2024 WADA Prohibited List stakeholder consultation: review Dutch stakeholders

July 17, 2023

We would like to thank the *Prohibited List Expert Advisory Group (LiEAG)* for giving us the opportunity to review the *DRAFT 2024 Prohibited List International Standard*.

We would also like to thank Dr. Audrey Kinahan for the stakeholder letter addressing the comments submitted by the stakeholders during the consultation of the draft 2023 List.

Fourfold contribution

In line with previous years our contribution is composed by the four Dutch stakeholders, being:

- Ministry of Health, Welfare and Sport
- Netherlands Olympic Committee*Netherlands Sports Confederation (NOC*NSF)
- NOC*NSF Athletes' Commission
- Doping Authority Netherlands

On behalf of these four stakeholders we would like to ask you to treat our review as a fourfold contribution to your consultation process.

Review criteria

We use the following criteria to review the DRAFT 2024 Prohibited List.

The proposed changes to the *Prohibited List* should:

- Be based on a transparent decision-making process
- Be easily explainable to the sports community
- Have strong focus on catching intentional cheaters
- Protect athletes who have no malicious intentions
- Have minimal interference with good medical practice

We feel these criteria help us to focus on the interests of our most important target group: the true athletes. They should benefit the most from the amendments we put into practice.

Comments for 2024 Prohibited List

Substances of abuse

- We thank Dr. Audrey Kinahan for addressing the comment regarding the compatibility of having substances identified both as a non-*Specified substance* and listed as *Substance of abuse*.

S0. Non-Approved Substances

- We welcome the addition of 2,4-dinitrophenol (DNP) and troponin activators (e.g. reldesemtiv and tirasemtiv) as examples of prohibited substances to the List.

S1. Anabolic Agents

- We welcome the addition of trestolone (7α-methyl-19-nortestosterone, MENT), dimethandrolone (7α,11ß-Dimethyl-19-nortestosterone) and 11ß-methyl-19 nortestosterone as examples of nandrolone (19-nortestosterone) analogs to the List.

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

- We support the rewording of S2.2.1 for clarity to highlight that Gonadotrophin-Releasing Hormone (GnRH) agonist analogs (e.g. buserelin, deslorelin, goserelin, histrelin, leuprorelin, nafarelin and triptorelin) are prohibited in males.
- We welcome the addition of histrelin (S2.2.1) tetracosactide (ACTH 1-24) (S2.2.2) and ibutamoren (MK-677) (2.2.4) as examples of prohibited substances to the List.

S4. Hormone and Metabolic Modulators

- We support the inclusion of Rev-Erb-α agonists to the List. We also welcome the addition of SR9011 as an example.

S5. Diuretics and Masking Agents

- We support the editorial changes made in this section to improve clarity.
- We welcome the addition of conivaptan and mozavaptan as examples of vaptan drugs.

M1. Manipulation of Blood and Blood Components

- We are very happy with the planned decision to allow the donation of plasma and plasma components by plasmapheresis. As you know the Netherlands has been promoting this change for years.

Tramadol (S7)

- The LiEAG have concluded that the use of tramadol should be prohibited In-competition. The *2024 Summary of Major Modifications and Explanatory Notes* states: *"Monitoring data has indicated significant Use in sports like cycling, rugby and football."*

  Since we haven't received the most recent 2022 Monitoring Program Figures, we rely on the figures available until 2021. These monitoring data show no significant Use of tramadol in football. It also shows a sport-specific prohibition of tramadol in cycling is working well, leaving only rugby with concerning tramadol findings, despite a clear drop in 2021 (1.69% > 2.14% > 2.70% > 0.86%).

  We believe the Prohibited List should have minimal interference with good medical practice and protect athletes with no malicious intentions. Prohibiting tramadol means more common medical interventions are now deemed unappropriated. We know athletes can always apply for a TUE, but these applications increase the administrative burden for athletes, physicians and the TUE committees. It can even draw athletes with no malicious intentions into disciplinary cases when the TUE application is not

granted as the paperwork was deemed insufficient, or alternative permitted treatment appeared to be available in retrospect.

Based on the available monitoring data and our review criteria, we cannot support a sport-wide prohibition of tramadol.

S9. Glucocorticoids

- We advise the LiEAG to keep informing the anti-doping community of any changes in the glucocorticoids washout periods via the *Summary of Major Modifications and Explanatory Notes* on an annual bases.

THC / cannabinoïden (S8)

Firstly, in our view cannabinoids should not be part of the anti-doping program. Cannabinoids most likely have a negative impact on athletic performance.

Secondly, the scientific review of the status of cannabis, previously initiated by the LiEAG, is solely concentrated around the status of delta9-tetrahydrocannabinol (THC). All the other prohibited cannabinoids are fully ignored by the LiEAG, which raises the question what the justification is for the prohibition of these substances. We ask the LiEAG again to provide this justification or to allow the use of all cannabinoids except THC.

Thirdly, if laboratories would analyze samples for the full spectrum of prohibited natural cannabinoids (and not only THC) they would find a considerable number of AAFs caused by the use of seemingly permitted products like cannabidiol (CBD) oil and hemp products. For references, please see the work from Cologne, Mareck et al (2020, https://doi.org/10.1002/dta.2959). If all cannabinoids (except CBD) will remain prohibited, we again suggest to give clear (publicly available) instructions to the laboratories on the testing menu requirements for cannabinoids and/or revisiting reporting levels for all prohibited natural cannabinoids.

Fourthly, as stated by the LiEAG in the addendum *"cannabidiol (CBD) was removed from the Prohibited List, allowing Athletes who wish to use it to have access to the non-psychoactive component of cannabis".* This however, does not work in practice as there are no CBD products available free from (traces of) THC. This is even true for medical grade CBD products. Despite having an urinary threshold of 150 ng/mL, the *Use* of any amount of THC is still prohibited in-competition. Athletes therefore, do not have access to CBD in-competition. We ask the LiEAG again to find a practical solution for this situation.

Comments for future consideration

Substances of abuse

- Only four 'classical' substances are currently listed as *Substances of abuse*. Use of more 'modern', synthetic substances with mimicking effects is not eligible for lighter sanctioning. We propose to add the synthetic substances with mimicking effects to the *Substances of abuse* list as well, as it would lead to a more balanced sanctioning regime. The LiEAG could start with the synthetic stimulants 3-MMC and 4-FA.

S3. Beta-2 agonists

- We thank Dr. Audrey Kinahan for addressing WADA's ongoing work to allow permitted inhaled therapeutic doses of beta-2 agonists.

- We still advise the LiEAG to simplify the daily dosing time intervals for salbutamol. The current daily dosing time intervals are hard to explain to the sports community and therefore cause a risk for athletes who have no malicious intentions.

- The Prohibited List states: "*The presence in urine of salbutamol in excess of 1000 ng/mL or formoterol in excess of 40 ng/mL is not consistent with therapeutic use of the substance and will be considered as an Adverse Analytical Finding (AAF) unless the Athlete proves, through a controlled pharmacokinetic study, that the abnormal result was the consequence of a therapeutic dose (by inhalation) up to the maximum dose indicated above."*

  Over the last years, it became obvious that the practical framework for performing such a controlled pharmacokinetic study is not clear enough. We therefore reiterate our proposal from last years to make this framework more clear and suggest WADA to publish an additional guideline document for performing controlled pharmacokinetic studies, keeping in mind that recreating true competitive circumstances is virtually impossible, as the Froome-case has shown.

<u>S4. Hormone and metabolic modulators</u>

- We thank Dr. Audrey Kinahan for addressing the possible abuse of thyroid hormones and the recent work of the LiEAG members outlining their views on this subject. We nevertheless reiterate our stance that thyroxine, triiodothyronine, Thyroid Stimulating Hormone (TSH) and Thyrotropin-Releasing Hormone (TRH) should be added to the *Prohibited List*. Thyroid hormones do not only meet the criteria for inclusion to the List, in the Netherlands we also received serious indications that thyroid hormones were being misused in elite sport.

- We thank Dr. Audrey Kinahan for addressing the current prohibited status of clomifene for women. Nevertheless, we reiterate our proposal to allow the use of clomifene for women, as - in our view - the balance of available evidence clearly favors permitting clomifene for female athletes.

<u>S5. Diuretics and masking Agents</u>

- The *Prohibited List* states: *"The detection in an Athlete's Sample at all times or In-Competition, as applicable, of any quantity of the following substances subject to threshold limits: formoterol, salbutamol, cathine, ephedrine, methylephedrine and pseudoephedrine, in conjunction with a diuretic or masking agent (except topical ophthalmic administration of a carbonic anhydrase inhibitor), will be considered as an Adverse Analytical Finding (AAF) unless the Athlete has an approved Therapeutic Use Exemption (TUE) for that substance in addition to the one granted for the diuretic or masking agent."*

  We still feel the current rules could lay a disproportionate burden on the athlete, especially when (1) a diuretic is administered in course of medical emergency and (2) the Athlete's Sample is collected *Out-of-Competition*. We also question the need for this policy, considering the current analytical abilities of the WADA accredited laboratories. We therefore reiterate our request from last years to stop this 'double TUE' policy.

<u>M1. Manipulation of blood and blood components</u>

- We thank Dr. Audrey Kinahan for addressing our proposal regarding the relocation of M1.2. to S2, as it seems odd to mention prohibited substances in a prohibited methods section. We acknowledgethe conclusion of the LiEAG re-stating that the current

classification is more accurate, with M1.2 dealing with manipulation to enhance oxygen uptake, while S2.1 deals with increasing red blood cell production.

S6. Stimulants

- We reiterate our suggestion of last year to add methoxysynefrine as an example of a specified stimulant. This substance is listed in doping trafficking reports and based on its chemical structure we suspect it to have a strong amphetamine-like effect.

S7. Narcotics

- The abuse of narcotics is limited and if these substances are abused, it constitutes medical malpractice more than doping use. Furthermore, in order to get a TUE, Registered Testing Pool athletes need to declare exactly which narcotics in what dosage will be given to them prior to surgery. This often causes practical challenges for the athlete, the doctor, as well as the TUE Committee. We therefore reiterate our proposal to adopt a more practical policy for the use of narcotics and allow their use in the course of hospital treatment, surgical procedures and clinical diagnostic investigations. This policy would be in line with the policy on intravenous infusions in section M2.2.

Monitoring Program

- It is our feeling that a number of substances could be removed from the *Monitoring Program* as the required prevalence data should be obtained by now. This especially accounts for the stimulants bupropion, caffeine, phenylephrine, phenylpropanolamine, pipradrol and synephrine. They have been included in the Monitoring Program since its start in 2009.

- We acknowledge the removal of salmeterol and vilanterol from the *Monitoring Program* as the required prevalence data were obtained.

- We acknowledge the addition of tapentadol and dihydrocodeine to the *Monitoring Program* to monitor patterns of use In Competition.

- We ask WADA to change the confidential status of the *Monitoring Program Figures* and make them publicly available.