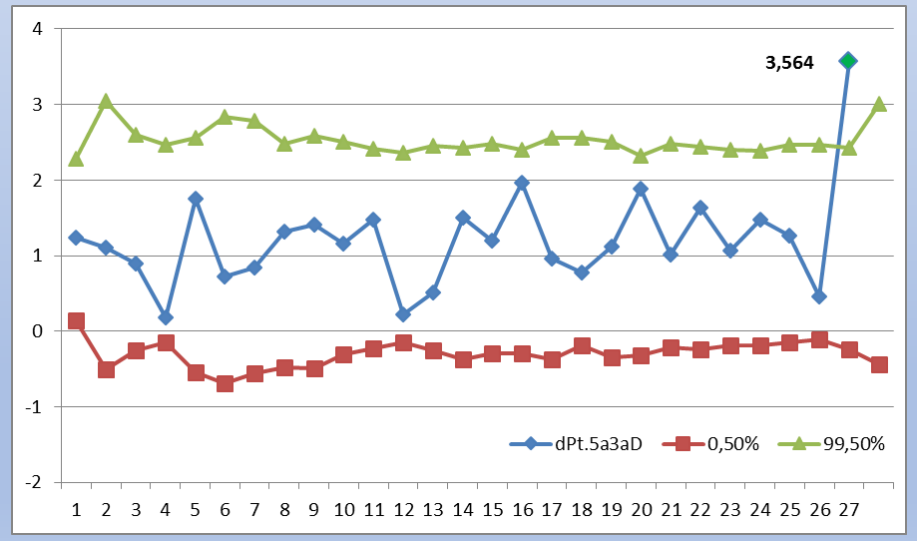
IRMS Bayesian approach $\Delta\delta_{ERC-TC}$(‰)

$\Delta\delta_{ERC-TC}$(‰)









PPV = 99,9999991 %

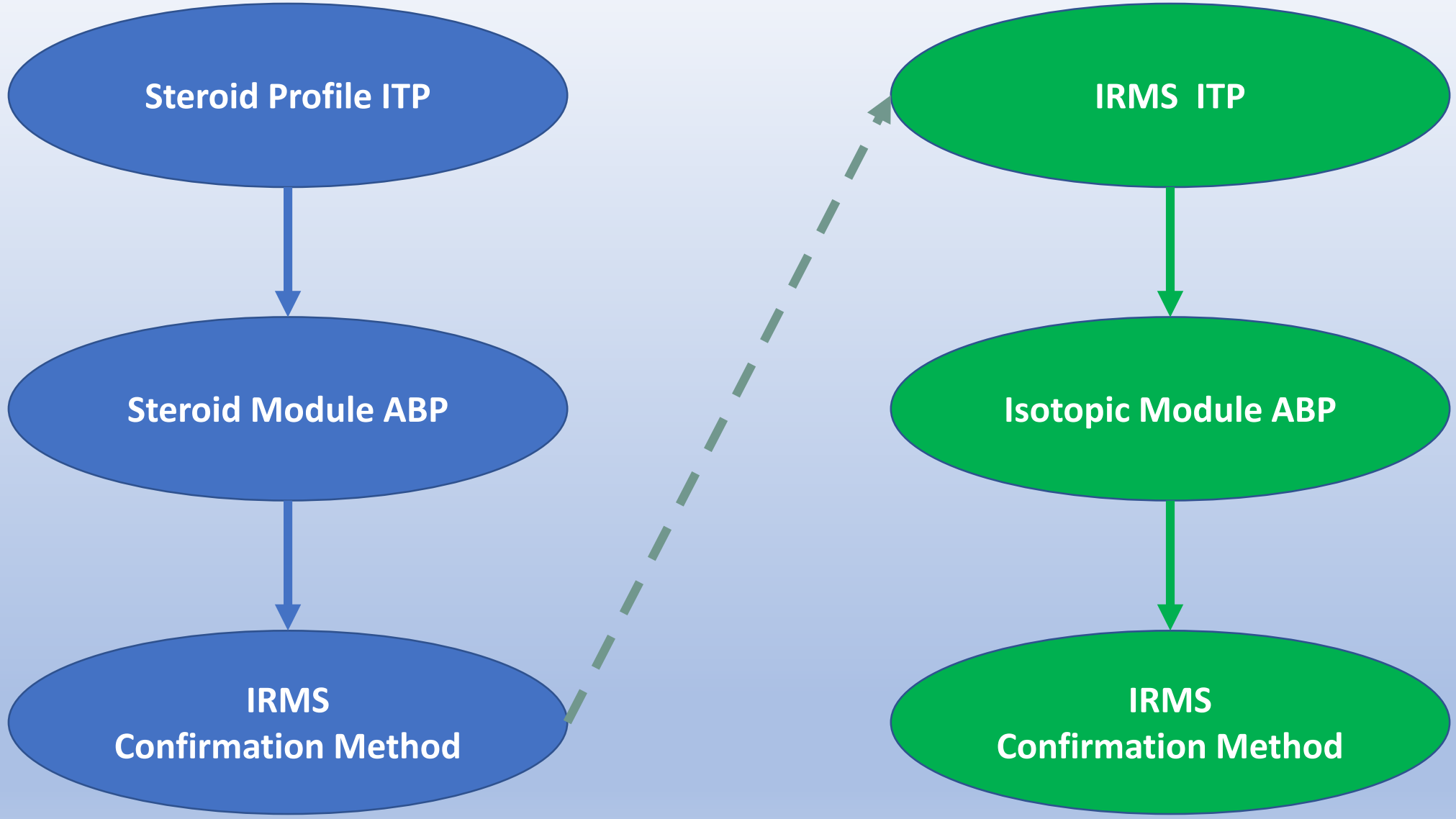
PPV = 99,999998 %

Methods comparison

Time window of detection (h)

		Methods			
	Case	WADA Lab	ABP SP module	WADA TD2016IRMS	IRMS Bayesian
Androstenedione 100 mg p.o.	1	25.5	11.5	33.5	**38.5**
	2	23.75	13.5	28.7	**37.5**
	3	32	15	54.0	**59.5**
T gel 4 x 50 mg (every 24 h)	1	0	72 (??)	96	**> 104**

It is evident that IRMS values evaluated with a Bayesian approach, increase the sensitivity of the technique


Steroid Profile ITP
Steroid Module ABP
IRMS
Confirmation Method
IRMS ITP
Isotopic Module ABP
IRMS
Confirmation Method

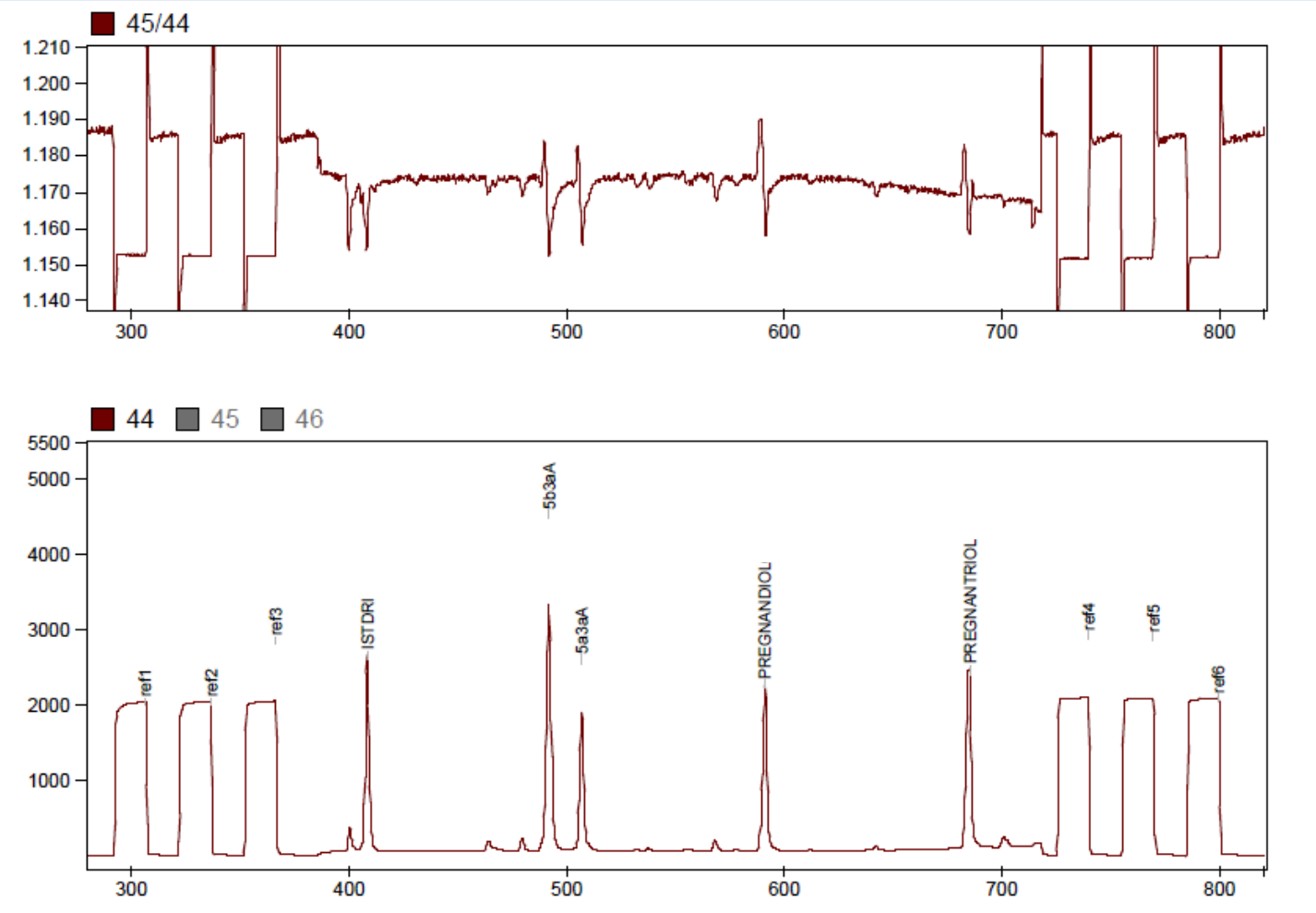
One GC/C/IRMS analysis per Sample

Positive QC

GC: Agilent 6890;
Column :
HP-5MS : 5% Phenylmethylsilicone
Injector T: 280°C
Oven program:
150°C (1')-
@25°C/min- 260°C (3')-
@ 40°C/min-310°C (2.7 min)

Injection: 2 µL Splitless

GC/C/IRMS
Thermo Delta Advantage



Run time 15' / sample

Analysis Sequence

Confirmation

Z:\RI-002\sequenze\160212.seq

Row	Peak Center	GC Method	Identifier 1	Identifier 2	Method
1	X	RI.6890	USPRI-002	1-7-8	RI.met
2	X	RI.6890	USPRI-002	2-6	RI 2-6.met
3	X	RI.6890	USPRI-002	5-9	RI 5-9.met
4	X	RI.6890	USPRI-002	3-6PT	RI 3-6PT.met
5	X	RI.6890	BURRI-003	1-7-8	RI.met
6	X	RI.6890	BURRI-003	2-6	RI 2-6.met
7	X	RI.6890	BURRI-003	5-9	RI 5-9.met
8	X	RI.6890	BURRI-003	3-6PT	RI 3-6PT.met
9	X	RI.6890	16A00561	1-7-8	RI.met
10	X	RI.6890	16A00561	2-6	RI 2-6.met
11	X	RI.6890	16A00561	5-9	RI 5-9.met
12	X	RI.6890	16A00561	3-6PT	RI 3-6PT.met
13	X	RI.6890	16A01061	1-7-8	RI.met
14	X	RI.6890	16A01061	2-6	RI 2-6.met
15	X	RI.6890	16A01061	5-9	RI 5-9.met
16	X	RI.6890	16A01061	3-6PT	RI 3-6PT.met
17	X	RI.6890	16A01075	1-7-8	RI.met
18	X	RI.6890	16A01075	2-6	RI 2-6.met
19	X	RI.6890	16A01075	5-9	RI 5-9.met
20	X	RI.6890	16A01075	3-6PT	RI 3-6PT.met
21	X	RI.6890	16A01082	1-7-8	RI.met
22	X	RI.6890	16A01082	2-6	RI 2-6.met
23	X	RI.6890	16A01082	5-9	RI 5-9.met
24	X	RI.6890	16A01082	3-6PT	RI 3-6PT.met
25	X	RI.6890	16A01227	1-7-8	RI.met
26	X	RI.6890	16A01227	2-6	RI 2-6.met
27	X	RI.6890	16A01227	5-9	RI 5-9.met
28	X	RI.6890	16A01227	3-6PT	RI 3-6PT.met
29	X	RI.6890	MIXdCERT-CONTR	FIN	RI delta certif.met
30	X	RI.6890	MIXRI2		RI 2.met
31	X	RI.6890	MIXRI		RI.met
32		Disabled	OSSIDAZIONE 3 ORE		Ox 3h.met

PQC
NQC

5

Screening

Z:\RI-002\sequenze\2015\150525A.seq

Row	Peak Center	GC Method	Identifier 1	Identifier 2	Method
1	X	RI.6890	USPRI	1-2	RI 2.met
2	X	RI.6890	BURRI	1-2	RI 2.met
3	X	RI.6890	15L0934 15A02618	1-2	RI 2.met
4	X	RI.6890	15L0934 15A02619	1-2	RI 2.met
5	X	RI.6890	15L0934 15A02620	1-2	RI 2.met
6	X	RI.6890	15L0934 15A02621	1-2	RI 2.met
7	X	RI.6890	15L0934 15A02622	1-2	RI 2.met
8	X	RI.6890	15L0936 15A02628	1-2	RI 2.met
9	X	RI.6890	15L0936 15A02629	1-2	RI 2.met
10	X	RI.6890	15L0936 15A02630	1-2	RI 2.met
11	X	RI.6890	15L0936 15A02631	1-2	RI 2.met
12	X	RI.6890	15L0936 15A02632	1-2	RI 2.met
13	X	RI.6890	15L0936 15A02633	1-2	RI 2.met
14	X	RI.6890	15L0934 15A02634	1-2	RI 2.met
15	X	RI.6890	15L0934 15A02635	1-2	RI 2.met
16	X	RI.6890	15L0944 15A02651	1-2	RI 2.met
17	X	RI.6890	15L0944 15A02652	1-2	RI 2.met
18	X	RI.6890	15L0944 15A02653	1-2	RI 2.met
19	X	RI.6890	15L0944 15A02654	1-2	RI 2.met
20	X	RI.6890	15L0944 15A02655	1-2	RI 2.met
21	X	RI.6890	15L0944 15A02656	1-2	RI 2.met
22	X	RI.6890	15L0944 15A02657	1-2	RI 2.met
23	X	RI.6890	15L0944 15A02658	1-2	RI 2.met
24	X	RI.6890	15L0944 15A02659	1-2	RI 2.met
25	X	RI.6890	15L1011 15A02860	1-2	RI 2.met
26	X	RI.6890	15L1011 15A02861	1-2	RI 2.met
27	X	RI.6890	15L1011 15A02862	1-2	RI 2.met
28	X	RI.6890	MIXdCERT-CONTR	FIN	RI delta certif.met
29		Disabled	OSSIDAZIONE 3 ORE		Ox 3h.met

PQC
NQC

25

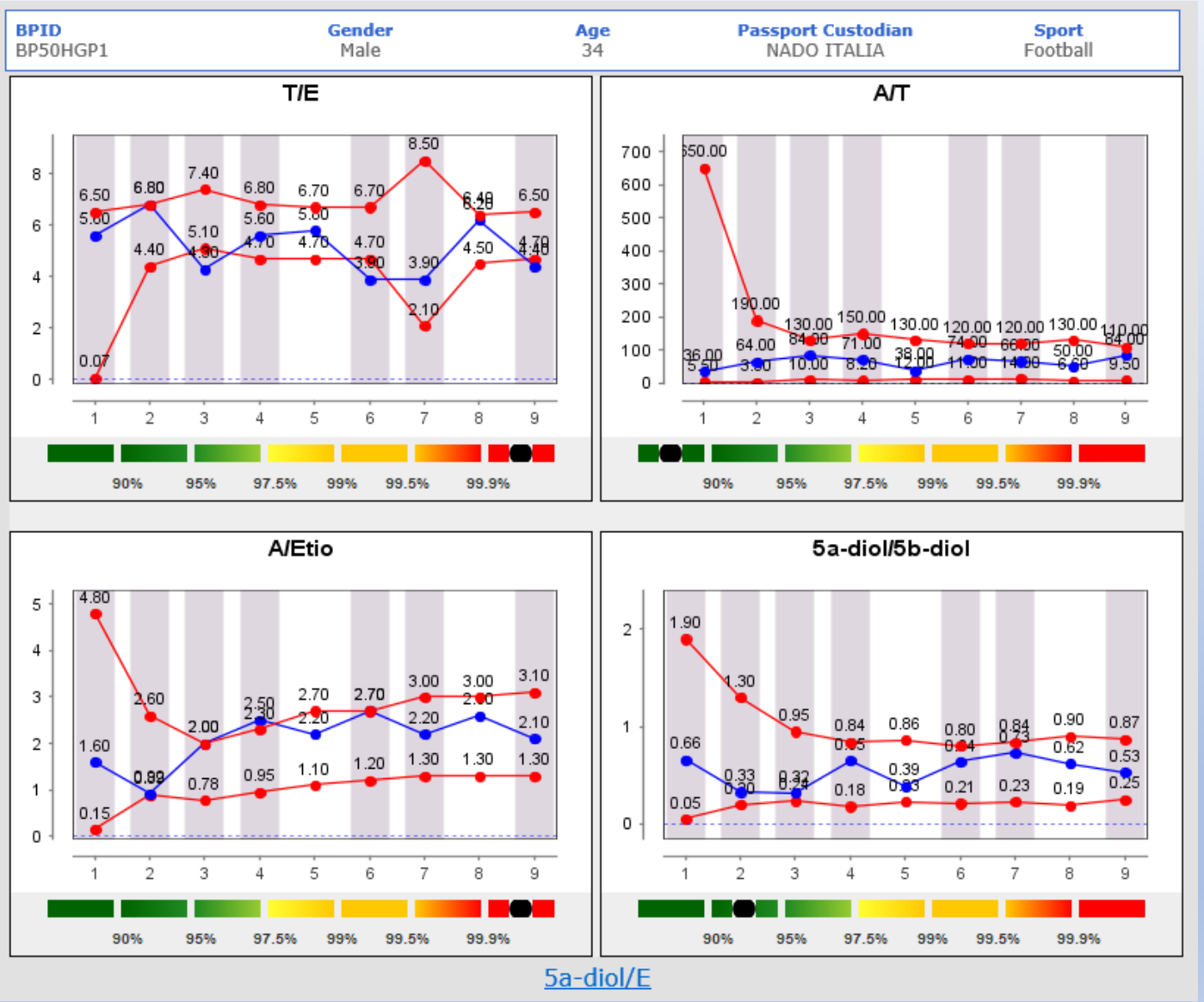
Increasing workload capacity

Step	h	
3-12 mL Urine	3	
Free fraction removal		
Hydrolysis + L/L		
HPLC / sample	0,7	1,7
4-5 Injections / sample	1	
Total time for 30 samples		54
Injections per sequence		> 120

Step	h	
6 mL Urine	2	
No Free fraction removal		
Hydrolysis + L/L		
HPLC / sample	0,3	0,6
1 Injection / sample	0,3	
Total time for 30 samples		19,4
Injections per sequence		< 35

Real passports

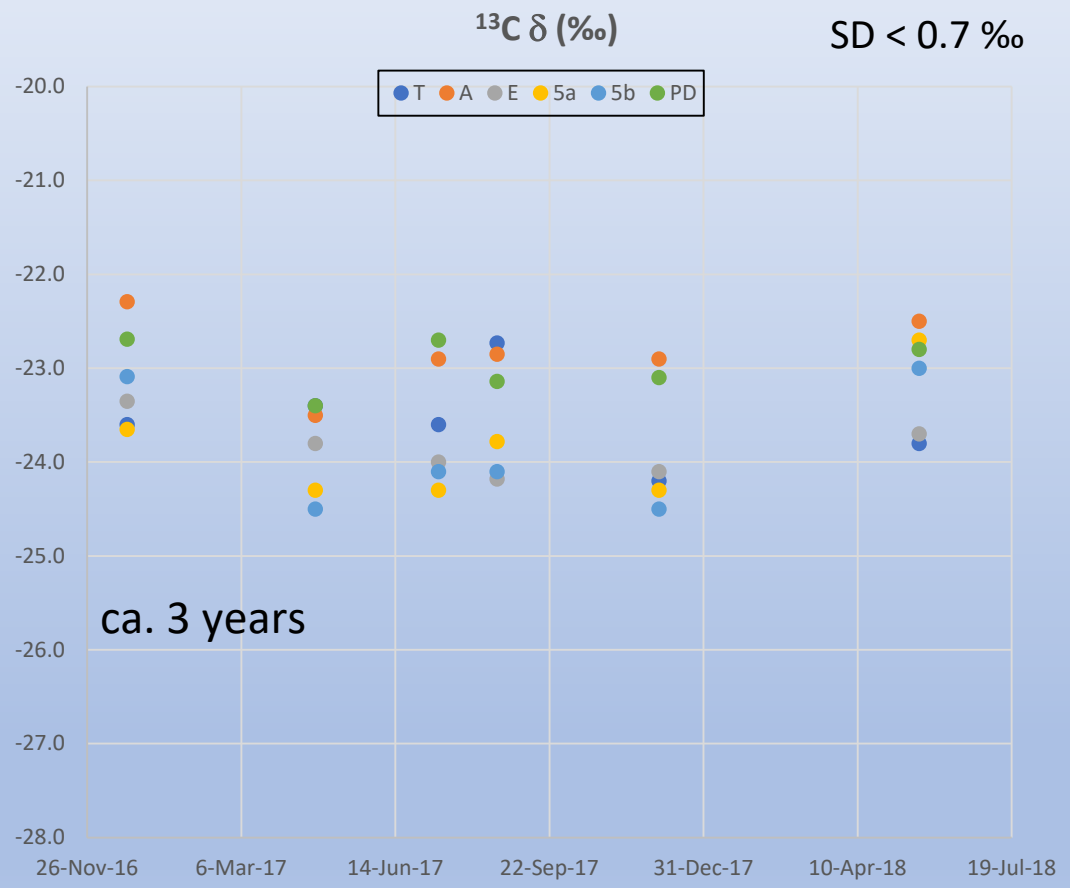
Steroid Module

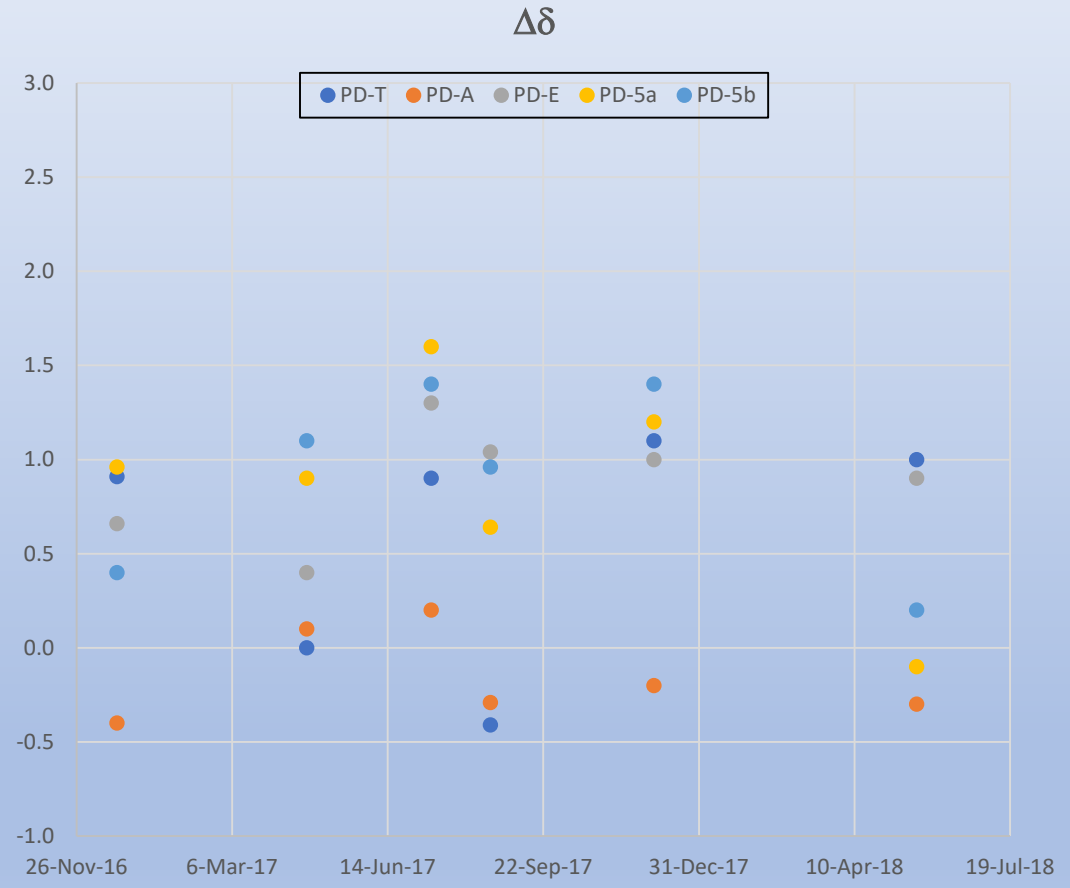


Samples collected 2015-2018

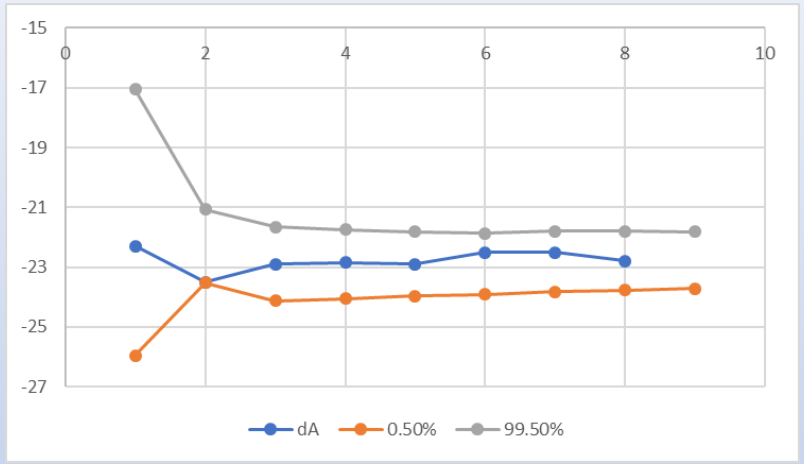
Isotopic Module

IRMS data are stable





Isotopic Module



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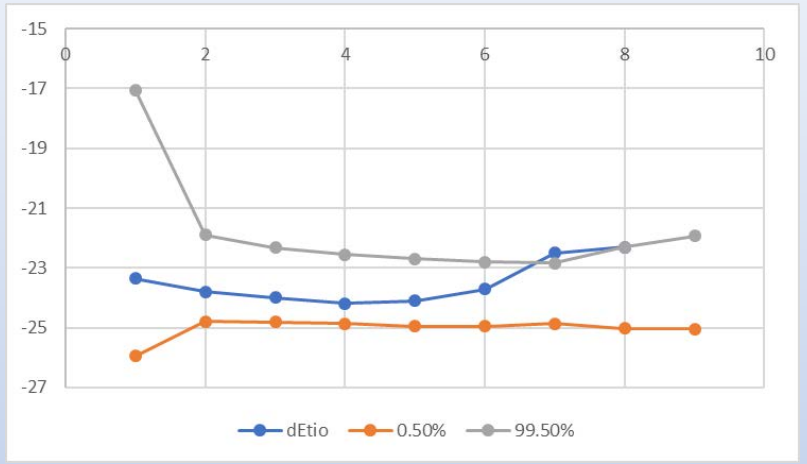

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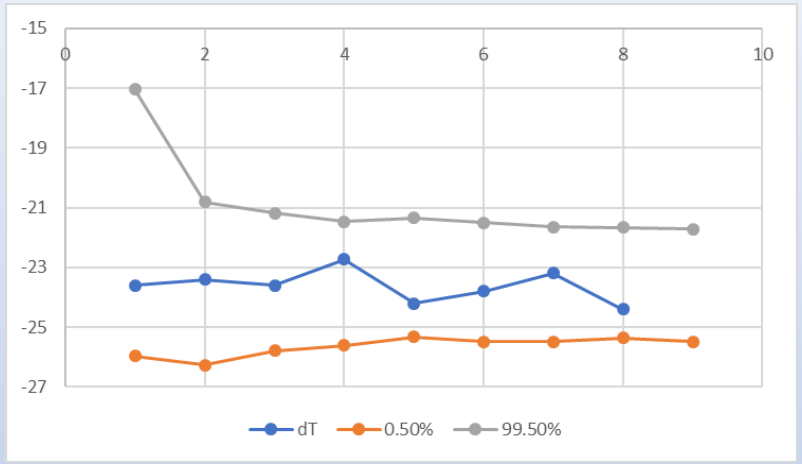

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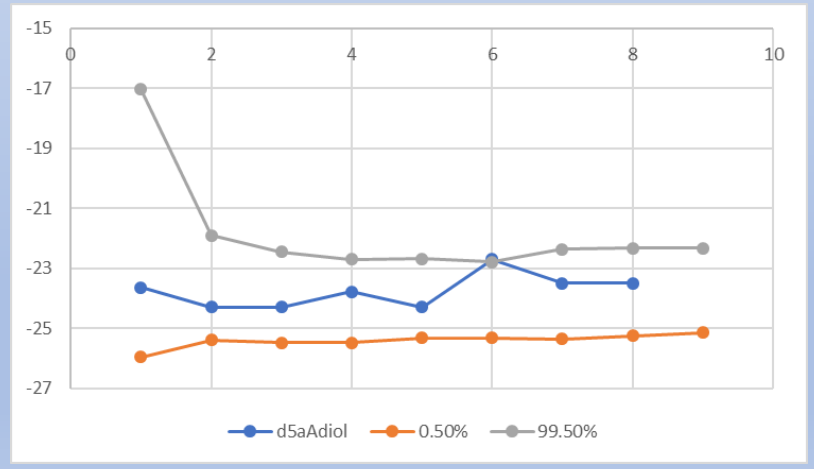
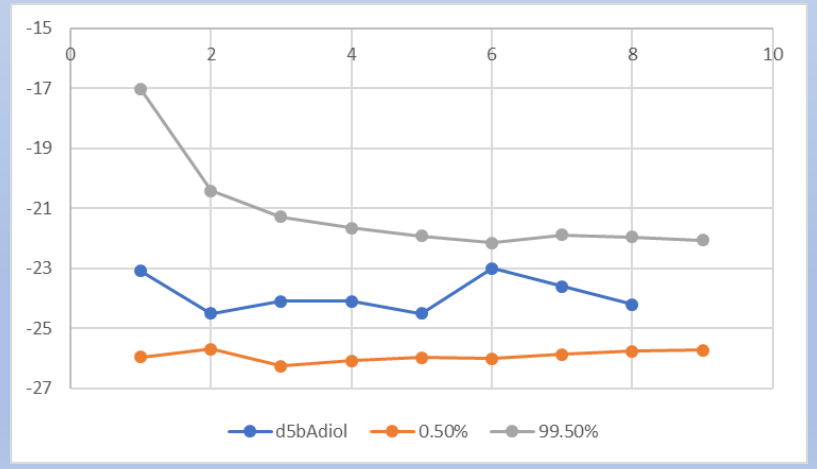


5aAdiol



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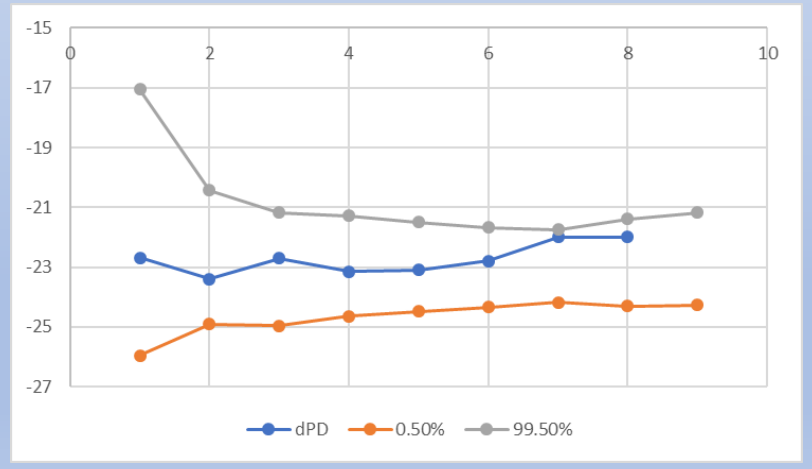
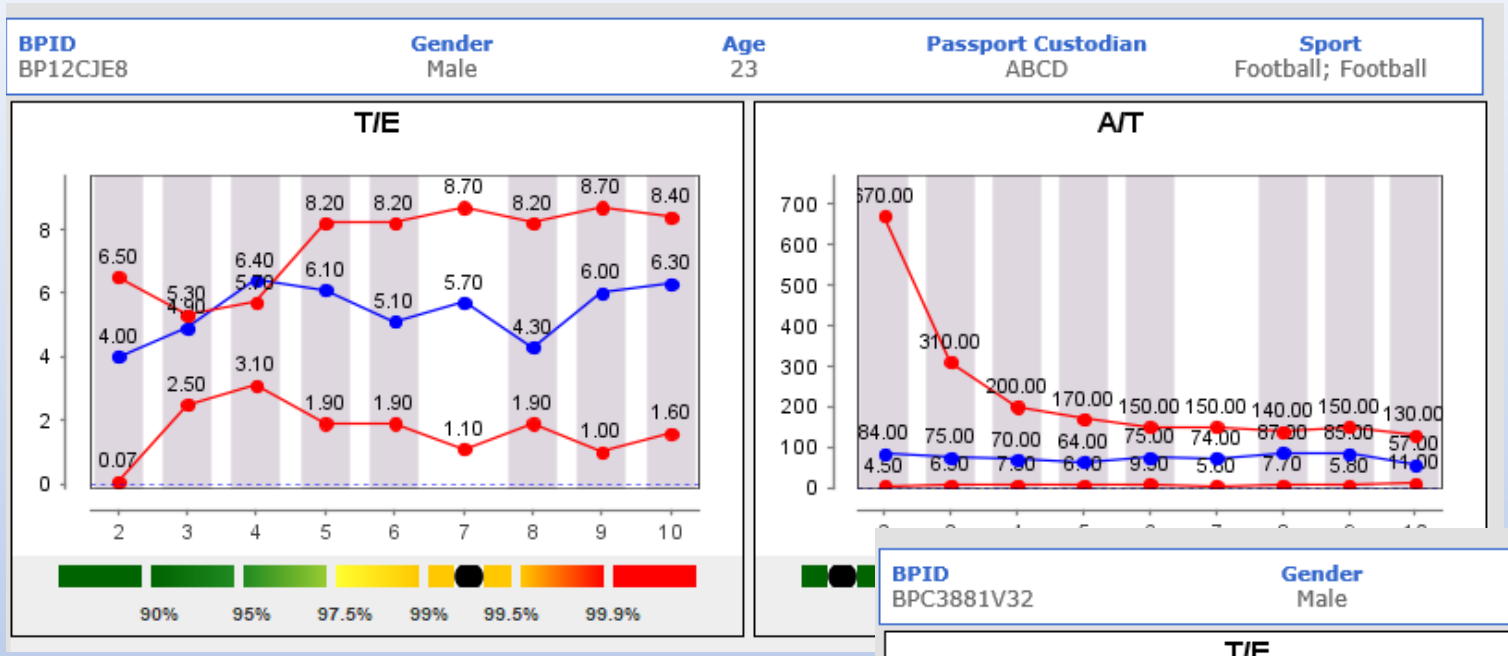
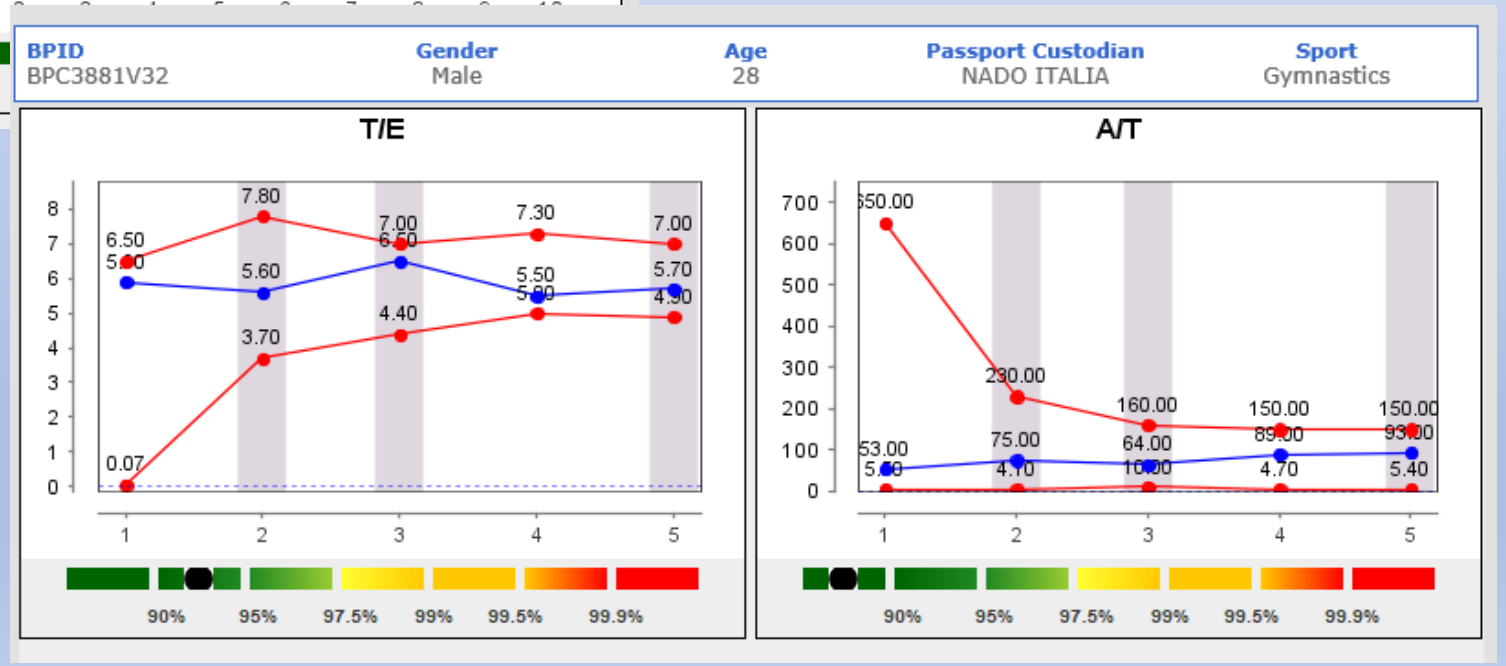


PD

Steroid Module

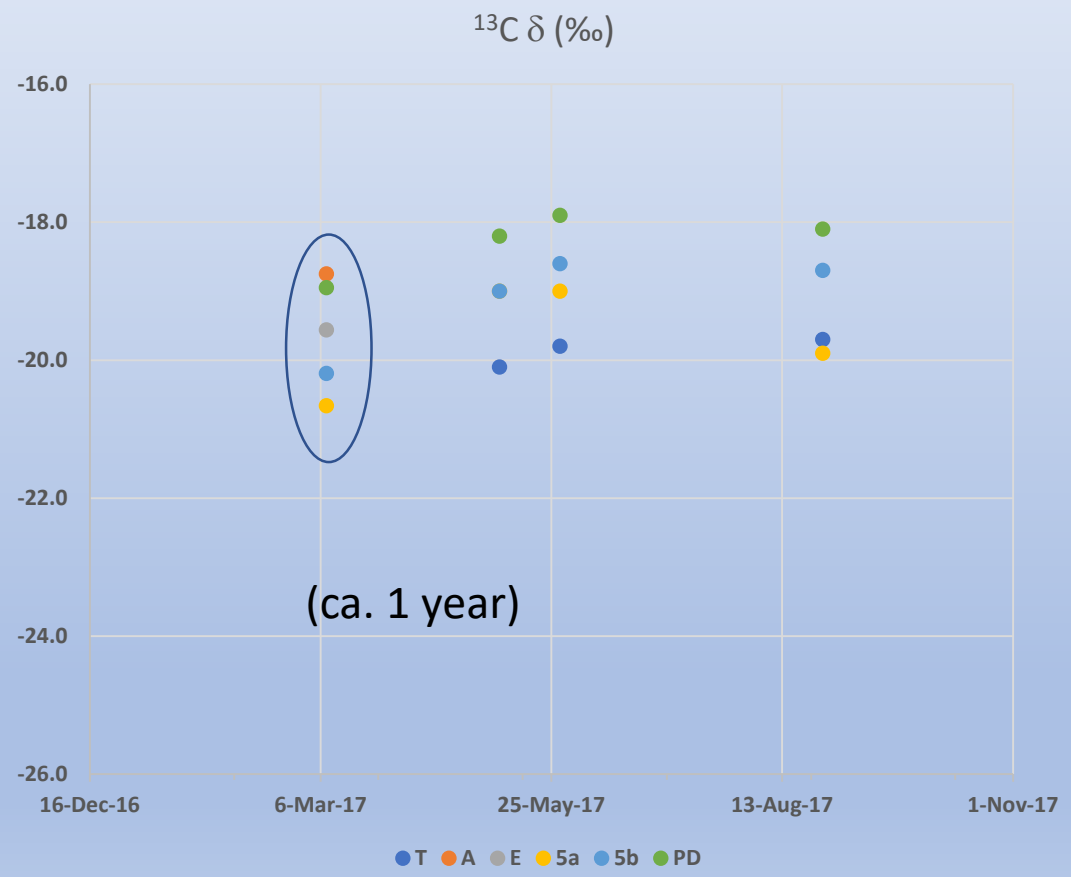


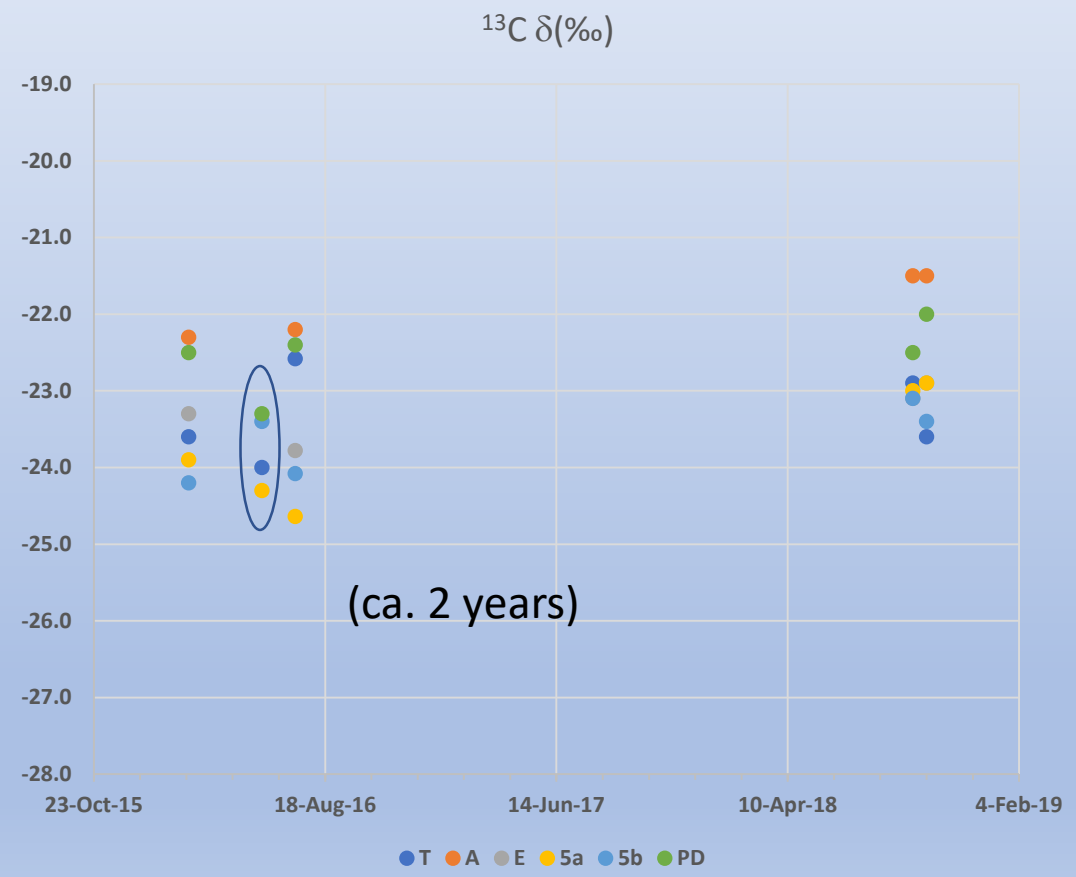


2 Laboratories involved

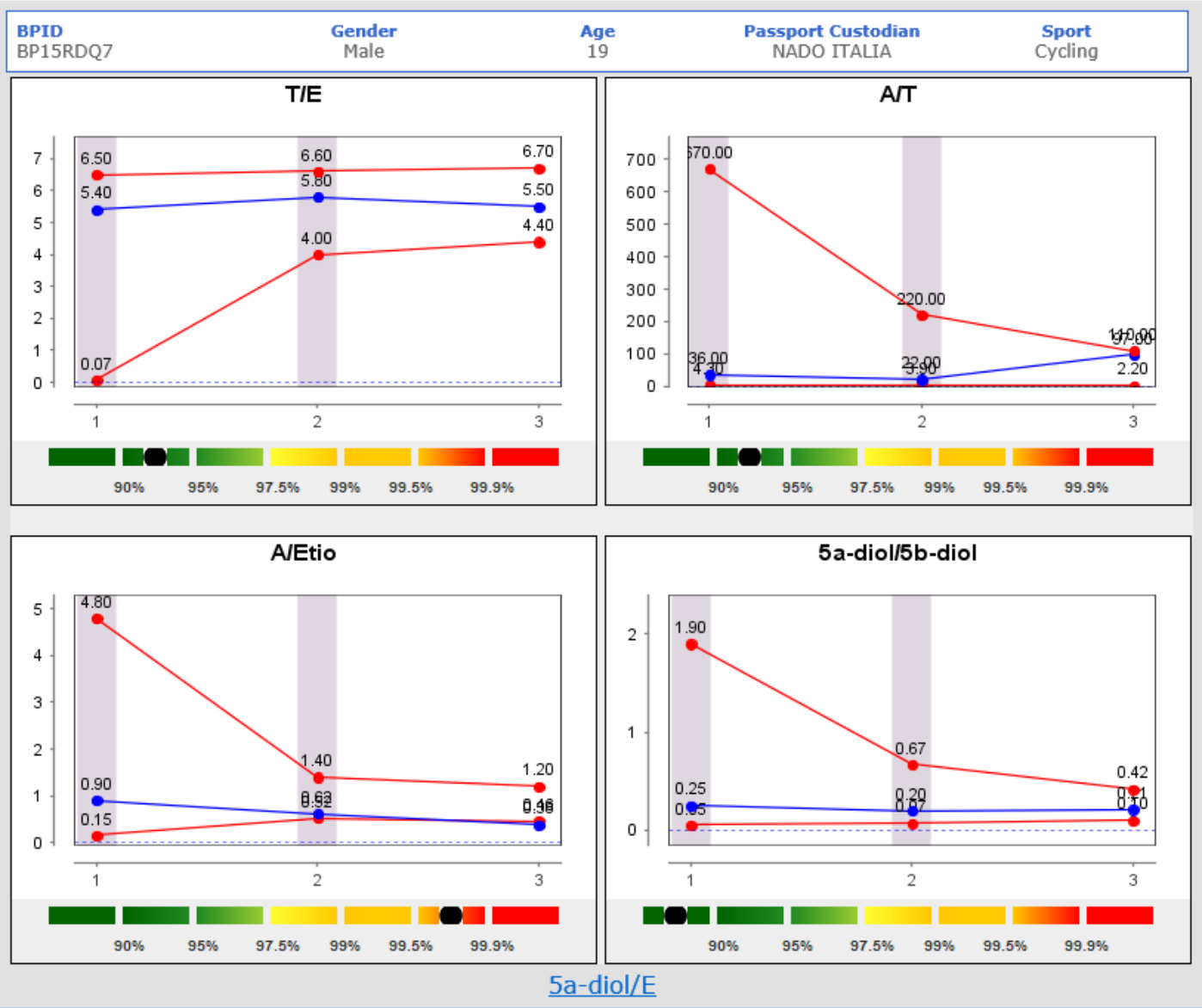
Isotopic Module

2 Laboratories involved





Steroid Module



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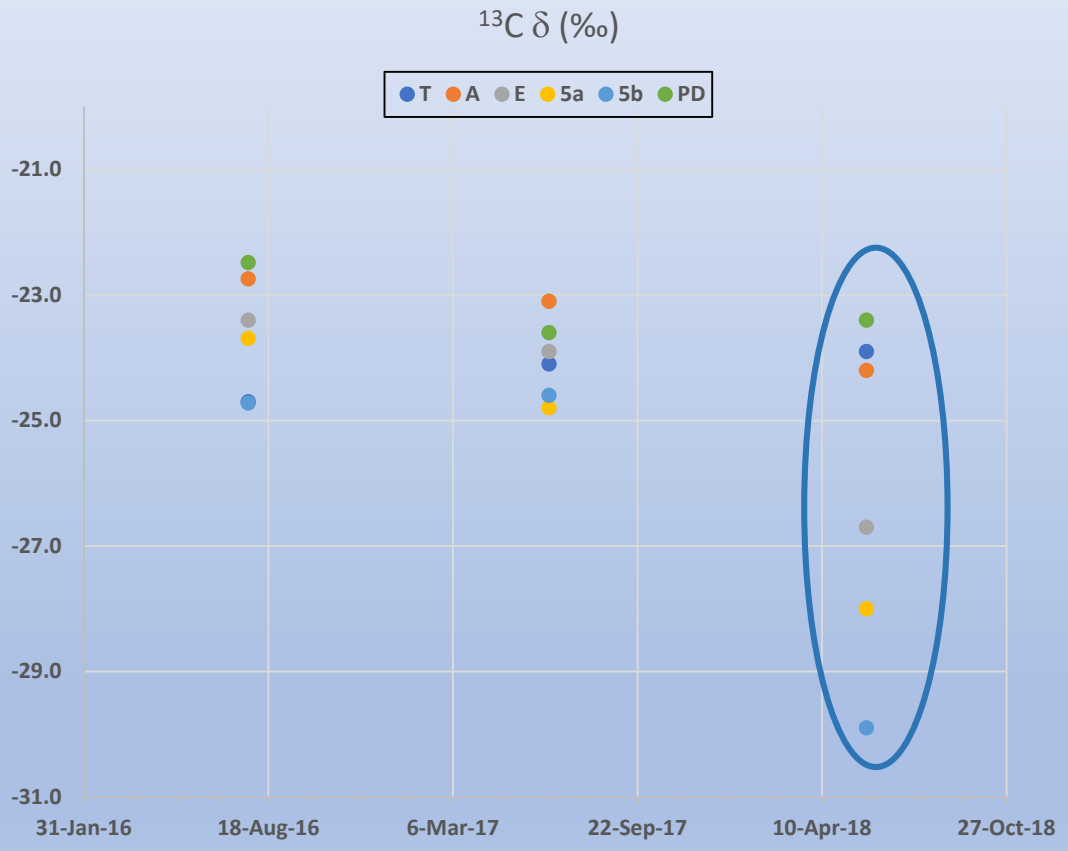

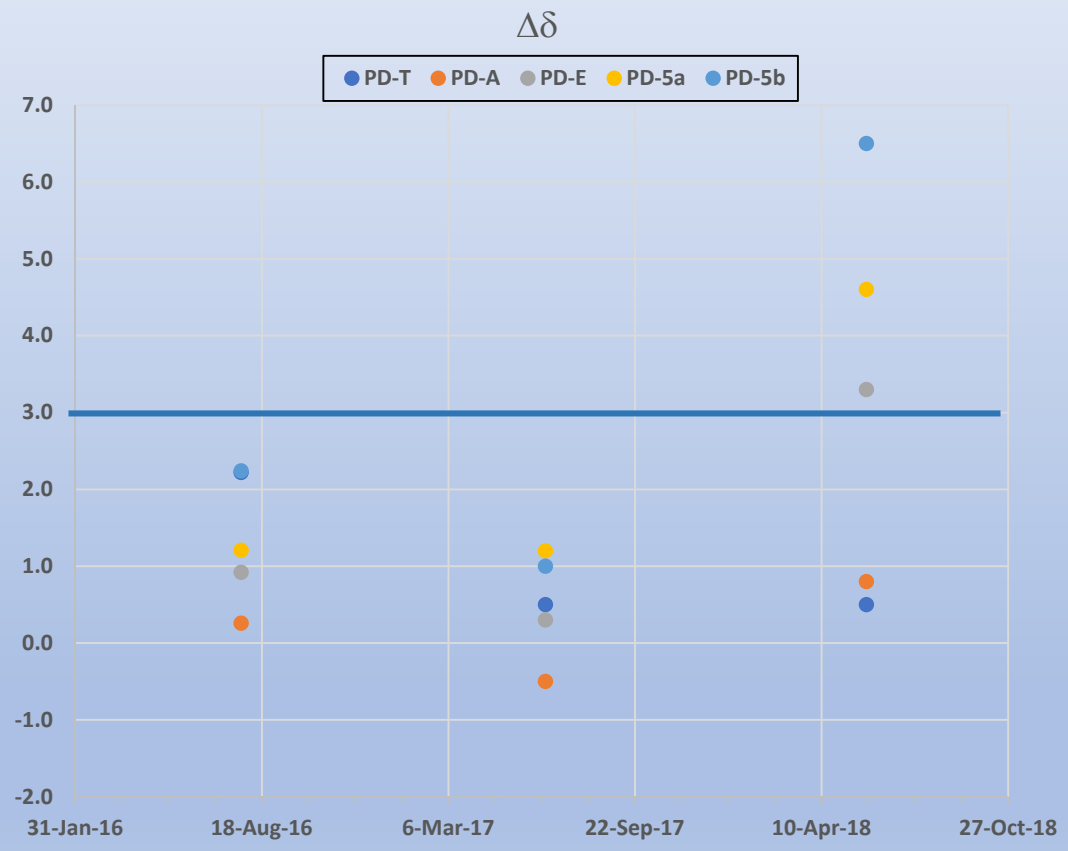

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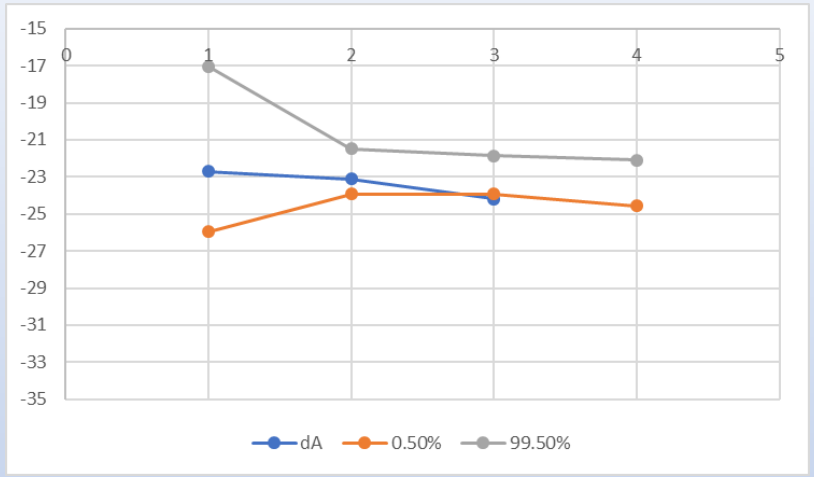

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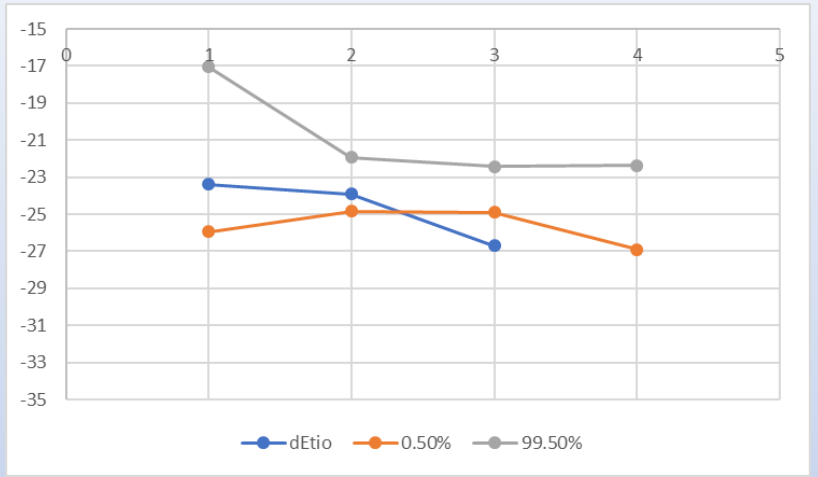

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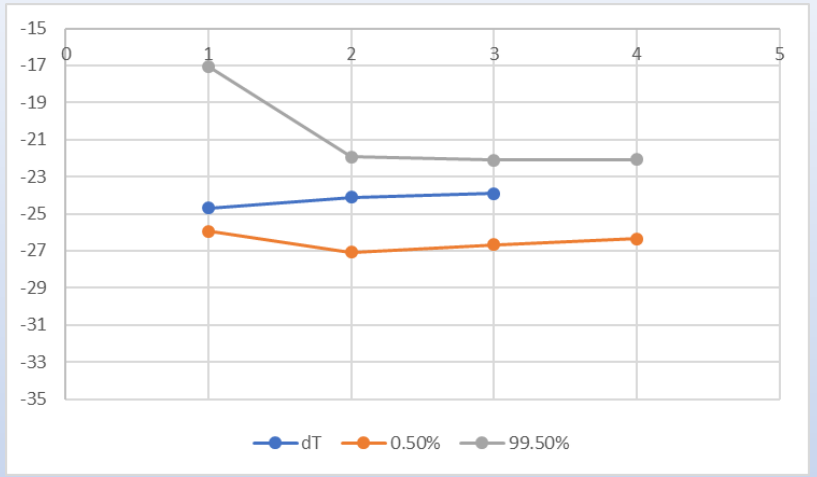

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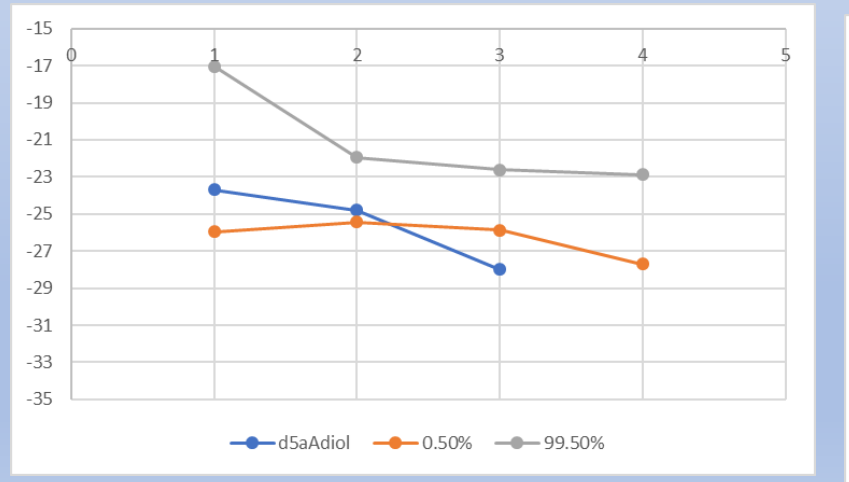

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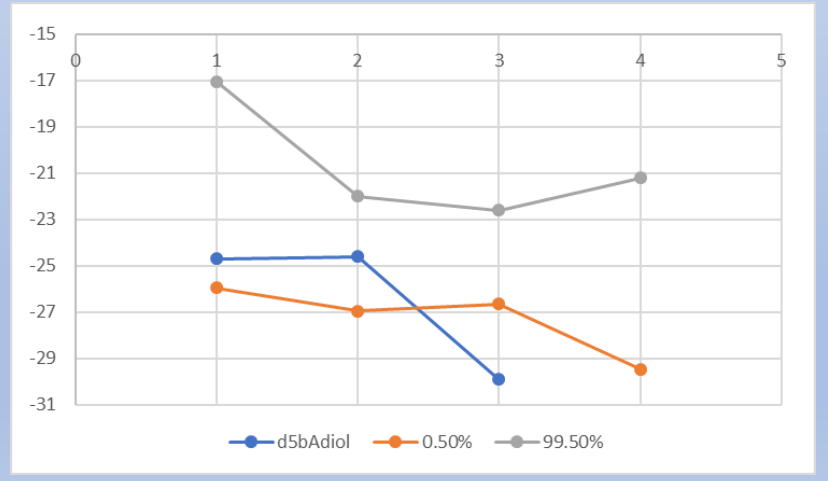

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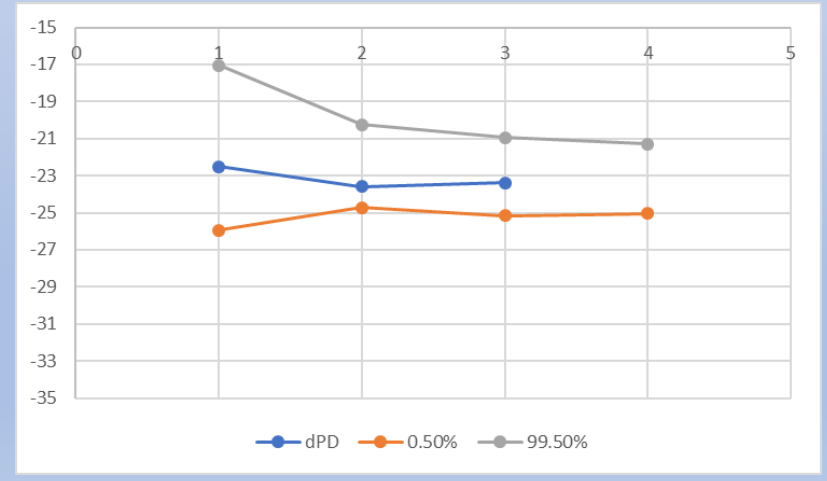

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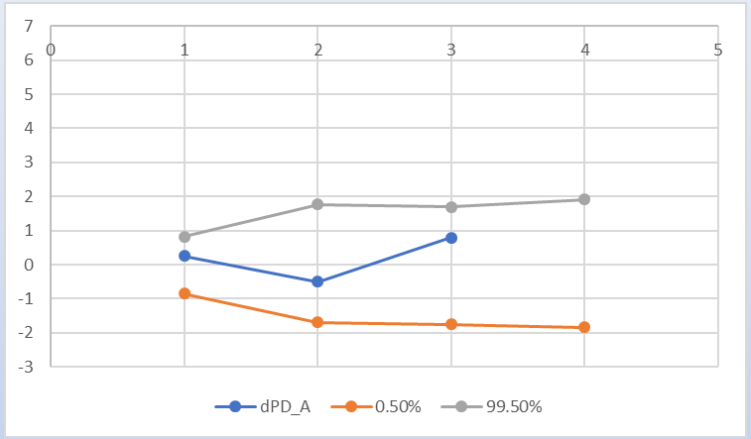
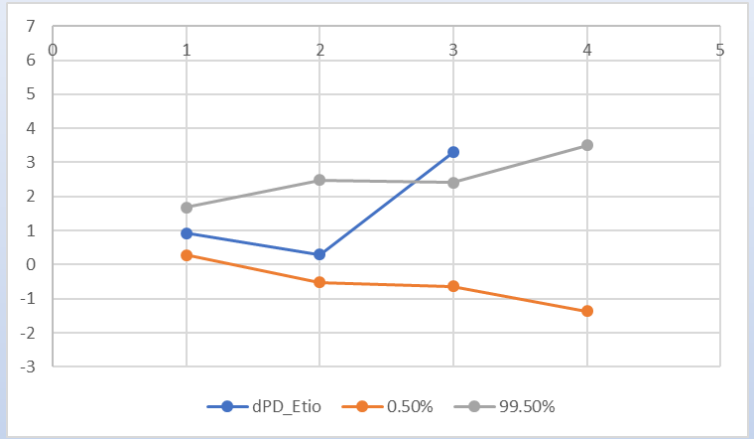
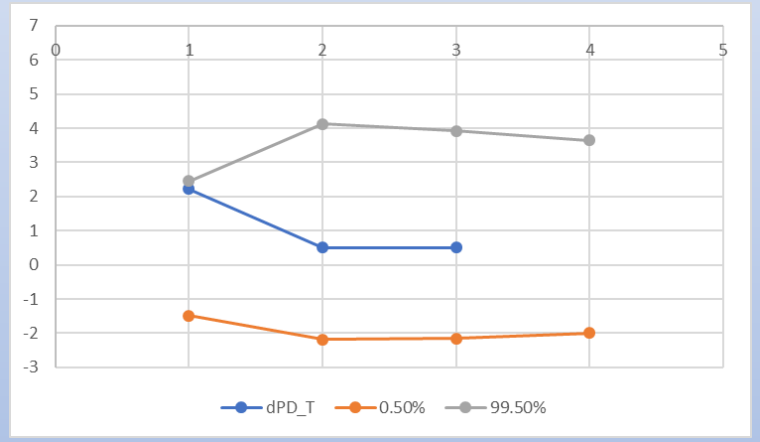
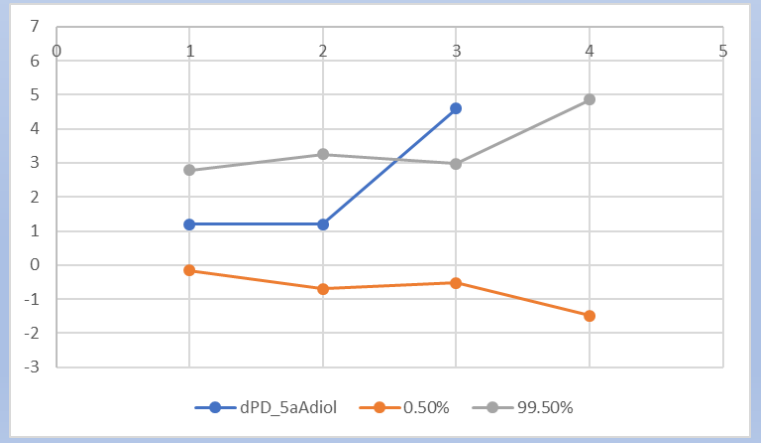
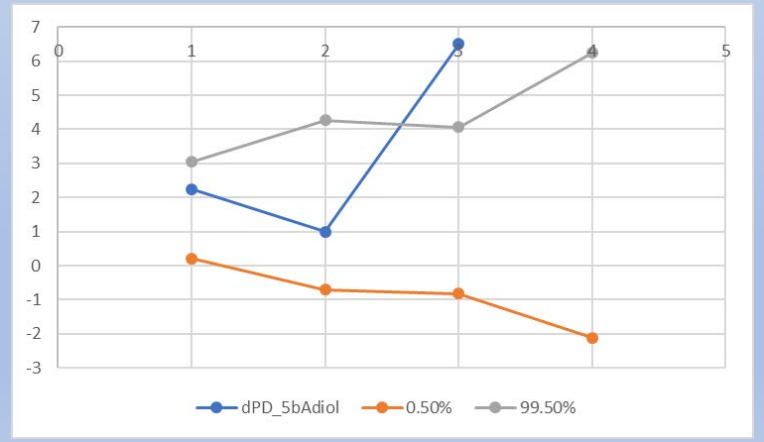
Isotopic Module



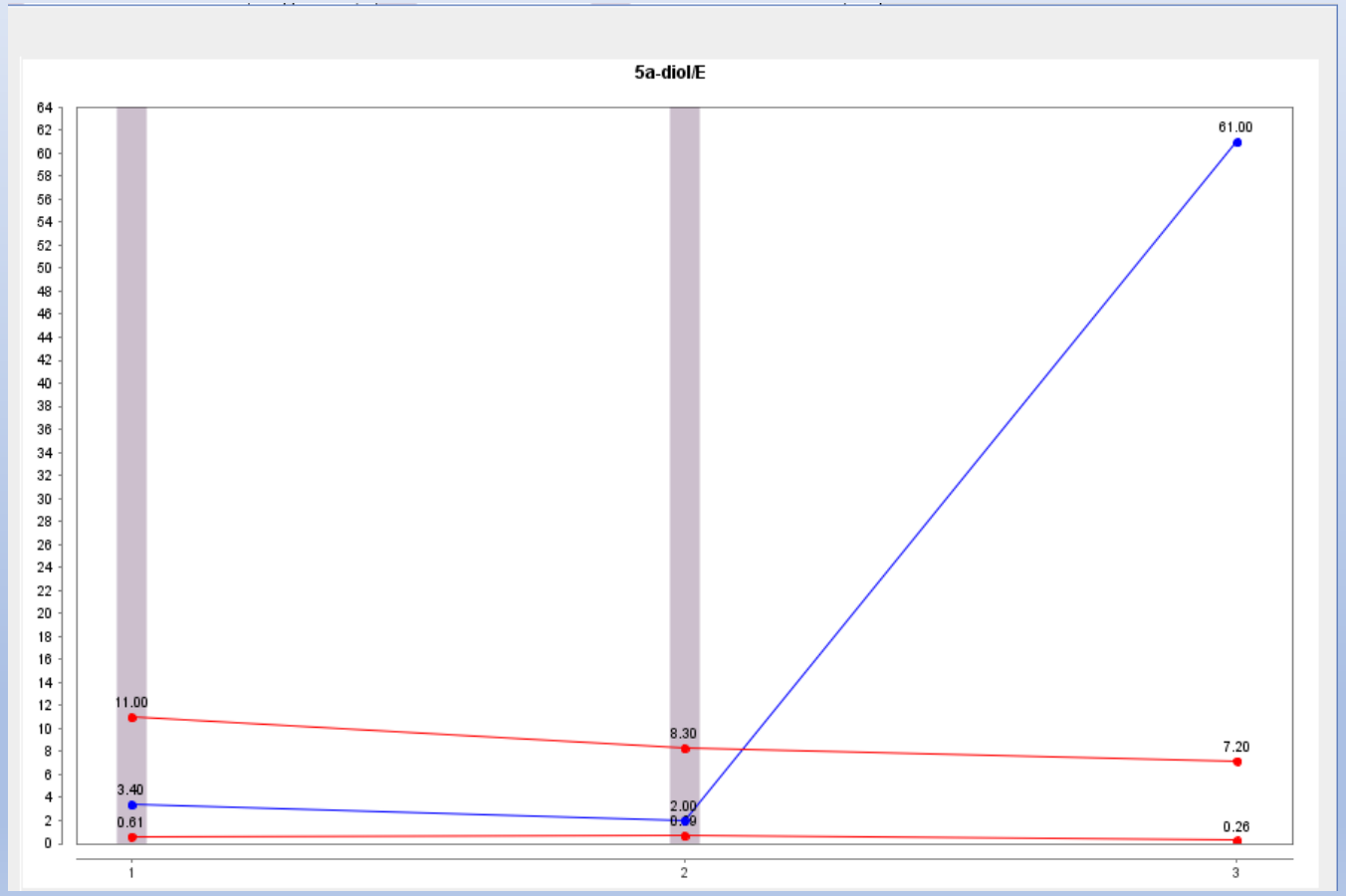








……. But the steroid module of the ABP has some additional information



Conclusions and Future Perspectives

IRMS Bayesian model:

- Improves the sensitivity for the detection of doping with pseudo endogenous steroids
- The simplicity and the same approach used for the Steroid Profile Adaptive Model should allow an easy inclusion in the Athlete Biological Passport
- The use of IRMS should be extended not only to confirmations

Future

- Greater harmonization among Laboratories is needed
- Study of potential confounding factors needed

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- My IRMS colleagues @ the Laboratorio Antidoping FMSI

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