# **APMU and IRMS cases management**

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Catalonian Antidoping Laboratory, IMIM, Barcelona

2<sup>nd</sup> IRMS Workshop, London, United Kingdom, September 2023





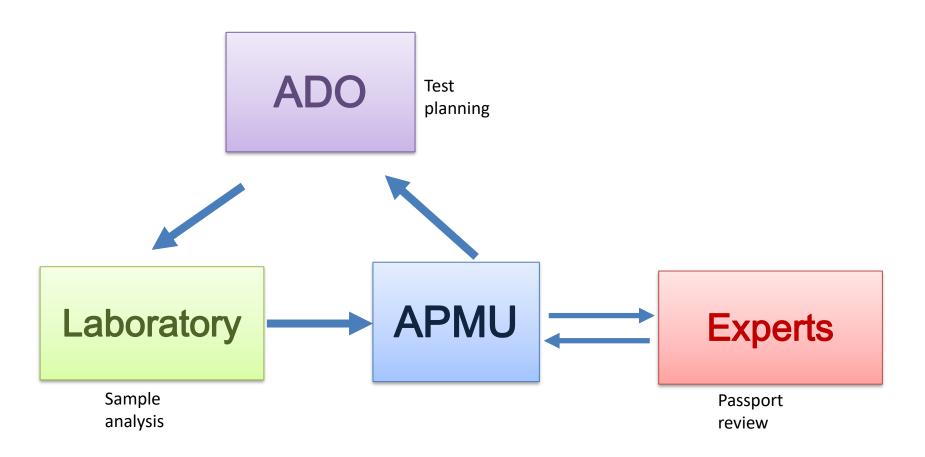
## Outline of the presentation

1. APMU inner workings

2. Management of IRMS cases



## Athlete Biological Passport



APMU (Athlete Passport Management Unit)
Administration and management of the ABP program

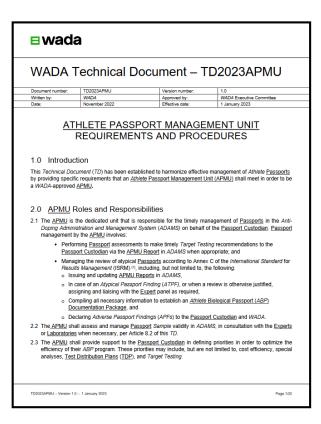


#### **APMU**

#### TD2023APMU

WADA Technical Document - Athlete Passport Management Units. Requirements and Procedures.

- Harmonize the effective management of Passports:
  - APMU roles and responsibilities
  - APMU requirements (hosting, personnel, confidentiality, security, experts panel)
  - APMU approval process
  - Maintaining WADA approval
  - Passport management



SOP BL059 : Catalonian Antidoping Laboratory APMU



## Catalonian APMU inner workings

- 1. Personnel
- 2. Confidentiality and security



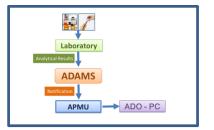
3. Expert panel

4. ADO – Passport custodian

5. Passport management

**Experts** 





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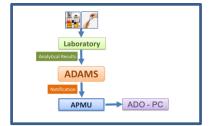
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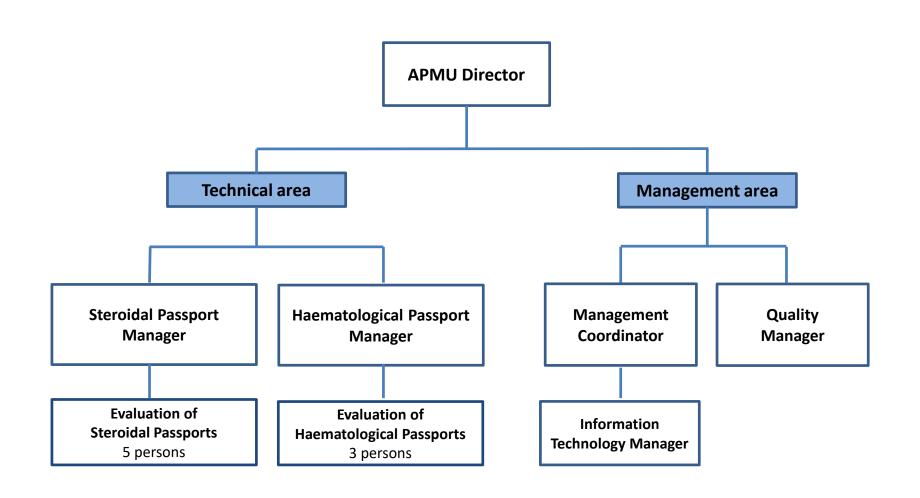


#### **APMU Personnel**

- Personnel is the key in the APMU work:
  - Highly trained individuals
  - Knowledge of analytical methods
  - Scientific expertise relevant to passport review
  - Research activity relevant for ABP
  - Experience in QA/QC programs
  - Knowledge retention: long-term stability of APMU quality



## APMU personnel - Organization Chart



# APMU Personnel – internal qualification

#### **Candidates for qualification**

- Expertise in WADA accreditation, ISO17025 accreditation
- Minimum experience of 2-3 years in anti-doping science
- Good understanding of the objectives of the ABP
- Knowledge of analytical methods:
  - Steroidal module: analysis of steroid profile, GC/C/IRMS
  - Haematological module: analysis of haematological parameters, analysis of ESAs, detection of homologous blood transfusions
  - Endocrine module: GH Biomarkers test, GH Isoforms method
- Participation in research projects relevant for ABP:
  - Detection of endogenous anabolic steroids use
  - Metabolism of anabolic steroids
  - Confounding factors of steroidal or haematological passports

#### RESEARCH ARTICLE

WILEY

RESEARCH ARTICLE

WILEY

#### Effect of glucocorticoid administration on the steroid profile

Sergi  $Coll^{1,2}$   $\boxed{0}$  | Xavier Matabosch<sup>1</sup> | Lorena Garrostas<sup>1</sup> | Clara Perez-Maña<sup>3,4</sup> | Rosa Ventura<sup>1,2</sup>

Abstract

The effect of tea consumption on the steroid profile

<sup>1</sup>Catalonian Anti-Doping Laboratory, Doping Control Research Group, IMIM, Hospital del Mar, Barcelona, Spain

Abstract

<sup>1</sup>Catalonian Anti-Doping Laboratory, Doping Control Research Group, IMIM, Hospital del Mar. Barcelona, Spain

The steroid profile (SP) is a powerful tool to detect the misuse of endogenous anabolic andro-

# APMU Personnel – internal qualification

#### **Step 1: Demonstration**

- Documentation: SOPs BL059, TD2021APMU, (TD2021EAAS), ADEL ABP Guide, ABP Operating Guidelines
- Theoretical sessions on ABP and ABP modules
- The Manager shows the candidate how to evaluate the passports:
  - ADAMS system access
  - Demonstration of the passport evaluation in ADAMS
  - Criteria of evaluation



#### **Step 2: Training**

- The candidate performs the evaluation of passports under the supervision on the manager.
- The candidate prepares the APMU reports that are, then, submitted by the manager after review.



#### **Step 3: Evaluation of the candidate**

- Test: evaluation of passports of different complexity.
- If the evaluation is correct -> qualification to evaluate passports.





# APMU Personnel – additional training

- WADA training
- ADEL training (webminars and courses)
- APMU Newsletters (WADA)
- Training in other APMUs
- ABP Symposiums
- Conferences
- Scientific literature



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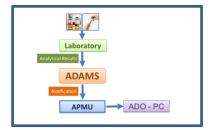
3. Expert panel

4. ADO – Passport custodian

5. Passport management

**Experts** 





# **APMU Confidentiality and Security**

#### Confidentiality:

- Signature of the WADA APMU Code of Ethics
- Signature of Code of Ethics for Laboratories



#### Security:

- APMU located in the facilities of the Laboratory
   Access restricted to laboratory personnel (electronic control)
- APMU data: stored in an APMU specific folder of the data server of the Laboratory

Access restricted to APMU personnel

 Access to the APMU specific folder through a remote desktop using username and password for identification.



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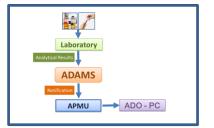
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**Experts** 





#### **APMU Expert Panel**



- APMU dedicated email account: <u>catalonianapmu@imim.es</u>
- Ensure timely evaluation (1-2 days):
  - The Experts inform of the periods they will be unavailable (holidays,...)
  - Communication via email of new passports review requests
- Review of passports:
  - Equitable allocation of passports between Experts
  - Expert review of suspicious and also normal passports
- Fluid communication with experts is important:
  - During the whole process: review of passports, preparation ABP Doc Pack, ...
  - APMU doubts in Expert reports, validity of samples,...

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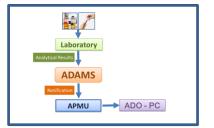
Expert panel

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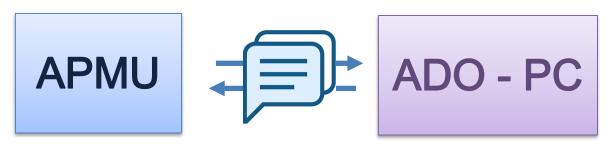
5. Passport management

**Experts** 





#### Passport custodian



- APMU dedicated email account: <u>catalonianapmu@imim.es</u>
- APMU -> PC:
  - APMU inner workings
  - Changes in TD (APMU, EAAS,...)
  - Doubts in APMU reports
  - Invalid samples
  - Additional information (competition schedule, altitude schedule, TUE...)
  - Possible typing errors in results,...
- PC-> APMU:
  - Information relevant for the evaluation of the Passport (investigation)

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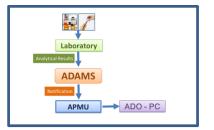
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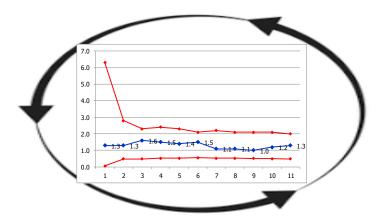
5. Passport management

**Experts** 





- a. Evaluation of Passports
- b. APMU report
- c. Follow-up of Passports with recommended actions





#### a. Evaluation of passports

- > Evaluation of passports: Guarantee timely evaluation
  - Daily evaluation (response in 1-3 days)
    Every day one person performs evaluation; normally, 2 persons involved/week per module
  - Personalized ADAMS accounts
  - Control of passports evaluated (e.g. notifications per day, per PC)
  - Evaluation of all Passports (normal and atypical)
  - APMU reports of suspicious Passports always submitted by Manager
- Periodical meetings (weekly) with Managers and Director:
  - Difficult cases: suspicious samples and Adverse Passport Findings
  - New patterns: agreed evaluation; wordings for APMU report
  - Number of passports evaluated
  - Organization of work (e.g. increase the number of evaluators)
  - Improvements in the process of evaluation/management of passports
  - External news: updates in TDs, ...





#### b. APMU report

#### Format and wordings Catalonian APMU:

- Homogeneous within our APMU
- Format: Date. Sample code. Recommendation Wording.

05/05/2023 Sample 8888888

Normal

26/07/2023 Sample 9999999: Because of high T/E, SP confirmation is required including IRMS analyses.

#### Wordings:

Type of sample		APMU comment
Suspicious		
	T/E	Because of high T/E, SP confirmation is required including IRMS analyses. Please, keep this sample until further evaluation of the profile.
	T/E	BPID with high T/E. Since IRMS analyses have not been performed since 20XX, IRMS analysis on sample XXXXXX is recommended in order to demonstrate that the elevated T/E is physiologically normal.
	т	Because of T concentration higher than X ng/mL, SP confirmation is required including IRMS analyses. Please, keep this sample until further evaluation of the profile.
	A and/or Etio	Because of (A/Etio) concentration higher than 10000 ng/mL, SP confirmation is required including IRMS analyses. Please, keep this sample until further evaluation of the profile.
	5aAdiol	Because of 5aAdiol concentration higher than X ng/mL, SP confirmation is required including IRMS analyses. Please, keep this sample until further evaluation of the profile.
Negative		
	Confirmed	SP confirmation and IRMS results do not confirm the exogenous origin. Data are included in the physiological variability. The BPID is now considered normal
Others		
	SG	LR specific gravity (X) deviates from DCF value (Y). Please, confirm laboratory specific gravity.
	degradation	Sample has been automatically invalidated because of microbial degradation.
	Conf factors	Presence of confounding factors (ethylglucoronide, finasteride, ketoconazole or similar, 'others') that may alter the SP.
	5a-reduct inh	Presence of 5a reductase inhibitors which are altering the alpha pathway of the endogenous steroids metabolism. This athlete should be tested on a regular basis.

A/Etio and 5aAdiol/5bAdiol are coherent with 5a-reductase since (...). However, this confounfing factor has not been reported by the lab.

#### c. Follow-up of passports

- Excel sheet to follow-up the Passports with recommended actions
- Follow-up of Steroidal Passports:

	Núm passaport BPID	Codi mostra	Motiu del seguiment	Persona 1a revisió	Data 1a revisió	Seguiment 1	Seguiment 2
•	xxxxxxxx	ууууууу	28/06/2022 Sample yyyyyyy: Because of high T/E, SP confirmation is required including IRMS analyses.	SCC	28/06/2022	29/07/2022 Sample yyyyyyy: SP confirmation and IRMS results do not confirm the exogenous origin. Data are included in the physiological variability. The BPID is now considered normal	
V	XXXXXXXX	ууууууу	28/06/2022 Sample yyyyyyy: Because of high T/E, SP confirmation is required including IRMS analyses.	SCC	28/06/2022	29/07/2022 Sample yyyyyyy: SP confirmation and IRMS results do not confirm the exogenous origin. Data are included in the physiological variability. The BPID is now considered normal	
	XXXXXXXX	ууууууу	30/06/2022 Sample yyyyyyy: Because of high T/E, SP confirmation is required including IRMS analyses.	SCC	30/06/2022		
•	XXXXXXXX	ууууууу	01/07/2022 Sample yyyyyyy: Because of A concentration higher than 10000 ng/mL, SP confirmation is required including IRMS analyses	SCC	01/07/2022	29/07/2022 Sample yyyyyyy: SP confirmation and IRMS results do not confirm the exogenous origin. Data are included in the physiological variability. The BPID is now considered normal	
V	XXXXXXXX	ууууууу	01/07/2022 Sample yyyyyyy: Because of high T/E, SP confirmation is required including IRMS analyses.	SCC	01/07/2022	29/07/2022 Sample yyyyyyy: SP confirmation and IRMS results do not confirm the exogenous origin. Data are included in the physiological variability. The BPID is now considered normal	

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# IRMS cases management

#### Catalonian APMU activity

	2021	2022	2023 (1st semester)
IRMS confirmations requested	230	205	113

## IRMS cases management

#### Catalonian APMU activity

	2021	2022	2023 (1st semester)
IRMS confirmations requested	230	205	113
IRMS confirmations performed	85 (37 %)	84 (41 %)	51 (45 %)
SSP-CPR (1st sample)	43	32	38
Atypical BPID	42	52	13
IRMS AAFs	7 (8.2 %)	3 (3.5 %)	2 (3.9 %)
SSP-CPR (1st sample)	6	1	1
Atypical BPID	1	2	1

## IRMS cases management

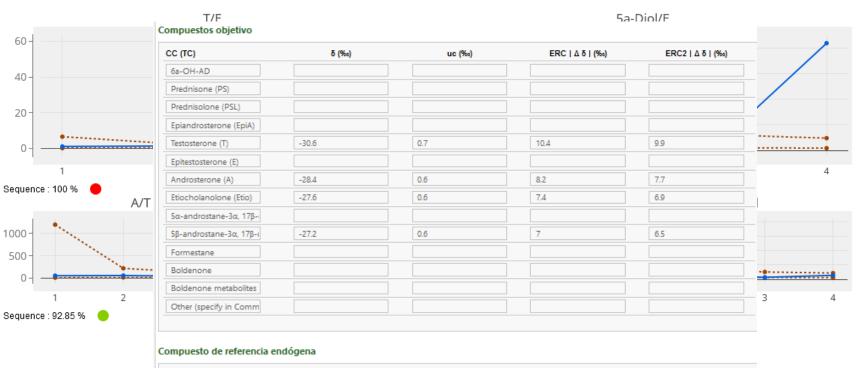
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#### Catalonian anti-doping lab IRMS activity

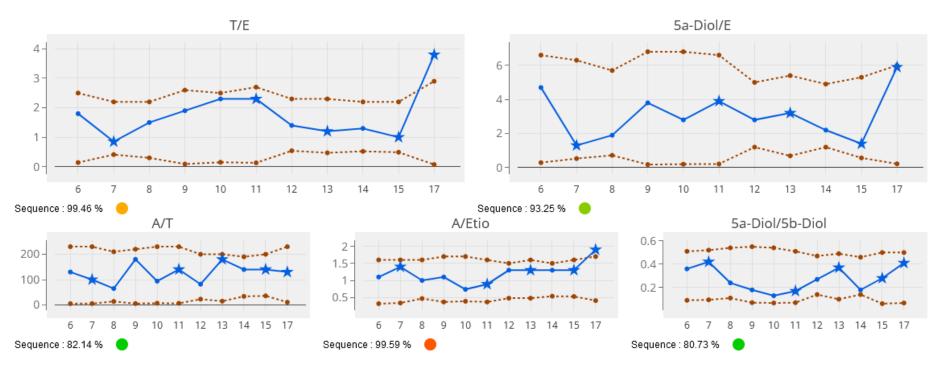
	2021	2022	2023 (1st semester)
IRMS tests (T and metabolites) conducted in our lab	192	141	104
IRMS AAFs	5 (2.6 %)	4 (2.8 %)	3 (2.9 %)

Case 1: AAF Gender: Male, 27 y/o Sport/discipline: Powerlifting



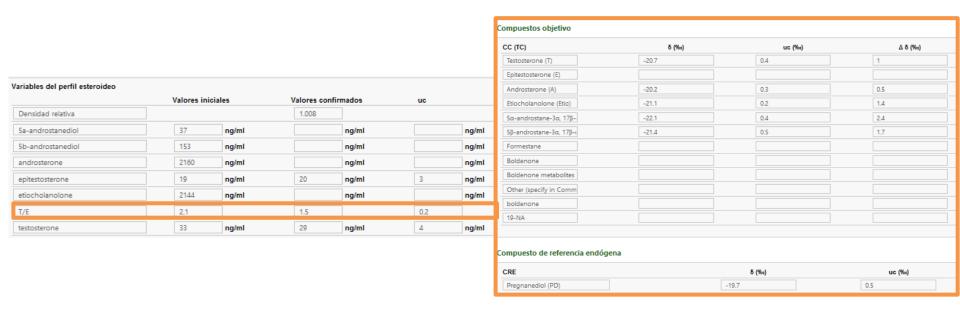
Sample	T/E	5a	CRE *	anediol (PD)			δ (‰) * -20.2		uc (9	io) *	A	Etio
4	59	2	ERC2 (p	para AAF / ATF) *			δ (‰) *		uc (9	io) *	2500	4000
3	1.5	O.	11-keto	U.35	O-Etic U.U/	42	-20.7 <b>3</b> /	21	0.6 <b>Z</b> D	330	1600	2900
2	1.5	1	.5	0.65	0.15	57	46	41	61	420	2600	4000
1	0.9	0	.9	0.70	0.15	55	21	24	21	140	1100	1600

Case 2: AAF Gender: Male, 38 y/o Sport/discipline: Athletics/Jumps

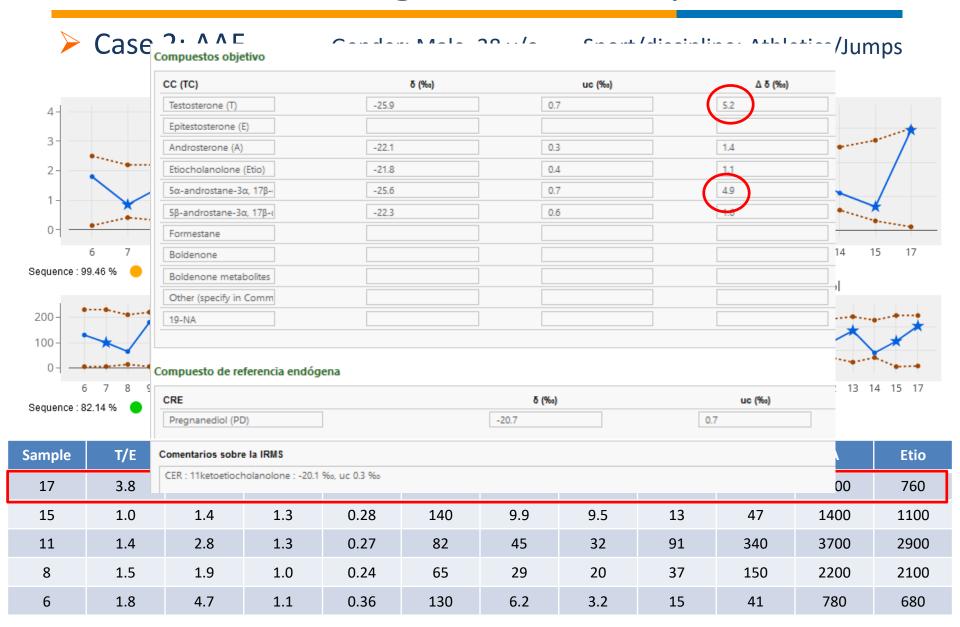


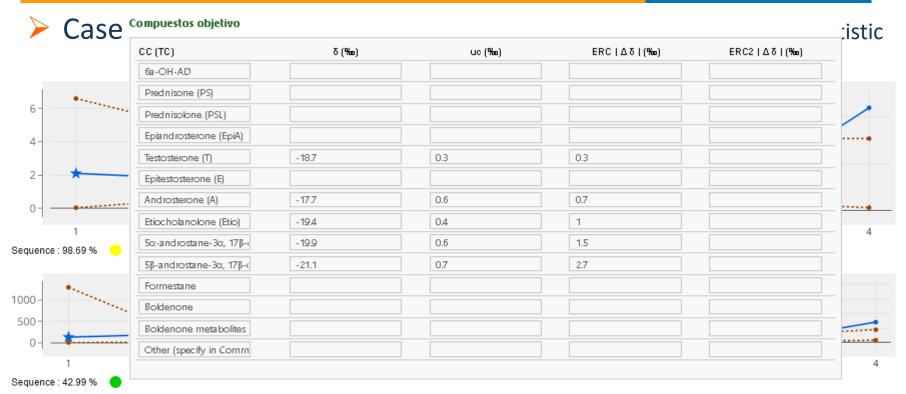
Sample	T/E	5a/E	A/Etio	5a/5b	A/T	Т	E	5a	5b	А	Etio
17	3.8	5.9	1.9	0.41	130	11	3.0	18	42	1500	760
15	1.0	1.4	1.3	0.28	140	9.9	9.5	13	47	1400	1100
11	1.4	2.8	1.3	0.27	82	45	32	91	340	3700	2900
8	1.5	1.9	1.0	0.24	65	29	20	37	150	2200	2100
6	1.8	4.7	1.1	0.36	130	6.2	3.2	15	41	780	680

Case 2: AAF Gender: Male, 38 y/o Sport/discipline: Athletics/Jumps



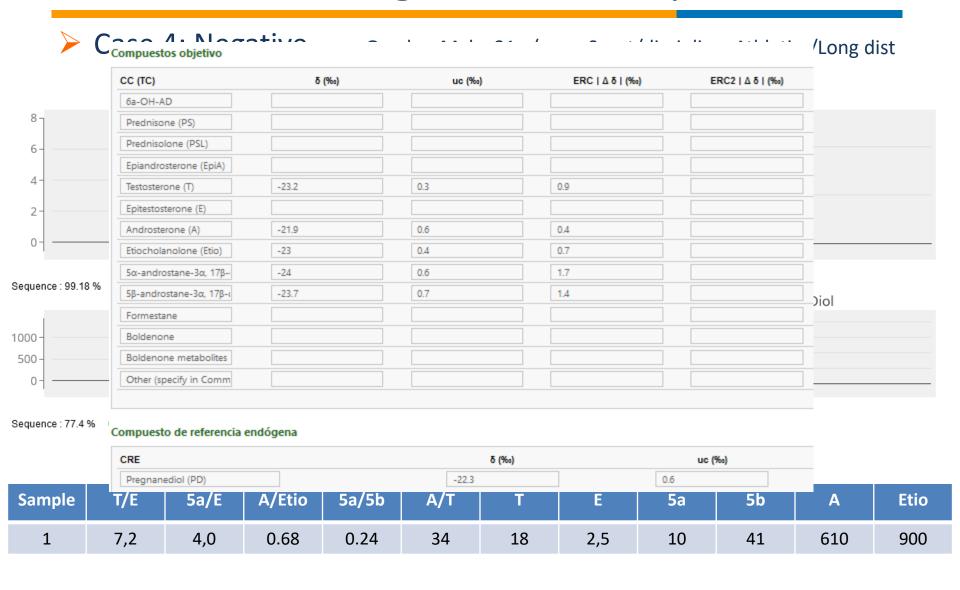
Sample	T/E	5a/E	A/Etio	5a/5b	A/T	Т	Е	5a	5b	Α	Etio
17	3.8	5.9	1.9	0.41	130	11	3.0	18	42	1500	760
15	1.0	1.4	1.3	0.28	140	9.9	9.5	13	47	1400	1100
11	1.4	2.8	1.3	0.27	82	45	32	91	340	3700	2900
8	1.5	1.9	1.0	0.24	65	29	20	37	150	2200	2100
6	1.8	4.7	1.1	0.36	130	6.2	3.2	15	41	780	680





#### Compuesto de referencia endógena

Comple	CRE					δ (%	o)		Falls					
Sample	T/E	Pregnanediol (PD)		Pregnanediol (PD)		Pregnanediol (PD)		Pregnanediol (PD) -184		C	).6		Etio	
4	4.0	11	0.92	0.70	240	10	3.0	32	46	2400	2600			
3	1.4	3.0	0.82	0.30	220	14	10	31	100	3000	3600			
2	1.8	4.1	0.71	0.17	180	15	8.7	36	220	2800	4000			
1	2.1	2.8	0.48	0.10	130	8.3	3.9	11	110	1100	2200			



#### Conclusions

- Timely evaluation of passports requires good organization within APMU
- Guarantee expertise of staff and training
- Knowledge retention
- Good communication with Experts and Passport Custodians
- TA should always follow APMU recommendations



