

# SUMMARY OF MAJOR MODIFICATIONS AND EXPLANATORY NOTES

## 2019 PROHIBITED LIST

### Substances and methods prohibited at all times (In- and Out-of-Competition)

#### Prohibited Substances

##### S1 ANABOLIC AGENTS

###### 1a Exogenous Anabolic Androgenic Steroids

- 4-hydroxytestosterone was transferred to class S1.1b, "Endogenous Anabolic Androgenic Steroids (AAS)", since this substance can be formed endogenously at low concentrations.
- Bolandiol was removed, since it constitutes one of the isomers of 19-norandrostenediol, which is already included under class S1.1b.

###### 1b Endogenous AAS and their *Metabolites* and isomers, when administered exogenously

- The title of S1.1b "Endogenous Anabolic Androgenic Steroids when administered exogenously" was changed to: "Endogenous AAS and their *Metabolites* and isomers when administered exogenously" to clarify that ALL endogenous AAS and their *Metabolites* and isomers are prohibited when administered exogenously. Therefore, the listed examples now include the endogenous AAS and some of their *Metabolites*/isomers.
- The examples of *Metabolites* and isomers of endogenous AAS were simplified, leaving only those endogenous substances that are currently known to be available in nutritional supplements or that may be used as masking agents (e.g. to affect the "steroid profile"). The currently named examples are:
  - 7 $\alpha$ -hydroxy-DHEA;
  - 7 $\beta$ -hydroxy-DHEA;
  - 4-androstenediol (androst-4-ene-3 $\beta$ ,17 $\beta$ -diol);
  - 5-androstenedione (androst-5-ene-3,17-dione);
  - 7-keto-DHEA;
  - epiandrosterone (3 $\beta$ -hydroxy-5 $\alpha$ -androstan-17-one);
  - epi-dihydrotestosterone (17 $\beta$ -hydroxy-5 $\beta$ -androstan-3-one);
  - epitestosterone.
- All other substances previously listed as examples of *Metabolites*/isomers of endogenous AAS were removed

as specific examples of this class; however, such substances remain prohibited if administered exogenously. The *Prohibited List* usually does not list *Metabolites*, unless it provides useful information to either *Athletes* or stakeholders. The removed *Metabolites* may have multiple names and are not known to be available in nutritional supplements or to have biological activity.

- The analysis of several of these *Metabolites*, as *Markers* of the exogenous administration of endogenous AAS is already covered in specific WADA Technical Documents: 19-Norandrosterone and 19-Noretiocholanolone are *Metabolites* of the 19-norsteroids, Nandrolone, 19-Norandrostenediol and 19-Norandrostenedione, and are covered in the TD19NA; Androsterone, Etiocholanolone, 5 $\alpha$ -androstane-3 $\alpha$ ,17 $\beta$ -diol (5 $\alpha$ Adiol) and 5 $\beta$ -androstane-3 $\alpha$ ,17 $\beta$ -diol (5 $\beta$ Adiol), which are *Metabolites* of Testosterone and its precursors, are defined as *Markers* of the "steroid profile", and are covered in the TDEAAS and TDIRMS; All the other substances previously listed (androstane- and androstenediols), if administered exogenously, are also monitored through GC/C/IRMS analysis of the *Markers* of the "steroid profile" (TDIRMS).
  - 2-Androstenone (5 $\alpha$ -androst-2-ene-17-one) was transferred to class S4.1 Aromatase Inhibitors, which better reflects its biological activity. Analogues and isomers of this substance were also included in S4.1, namely 2-Androstenol (5 $\alpha$ -androst-2-en-17-ol), 3-Androstenol (5 $\alpha$ -androst-3-en-17-ol) and 3-Androstenone (5 $\alpha$ -androst-3-en-17-one);
  - Epiandrosterone (3 $\beta$ -hydroxy-5 $\alpha$ -androstan-17-one) was added as an example, since this substance is available in nutritional supplements.
- ###### 2 Other Anabolic Agents:
- Ostarine is now also listed by its International Non-proprietary Name (INN), enobosarm.

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## S2 PEPTIDE HORMONES, GROWTH FACTORS, RELATED SUBSTANCES, AND MIMETICS

- More examples of Hypoxia-inducible factor (HIF) activating agents were added. These are daprodustat (GSK1278863) and vadadustat (AKB-6548), while the reference name of molidustat, BAY 85-3934, has been included.
- The title of S2.2 was changed to “Peptide Hormones and their Releasing Factors”, more accurately reflecting the substances in this class.
- Ghrelin and hexarelin are now listed by their INNs, lenomorelin and examorelin, respectively.
- Macimorelin was added as an example of a growth hormone secretagogue.

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## S3 BETA-2-AGONISTS

- Tretoquinol (trimetoquinol) is a beta-2 agonist and was added as an example to S3. It is an ingredient in oral cold and flu medications, particularly in some countries in Asia.

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## S4 HORMONE AND METABOLIC MODULATORS

- 2-Androst-2-ene-17-one (5 $\alpha$ -androst-2-ene-17-one) was transferred from S1.1b to this class, which better reflects its biological activity. Analogues and isomers of this substance were also included in S4.1, namely 2-Androst-2-en-17-ol (5 $\alpha$ -androst-2-en-17-ol), 3-Androst-3-en-17-ol (5 $\alpha$ -androst-3-en-17-ol) and 3-Androst-3-en-17-one (5 $\alpha$ -androst-3-en-17-one).
- The title of S4.4 was changed to: “Agents preventing Activin receptor IIB activation”, and several examples are listed. These include myostatin inhibitors such as myostatin-neutralizing antibodies (e.g. domagrozumab, landogrozumab, stamulumab), myostatin-binding proteins (e.g. follistatin, myostatin propeptide), agents reducing or ablating myostatin expression, activin receptor IIB competitors such as e.g. decoy activin receptors (e.g. ACE-031), anti-activin receptor IIB antibodies (e.g. bimagrumb), and activin A-neutralizing antibodies. This change was made to reflect the multiple ways in which this receptor can be affected.

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## Prohibited Methods

### M3 GENE AND CELL DOPING

- The title of this class was changed to: “Gene and Cell Doping”, in order to reflect that cells were already included in M3.3. Stem cells are not prohibited for treating injuries as long as their use restores normal function of the affected area and does not enhance function. The term “post-transcriptional” was added to the list of examples to more completely define the processes that can be modified by gene editing.

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## Substances and Methods Prohibited In-Competition

- The wording of the opening sentence was modified to harmonize with Article 4.2.2 of the Code as well as other sections of the List. In this regard, the word “categories” was replaced by “classes”.

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### S6 STIMULANTS

- For consistency in chemical nomenclature, 1,3-dimethylbutylamine is also represented as 4-methylpentan-2-amine. Two additional analogues of methylhexaneamine were added as examples: 5-methylhexan-2-amine (1,4-dimethylpentylamine) and 3-methylhexan-2-amine (1,2-dimethylpentylamine).
- Dimethylamphetamine is now listed by its INN dimetamfetamine. Other amphetamine compounds were standardized to align with the INN.

## Substances Prohibited in Particular Sports

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### **P1** BETA-BLOCKERS

- Bunolol is a racemic mixture of levobunolol and bunolol, so levobunolol was removed as an example in P1.

\* For further information on previous modifications and clarifications please consult the Prohibited List Q & A on [www.wada-ama.org/en/questions-answers/prohibited-list-qa](http://www.wada-ama.org/en/questions-answers/prohibited-list-qa)