2022 WADA Prohibited List stakeholder consultation: review Dutch stakeholders

16 July, 2021

We would like to thank the *Prohibited List Expert Group (LiEG)* for giving us the opportunity to review the *DRAFT 2022 Prohibited List International Standard*.

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 2022 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

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. 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.

- Since "*Substances of abuse are substances that are identified as such because they are frequently abused in society outside of the context of sport*" and *Specified substances* are substances "*which are more likely to have been consumed or used by an Athlete for a purpose other than the enhancement of sport performance*" it feels odd to have cocaine identified as a non-*Specified substance* and, at the same time, listed as *Substance of abuse*. In our ADRV experience cocaine is very rarely abused with the purpose to enhance sport performance. For the sake of consistency, we therefore propose to keep cocaine listed as a *Substance of Abuse*, but to identify it as a *Specified substance* instead of a non-*Specified substance.*

S1. Anabolic agents

- We support the decision to transfer tibolone from S1.2 to S1.1.

- Using alphabetical order, ebonosarm (ostarine) should be placed before LGD-4033 (ligandrol).

S2. Peptide hormones, growth factors, related substances, and mimetics

- No comments

S3. Beta-2 agonists

- We do not support the proposed modification of the daily dosing time intervals for salbutamol. The new exception is harder to explain to the sports community and therefore causes a higher risk for true athletes. It also interferes more with good medical practice.
    - According to the *Summary of major modifications and explanatory notes* the modification is proposed to reduce the risk of any potential *Adverse Analytical Finding* arising after high doses are taken at once. This is true for a 12 hour time interval (from 800 to 1200 microgram), but at the same time the risk for an eight hour time interval gets higher since the maximum allowed total intake for this time interval is reduced by 25% (from 800 to 600 microgram).
    - Athletes using 400 microgram *Cyclocaps* can take one dose per 8 hours under the suggested rules, while they can take two doses per 12 hour time interval under the current rules.
    - Athletes need to be more careful during the third 8 hour time interval in 24 hours, as taking three successive maximum allowed intakes per eight hour time interval will lead to exceedance of the maximum allowed intake per 24 hour time interval by 200 microgram (1800 versus 1600 microgram).

  We suggest the LiEG to use just one intake limit with one time interval. We prefer to only use 1600 micrograms per 24 hours from the start of any dose as it is in line with the 24 hour time intervals used for all the other beta-2 agonist exceptions.

- Although we have understood it is not easy from a laboratory analytical point of view, we recommend to further study the pharmacokinetics of terbutaline in order to find a solution to permit the use of terbutaline up to the manufacturer's maximum recommended metered dose as well. This would further minimize the interference with good medical practice as terbutaline is one of the regular medications in the treatment of asthmatics in our country.

- 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

- The presumed misuse of thyroxine by Dutch athletes was a major issue in the last couple of years. We therefore 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. We believe there are no potential performance or AAS post-cycle benefits for women to use it. 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 favours 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, 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."*

  Although we understand the rationale of this policy, we feel it 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. Therefore, we 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.:

    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.

M2. Chemical and physical manipulation

- No comments

M3. Gene and cell doping

- No comments

S6. Stimulants

- We welcome the proposed minor modifications:
    - To change *imidazole derivatives* into *imidazoline derivatives* to distinguish between generic imidazole derivatives and sympathomimetic imidazolines.
    - To clarify that the urinary threshold of 5 µg/mL applicable to findings of cathine refers to both isomers of norpseudoephedrine.
    - To add ethylphenidate, 3-methylnaphthidate and 4-fluoromethylphenidate as examples of methylphenidate analogues.
    - To add hydrafinil (fluorenol) as an example of an analogue of modafinil and adrafinil

- 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.

S8. Cannabinoids

- Substances such as cannabinoids, that most likely have a negative impact on athletic performance - and only theoretically might be able to have a very marginal potency to increase performance - should not be part of the anti-doping program. We cannot help but feel that the listing of cannabinoids is predominantly a political statement, rather than a logical outcome of weighing the Code criteria. The review published in 2011 by Marilyn Huestis, Irene Mazzoni, and Olivier Rabin (https://doi.org/10.2165/11591430-000000000-00000) is outdated and we feel it is a topic that should be re-addressed by numerous experts. We offer our help in such an endeavor. Based on our current knowledge we find that the inclusion of cannabinoids does not add value to the *Prohibited List*. In fact, it harms the credibility of all our anti-doping efforts.

- If laboratories would currently consider to 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 CBD oil and hemp products. For references, please see the work from Cologne, like Mareck et al (2020, https://doi.org/10.1002/dta.2959) and the group's upcoming *Recent advances in doping analysis (29)* publication. If all cannabinoids except CBD will remain prohibited, we suggest to give clear instructions to the laboratories on the testing menu requirements for cannabinoids and/or revisiting reporting levels for all prohibited natural cannabinoids.

S9. Glucocorticoids

- We would like to thank the LiEG for providing detailed reasoning for their decision to prohibit all injectable routes of administration for glucocorticoids during the *In-Competition* period. We also would like to thank the LiEG for providing washout periods following administration of glucocorticoids to be used to decide whether a *Therapeutic Use Exemption* (TUE) may be required.

- From a legal perspective, we can understand the decision to prohibit all injectable routes of administration for glucocorticoids during the *In-Competition* period. As is written in the *Summary of major modifications and explanatory notes* there is "*sufficient data available to show that the same systemic concentrations as existing prohibited routes can be achieved after administration by local injection at licensed therapeutic doses*". It was impossible to set a clear reporting level to differentiate administration by local injection from existing prohibited routes of administration under the current rules. Hence, we support the LiEG's search for a better solution.

  However, based on our review criteria, we do have some concerns regarding the proposed new rules:
  - The *Prohibited List* should have minimal interference with good medical practice and protect athletes with no malicious intentions. Prohibiting all injectable routes of administration 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. It can also cause athletes to

unnecessarily undergo surgery, as alternative permitted treatment, to treat common medical conditions like bursitis or neuralgia.

- The *Prohibited List* should have strong focus on catching intentional cheaters while protecting athletes with no malicious intentions. Glucocorticoids are catabolic substances. In our understanding, only endurance athletes seem to be able to fractionally and briefly enhance their performance by the use of glucocorticoids. Over longer period of time the use of glucocorticoids decreases performance. Figures from the *2020 Monitoring Program* clearly show the prevalence of glucocorticoid use is relatively low. It also reveals equal use *In-Competition* (1.8%) compared to *Out-of-Competition* (1.7%). If the use of glucocorticoids was abused by a substantial number of athletes to enhance performance, the percentage *In-Competition* would not only be higher than 1.8%, it would also be much higher In-Competition than *Out-of-Competition.* Even if we look at the figures per sport, only in wrestling the percentage *In-Competition* (4.3%) is twice as high compared to *Out-of-Competition (2.1%).* Therefore, we suggest to introduce a more targeted approach by leaving the decision to the International Federations. For example, via a so called sport-specific *Ban on injections* or *No needle policy*.
- The *Prohibited List* should be easily explainable to the sports community. With seven basic variables leading to five different washout periods ranging from three to 60 days, it is really not. On top of that, the *Prohibited List* will only become publically available just over 90 days before the rules will be in force. With a maximum washout period of 60 days, the implementation of the rules might become a tremendous educational challenge.

<u>Index</u>

- The *Prohibited List* was redesigned last year. Although we welcome the improvements in navigation and usability, we feel the use of an index is abundant and as a result is only leading to more work (and potential mistakes) when translating the *Prohibited List* in other languages. Also, we have received several questions in the past year regarding the listing of permitted substances such as xylometazoline in the index – it confuses the doctors who use the Prohibited List as a reference.

<u>Monitoring Program</u>

- We support the removal of bemitil and glucocorticoids from the *Monitoring Program* as the required prevalence data were obtained.

- It is our feeling that more 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.

- On 14 May WADA published the 2019 Monitoring Program Figures. The document is clearly marked as being 'confidential'. The accompanying letter also states the document "*is being shared on a confidential basis".* We always assumed the Monitoring Program Figures were publicly available documents. We think it is important to be open and transparent in our field of work and feel we have a duty to explain why we make certain decisions. This includes sharing aggregate data. Therefore, we ask WADA to change the confidential status of the Monitoring Program Figures and make them publicly available.