WORLD ANTI-DOPING AGENCY
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WORLD ANTI-DOPING AGENCY
Health, Medical & Research (HMR) Committee Meeting Minutes
September 3rd-4th, 2009

Participants:

Pr. Arne Ljungqvist (AL), Chairman	Attending
Pr. Kamal Al-Hadidi (KA)	Attending
Pr. Eduardo De Rose (EDR)	Attending
Dr Jiri Dvorak (JD)	Attending
Pr. Theodore Friedmann (TF)	Attending
Pr. David Gerrard (DG)	Attending
Pr. Luis Horta (LH)	Attending
Dr. Manikayasagam Jegathesan (MJ)	Attending
Pr. Per Wiik Johansen (PJ)	Attending
Pr. Ichiro Kono (IK)	Attending
Dr. Jean-Claude Mbanya (JCM)	Attending
Dr. José Antonio Pascual (TP)	Attending
Dr. Babette Pluim (BP)	Attending
Dr. Patrick Schamasch (PS)	Attending
Dr. Gary Wadler (GW)	Attending

WADA Staff

Dr. Osquel Barroso (OB)	Attending
Dr. Irene Mazzoni (IM)	Attending
Dr. Olivier Rabin (OR)	Attending

Guest

Dr. Fabio Pigozzi (IUSM, University of Rome) representing FIMS.

1. Welcome and Review of the Agenda

- Mr. David Howman and Prof. Arne Ljungqvist welcomed the Committee members.
- The Resignation of Pr. Tim Noakes was noted.
- Two new members of the HMR Committee, Prof. Kamal Al-Hadidi and Dr. Manikayasagam Jegathesan were introduced.
- The Agenda was approved.

2. Review of 2010 Prohibited List, report from the List Subcommittee and recommendation to the Executive Committee

- The 2010 Draft of the Prohibited List prepared by the List Committee was presented by Dr Gary Wadler, Chairman of the List Committee. The proposed changes were for the most part accepted by the HMR Committee and some points were further discussed:
    1. The introductory paragraph was modified to reflect changes in S.2 section;

2. The International Nonproprietary Name (INN) for methyltrienolone (metribolone) was included;
3. The "Comment to class S1.1b" (Anabolic Agents) was transferred from the Prohibited List to another WADA document to be determined by the WADA Laboratory Committee. The List Committee also recommended the HMR Committee to encourage the Laboratory Committee to speed up the implementation of the *Athlete's* steroid profiles, so that other markers in addition to the T/E ratio will could be used to declare an *Adverse Analytical Finding;*
4. The "Comment to class S2" (Peptide Hormones, Growth Factors and Related Substances) was deleted from the Prohibited List and will be included in another WADA document to be determined by the WADA Laboratory Committee;
5. The title of S2 class was modified to "Peptide Hormones, Growth Factors and Related Substances" to better define the substances under this category;
6. To reflect the growing number of substances available under S2, methoxy polyethylene glycol-epoetin beta (CERA) was included as an example of new erythropoeisis-stimulating substances available and additional examples of growth factors affecting muscle, tendon or ligament protein synthesis/degradation, vascularisation, energy utilization, regenerative capacity or fibre type switching [e.g. Platelet-derived Growth Factor (PDGF), Fibroblast Growth Factors (FGFs), Vascular-Endothelial Growth Factor (VEGF), Hepatocyte Growth Factor (HGF)] were included as well;
7. The status of Platelet-derived preparations (e.g. Platelet Rich Plasma, "blood spinning"), was clarified. They are prohibited and require a TUE if administered intramuscularly and a declaration of use for other routes of administration. Since there is not a unique protocol to obtain these preparations the Committee also encouraged independent research on this method;
8. The List Committee had recommended that salbutamol, salmeterol, terbutaline, fenoterol and procaterol by inhalation should only require a declaration of use rather than a TUE. However, some of these medications can be obtained as oral or intravenous preparations as well. In addition, WADA is conducting studies to determine thresholds to distinguish inhaled from systemic administration. Therefore, until those studies are completed, the HMR Committee decided to change for now the requirements for the therapeutic use of salbutamol and salmeterol by inhalation. These two beta2-agonists now need a declaration of use and no longer a TUE when administered by inhalation while any other inhaled beta-2-agonists still require a TUE. The International Standards for TUE will be changed accordingly;
9. It was clarified that the maximum dose for the controlled pharmacokinetic study for salbutamol cannot exceed the maximum therapeutic dose for inhaled salbutamol (1600 µg/day);
10. Two other examples of aromatase inhibitors, namely androstene-3,6,17 trione (6-oxo) and androsta-1,4,6-triene-3,17-dione (androstatrienedione) were included in view of their wide availability as components of nutritional supplements;
11. The prohibited status of the plasma expander glycerol (oral and intravenous) and the non-prohibited status of pamabrom, a weak diuretic largely available as a combined over-the-counter medication, were clarified in the 2010 List;
12. The status of supplemental oxygen was changed and is no longer prohibited as there is little evidence that it can be performance enhancing;
13. Proteases were included as an example of sample adulteration in Prohibited Methods M2 and the definition of Gene Doping was reworded to make it clearer;
14. The status of intravenous infusions was reviewed and now reads: "Intravenous infusions are prohibited except for those legitimately received in the course of hospital admissions or clinical investigations";
15. Three stimulants were added to the close list of non-specified stimulants: benfluorex, prenylamine, as both are known to metabolize to non-specified stimulants

(amphetamine or norfenfluramine) and methylhexaneamine as it is a non-therapeutic substance;

16. Pseudoephedrine was reintroduced in the Prohibited List as a specified stimulant because: a) results from the Monitoring Program over the past 5 years have shown a sustained increase in urinary concentrations of pseudoephedrine in athletes, b) there was clear evidence of abuse in some sports and regions and c) the available scientific literature demonstrated its performance enhancing effects at certain doses. Given the wide availability of pseudoephedrine-containing medicines, pseudoephedrine was reintroduced in the 2010 List with a urinary threshold of 150 µg/mL based on the results from controlled excretion studies done by WADA as well as the literature;

17. There were no changes in the Glucocorticoid class and the HMR Committee supported that WADA continues to conduct studies to differentiate administration by inhaled, intra-articular and systemic routes with the objective to establish thresholds based upon urinary concentrations;

18. It was clarified that synthetic cannabinoids are covered in class S8 (Cannabinoids);

19. Any references to the International Paralympic Committee (IPC) for alcohol and beta-blockers classes were deleted, as the responsibility for testing in the sports of Boules and Archery has been transferred from IPC to the World Bowling Federation and the International Archery Federation (FITA), respectively.

3. Review and recommendation for the 2009 research projects

- The HMR Committee was informed of the outcome of the implementation of WADA's new web-based platform for grant submission. The platform was greatly appreciated both by the applicants as well as by WADA research grant's management.
- Members of the HMR Committee responsible for organizing the peer-review process and WADA staff presented a summary of the evaluations received from the external independent reviewers in their field.
- A ranking of projects within each category was made and 33 projects were selected.
- For several projects, budgetary revisions were recommended, especially when coming from the same laboratory and involving the same personnel.
- Two projects from one group were considered to present extensive overlap and therefore a unified project was recommended.
- One project was considered important but risky. Therefore, a pilot project of one year duration was recommended with a greatly reduced budget, with further evaluation of the outcomes at the end of the granting period.
- One extension project was approved with the condition that the Final report from the previous project due in May 2010 shows considerable success.
- One project was favorably reviewed but the HMR Committee pointed out that there was extensive overlap with an ongoing project. Therefore, it was proposed that the project is tailored so that there are no redundancies with the existing grant.
- One project aimed to established thresholds for 4 common inhaled beta-2 agonists. The HMR Committee recommended asking the investigators to add procaterol to the project, as it is widely used in Asia.

4. Report from TUE Subcommittee

- Dr David Gerrard, Chairman of the TUE Committee gave an update on the TUE Subcommittee activities during 2009.
- Review of TUE applications: There was a backlog of reviews of TUE due to the absence of WADA's Medical Director. Furthermore, almost half of the applications are incomplete.
- There was a high load of applications for asthma medications. The cost of bronchial provocation tests on the athletes' budgets was acknowledged by the TUE Committee.

- An International TUE Symposium in collaboration with the Council of Europe will take place in Strasbourg in December 2009. The program includes case presentations, medical information and TUE and ethical reviews.
- There was an update on Medical Conditions for which the Minimal Standards of Best Clinical Practice have been completed. These included: hypogonadism & hormone deficiencies; attention deficit hyperactivity disorder; narcolepsy; insulin-dependent diabetes; renal failure/transplantation; asthma and hypertension. The work is in progress for other conditions such as musculoskeletal conditions, medical use of IV infusions and female adrenal insufficiency.
- The HMR Committee was informed that mutual recognition of TUEs granted by different Federations does not occur all the time. The HMR Committee believed that the increased use of ADAMS with time will help to improve this situation.
- The TUE Committee Chairman concluded his report stressing the need for medical guidelines for different pathologies including the establishment of minimum diagnostic criteria, medical collaboration and mutual recognition of TUEs and the importance of having a consistent TUEC process that is fair to all athletes.

5. Report from Laboratory Subcommittee

- Pr, Luis Horta, Chairman of the Laboratory Subcommittee, gave an update on the Laboratory Subcommittee activities.
- There was no false positive reported in the Proficiency Testing program but some corrective actions were taken for some false negatives or unsatisfactory quantitative results.
- All laboratories were re-accredited except for the Ankara and Penang Laboratories due to poor technical performance. The two laboratories were later re-instated following proper corrective actions received by WADA.
- One of the main objectives of the Laboratory Subcommittee for 2009 and 2010 was and will be to develop a strategy aimed at incrementing the consistency of the steroid profile data across the accredited laboratories in order to be ready for the application of the athlete's steroid longitudinal profile.
- Two Educational Tests will be completed during 2009 (hCG and 19-NA).
- There have been significant improvements in the Documentation Packages.
- The New Delhi and Bucharest laboratories received WADA accreditation in 2009.
- The Kazakhstan laboratory successfully completed six WADA proficiency testing rounds but the Kazakhstan government has not yet ratified the UNESCO Convention against Doping in Sport, which is a pre-requisite for accreditation.
- The WADA Executive Committee preselected three laboratories as candidates for the WADA accreditation process: the Buenos Aires laboratory in Argentina, the Mexico laboratory in Mexico and the Doha laboratory in Qatar.
- The initial visit to the Vancouver satellite laboratory for the 2010 Winter Olympic Games was conducted by Victoria Ivanova, WADA Scientific Project Manager. In addition, Prof. Christiane Ayotte, Director of the Montreal and the Vancouver satellite doping laboratories, updated the Subcommittee on the laboratory preparations.
- Version 6.0 of International Standards for Laboratories came into effect on January 1st, 2009. Several Technical Documents continued to be reviewed by the Laboratory Subcommittee along the year and those finished came into effect. It was expected that all Technical Documents will be finished by December 2009.
- ILAC-WADA collaboration: a meeting will take place in October 2009.
- A working group was established to study the effects of alcohol on the T/E ratio.
- The Subcommittee agreed that extreme low doses of formestane should be considered endogenous.

4. Report from the Gene Doping Panel

- Pr. Ted Friedmann, Chairman of the Gene Doping Panel, summarized the recommendations of the Gene Doping Panel with regards to the research projects on gene doping.
- The Panel stressed the importance of evolving the strategy vis-à-vis projects that attempt to identify molecular signatures for doping in general and gene doping in particular, as science progressed and results were becoming available. It was concluded that these studies are complicated to interpret so the Panel recommended to stop accumulating data and to attempt starting validation in humans as soon as possible. To this end, good candidate genes and molecular markers should be identified; once this is done, experiments should be designed to minimize variables (e.g. one laboratory and reagents, one technique) and see whether these candidate molecular signatures can be validated.
- During the review of the 2009 grants for gene doping, these Gene Doping Panel recommendations were taken into account.

5. Athlete's Passport

- Dr Olivier Rabin gave an update on the Athlete's Passport. The Passport has 2 modules: a- hematological; b- endocrine (subdivided in: i- steroids, ii- other). There has been good progress and a few antidoping organizations (e.g. UCI) are currently implementing the Hematological Passport. Guidelines are being finalized for the hematological module e.g. blood collection, shipping, quality control, period of resting before venipuncture. A proposal is expected to be presented to the WADA Executive Committee in December. The steroid profile is of high interest as well; the variables to be tested have been presented and there are 3 WADA accredited laboratories (Lausanne, Montreal, Cologne) involved in the development phase.
- It is envisaged that when an athlete profile deviates, the athlete can be prosecuted if there are no justifying pathophysiological reasons.
- It is foreseeable that the Athlete's passport and the regular testing will be co-implemented as not all Prohibited substances can be followed through the Passport.

7. Therapeutic use of growth factors, stem cells and Platelet-Rich Plasma

- The issue of Platelet-Rich Plasma (PRP) and growth factors was addressed by the List and HMR Committees and is reflected in the modifications introduced in class S2.
- Use of Stem Cells: some athletes appear to be using stem cells to speed up healing and recovery from injuries. AL informed that the International Olympic Committee intends to convene a consensus meeting on the state of the art of stem cell, platelet-rich plasma and other growth factors procedures in April 2010. WADA, due to its activities in the field, requested to be invited.

8. Blood Doping Symposium

- Drs Ichiro Kono and Olivier Rabin gave an update on the Blood Doping Symposium that will take place in Tokyo in November 2009.
- The Symposium is sponsored by the Japanese Government, the Japan Anti-Doping Agency and WADA. Dr Kono especially thanked the Japanese authorities.
- The main subjects include blood transfusions (autologous, homologous), EPO and analogues, Hematological module of the Athlete Passport, what has been achieved to date and future directions.
- There will be local and international experts in the field.

9. B sample

- B sample: : There have been discussions in the anti-doping field on whether a B sample is still necessary as, due to improvements in analytical techniques along the years, the probability that a B sample will not match the A sample is negligible. WADA will write a position paper which will be discussed during the 2010 HMR Committee meeting and the outcome submitted to the Executive Committee.

10. Worldwide Drug Information Database

- Dr Rabin informed the HMR Committee that WADA was working with Pharmaceutical Press (Martindale) to set up a worldwide information database on prohibited substances in sports. Martindale has already published a pocket book on prohibited substances in sports and now a web-based approach will follow.
- Other anti-doping agencies which have already established similar databases have been invited for a meeting to exchange experiences and ideas on the subject, to be held in Montreal on November 19th, 2009. The List Committee has agreed to be consulted when needed to clarify the status of drugs.
- It will be originally launched in English and French.
- The HMR Committee fully supported the project.

11. Presentation by Dr Ted Friedmann

- Dr Ted Friedmann gave a presentation on the WADA-sponsored bioinformatics project at University of California San Diego (UCSD).
- The rationale for cross-study analyses of different WADA-sponsored molecular signature projects was that these studies use disparate chemical and biological agents, experimental platforms and designs and analytical methods.
- As a consequence, important parts of a genetic doping signature may be overlooked in individual genetic and proteomic studies.
- The bioinformatics unit is now functional and allows secured uploading and downloading of data from a remote host (WADA grantees).
- A large number of in-house analytical programs are available at UCSD for centralized comparison of available datasets from participating WADA laboratories and for use by participating laboratories.
- Some datasets were compared and preliminary results showed that there may be some molecular signatures associated with hypoxia and IGF-I.
- Future steps will be directed towards validation in the first place as well as to obtain additional datasets from other WADA investigators.

12. Any Other Business

- *Adverse Analytical Findings* and Positive *Samples*: It is well known that not all *Adverse Analytical Findings* result in Anti-Doping Rules Violations (ADRV), because they could be due to medications allowed with a TUE. In view of this, all Federations were requested to submit the number of positive doping samples for the compiled laboratory statistics but many of them have yet to comply. There was a proposal by Dr Jiri Dvorak to add a new column to the compiled statistics of *Adverse Analytical Findings* so to include the real positive cases.
- Research capabilities: Although WADA has the greatest share of grant funding for anti-doping, some Federations and national anti-doping organizations also fund research projects in the field. In order to more effectively use overall antidoping research capabilities, it was proposed to convene a meeting with other research funding organizations in order to share information and ideas on how to better use the money and resources available.
- Toolkit for Sports Physicians: David Julien (DJ), WADA's Education Department Manager, informed the HMR Committee that the Education Department is preparing a toolkit for Sports

Physicians, including information on prohibited substances, dangers to athlete's health and sport medicine ethics. WADA Science Department was already collaborating and DJ requested help from the HMR Committee to develop the chapter on Alternatives to doping. Since some parts of the toolkit could be complemented by the IOC's Sport Medicine Manual it was recommended to work closely with the IOC Medical Commission to avoid redundancies.

12. Next meeting

- The next HMR Committee meeting is scheduled for September 2-3, 2010.
- The meeting is adjourned.