DOPING AUTORITEIT

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Regarding: Netherlands reaction to draft 2013 Prohibited List International Standard (a shared submission of four stakeholders)

Capelle aan den IJssel, 29 June 2012

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

Thank you very much for the invitation to review the draft 2013 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 are particularly grateful that, by starting to use the new interface WADAConnect this year, all stakeholders' comments are shared within the anti-doping community. As you know, that has been our preference since the first Prohibited List was published by WADA in 2004; we can even foresee a publicly available overview of all comments in the future because we firmly believe that anti-doping policies are strengthened by as much transparency as possible.

We are especially looking forward to reading the various proposals deriving from athlete's committees, as they play a pivotal role in our work.

Because of this new initiative, we have chosen to repeat some of our general and specific comments from previous years as we would like to share these with our international colleagues.

General comments

We feel it is important that a Prohibited List International Standard is compiled on the basis of the following characteristics:

- it minimises the impact on good-willing athletes, which means it is as short as possible, but as long as necessary;
- it minimises the requirements for good-willing physicians and other support personnel;
- it does not interfere with guidelines of good medical practice and focuses on the issue of doping in sports;
- it optimises the possibility to catch cheating athletes and their supporting personnel by prioritising on the criterion of performance enhancement;
- it is 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 following 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.

We would like to emphasise that these characteristics should not only lead to discussions on whether certain substances or groups of substances could be added or removed from the Prohibited List. Other possible solutions to strengthen anti-doping efforts include raising reporting thresholds, changing the rules on sanctioning for these substances, and/or limiting their prohibited status to certain sports known to have problems regarding this particular group of substances. It is important to find a balance between effective anti-doping regulations and the impact that these regulations have on the lives of athletes and the work of their supporting personnel.

We are aware that part of these changes are also considered in the current consultation phase of a revised World Anti-Doping Code, but the current Code already allows for prioritising certain aspects of potentially prohibited substances and methods. These discussions need to be held at all levels of the World Anti-Doping Program. We kindly ask WADA to acknowledge our firm opinion in this regard, and to choose solutions that recognise the different views that exist rather than deciding in a manner which completely rejects the strongly held views of one or more Anti-Doping Organisations.

From these principles, we have derived three concrete proposals for further improvement of the annual process to update the Prohibited List.

More transparency
We welcome the "Summary of modifications and explanatory notes" that annually accompanies the release of a new Prohibited List International Standard. Yet, we feel that the process of drafting the Prohibited List and collating comments from stakeholders would benefit from even more transparency. Every single change in the Prohibited List should be accompanied by an explanation why it was decided to make this change and this years draft still leaves several questions unanswered (as we will point out in the specific sections below). This would help both the support of the Prohibited List and the educational efforts when introducing a new Prohibited List to the athletic community (including support personnel).

More clarity
Together with transparancy, we feel that more clarity (and perhaps more guidance) is needed on certain substances that fall under the text "similar chemical structure or similar biological effect(s)". In the past we have had several instances where WADA's interpretation of certain substances was different than we had thought initially, which makes it difficult to give clear and proper information to our "clients". Apparently, some sort of list exists in the WADA's office that gives guidance on the issue whether certain substances, that are not specifically mentioned on the Prohibited List, are in fact

prohibited or not. Perhaps more examples could be mentioned on the Prohibited List itself, or another solution could be that WADA would make their interpretation public. This could be a first step towards a global overview of permitted and prohibited medicines, which would help all countries. As you know, many countries already publish their own lists of permitted and prohibited medicines on their own initiatives.

Working symposium
Finally we feel that the Prohibited List International Standard is so important that it merits a special working symposium on the contents and principles of the Prohibited List. There are obviously very different views on an "optimal" Prohibited List around the world, and some important issues are best discussed at large, instead of being tackled once a year in written comments. Examples are the possible elimination of the current differences in prohibiting substances in and/or out-of-competition, the absence of potentially harmful performance enhancing substances such as thyroid hormones and nicotine and the presence of substances where these properties are doubtful (e.g. cannabinoids, narcotics, and alcohol). Especially now the process towards the Revision of the World Anti-Doping Code is fully underway it is important to provide a platform to find a common approach regarding all Prohibited List issues, especially the most controversial ones. This way, the Prohibited List International Standard could be supported by a much larger proportion of all stakeholders than in the current situation, which would seriously strengthen the World Anti-Doping Program.

Specific comments

S0
The proposed new text on "veterinary use" is supported.

S1
The proposed changes in section S1-1 are generally supported, but it remains unclear why these particular INN and IUPAC names are used. We were advised by the Royal Dutch Pharmacists Association that they have different IUPAC names in their databases. All names that are marked yellow in the attached Excel-document are official IUPAC names according to the handbooks of the Royal Dutch Pharmacists Association (see excerpts in the attached pdf-file) but are different from the names that are listed in the Prohibited List International Standard. It is unclear to us how it is possible that two different IUPAC-names can exist.

- We would like to suggest that generally available IUPAC-names are used consistently in this section; see our attached documentation. We are, of course, willing to assist in helping to find one common approach regarding the used names for anabolic agents.

Even though the issue of clenbuterol-contaminated food stuffs has somewhat subsided during the last year, we still feel that more attention to this problem is warranted. The current status, where all athletes are advised to be extremely cautious with meat originating from China and Mexico, is not very reassuring to athletes who participate in events in those countries, and it is still unknown what the risks are of meat originating from countries in the rest of Asia, South America and Africa (assuming that the existing regulatory systems in Europe, North-America, and Oceania are sufficient to exclude meat contamination with doping substances in those continents). Hence, the current situation is not satisfactory. The current rules of the World Anti-Doping Program allow for tackling new unexpected cases, but these procedures take several months, and the damage done to the athlete during these procedures (in terms of procedural costs, publicity, emotional stress and possibly loss of employment) cannot be repaired.

- We would like to ask WADA, and particularly both the List Committee and the Laboratory Committee, to try and find a solution for potential unintentional Adverse Analytical Findings regarding steroids-in-meat. We feel that the World Anti-Doping

Program should protect good-willing athletes at all times. A possible solution that could be implemented is to raise the reporting levels for certain substances for all WADA-accredited laboratories. Other possible solutions might be to introduce the possibility to report "atypical" findings below a certain threshold, or to further study specific analytical approaches that may discern intentional use from unintentional use through food (presumably meat) consumption.

It is surprising to see that both nandrolone and 19-norandrosterone are still listed in section S1-1a ("Exogenous AAS"). It has been known for years that these substances can be produced endogenously, and several Technical Documents related to the International Standard for Laboratories have accommodated for this. Please allow us to give two examples: Kicman has stated "adverse findings for nandrolone are frequent, but this steroid and 19-norandrostenedione are also produced endogenously" (Biochemical and physiological aspects of endogenous androgens; Handb Exp Pharmacol 2010; 195:25-64) and Strahm et al. have written "it may be expected that endogenous 19-NA levels of 15 ng/mL could be measured in urine specimens collected during pregnancy" (Profiling of 19-norandrosterone sulfate and glucuronide in human urine: implications in athlete's drug testing; Steroids 2009; 74:359–364).

- 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

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 2011 and 2012 explained this status, but when the Prohibited List 2013 comes into effect this remark 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".

- Since the methods of injecting "Platelet Rich Plasma" (PRP) or "Platelet Leukocyte Gel" (PLG) involve prohibited growth factors (like IGF-1), we feel it is necessary to explain the permitted status of these methods in therapeutic settings in the Prohibited List itself, in order to avoid any confusion. 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

Over the past few years, scientific literature has well established that inhaled β2-agonists have no performance enhancing effect on endurance, strength and sprint performance in healthy athletes. 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.

Moreover, the sudden introduction of a maximal dose for formoterol of 36 micrograms over 24 hours has surprised us in September 2011. The 2012 "Summary of major modifications and explanatory notes" document stated that "inhaled formoterol at therapeutic doses is no longer prohibited", but this is not the case. In many countries in the world, including the Netherlands, the maximal therapeutic dose is higher, with a

maximum of 72 micrograms per day. The current rule does not take national differences into account, and therefore presents only part of the solution for this particular substance; it adds in fact confusion to an already complicated group of substances. It would be much clearer to both athletes and their physicians if all therapeutic doses of formoterol would be permitted. It is even more puzzling since no clarification has been given in the explanatory note on why this restriction in dose would be necessary, and no official explanation is given in the decision to introduce a new urinary threshold of 30 nanograms per millilitre.

➢ We strongly request that WADA will allow the use of all inhaled β2-agonists, including globally accepted standard therapeutic doses of formoterol. We would also welcome a public explanation on the urinary threshold for formoterol. Ultimately, we would favour the introduction of new thresholds for terbutaline, fenoterol, and other β2-agonists.

S4

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.

➢ Please provide the rational (scientific, practical or otherwise) for permitting two substances that are currently banned.

S5

We are in agreement with the proposed change, and very happy that a decision has been made regarding the threshold value of glycerol.

The final paragraph, on the TUE-requirement for threshold substances under certain circumstances, remains to be superfluous in our eyes. 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, deserves a better explanation on the necessity of this rule, or can be omitted.

M1

The recent discussions in Germany on the issue whether so-called "UV treatment of blood" constitutes blood doping (or not) revealed that a more clear definition is needed for blood doping. The new wording in section M2-3 overlaps this debate and we feel it is better to combine the two prohibitions into one section.

➢ We propose that the method of blood doping should be defined better, for example "Blood doping is the (re)introduction of any quantity of blood or blood component(s) into the circulatory system. Blood components include autologous, homologous or heterologous blood or red blood cell products of any origin."

Both in our proposal and in the proposed draft for the 2013 Prohibited List hemodialysis, plasmapheresis, and plateletpheresis are prohibited. In our eyes, this is not really necessary as these medical procedures are not performance enhancing in normal, healthy athletes and do not pose a direct threat towards doping use.

➢ We would like to ask you to consider to permit hemodialysis, plasmapheresis and plateletpheresis, for example by adding a clear remark that these procedures are permitted "when legitimately executed in hospital settings". In the current draft, it is

mentioned that plasmapheresis would require a TUE in the future, but this is not a clear solution since this procedure would not fulfil regular TUE requirements (it is not therapeutic use – it is a therapeutic gift). Therefore, if this procedure remains to be prohibited, a new guideline is necessary on how TUE-committees should handle such requests.

M2
Besides the comment made above in section M1, there is the small issue that in this section the word "prohibited" is used twice (both in the general sentence and in two of the three subsections).

➢ For consistency reasons, the words "is prohibited" and "are prohibited" should be deleted in subsections 1 and 2.

M3
The change in this section is supported, but we would like to make two additional comments. Firstly, although the proposed change is minimal, we would prefer a more constant definition of gene doping over time, unless new insights must be reflected in this section. Secondly, we received some questions in the course of 2012 whether the prohibition of "The use of normal … cells" also includes PRP (see our comments made above in section S2) or allergen immunotherapy. This should not be the case in our eyes. So, in spite of our first comment, we would like to have this issue addressed in the definition of gene doping.

➢ We would like you to make clear that medical interventions such as PRP (see section S2) and allergen immunotherapy are not included in the definition of gene doping. Once this is clear, we would like to ask you to leave the definition of gene doping unchanged for some time, unless new insights regarding this topic require otherwise.

S6
The explanatory regarding methylhexaneamine is very much appreciated. This is a substance where inadvertent doping is a constant threat.

S7
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 relation to (questions about) abundant poppy seed use or TUE-applications regarding surgery and concomittant painkillers.

➢ 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. 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.

S8
Whether cannabis use in sports should be prohibited and sanctioned by means of anti-doping rules will probably always remain a controversy. We welcomed the publication about "Cannabis in sport - anti-doping perspective" by Huestis et al in 2011 (Cannabis in sport: anti-doping perspective; Sports Med 2011; 41(11):949-966). It is tempting to write an elaborate reaction to their views, but this would result in a too much detailed discussion. In short we feel that their arguments, however eloquently put, have not changed our opinion, namely that the use of a substance that is most likely to have a negative impact on athletic performance 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 smoking in their private lives or speeding when driving a

car in rural areas. These activities, however, are not doping issues, and they should not lead to the severe doping sanctions.

- We would like to ask WADA to try and find a solution that recognises our view (which we know is shared by many other stakeholders) as well as other views that exist in the world regarding the issue of "cannabinoids and doping". This might be arranged by changes in the Prohibited List or in other WADA documents, e.g. raising the reporting threshold or changing the sanction regimen in case of a first cannabis offence. From a principal point of view, 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 work from Brenneissen et al. (Anal Bioanal Chem (2010) 396:2493–2502) gives examples on how to solve this fundamental issue in the case of cannabinoids.

- As a minor point: for the sake of consistency, all prohibited substances should be printed in bold.

S9 / P1 / P2
No comments.

The 2013 Monitoring Program
One new addition is proposed, and as always we support the increase of knowledge by gathering new data. But we would like to emphasise beforehand that the presence of a certain substance in an athlete's sample does not constitute abuse. A certain prevalence will provide little information unless it can be compared with prevalences in other cohorts, such as sub-elite athletes or age-matched controls.

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

With sincere greetings and the best wishes in your efforts to compile the final version of the 2013 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
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