# Prohibited List of Substances and Methods

# 1. How does a substance or method make it to the prohibited list?

The WADA Prohibited List may include any substance and methods that satisfy any two of the following three criteria:

- 1. It has the potential to enhance or enhances sport performance;
- 2. It represents an actual or potential health risk to the Athlete;
- 3. It violates the spirit of sport (this definition is outlined in the Code).

Substances or methods which mask the effect or detection of prohibited substances are also prohibited. In addition, a substance which has not been approved for human use is likely to be prohibited as well.

The Prohibited List is reviewed annually in consultation with scientific, medical and anti-doping experts to ensure it reflects current medical and scientific evidence and doping practices. The Prohibited List comes into effect on January 1st of each year and is published by WADA three months prior to coming into force; however, in exceptional circumstances, a substance may be added to the Prohibited List at any time.

# 2. What is the status of platelet derived preparations (PRP)?

Platelet derived preparations (PRP) are not prohibited. Despite the presence of some growth factors, plateletderived preparations were removed from the Prohibited List as recent studies on PRP do not demonstrate any performance enhancement beyond a potential therapeutic effect.

Note that individual growth factors from any other source remain prohibited under S.2.

### 3. Is Plasmapheresis prohibited?

The status of plasmapheresis is different for plasma donors and recipients:

- For the plasma donor, plasmapheresis is prohibited under section M1.1 because the donor's own red blood cells (and other blood components) are being reintroduced back into their own circulatory system after the plasma or blood components have been separated outside of the person's body.
- For the plasma recipient, who is receiving plasma from a different donor, plasmapheresis is not prohibited under M1.1 or M1.3 as the patient receives only plasma, but not whole blood or red blood cells. For the plasma recipient, plasmapheresis would only be prohibited under M2.2 if it is not legitimately received in the course of hospital treatment when the volume is more than 100 mL per 12 hour period.

# 4. Is Intravenous Laser Therapy prohibited?

Intravenous laser therapy is prohibited under M1.3 as defined by "Any form of intravascular manipulation of blood..."

#### 5. What is the status of methylhexaneamine (MHA)?

MHA is known by many different names, including, but not limited to, dimethylamylamine, 1,3dimethylamylamine, dimethylpentylamine, methylhexamine, methylhexanamine, 1,3-dimethylpentylamine. It is prohibited In-Competition only as a specified stimulant under Section 6.b.

MHA is a stimulant that was sold as a medicine up to the early 1970s, but is no longer used for medical treatment. MHA is currently included as a constituent of some dietary supplements sold today, including via the Internet.

#### 6. Does geranium oil contain methylhexaneamine (MHA)?

Scientific studies have clearly demonstrated that natural geranium oil does not contain MHA. The use of geranium oil cannot be considered as being the source of MHA or related metabolites in a urine sample collected for anti-doping purposes. However, athletes should be aware that MHA has been marketed under various names, including "geranium oil" so athletes should be <u>extremely</u> cautious about using supplements with this "ingredient".

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MHA is prohibited *In-Competition* only as a stimulant under section S6.b.

#### 7. What is the status of clenbuterol?

Clenbuterol is an anabolic agent that prohibited at all times (i.e., both in- and out-of-competition). There is no threshold under which this substance is not prohibited.

At present, and based on expert opinions, there is no plan for WADA to introduce a threshold level for clenbuterol.

It is possible that under certain circumstances the presence of a low level of clenbuterol in an athlete sample can be the result of food contamination. However, each case is different and all aspects and context of the case need to be taken into account during the results management process. According to the World Anti-Doping Code, the athlete has the opportunity to explain how a prohibited substance entered their body during the results management and/or or hearing phase of their case.

WADA is working closely with specific countries, International Federations and event organizers to help minimize the risk of meat contamination. Food contamination as a public health issue is primarily a matter for governments to resolve.

#### 8. What is a 'specified substance'?

It should be clear that all substances on the Prohibited List are prohibited. The sub-classification of substances as "Specified" or "Non-Specified" are important only in the sanctioning process.

A "Specified Substance" is a substance which potentially allows, under defined conditions, for a greater reduction of a sanction when an athlete tests positive for that particular substance.

The purpose of the sub-classifications of "Specified" or "Non-Specified" on the Prohibited List is to recognize that it is possible for a substance to enter an athlete's body inadvertently, and therefore allow a tribunal more flexibility when making a sanctioning decision.

"Specified" substances are not necessarily less effective doping agents than "Non-Specified" substances, nor do they relieve athletes of the strict liability rule that makes them responsible for all substances that enter their body.

#### 9. What is the status of colostrum?

Colostrum is not specifically prohibited, however it can contain certain quantities of IGF-1 and other growth factors which are prohibited and can influence the outcome of anti-doping tests. Therefore, WADA does not recommend the ingestion of this product.

#### 10. What is the status of deer antler velvet spray?

Deer Antler Velvet Spray may contain IGF-1, which is a prohibited substance and has been included on the Prohibited List for many years. On the other hand, very small quantities of IGF-1 can be found naturally in animal products (e.g. colostrums, deer antler velvet).

There can be no guarantee that IGF-1 taken orally will not influence the plasma level of IGF-1, which may influence the result of anti-doping tests.

WADA recommends that athletes exercise extreme caution with this supplement because it could lead to a positive test. Athletes who use these types of products do so at their own risk.

In addition, like other supplements, these products may contain prohibited substances not disclosed on the product label.

## 11. Why is glycerol no longer prohibited ?

Effective 1 January 2018 glycerol was removed from the Prohibited List. This decision comes in consideration of the information published in scientific articles since 2012 that particularly addresses the ability of glycerol to influence the athlete's plasma volume and parameters of the Athlete Biological Passport (ABP), where the magnitude of glycerol-derived effects is regarded as minimal.

#### 12. Is Dialysis a Prohibited Method?

Dialysis (also known as hemodialysis) is a medical treatment for patients with kidney failure. Dialysis is a prohibited method under M1.1, as blood is taken out from the patient and filtered, before being reintroduced back into the patient's circulatory system. An athlete needing dialysis treatment requires a Therapeutic Use Exemption.

#### 13. How are substances named and catetgorised on the Prohibited List?

WADA names substances according to the following convention:

- For substances that have been given an International Non-proprietary Name (INN), as published by the World Health Organisation, this name is used first.
- Only when the commonly-used name of a substance is better known than the INN, this commonly-used name appears in parenthesis.
- When the INN is not known, the International Union of Pure and Applied Chemistry (IUPAC) nomenclature is used, accompanied in some cases by the commonly-used name. As INNs are generated, the Prohibited List evolves with the addition of the INN and if deemed beneficial, the previous IUPAC name may be still included for a period of time.
- Common examples of substances and methods are provided in all sections but these examples are not exhaustive.

#### 14. What is the status of mannitol used by inhalation?

Mannitol by inhalation is permitted e.g. to perform bronchial provocation testing in asthma.

Mannitol is only prohibited when administered intravenously.

#### 15. Are eye drops containing brinzolamide or dorzolamide prohibited?

Carbonic anhydrase inhibitors dorzolamide and brinzolamide, when administered topically in the eye, are not prohibited. The rationale behind this exception is these drugs do not have a diuretic effect when topically applied.

#### 16. What is the status of eye drops containing beta-blockers?

Eye drops containing beta-blockers **are** prohibited in particular sports under section P1 because the ophthalmic administration of beta-blockers results in systemic concentrations of the drugs similar to when the medication is taken orally.

# 17. What is the status of intravenous injections or infusions as part of a medical procedure?

Intravenous infusions or injections are not prohibited if they are legitimately received in the course of a hospital treatment, surgical procedure or clinical investigation or if they do not exceed 100 mL per 12 hour period. Otherwise they require a Therapeutic Use Exemption.

#### 18. Why are intravenous injections or infusions prohibited?

The intent of section M2.2 is to prohibit hemodilution, overhydration and the administration of prohibited substances by means of intravenous infusion. An intravenous infusion is defined as the delivery of fluids through a vein using a needle or similar device.

The legitimate medical uses of intravenous infusions may not need a Therapeutic Use Exemption in certain settings (hospital treatment, surgical procedures or clinical investigations). In other situations, such as trauma with or without blood loss, severe dehydration, intractable vomiting, the athlete should receive appropriate treatment and apply for a retroactive Therapeutic Use Exemption as soon as reasonable.

Injections with a simple syringe are not prohibited as a method if the injected substance is not prohibited and if the volume does not exceed 100 mL every 12 hours.

# 19. Why is pseudoephedrine prohibited at certain concentrations?

Pseudoephedrine is a specified stimulant prohibited *In-Competition* only at a urinary threshold of 150  $\mu$ g/mL. This decision was based on the results of controlled excretion studies as well as scientific literature indicating that only high doses of pseudoephedrine improved sports performance.

Given the wide availability of pseudoephedrine, particularly as a component of multi-ingredient cold and influenza treatments, athletes and their support personnel should be advised the following.

- Athletes should stop taking Pseudoephedrine-containing medicines at least 24 hours before competition. For therapeutic applications during the *In-Competition* period, consider the use of alternative permitted medications in consultation with a physician, or apply for a Therapeutic Use Exemption for the use of Pseudoephedrine for therapeutic reasons.
- The established urinary threshold level of 150 µg/mL may be reached (rarely, but possibly) in some individuals within 6-20 hours of taking some long-acting therapeutic formulations.
- The threshold level of 150 μg/mL has been established based on the intake of therapeutic doses of pseudoephedrine, defined as a maximum daily dose of 240 mg pseudoephedrine taken either as:
  - four daily oral administrations (one every 4-6 hours) of a 60 mg (or 2 x 30 mg) immediate release preparation (i.e. tablet, capsule or liquid) or
  - o two daily administrations (one every 12 hours) of a 120 mg extended release preparation
  - o one daily administration of a 240 mg extended release preparation.
- As an example, a single daily dose of 3 x 60 mg tablets would be a supratherapeutic dose that may lead to an Adverse Analytical Finding.

# 20. Are all drugs not mentioned on the Prohibited List permitted?

The fact that a substance is not on the Prohibited List does not mean that it is not prohibited since most categories only include some common examples and are not exhaustive.

In addition, section S0 (Non-approved substances) includes substances used for doping which are not included in other sections of the Prohibited List that are not approved by any governmental regulatory health authority for human therapeutic use. This includes drugs under pre-clinical or clinical development, discontinued drugs, designer drugs or veterinary drugs. A designer drug is defined as a synthetic analogue of a legally restricted or prohibited drug, devised to circumvent drug laws.

Most prohibited substances fall in one of the S1 to S9 categories. Therefore, only in rare occasions a substance is included in S0 after a case-by-case evaluation.

#### 21. Is catheterization permitted?

Catheterization may be necessary for medical purposes. It is only prohibited if used to tamper or attempt to tamper with the integrity of a sample or sample collection.

# 22. What is the difference between a "delivered" vs "metered" dose from my asthma inhaler?

For beta-2-agonists, given by ANY device, the amount of drug can be expressed in two ways:

- 1. Metered Dose the quantity of drug substance contained in the delivery device (inhaler)
- 2. **Delivered dose** the amount of drug that is available to the lungs; delivered from the mouthpiece of the inhalation device.

The Prohibited List refers to the **delivered dose for formoterol** and the **metered dose for salbutamol and salmeterol** to reflect the most common labelling practices around the world.

The labelling convention of asthma inhalers may vary between countries – to determine the delivered dose of a product in a particular country, read the accompanying medical literature and labelling of the inhalation device you are using. Note that there are many different types of inhalers; a Metered Dose Inhaler (MDI), i.e. a "puffer" is one type. Other delivery devices include, but are not limited to: Diskus, Turbuhalers, Ellipta, Aerolizer, Genuair.

#### 23. What is the status of vitamin B12, as it contains cobalt?

Vitamin B12 is not prohibited because the cobalt present does not have the same effects as elemental cobalt or cobalt salts. In addition, the amount of cobalt that is naturally contained in food is not significant and would not be enough to act as a doping agent. However, if a dietary supplement includes cobalt, for example inorganic cobalt or cobalt salts, then it would be considered prohibited.

#### 24. Are hypoxic chambers permitted?

Hypoxic chambers artificially induce hypoxic conditions. Their use is not prohibited by WADA, however some sporting authorities ban the use of hypoxic chambers during competitions under their sport rules. Athletes must check the rules that apply to hypoxic chambers with the sporting authorities governing the events they compete in.

#### 25. What is the status of higenamine?

Higenamine is prohibited under S3 as a non-selective beta-2-agonist. Higenamine is documented to be a constituent of the plant *Tinospora crispa*, which can be found in some dietary supplements.

#### 26. What is the status of supplemental oxygen?

Supplemental oxygen administered by inhalation, but not intravenously, is permitted. However, some sports authorities may prohibit its use in their regulations. Athletes must check the rules that apply to supplemental oxygen use with the sporting authorities governing the events they compete in.

#### 27. Can I test positive for phenylethylamine through food consumption?

Regular food consumption will not yield sufficient levels of phenylethylamine to result in an Adverse Analytical Finding.

#### 28. What is the status of stem cell treatment?

Non-transformed stem cells used alone (with no growth factor or other hormones added) for healing injuries are not prohibited as long as they return the functioning of the affected area to normal and do not enhance it.

## 29. What is the status of Actovegin?

Actovegin is a deproteinized calf serum. According to the manufacturer, it contains peptides, amino acids, nucleic acids but does not contain cells or proteins. Independent analysis of the product has not detected prohibited growth factors, proteins in general, or steroids. So based on this, Actovegin is not prohibited except if it is used as an intravenous infusion or injection of more than 100 mL each 12 hours.

#### 30. What is gene editing?

Gene editing is a type of genetic engineering in which DNA is manipulated at specific sites. Gene editing technology has advanced impressively in recent years and is a promising gene therapy technique for the treatment of, for example, genetic diseases or cancer; at this point only a few early stage clinical trials are taking place worldwide. This has prompted WADA to evaluate possible misuses of gene editing for doping and as a consequence, has included these technologies in the definition of Gene Doping in the 2018 Prohibited List. Despite sensational and scientifically unfounded claims occasionally seen in the media, WADA is not presently aware of any athletes who are gene doping. Nevertheless we want to be ahead of the game and make it clear that when or if such techniques as gene editing would be used to enhance performance beyond a return to normal function, then it would be prohibited.

### 31. Why is alcohol no longer prohibited?

Effective 1 January 2018, and after careful consideration and extensive consultation, Alcohol is excluded from the Prohibited List. The intent of this change is not to compromise the integrity or safety of any sport where alcohol use is a concern, but rather to endorse a different means of enforcing bans on alcohol use in these sports. The International Federations (IF) affected by this change were alerted sufficiently in advance in order to amend their rules and to put in place protocols to test for alcohol use and appropriately sanction athletes who do not abide by the rules of their sport. Control of the process will allow IF more flexibility in applying rules or thresholds as they see fit. The National Anti-Doping Organizations are no longer obliged to conduct tests but may assist IF and National Federations where appropriate.

#### 32. What is the status of nebulizers?

Nebulizers are by definition inhalation devices and thus not prohibited as a method. However, the inhalation of salbutamol in doses recommended by the manufacturer is most likely to result in urinary levels of salbutamol exceeding the urinary threshold of 1,000 ng/ml and thus, the use of salbutamol with a nebulizer requires a TUE. However, a TUE for nebulized salbutamol would be granted only in rare situations, such as a severe acute asthma attack treated in an emergency room setting. In otherwise healthy adults, the use of metered dose inhalers with a spacer has been demonstrated as effective as the nebulized drug in managing acute exacerbations of asthma.

#### 33. What is the status of levosalbutamol (levalbuterol)?

Levosalbutamol (also known as levalbuterol) is prohibited at all times as it is a beta-2-agonist. This drug is different from the regularly prescribed salbutamol. Salbutamol consists of the racemic mixture of the R- and S- enantiomers. Levosalbutamol consists only of the R-enantiomer. Unlike salbutamol, there are no exceptions for the use of levosalbutamol based on any therapeutic dose. A Therapeutic Use Exemption must be applied for and granted before using levosalbutamol.

#### 34. What is the status of arformoterol?

Arformoterol is prohibited at all times as it is a beta-2-agonist. This drug is different to from the regularly prescribed formoterol Formoterol consists of a racemic mixture of R- and S- enantiomers. Arformoterol consists only of the R-enantiomer. Unlike formoterol, there are no exceptions for the use of arformoterol based on any therapeutic dose. A Therapeutic Use Exemption must be applied for and granted before using arformoterol.

# **Dietary and Nutritional Supplements**

# 1. Are supplements safe to take?

Extreme caution is recommended regarding supplement use.

The use of dietary supplements by athletes is a serious concern because in many countries the manufacturing and labeling of supplements do not follow strict rules, which may lead to a supplement containing an undeclared substance that is prohibited under anti-doping regulations. A significant number of positive tests have been attributed to the misuse of supplements and attributing an Adverse Analytical Finding to a poorly labeled dietary supplement is not an adequate defense in a doping hearing.

The risks of taking supplements should be weighed against the potential benefit that may be obtained, and athletes must appreciate the negative consequences of an Anti-Doping Rule Violation as a result of taking a contaminated supplement.

Use of supplement products that have been subjected to one of the available quality assurance schemes can help to reduce, but not eliminate, the risk of an inadvertent doping infringement.

# 2. Can a dietary/nutritional supplement company have their supplements tested by WADA?

The World Anti-Doping Agency (WADA) is not involved in the testing of dietary/nutritional supplements.

The Laboratory Code of Ethics, in the International Standard for Laboratories (Section 4.4 of Annex B), states that WADA-accredited laboratories shall not engage in analyzing commercial material or preparations (e.g. dietary supplements) unless specifically requested by an Anti-Doping Organization as part of a doping case investigation. The Laboratory shall not provide results, documentation or advice that, in any way, suggests endorsement of products or services.

#### 3. Can a supplement company have their products approved by WADA?

WADA is not involved in any certification process regarding supplements and therefore does not certify or endorse manufacturers or their products. WADA does not control the quality or the claims of the supplements industry which may, from time to time, claim that their products have been approved or certified by WADA.

If a company wishes to promote its products to the sport community, it is their responsibility as a manufacturer to ensure that the products do not lead to any anti-doping rule violation. Some third-party testers of supplements exist, and this may reduce the risk of contamination but not eliminate it.

# Cannabinoid

#### 1. What is a cannabinoid?

A cannabinoid is a compound produced by the cannabis (marijuana) plant or synthesized as a chemical (synthetic cannabinoid). Of more than 100 cannabinoids in the plant, delta-9-tetrahydrocannabinol (THC) is the main psychoactive compound, which alters the mind or behavior. Other cannabinoids include cannabidiol (CBD), cannabinol (CBN), and cannabigerol (CBG). Since the mid-2000's, many different synthetic cannabinoids were produced in illegal laboratories and sold as drugs to mimic the effects of THC.

#### 2. Which cannabinoids are prohibited?

All natural and synthetic cannabinoids are prohibited except for cannabidiol (CBD). Cannabis, hashish and marijuana are prohibited. Products, including foods and drinks, containing cannabinoids, are also prohibited. All synthetic cannabinoids that mimic the effects of THC are prohibited.

# 3. Is Cannabidiol (CBD) oil prohibited?

CBD is not prohibited; however, athletes should be aware that some CBD oils and tinctures extracted from cannabis plants, may also contain THC and other cannabinoids that could result in a positive test for a prohibited cannabinoid.