DOPING AUTORITEIT

Regarding: Netherlands reaction to draft 2014 Prohibited List International Standard (a shared submission of four stakeholders)

Capelle aan den IJssel, 19 July 2013

Dear Mr. Howman and members of WADA's Prohibited List Expert Group,

Thank you very much again for the invitation to review the new draft of the Prohibited List International Standard. With this letter, I would like to provide you with the comments of four Dutch stakeholders, being:

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

On behalf of these four organisations I would like to ask you to treat this letter as a fourfold contribution to your consultation process.

As usual, we have used our continuous relationship with athletes, physicians, pharmacists, and scientists over the previous year to collate our remarks and comments.

Introduction

We thank you for the changes that were introduced in the Prohibited List last year; we feel the Prohibited List has increased in strength because of the changes that were introduced. We hope that with the continuous support of all stakeholders the process of improving the Prohibited List International Standard will continue. The current discussions on the new World Anti-Doping Code may obviously impact the Prohibited List as well, but this is something that will be taken into account next year.

In September last year we were caught off guard by two major changes in the final version of the 2013 Prohibited List (in sections S3 regarding the new maximum allowed dose for formoterol and M1 regarding the definitions of blood manipulations) without a possibility to comment on them. Therefore, we will comment on these changes in this letter as well.

An extra surprise was the decision by WADA's Executive Committee in May this year to increase the threshold level for carboxy-THC to 150 ng/ml. We will comment on the contents and consequences of this decision in section S8, but from a principal point of view we would like to ask WADA not to make such far-reaching decisions without appropriate consultation and without scientific reasoning. Practically speaking, the new rule came into effect overnight, rendering many of our educational materials useless. The annual process of announcing a new Prohibited List around October 1st which comes into effect the following January 1st suits the educational role of all ADOs much better.

General comments
As always, we have followed the subsequent characteristics in reviewing the Prohibited List International Standard:

- the List should optimise the possibility to catch cheating athletes and their supporting personnel by prioritising on the criterion of performance enhancement;
- it should minimise the impact on good-willing athletes, which means it is as short as possible, but as long as necessary;
- it should minimise the requirements for good-willing physicians and other support personnel;
- it should not interfere with guidelines of good medical practice and focus on the issue of doping in sports;
- it should be easily explainable to athletes, their support personnel and the general public, so these groups will not be alienated from anti-doping efforts in general.

By adhering to these characteristics, we feel that the Prohibited List will be optimally focussed, practical, and understandable to everyone involved, thereby strengthening the World Anti-Doping Program. Generally speaking, there are two keywords that arise from our proposals and comments:

Clarity
The Prohibited List should be clear to everyone involved. It should, for example, aim to minimize the practical impact of the catch-all phrase "similar chemical structure or similar biological effect(s)" and it should be easy to understand why certain groups of substances are prohibited, whereas others are not. The current version of the "Summary of major modifications and explanatory notes" explains some decisions, but unfortunately not all.

Transparency
WADA should not hesitate to publicly explain the outcomes of the decisions that are ultimately made by the Prohibited List Expert Group. The annual process that is followed is strong, and by explaining its sturdiness the support of the Prohibited List will increase. WADA's explanations to exclude powerful substances such as nicotine and thyroid hormones and to include substances about which there continues to be a debate regarding their preferred doping-status, such as cannabinoids and glucocorticosteroids, will focus discussions and, ultimately, enable even stronger support amongst a larger group of people.

The importance of these keywords was recently stressed by the report of the independent Dutch anti-doping commission, that was commissioned to study the 'doping culture' and anti-doping measures in Dutch cycling. Many cyclists mentioned in their interviews that the current Prohibited List contains several substances that cannot be regarded to be performance enhancing in many sports, which makes that the entire list is taken less seriously. It is one of the rationalisations that cyclists used to explain their doping use.

Specific comments

S1

Both nandrolone and 19-norandrostenedione are still listed in section S1-1a ("Exogenous AAS") even though it has been known for years that these substances can be produced endogenously. For example, Hemmersbach and colleagues stated in 2006 "The first reports of human, in vivo production of nandrolone in the ovarian follicle were published 15–20 years ago" (Biomed Chromatogr 20(8): 710-717) and Kicman has stated in 2010 "adverse findings for nandrolone are frequent, but this steroid and 19-norandrostenedione are also produced endogenously" (Handb Exp Pharmacol 2010; 195:25-64).

- We strongly suggest that both nandrolone and 19-norandrosterone are moved to section b of S1-1. Since they can be produced endogenously, that would be a more suitable place.

S2

We are surprised to see that the phrase "and their releasing factors" is deleted in group S2-1, especially since the pharmaceutical market for erythropoiesis-stimulating agents (ESAs) seems to be blossoming. There is no explanation given for this change in the "Summary of major modifications and explanatory notes".

- Since the term "ESAs" has become commonplace in haematology, we feel it is more logical to specifically include the releasing factors of these agents in the Prohibited List as well. If WADA would decide otherwise, this is a change that requires an explanation.

In January 2011, we welcomed the removal of the methods of injecting "Platelet Rich Plasma" (PRP) or "Platelet Leukocyte Gel" (PLG) in therapeutic settings from this section. The Explanatory Notes to the Prohibited List International Standard explained this status in previous years, but when the Prohibited List 2014 comes into effect these remarks will no longer be easily available. This could present problems, especially since PRP could fit into the current definition of "gene doping", which includes "the use of normal … cells".

- In order to avoid confusion we feel it is necessary to explain the permitted status of therapeutical PRP and PLG in the Prohibited List itself. This could, for example, be done in a similar way to the remarks regarding felypressin (in section S5) or imidazole and adrenaline (in section S6).

S3

The rules for all inhaled β2-agonists should be in line with each other. Over the past few years, scientific literature has well established that inhaled β2-agonists have no proven performance enhancing effect on endurance, strength and sprint performance in healthy athletes (see e.g. Pluim et al., Sports Med 41(1): 39-57, 2011). In this light, it is very surprising to have different rules for salbutamol, salmeterol, and formoterol on one hand, and terbutaline, fenoterol and other similar substances on the other hand. In fact, this demarcation in the anti-doping rules is interfering in a physician's decision to prescribe certain medication. We have had several cases already where an athlete has been using a particular β2-agonist for many years, and partly because of this optimal medication the required drop in lung function parameters during a provocation test was not reached. In such cases, the athlete is caught between the doping rules and their personal optimal medication regimen, but because of the current rules they often opt to switch their medication to salbutamol. This is a real-life example where anti-doping rules interfere too much in the physician-patient relationship, and with guidelines of good medical practice.

In addition, we were surprised to see the change in the maximum allowed delivered dose for formoterol in the final Prohibited List, released on 10 September 2012. The direction of the change (an increase in the allowed dose) was welcomed as it followed the principles of our previous recommendations, but in our view this is still perceived as only part of the total solution.

➢ We strongly suggest that WADA will allow the use of all inhaled β2-agonists, including terbutaline and fenoterol, at least up to official pharmaceutical delivery dosages.

S4

No changes have been proposed, but our comment from last year is still valid: the decision to move insulins to section S4 without copying the words "releasing factors" and "other substances with similar chemical structure or similar biological effect(s)" means that the substances exenatide and liraglutide are permitted per 1-1-2013. We are curious about the backgrounds that have led to this decision. Moreover, from a methodological point of view, it is strange to move insulins (which are, by definition, peptide hormones) out of the group that is labelled "Peptide hormones, Growth factors and related substances" into an other group of prohibited substances.

➢ Please provide the rational (scientific, practical or otherwise) for permitting two substances that have been banned in the past and for the decision to remove a peptide hormone out of the group labelled "Peptide hormones…".

➢ As a minor point: for the sake of consistency, it would be better to conclude each subsection with a semicolon (;) and to conclude the final subsection (in this case 5) with a period (.), just like has been done in sections S3 and M3.

S5

No changes have been proposed, but our comment from last year is still valid: the final paragraph, on the TUE-requirement for threshold substances under certain circumstances, seems not to be necessary on the basis of the information that we possess. The instances that this would happen are very, very rare and we are not aware of any actual anti-doping rule violation that has been committed on the basis of this paragraph. It is doubtful whether any anti-doping organisation would be confident enough to start a case based on this prohibition if such a situation occurs. Moreover, the current wording ("any quantity of a substance subject to threshold limits") opens the way for inadvertent violations, for example when codeine has been used and morphine-metabolites can be found in an athlete's urine.

➢ The final paragraph, on the TUE-requirement for threshold substances under certain circumstances, merits a better explanation on the necessity of this rule, or can be omitted.

M1

Thank you for changing the definitions of "Blood Manipulations" in September last year. These have made it more clear which actions are prohibited, and which are not. In our view these new texts also mean that the altruistic act of plasmapheresis is prohibited, which in our opinion does not serve a specific anti-doping purpose. But at the same time we have not yet been confronted with any practical problems regarding these changes.

M2

No comments.

M3
The texts on Gene Doping remain unchanged, which on the one hand is good since the annually occurring changes over the last few years made this method difficult to interpret. But on the other hand the current texts still seem to include permitted therapies such as PRP (see our comments made above in section S2) and allergen immunotherapy. We feel that this should not be the case.

➢ We would like to ask WADA to make clear that medical interventions such as PRP and allergen immunotherapy are not included in the definition of gene doping. This does not necessary require a change in the definition; a solution might be to specifically allow these therapeutic methods just like the sentences addressing the status of felypressin (in section S5) or imidazole and adrenaline (in section S6), or to address this issue in the "Explanatory Note".

S6
We support the proposed texts; they follow our general characteristics outlined in the introduction of our comments, being a call for more clarity and transparency.

S7
No changes have been proposed, but our comment from last year is still valid: to our knowledge, the abuse of this category of substances is very, very limited and if they are abused, it constitutes medical malpractice more than doping use (i.e. it is not a case where an unfair competitive edge is being sought). Frankly, we only encounter this section in combination with (questions about) abundant poppy seed use or TUE-applications regarding surgery and concomittant painkillers.

➢ We suggest that a remark could be made that the use of narcotics is allowed during surgical interventions, much like the remark on intravenous infusions in section M2-2, or that this section can be deleted altogether. Following the general characteristics we described earlier, we feel that this section is less important than other sections on the Prohibited List and that its practical influence should be lessened even further.

S8
We are of the opinion that the use of a substance that is most likely to have a negative impact on athletic performance (such as cannabis) should not be part of the anti-doping program, especially when its use has been out-of-competition. Athletes, being role models to the young, should not be using marihuana nor should they engage themselves in morally objectionable activities such as speeding when driving a car or even smoking in their private lives. These activities, however, are not doping issues, and they should not lead to severe doping sanctions. We are aware of the various views that exist on this issue, but we would like to ask you to try and find a solution that is less rigorous than the current prohibition.

Given the fact that cannabis is still part of the Prohibited List, we welcome the practical consequences of the recent decision by WADA's Executive Committee to increase the threshold level for carboxy-THC to 150 ng/ml as we can expect a 75% drop in cannabis cases because of this new rule. Still, it would have been better if this decision would have been backed by scientific data and if a draft-decision had been circulated among the various stakeholders, including an explanation of WADA's views on this issue.

At a fundamental level, we feel it is unfair to sanction athletes on the basis of presence of a long-lasting metabolite in an athlete's sample when this particular substance is only prohibited in-competition. The higher threshold will certainly diminish this problem, but it is not likely to eliminate it. The work from Brenneissen et al. (Anal Bioanal Chem (2010) 396:2493–2502) and Mareck et al. (Drug Test Anal (2009) 1(11-12): 505-510) gives examples on how to solve this fundamental issue in the case of cannabis. Those solutions would give better founded alternative approaches than the introduction of a new arbitrary threshold.

- If cannabis is to remain on the Prohibited List, we suggest the introduction of new approaches to test for the use of cannabis in-competition, such as (the glucuronides of) the pharmacologically active delta9-tetrahydrocannabinol and/or 11-hydroxy-delta9-tetrahydrocannabinol. This would allow a better measure of 'in-competition use' than the use of a threshold in carboxy-THC.
- As a minor point: for the sake of consistency, all prohibited substances should be printed in bold, as is the case in all other sections of the Prohibited List.

S9 / P1 / P2 / Monitoring Program
No comments.

Concluding remarks
In case the work of the Expert Group can be helped by explaining our proposals in more depth or by providing alternative proposals or more data we would be more than happy to assist.

With sincere greetings and the best wishes in your efforts to compile the final version of the 2014 Prohibited List,

Also on behalf of the Ministry of Health, Welfare, and Sports, the Netherlands Olympic Committee*Netherlands Sports Confederation (NOC*NSF), and the NOC*NSF Athletes' Commission,

Anti-Doping Authority the Netherlands

Herman Ram
CEO