

Pharmacological aids to Performance: challenges of the prohibited list

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IMIM- Hospital del Mar Medical Research Institute, Barcelona
Chair, IPC Anti-Doping Committee



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1.- Doping: Treating vs Eating

2.- Drugs and more: *The Prohibited List*

3.- Enforcement: Testing

- Analytical approach
- TDSSAs

4.- Food: *Supplements*

5.- Regulations: Athlete Support Personnel

1. Doping: Treating vs Eating

- “**Anti-doping rules**, like competition rules, are sport rules governing the conditions under which sport is played” (World Anti-doping Code 2015).
- What do these AD rules say?: Doping is prohibited !
- What is Doping?
 - **Conceptual Definition**
“use pharmacological aids to improve performance”: *The Prohibited List*



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1. Doping: Treating vs Eating

- **Structure of the Prohibited List**

Substances and Methods Prohibited at all times

- S0. Non-Approved Substances
- S1. Anabolic Agents
- S2. Peptide Hormones, Growth Factors, Related Substances and mimetics
- S3. Beta-2 Agonists
- S4. Hormone and Metabolic Modulators
- S5. Diuretics and Masking Agents

- M1. Manipulation of Blood and Blood Components
- M2. Chemical and Physical Manipulation
- M3. Gene Doping

Substances Prohibited In Competition

- S6. Stimulants
- S7. Narcotics
- S8. Cannabinoids
- S9. Glucocorticoids

Substances Prohibited in Particular Sports

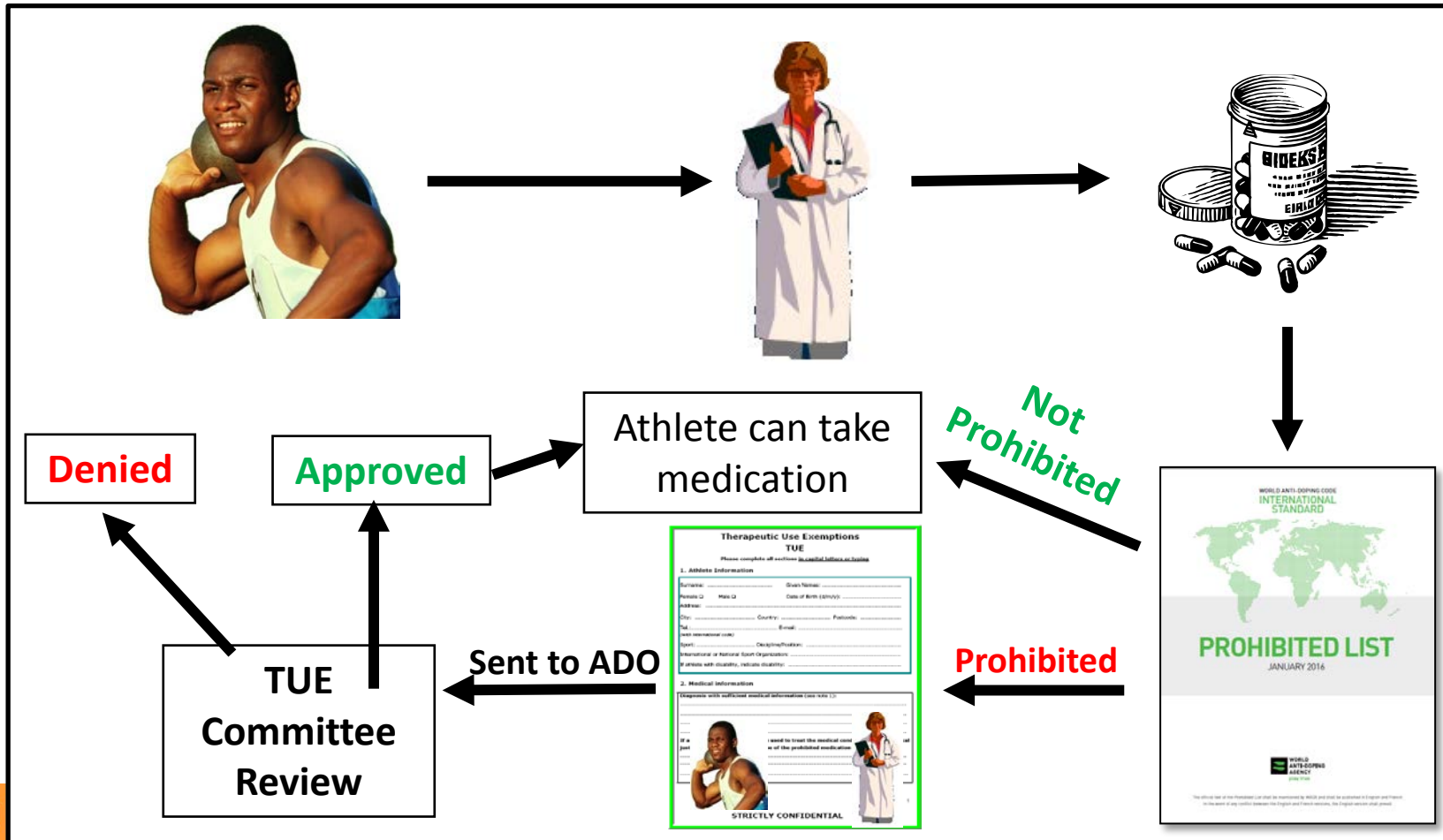
- P1. Alcohol
- P2. Beta-Blockers



1. Doping: Treating vs Eating

- What if an Athlete needs treatment with a Prohibited Substance?

Always ask for a Therapeutic Use Exemption (TUE).



1. Doping: Treating vs Eating

- Why Treating vs Eating ?
'We are what we eat' (ingest or be exposed to)
- What is the definition of ... food?
- Are 'nutritional supplements' drugs or food?
- Does a proper diet covers all nutritional needs of an athlete?
- Is there anything unethical in using nutritional supplements containing substances [drugs ?] that cannot be considered food?



Let's start by 'TREATING'

2. Drugs and more: *The Prohibited List*

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Substances Prohibited in Particular Sports

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- P2. Beta-Blockers



2. Drugs and more: *The Prohibited List*

- Structure of the Prohibited List

S0. Non-Approved Substances



S0 NON-APPROVED SUBSTANCES

Any pharmacological substance which is not addressed by any of the subsequent sections of the *List* and with no current approval by any governmental regulatory health authority for human therapeutic use (e.g. drugs under pre-clinical or clinical development or discontinued, designer drugs, substances approved only for veterinary use) is prohibited at all times.

“Governmental regulatory health authority?
Stringent Regulatory Authorities (SRAs)” as defined by the WHO.

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2. Drugs and more: *The Prohibited List*

- Structure of the Prohibited List



S2. Peptide Hormones, Growth Factors, Related Substances and mimetics

S2.1 Erythropoietin-Receptor Agonists

S2.1.1 Erythropoiesis-Stimulating Agents (ESAs)

- EPO and analogues
(*epoetins, darbepoetin, pegserpoetin, EPO-Fc*)
- EPO mimetic peptides (EMPs)
(*peginesatide, CNTO 530,...*)

S2.1.2 Non-erythropoietic EPO-receptor Agonists (*ARA-290, Asialo-EPO, Carbamylated EPO*)

S2.2 Hypoxia-Inducible Factor (HIF) stabilizers

(e.g. cobalt, FG-45921, ...)

Russian athletes admit Xenon doping at Winter Olympics
Drug has same effect as outlawed EPO which boosts oxygen-carrying blood cells

2. Drugs and more: *The Prohibited List*

- Structure of the Prohibited List

S2. Peptide Hormones, Growth Factors, Related Substances and mimetics

**S2.3 Chorionic Gonadotrophin (CG)
Lutenizing Hormone (LH)
and their releasing factors in males**
(*buserelin, gonadorelin*).

**S2.4 Corticotrophins
and their releasing factors**
(*corticotropin*).



2. Drugs and more: *The Prohibited List*

- Structure of the Prohibited List

S2. Peptide Hormones, Growth Factors, Related Substances and mimetics

S2.5 Growth Hormone (GH)

releasing factors and its analogues

(e.g. *GHRH*, *CJC-1295*, *sermorelin*, *tesamorelin*)

Growth Hormone secretagogues (GHS)

Ghrelin and mimetics (*anamorelin*, *ipamorelin*)

GH-releasing peptides (GHRPs)

(e.g. *alexamorelin*, *GHRP-6*, *hexamorelin*, *pralmorelin*,...)

Additional prohibited growth Factors

FGFs, HGFs, IGF-1, MGFs, PDGF, VEGF and any other growth factor affecting muscle, tendon or ligament.



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2. Drugs and more: *The Prohibited List*

- Structure of the Prohibited List

S4. Hormones and metabolic modulators

S4.1 Aromatase inhibitors

(6-oxo, aminoglutethimide, androstatrienedione, testolactone, anastrozole, letrozole, exemestane, formestane)

S4.2 Selective estrogen receptor modulators (SERMs)

(raloxifene, tamoxifen, toremifene)

S4.3 Other anti-estrogenic substances

(clomiphene, cyclofenil, fulvestrant)

S4.4 Agents modifying myostatin function(s)

(myostatin inhibitors)



2. Drugs and more: *The Prohibited List*

- Structure of the Prohibited List

S4. Hormones and metabolic modulators

S4.5 Metabolic modulators

S4.5.1 Activators of AMPK

(AICAR)

and PPAR δ agonists

(GW 1516)

S4.5.2 Insulins and insulin-mimetics

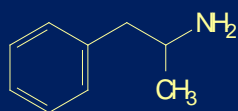
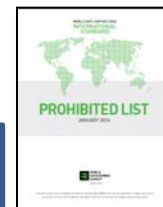
S4.5.3 Meldonium

S4.5.4 Trimetazidine



3. Enforcement: Testing

- Chemical structure of compounds



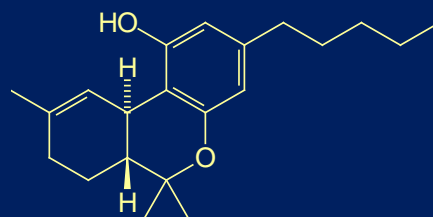
Amphetamine

PM: 135 Da



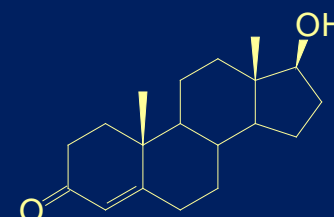
Morphine

PM: 285 Da



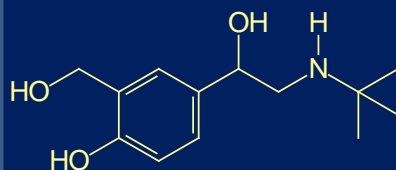
Δ^9 -THC

PM: 314 Da



Testosterone

PM: 288 Da



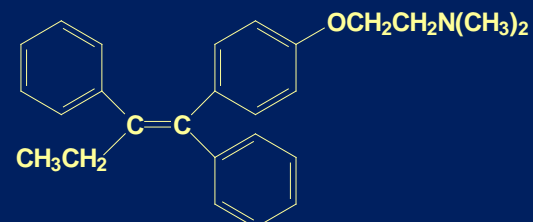
Salbutamol

PM: 239 Da



Aminogluthetimide

PM: 232 Da

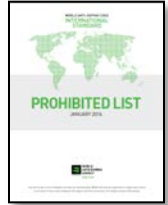


Tamoxifene

PM: 371 Da

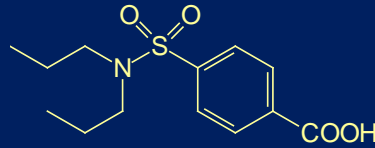
3. Enforcement: Testing

- Chemical structure of compounds



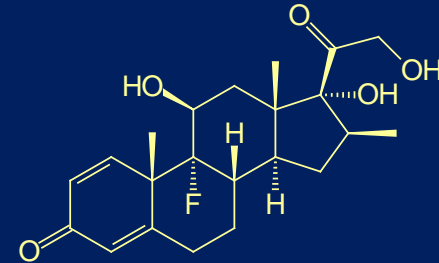
Furosemide

PM: 331 Da



Probenecid

PM: 285 Da



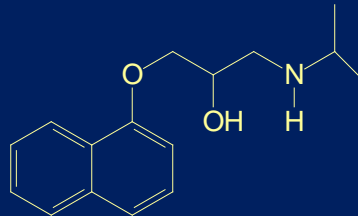
Betamethasone

PM: 393 Da



Alcohol

PM: 46 Da

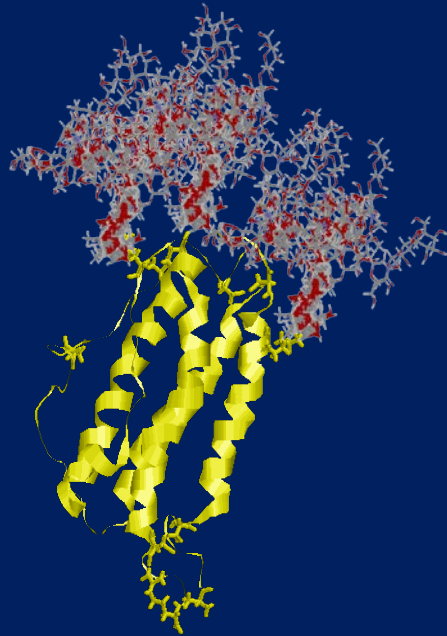


Propranolol

PM: 259 Da

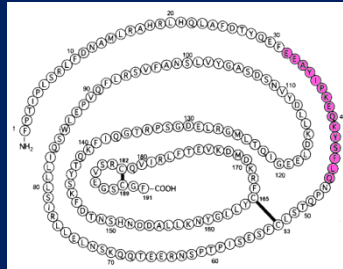
3. Enforcement: Testing

- Chemical structure of compounds



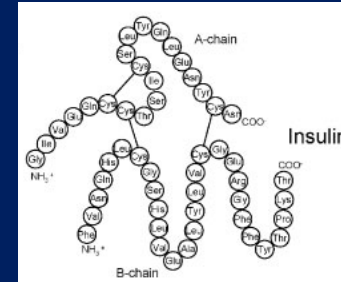
Erythropoietin (EPO)

PM: ~ 30,500 Da



Growth Hormone (hGH)

PM: ~ 22,000 Da



Insuline

PM: 5,806 Da

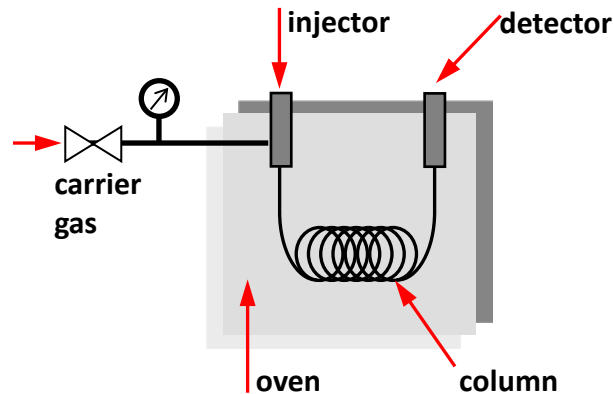


3. Enforcement: Testing

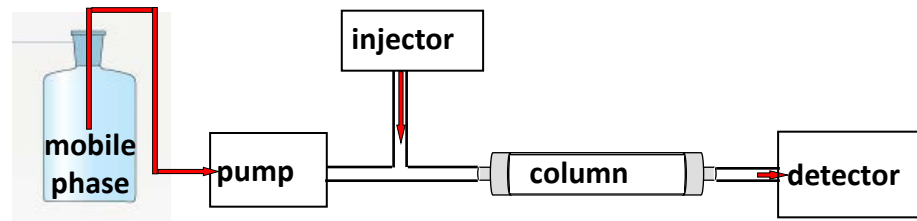
- Analytical Approaches

General purpose methods: GC/MSⁿ, LC/MSⁿ

Volatile compounds
(gas chromatography)



Non-volatile compounds
(liquid chromatography)



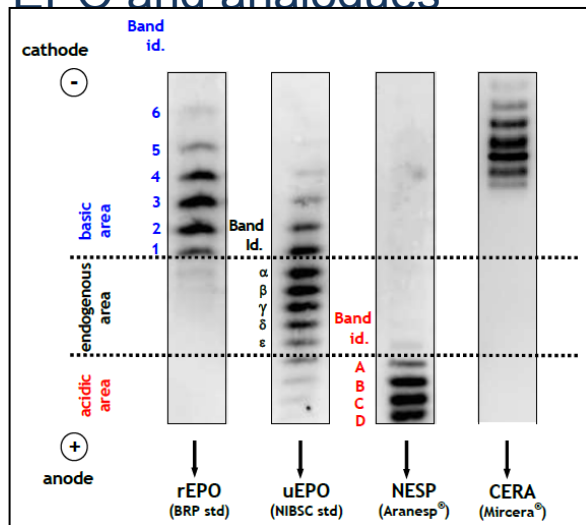
3. Enforcement: Testing

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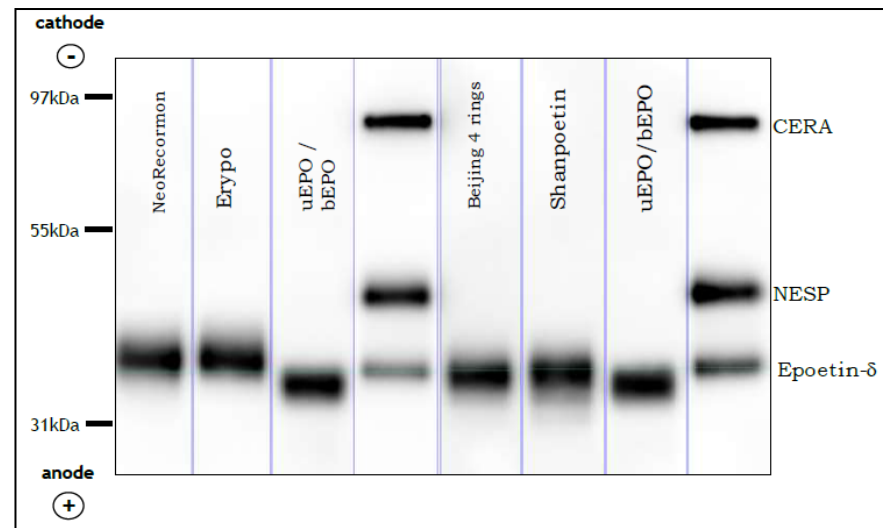
Singular methods: IEF, SAR-PAGE, Immunoassays, Flow cytometry, etc.



EPO and analogues IEF



SAR-PAGE



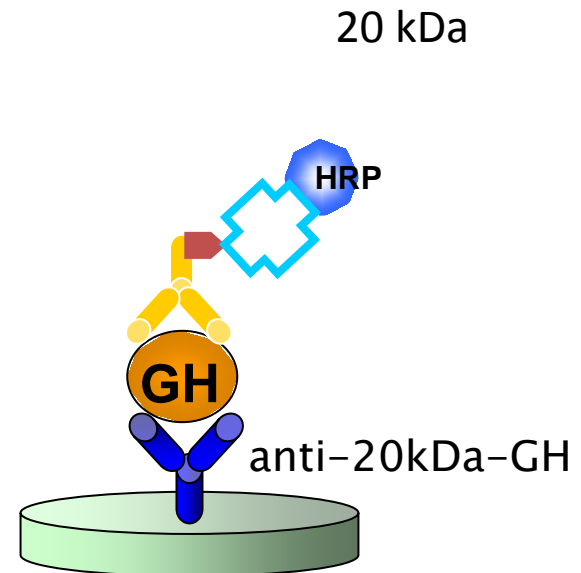
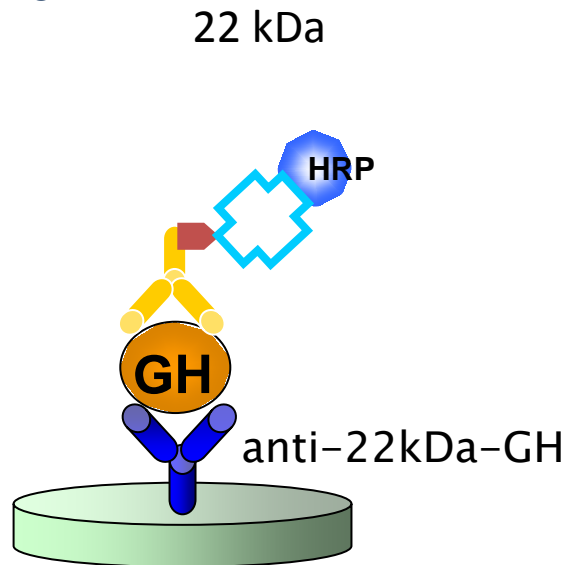
3. Enforcement: Testing

- Analytical Approaches

Singular methods: IEF, SAR-PAGE, IMMUNOASSAYS, etc.



Growth Hormone



3. Enforcement: Testing

- Selection of '**additional**' tests to perform





Chain of custody

000001



A Event details

Mission order

Date

Out of competition

In competition

No. of urine

No. of blood

Doping Control Station Manager

Doping Control Station

Transport box number

B Bottle codes

Sample codes	Analysis request						
	EPO	BT	HBOCS	HGH	CERA	ABP	Other

3. Enforcement: Testing

- WADA's Technical Document on Sport Specific Analysis (TDSSA)




SPORT	DISCIPLINE	PHYSIOLOGICAL ASSESSMENT				MINIMUM LEVELS OF ANALYSIS		
POWER & STRENGTH SPORTS		P&S	ME	CVE	NPD %	ESAs %	Insulins %	hGH & GHRFs %
MUSCULAR ENDURANCE		P&S	ME	CVE	NPD %	ESAs %	Insulins %	hGH & GHRFs %
CV ENDURANCE		P&S	ME	CVE	NPD %	ESAs %	Insulins %	hGH & GHRFs %
Aquatics	Long distance swim (800 m+)	3	4	5	30	30	2,5	5
	Open water	3	5	5	30	30	2,5	5
Athletics	Long distance (1500 m+)	1	2	5	10	60	2,5	5
Biathlon	Biathlon	4	5	5	NR	60	2,5	10
Canoe/Kayak	Dragon boat	2	3	4	50	10	2,5	5
	Long distance (1000 m)	3	3	4	30	30	2,5	5
	Marathon	2	3	5	30	30	2,5	5
	Ocean racing	2	2	4	40	15	2,5	5
Cycling	Cyclocross	3	4	4	10	30	5	10
	Mountain bike	3	4	4	15	30	5	10
	Road	2	5	5	15	60	5	10
	Track endurance	3	5	5	10	60	5	10
Modern Pentathlon	Modern pentathlon	4	3	3	85	5	0	5
Rowing	Rowing	4	5	5	NR	30	5	10
Skating	Speed/Long (1500 m+)	4	5	5	40	30	2,5	10
Skiing	Cross country	5	5	5	30	60	5	10
	Nordic combined	5	5	5	20	30	5	10
Triathlon	Triathlon	1	3	5	10	60	2,5	10
AIMING SPORTS		P&S	ME	CVE	NPD %	ESAs %	Insulins %	hGH & GHRFs %
PILOT SPORTS		P&S	ME	CVE	NPD %	ESAs %	Insulins %	hGH & GHRFs %
GYMNASTIC SPORTS		P&S	ME	CVE	NPD %	ESAs %	Insulins %	hGH & GHRFs %
BALL AND TEAM SPORTS		P&S	ME	CVE	NPD %	ESAs %	Insulins %	hGH & GHRFs %
COMBAT SPORTS		P&S	ME	CVE	NPD %	ESAs %	Insulins %	hGH & GHRFs %

3. Enforcement: Testing

- WADA's Technical Document on Sport Specific Analysis (TDSSA)




**WORLD
ANTI-DOPING
AGENCY**
play true

Appendix 2

Minimum Levels of Analysis for Sports and Disciplines for Athletes with Impairments

SPORTS	DISCIPLINE	ESAs %	GH & GHRFs %
Aquatics	IPC Swimming (100 m or less)	5	10
Aquatics	IPC Swimming Middle Distance (200-400 m)	10	5
Aquatics	IPC Swimming Long Distance (800 m or greater)	30	5
Archery	Para-Archery	0	0
Athletics	IPC Combined Events	15	10
Athletics	IPC Jumps	5	10
Athletics	IPC Sprint (400 m or less)	5	10
Athletics	IPC Throws	5	10
Athletics	IPC Middle Distance (800-1500 m)	30	5
Athletics	IPC Long Distance (3000 m or greater)	30	5
Badminton	Para-Badminton	5	5
Basketball	Wheelchair Basketball	5	5
Biathlon	IPC Biathlon	30	10
Bobsleigh	Para-Bobsleigh	5	5
Boccia	Para-Boccia	0	0
Canoe/Kayak	Para-Canoe Sprint	10	10
Curling	Wheelchair Curling	0	0
Cycling	Para-Cycling Track Sprint	5	5
Cycling	Para-Cycling Road	30	5
Cycling	Para-Cycling Track Endurance	30	5
DanceSport	IPC Wheelchair DanceSport	0	0
Equestrian	Para-Equestrian	0	0

1. Doping: Treating vs Eating

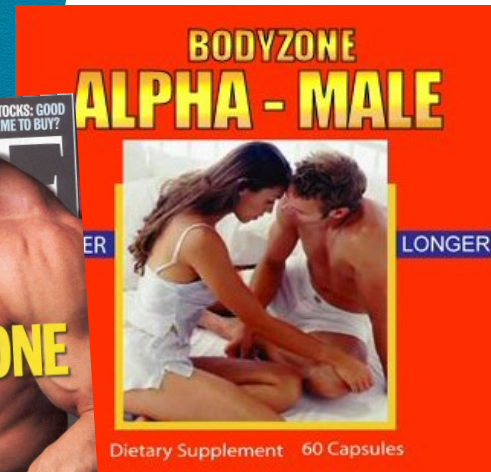
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'We are what we eat' (ingest or be exposed to)
- What is the definition of ... food?
- Are 'nutritional supplements' drugs or food?
- Does a proper diet covers all nutritional needs of an athlete?
- Is there anything unethical in using nutritional supplements containing substances [drugs ?] that cannot be considered food?



4. Food: *Supplements*

- Are nutritional supplements needed?
- Are nutritional supplements performance enhancing?
- Are nutritional supplements safe?

- Caffeine
- Creatine
- Ribose
- Bicarbonate / citrate
- Theophylline
- β -hydroxy- β -methyl-butirate (HMB)
- Glycerol
- Chromium picolinate
- Glutamine
- Carnitine
- Antioxidants
- Proteins and aminoacids
- Colostrum
- Rodhiola Rosea
- Vitamins
- Etc...



4. Food: *Supplements*

- Many athletes have produced adverse analytical findings (AAFs) attributed to the use of nutritional supplements.



- **They may be '*not-properly*' labeled**

- they may contain substances not mentioned or miss-spelled in the label. (e.g. natural extracts, synonyms, etc.)

- **They may get contaminated during the manufacturing process**

- residual contaminations may escape the GMP but be detected as doping.

- **They may contain drugs added intentionally**

- e.g. green tea containing diuretics, protein shakes containing anabolic steroids, etc.

4. Food: *Supplements*

<http://www.koelnerliste.com/en/cologne-list.html>



Cologne List®

more safety through tested products



- ✓ Nutritional supplements and products can contain banned substances.
- ✓ Cologne List® is a list of nutritional supplements which have been tested for such substances.
- ✓ By only using products which are on Cologne List® athletes reduce the risk of unintentionally becoming the victims of doping.
- ✓ Cologne List® is not a recommendation to athletes that they should use a nutritional supplement. Our goal is solely to provide better information and to improve transparency!

4. Food: *Supplements*

<http://www.usada.org>



About ▾ Testing ▾ Substances ▾ Science ▾ |



Celebrating USADA's
15th Anniversary

Learn more about the important events
that have contributed to USADA's success
in protecting the rights of clean athletes
for the last 15 years.



Athlete Express



Search Status of Medication



Supplement Information



Report Doping in Sport



Whereabouts Information



Therapeutic Use
Exemptions

4. Food: *Supplements*

<http://www.usada.org>



Supplement 411 High Risk List

Only the website version of this list is valid, and only on the day accessed.
If you are viewing a saved or printed version of this page then you are viewing
an out-dated, invalid High Risk List.

Brand Name ↑	Company	What the label says	Prohibited List Classification	Updated	Comments
1-Andro	IronMagLabs	The Supplement Facts panel lists "1-Androstene 3bol, 17-one"	Anabolic agents	2015-09-27	The product label lists one or more prohibited substances including "1-androstene 3b-ol, 17-one" which is also known as 1-androsterone or 1-DHEA.
1-Andro Liquid	Advanced Muscle Science (AMS)	The Supplement Facts panel lists "1-Androstene-3b-ol, 17-one"	Anabolic agents	2015-05-18	The product label lists a prohibited substance.
1-Andro RDe Chrome	Advanced Muscle Science (AMS)	The Supplement Facts panel lists "1-Androstene-3β-ol, 17-one"	Anabolic agents	2015-10-01	The product label lists a prohibited substance. Testing of Lot #1330 revealed the presence of 1-androstenediol and androsterone.
1024	Achievement Through Sciences (ATS) Labs	The Supplement Facts panel lists "7-methoxyflavone."	Anabolic agents	2015-08-07	Testing of a sample purchased June 2015 revealed the presence of boldione, methasterone, androsta-1,4,6-trienedione, and other prohibited substances.
17-Diol	Sports One Nutrition	The Supplement Facts panel lists "Epithio-17a-methyletioallocholanol" and "Methyl Synephrine"	Anabolic agents	2015-02-12	The product label lists one or more prohibited substances.
380 Preworkout	Aviva Nutrition	The Supplement Facts panel lists "Amperall (2-amino-4-methylpentane)"	Stimulants	2015-09-10	The product label lists a prohibited substance. The FDA has clarified that DMBA does not meet the definition of a dietary ingredient, and therefore dietary supplements that contain this ingredient are adulterated. To learn more see the FDA Statement on 1,3-Dimethylbutylamine (AMP, Amp Citrate, 4-AMP)
ABSolute Fuel	BioScience Institute Inc.	The Supplement Facts panel lists "Citrus Aurantium 30%	Stimulants	2015-09-29	Testing of Lot #13338007 revealed the presence of oxilofrine (also known as methylephedrine). The

5. Regulations: Athlete Support Personnel

- What is Doping?

- **Conceptual Definition**

“use pharmacological aids to improve performance”: *The Prohibited List*

- **Legal Definition (Art. 1 of The Code):**

“the occurrence of one or more anti-doping rule violations set forth in Art. 2”

Article 2:

2.1 presence of a prohibited substance (AAF)

2.2 use or attempted use

2.3 evading, refusing or failing to submit to a test

2.4 whereabouts failure

2.5 tampering or attempted tampering

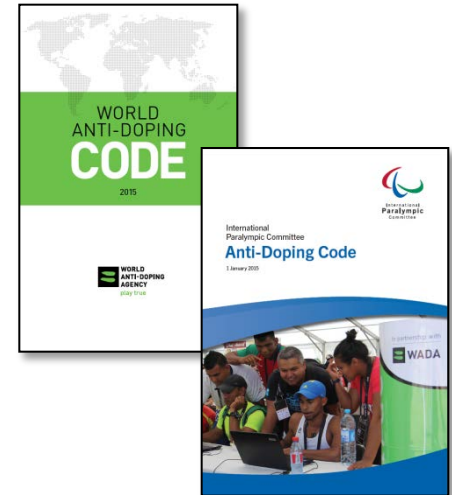
2.6 possession

2.7 trafficking or attempted trafficking

2.8 administration or attempted admin.

2.9 complicity

2.10 prohibited association



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2.5 tampering or attempted

2.6 possession

2.7 trafficking or attempted

2.8 administration or attempt

2.9 complicity

2.10 prohibited association



2.6.2 *Possession by an Athlete Support Person In-Competition of any Prohibited Substance or any Prohibited Method, or Possession by an Athlete Support Person Out-of-Competition of any Prohibited Substance or any Prohibited Method which is prohibited Out-of-Competition in connection with an Athlete, Competition or training, unless the Athlete Support Person establishes that the Possession is consistent with a TUE granted to an Athlete in accordance with Article 4.4 or other acceptable justification.*

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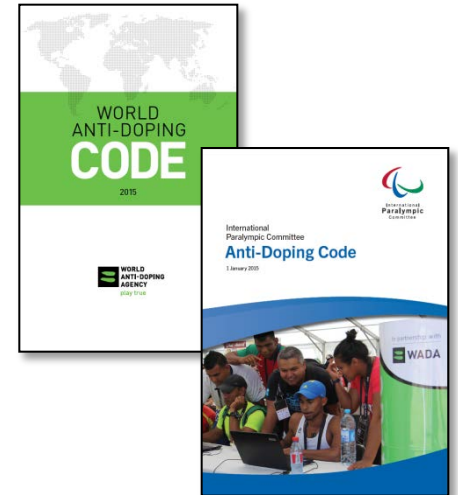
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- **Conceptual Definition**

“use pharmacological aids to improve performance”: *The Prohibited List*

- **Legal Definition (Art. 1 of The Code):**

“the occurrence of one or more anti-doping rule violations set forth in Art. 2”

Article 2:

2.1 presence of a prohibited substance (AAF)

2.2 use or attempted use

2.3 evading, refusing or failing to submit to a test

2.4 whereabouts failure

2.5 tampering or attempted tampering

2.6 possession

2.7 trafficking or attempted trafficking

2.8 administration or attempted administration

2.9 complicity


2.10 prohibited association

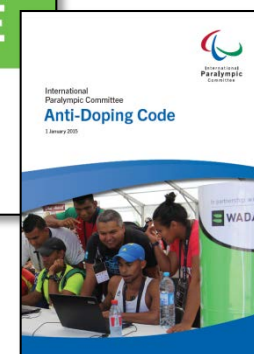
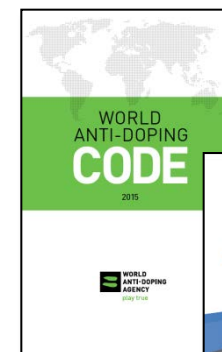


Association by an Athlete or other Person subject to the authority of an Anti-Doping Organization in a professional or sport-related capacity with any Athlete Support Person who:

2.10.1 If subject to the authority of an Anti-Doping Organization, is serving a period of Ineligibility; or

5. Regulations: Athlete Support Personnel

 WORLD ANTI-DOPING AGENCY			
<u>Last name</u>	<u>First name</u>	<u>Nationality</u>	<u>Suspension dates</u>
1 Acampora	Domenico	ITA	Until 19/01/2032
2 Agresti	Stefano	ITA	Life
3 Ahamdi	Rouhollah	IRI	Until 23/05/2018
4 Albuthabhak	Abdulhussein Majeed	IRQ	Until 05/01/2018
5 Al-Naimi	Hamad Salem	QAT	Until 19/01/2016
6 Anedda	Simone	ITA	Until 19/03/2040
7 Anzorov	Imran	RUS	Life
8 Ardingo Posca	Davide Alfredo	ITA	Until 17/03/2017
9 Aubut	Andre	CAN	Life
10 Babedzhanyan	Aleksandr	RUS	Until 24/12/2016
11 Baccin	Marco Jose	ITA	Until 13/01/2017
12 Barazza	Flavio	ITA	Until 02/12/2017
13 Barotti	Riccardo Stefano	ITA	Life
14 Basarab	Laurentiu	ROU	Life
15 Bellani	Fausto	ITA	Until 24/06/2016
16 Belova	L	BLR	Life
17 Bianchi	Vittorio Emanuele	ITA	Life
18 Bianculli	Massimo	ITA	Until 05/02/2024
19 Block	Mark	USA	Until 31/12/2018
20 Bonazzi	Fiorenzo Egeo	ITA	Until 16/01/2018
21 Borriello	Antonino	ITA	Until 28/04/2032
22 Brazuk	Maciej	POL	Until 18/09/2015
23 Buccella	Matteo	ITA	Until 21/05/2034
24 Busca	Stefano	ITA	Until 05/06/2033
25 Camerini	Maurizio	ITA	Life
26 Carella	Cinzia	ITA	Until 16/10/2032
27 Carlton	Fraser	JAM	Until 25/09/2017
28 Chiodi	Danilo	ITA	Until 21/04/2017
29 Chiste	Roberto	ITA	Until 22/10/2033
30 Ciappi	Giulano	ITA	Until 22/09/2017
31 Cimino	Americo	ITA	Until 20/02/2017
32 Coconi	Cesare	ITA	Life
33 Coletta	Gaetano	ITA	Until 22/05/2033
34 Cultrera	Corrado	ITA	Until 19/06/2017
35 Davila Jaramillo	Cesar Fabian	ECU	Until 04/12/2015
36 Del Fatti	Alessandro	ITA	Until 30/09/2030
37 Despotovic	Milan	SRB	Life
38 Destro	Renzo	ITA	Until 22/09/2017
39 Drummond	Jonathan	USA	Until 16/12/2022
40 Duquette	Maurice	CAN	Life
41 Esmer	Sevinc	TUR	Life
42 Evans	Lee	NGR	Until 16/02/2018
43 Evsukov	Eugenii	RUS	Until 14/06/2018
44 Fabbi	Ferruccio	ITA	Until 05/06/2033
45 Ferrari	Michele	ITA	Life
46 Florea	Dorel	ITA	Until 05/06/2033
47 Foresi	Luigi	ITA	Until 10/05/2019
48 Forti	Piero	ITA	Until 29/01/2033
49 Frediani	Viscardo	ITA	Life
50 Garcia del Moral	Luis	ESP	Life
51 Garipey	Jimmy	CAN	Until 18/01/2017
52 Gilmozzi	Giancarlo	ITA	Until 23/09/2016
53 Gilmozzi	Sebastian	ITA	Until 23/09/2016



5. Regulations: Athlete Support Personnel

- Consequences of Doping

- Sanctions (ineligibility periods)**

“the occurrence of one or more anti-doping rule violations set forth in Art. 2”

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2.6 possession

2.7 trafficking or attempted trafficking

2.8 administration or attempted admin.

2.9 complicity

2.10 prohibited association

10.3.3 For violations of Article 2.7 or 2.8, the period of *Ineligibility* shall be a minimum of four years up to lifetime *Ineligibility*, depending on the seriousness of the violation. An Article 2.7 or Article 2.8 violation involving a *Minor* shall be considered a particularly serious violation and, if committed by *Athlete Support Personnel* for violations other than for *Specified Substances*, shall result in lifetime *Ineligibility* for *Athlete Support Personnel*. In addition, significant

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10.3.4 For violations of Article 2.9, the period of *Ineligibility* imposed shall be a minimum of **two years, up to four years**, depending on the seriousness of the violation.

10.3.5 For violations of Article 2.10, the period of *Ineligibility* shall be **two years**, subject to reduction down to a minimum of one year, depending on the *Athlete* or other *Person's* degree of *Fault* and other circumstances of the case.

Thank you!



Institut Hospital del Mar
d'Investigacions Mèdiques