2023 WADA Prohibited List stakeholder consultation: review Dutch stakeholders

21 July, 2022

We would like to thank the *Prohibited List Expert Advisory Group (LiEAG)* for giving us the opportunity to review the *DRAFT 2023 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 2022 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 2023 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 addressing major modifications

Tramadol (S6)
The LiEAG have concluded that the use of tramadol should be prohibited In-competition. The *2023 Summary of Major Modifications and Explanatory Notes* states: *"While Union Cycliste Internationale's (UCI) 2019 prohibition of In-competition use significantly reduced the high prevalence of In-competition use, recent monitoring data shows trends of increasing use in other sports such as rugby and football."*

The monitoring data does not support this claim, as no real trends of increasing use in other sports can be observed. For all sports – cycling excluded - the percentage of tramadol findings have dropped over the past four years, 2018-2021 (0.50 > 0.45 > 0.38 > 0.21). The figure of 2018 (0.50) is also the highest percentage since its addition to the Monitoring Program. For football no real increase can be observed over the same time period (0.65 > 0.42 > 0.48 > 0.38). Only within rugby the percentage of tramadol findings seem concerning, 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 current monitoring data and our review criteria, we cannot support a sport-wide prohibition of tramadol.

THC / cannabinoïden (S8)
We would like to thank the LiEAG for initiating a scientific review of the status of cannabis in 2022. The addendum of the *2023 Summary of Major Modifications and Explanatory Notes* provides a clear overview of how the LiEAG came to its decision: "*Based on these three criteria defined by the Code, on the scientific evidence available, THC meets the criteria to be included on the List.*"

Firstly, we do not agree with the decision reached by the LiEAG. In our view cannabinoids should not be part of the anti-doping program. Cannabinoids most likely have a negative impact on athletic performance. The current scientific review does not change this view.

Secondly, the scientific review of the status of cannabis 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 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 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 CBD in-competition. We ask the LiEAG to find a practical solution for this situation.

Comments addressing minor modifications

- We support the addition of the following substances to the List:
  - antibodies of precursors of myostatin (S4.3)
  - solriamfetol (S6b)
  - dermorphin (S7)

- We welcome the addition of the following examples of substances to the List:
  - Androst-4-ene-3,11,17-trione (11-ketoandrostenedione, adrenosterone, 11-OXO) (S1.1)
  - 17α-methylepithiostanol (epistane) (S1.1)
  - ractopamine (S1.2 – *and not S1.b. as stated*)
  - apitegromab (S4.3)
  - torasemide (S5)
  - voxelotor (M1)
  - 1,3-dimethylamylamine en 1,3 DMAA (as alternative common names for 4-methylhexan-2-amine) (S6b)
  - 1,4-dimethylamylamine en 1,4-DMAA (as alternative common names for 5-methylhexan-2-amine) (S6b)

- We support the inclusion of minigolf – at the request of the World Mini-Golf Federation - as a sport where beta-blockers are prohibited (P1).

- We welcome the clarification that a Therapeutic Use Exemption is not required for topical ophthalmic administration of a carbonic anhydrase inhibitor (e.g. dorzolamide, brinzolamine) in conjunction with a threshold substance (S6).

- We support the addition of hypoxen (polyhydroxyphenylene thiosulfonate sodium) to the Monitoring Program.

- If tramadol is added to the List, we advise the LiEAG to note its removal from the Monitoring Program in the *2023 Summary of Major Modifications and Explanatory Notes*.

Comments for future consideration

<u>Substances of abuse</u>

- We thank Dr. Audrey Kinahan for addressing the comment regarding the compatibility of having cocaine identified as a non-*Specified substance* and listed as *Substance 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. This could lead to an unbalanced situation in which, for instance, the use of cocaine or MDMA will lead to a three-month ban and the use of a similar substance, like 3MMC, will lead to a two-year ban. The same applies to THC and synthetic cannabinoids with mimicking effects. This is a discrepancy that we feel should be avoided. We feel a much broader approach is more fair to tackle this unbalanced, primarily non-athletic, situation. Therefore, we propose to add the synthetic substances with mimicking effects to the *Substances of abuse* list as well.

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 and the challenges to distinguish terbutaline administered orally from inhalation.

- We 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.

S4. Hormone and metabolic modulators

- 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*.

- We reiterate our proposal to allow the use of clomifene for women. There are no convincing performance or AAS post-cycle benefits for women to use it. The use also poses no unusual medical risks for female athletes. Please see Handelsman, 2008 (https://doi.org/10.1038/bjp.2008.171) as a reference. At the same time, we receive multiple questions from women who suffer from fertility challenges. They need a TUE to start their clomifene therapy. Moreover, once the athlete starts the therapy, the substance can still be detected up to a year later, leading to numerous potential moments on which the athlete can be confronted with the fertility challenges again during and after doping controls. In our view the balance of available evidence clearly favors permitting clomifene for female athletes.

S5. Diuretics and masking Agents

- 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 thank Dr. Audrey Kinahan for addressing the comments made by the stakeholders regarding this topic. We also welcome the proposed exception of topical ophthalmic administration of a carbonic anhydrase inhibitor for the 2023 List. We nevertheless 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.

M1. Manipulation of blood and blood components

- We believe athletes, like any other person, should have the right to donate blood plasma. But since blood plasma donation involves the reinfusion of red blood cells, it is considered a prohibited method according to the current rules. This means that all athletes who perform their sport under the WADC - approximately 4.5 million people in the Netherlands – are not able to perform this noble and potentially lifesaving act. Also, no TUE can be granted since plasma donation does not meet at least one TUE criterion: athletes will not experience significant health problems if they abstain from this method. Furthermore, donating blood plasma cannot be considered to be performance enhancing and cannot be expected to influence the accuracy of the Athlete Biological Passport. Therefore, we feel this prohibition does not meet the criterion of proportionality and we reiterate our proposal to make an exemption to the current rules and explicitly allow blood plasma donation in medical settings for all athletes.

- It seems odd to mention prohibited substances in the prohibited methods section. Therefore, we reiterate our proposal to relocate M1.2. to S2:

  1.6 Agents artificially enhancing the uptake, transport or delivery of oxygen. Including but not limited to:
  Perfluorochemicals, efaproxiral (RSR13) and modified haemoglobin products, e.g haemoglobin-based blood substitutes and microencapsulated haemoglobin products, excluding supplemental oxygen by inhalation.

S6. Stimulants

- We suggest 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.

S9. Glucocorticoids

- All injectable routes of administration for glucocorticoids during the *In-Competition* period are prohibited since last year. This change raised some concerns regarding the interference of the rules with good medical practice, the increase in administrative burden for athletes, physicians and TUE committees and the potential risks for athletes with no malicious intentions. We therefore advise the LiEAG to review the new glucocorticoids practice on these points.

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