

Written Exam
529-0043-00S - Analytical Strategy
Summer 2016

Vorname : _____ Name : _____

- Zeit: 60 Min. Teilen Sie sich Ihre Zeit gut ein.
Time: 60 min, organize your time carefully.

- Sie können auf Englisch oder Deutsch antworten
Answers are accepted in German or English.

- Es sind alle Hilfsmittel mit Ausnahme von Computern und Telekommunikation erlaubt.
It is allowed to use all resources except for computers and communication devices.

- Unleserliche Texte, unklare Formulierungen oder unsaubere Skizzen können nicht bewertet werden. Bitte bemühen Sie sich um eine saubere Darstellung.
Unreadable text, unclear formulations or graphs are not graded. Please try to use clear illustrations and descriptions

- Schreiben Sie jedes abzugebende Blatt einzeln mit Ihrem Namen und Vornamen an.
Label every page with name and surname.

- Dieses Deckblatt ist ausgefüllt abzugeben. Die Aufgabenstellung ist ebenfalls einzureichen.
Please fill in the first page. Hand in all pages including cover page and questions.

- Wir bitten Sie um Fairness und wünschen Ihnen viel Erfolg!
We ask you for fairness and wish you good luck!

Prüfung Sommer 2016 / Analytical Strategy

(Answers can be given in German or English)

Olympic Summer Games, Rio 2016. You are responsible for establishing the laboratory for doping control. As opposed to spot checks (“Stichproben”) of only a few selected athletes, your task is to measure anabolic steroids for every athlete in certain teams (e.g., the Russian team, a total of 278 athletes, which has been accused of manipulating anti-doping efforts). This means that there will be many more samples to process than usual, although for a smaller number of substances. In the “Prohibited List” of the World Anti Doping Agency (WADA) there are 46 exogenous anabolic steroids explicitly listed (see attachment). Urine samples from the athletes are available, which immediately after collection will be split into two aliquots (A and B sample). Only one of these, the A sample is normally analyzed.

Answer the following questions:

1. Explain the idea behind having both an A and a B sample. What is important when taking samples for doping control during competition? (1P)
2. Discuss problems that could occur if only one sample exists. (1P)
3. What problems do you foresee if the two samples (A and B) were analyzed at different time points, and how could these be avoided? (1P)
4. Propose an analytical method for quantitative analysis of over 40 steroids in a large number of samples. Specify the analytical system as accurately as possible. (3P)
5. Among the anabolic steroids on the WADA prohibited list, there are “exogenous” (a) and “endogenous” (b) listed. Why is it important to distinguish between these? (1P)
6. What instruments, and how many of them would you buy to establish the analytical laboratory for doping control? Justify your answer with an estimation of time requirements for sample handling, sample preparation, and analytical run time, assuming that the lab operates continuously, 24 hours a day. (3P)
7. How would you organize the analytical protocol to be able to generate results that are robust and can serve as legal basis for banning athletes? What do you have to pay attention to when reporting positive doping results? (2P)
8. Standard analysis of urine is not only time-consuming but also problematic in terms of sampling (privacy). Suggest a rapid, non-invasive method to detect anabolic steroids for doping control. (2P)

(Max. 14 Points)

SUBSTANCES & METHODS PROHIBITED AT ALL TIMES

(IN- AND OUT-OF-COMPETITION)

PROHIBITED 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.

S1 ANABOLIC AGENTS

Anabolic agents are prohibited.

1. ANABOLIC ANDROGENIC STEROIDS (AAS)

a. Exogenous* AAS, including:

1-Androstenediol (5 α -androst-1-ene-3 β ,17 β -diol);
1-Androstenedione (5 α -androst-1-ene-3,17-dione);
1-Testosterone (17 β -hydroxy-5 α -androst-1-en-3-one);
4-Hydroxytestosterone (4,17 β -dihydroxyandrost-4-en-3-one);
19-Norandrostenedione (estr-4-ene-3,17-dione);
Bolandioli (estr-4-ene-3 β ,17 β -diol);
Bolasterone;
Boldenone;
Boldione (androsta-1,4-diene-3,17-dione);
Calusterone;
Clostebol;
Danazol ([1,2]oxazolo[4',5':2,3]pregna-4-en-20-yn-17 α -ol);
Dehydrochlormethyltestosterone (4-chloro-17 β -hydroxy-17 α -methylandrosta-1,4-dien-3-one);
Desoxymethyltestosterone (17 α -methyl-5 α -androst-2-en-17 β -ol);
Drostanolone;
Ethylestrenol (19-norpregna-4-en-17 α -ol);
Fluoxymesterone;
Formebolone;
Furazabol (17 α -methyl [1,2,5]oxadiazolo[3',4':2,3]-5 α -androstan-17 β -ol);

Gestrinone;
Mestanolone;
Mesterolone;
Metandienone (17 β -hydroxy-17 α -methylandrosta-1,4-dien-3-one);
Metenolone;
Methandriol;
Methasterone (17 β -hydroxy-2 α ,17 α -dimethyl-5 α -androstan-3-one);
Methyldienolone (17 β -hydroxy-17 α -methylestra-4,9-dien-3-one);
Methyl-1-testosterone (17 β -hydroxy-17 α -methyl-5 α -androst-1-en-3-one);
Methylnortestosterone (17 β -hydroxy-17 α -methylestr-4-en-3-one);
Methyltestosterone;
Metribolone (methyltrienolone, 17 β -hydroxy-17 α -methylestra-4,9,11-trien-3-one);
Mibolerone;
Nandrolone;
Norboletone;
Norclostebol;
Norethandrolone;
Oxabolone;
Oxandrolone;
Oxymesterone;
Oxymetholone;
Prostanazol (17 β -[[tetrahydropyran-2-yl]oxy]-1'H-pyrazolo[3,4:2,3]-5 α -androstanol);
Quinbolone;
Stanozolol;
Stenbolone;
Tetrahydrogestrinone (17-hydroxy-18 α -homo-19-nor-17 α -pregna-4,9,11-trien-3-one);
Trenbolone (17 β -hydroxyestr-4,9,11-trien-3-one);

and other substances with a similar chemical structure or similar biological effect(s).

b. Endogenous** AAS when administered exogenously:

Androstenediol (androst-5-ene-3 β ,17 β -diol);
Androstenedione (androst-4-ene-3,17-dione);
Dihydrotestosterone (17 β -hydroxy-5 α -androstan-3-one);
Prasterone (dehydroepiandrosterone, DHEA,
3 β -hydroxyandrost-5-en-17-one);
Testosterone;

and their metabolites and isomers, including but not limited to:

3 β -Hydroxy-5 α -androstan-17-one;
5 α -Androstane-3 α ,17 α -diol;
5 α -Androstane-3 α ,17 β -diol;
5 α -Androstane-3 β ,17 α -diol;
5 α -Androstane-3 β ,17 β -diol;
5 β -Androstane-3 α ,17 β -diol;
7 α -Hydroxy-DHEA;
7 β -Hydroxy-DHEA;
4-Androstenediol (androst-4-ene-3 β , 17 β -diol)
5-Androstenedione (androst-5-ene-3,17-dione);
7-Keto-DHEA;
19-Norandrosterone;
19-Noretiocholanolone.
Androst-4-ene-3 α ,17 α -diol;
Androst-4-ene-3 α ,17 β -diol;
Androst-4-ene-3 β ,17 α -diol;
Androst-5-ene-3 α ,17 α -diol;
Androst-5-ene-3 α ,17 β -diol;
Androst-5-ene-3 β ,17 α -diol;
Androsterone
Epi-dihydrotestosterone;
Epitestosterone;
Etiocholanolone.

2. OTHER ANABOLIC AGENTS

Including, but not limited to:

Clenbuterol, selective androgen receptor modulators (SARMs, e.g. andarine and ostarine), tibolone, zeranol and zilpaterol.

For purposes of this section:

* "exogenous" refers to a substance which is not ordinarily produced by the body naturally.

** "endogenous" refers to a substance which is ordinarily produced by the body naturally.

S2 PEPTIDE HORMONES, GROWTH FACTORS, RELATED SUBSTANCES AND MIMETICS

The following substances, and other substances with similar chemical structure or similar biological effect(s), are prohibited:

1. Erythropoietin-Receptor agonists:

- 1.1** Erythropoiesis-Stimulating Agents (ESAs) including e.g. Darbepoietin (dEPO); Erythropoietins (EPO); EPO-Fc; EPO-mimetic peptides (EMP), e.g. CNTO 530 and peginesatide; methoxy polyethylene glycol-epoetin beta (CERA).

- 1.2** Non-erythropoietic EPO-Receptor agonists, e.g. ARA-290; asialo EPO; carbamylated EPO.

2. Hypoxia-inducible factor (HIF) stabilizers, e.g. cobalt and FG-4592; and HIF activators, e.g. argon, xenon;

3. Chorionic Gonadotrophin (CG) and Luteinizing Hormone (LH) and their releasing factors, e.g. buserelin, gonadorelin and leuprorelin, in males;

4. Corticotrophins and their releasing factors, e.g. corticorelin;