WORLD ANTI-DOPING AGENCY
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# WORLD ANTI-DOPING AGENCY
# Health, Medical & Research (HMR) Committee Meeting Minutes
# September 2ND-3rd, 2010

## Participants:

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| 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. José Antonio Pascual (TP) | Attending |
| Dr. Babette Pluim (BP) | Attending |
| Dr. Patrick Schamasch (PS) | Attending |
| Pr. Chara Spiliopoulou (CS) | Attending |
| Dr. Gary Wadler (GW) | Attending |
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| Pr. Jean-Claude Mbanya (JCM) | Apologies |

WADA Staff

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| Dr. Osquel Barroso (OB) | Attending |
| Dr. Irene Mazzoni (IM) | Attending |
| Dr. Olivier Rabin (OR) | Attending |
| Dr. Alan Vernec (AV) | Attending |

Guest

Pr. 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.
- One new member of the HMR Committee, Prof. Chara Spiliopoulou, was introduced.
- The Agenda was approved.

## 2. Review of 2011 Prohibited List, report from the List Expert Group and recommendation to the Executive Committee

- The 2011 Draft of the Prohibited List, prepared by the List Expert Group (LEG) was presented by Dr Gary Wadler, Chairman of the LEG. All the proposed changes, except for one, were accepted by the HMR Committee and some points were further discussed:

    1. An introductory sentence emphasizing the status of drugs with no official approval and not covered by other sections of the Prohibited List was added;

2. To reflect the growing number of substances developed to stimulate erythropoiesis, hypoxia-inducible factor (HIF)-stabilizers were added as examples;
3. The non-proprietary name of Hematide was added (peginesatide);
4. Intra-muscular use of Platelet-Derived Preparations (PRP) was removed from the Prohibited List based on the lack of any evidence concerning the use of these methods for purposes of performance enhancement to date;
5. The LEG had recommended that formoterol by inhalation should not be prohibited. However, the HMR noted that formoterol could be obtained as an oral preparation as well and that WADA was conducting studies to determine thresholds to distinguish inhaled from systemic administration. Therefore, until those studies were completed, the HMR Committee decided that inhaled formoterol should remain prohibited;
6. All references to the declaration of *Use* were removed from the List;
7. Desmopressin was added to the Diuretics and Masking Agents section;
8. The last paragraph of the S5 section (Diuretics and Masking Agents) was revised to more clearly explain the consequences of detecting an exogenous threshold substance at a sub-threshold concentration in the presence of a diuretic or other masking agent;
9. Methods that consist of sequentially withdrawing, manipulating and reinfusing whole blood into the circulation were added to the M2 section (Chemical and Physical Manipulation);
10. For clarification purposes the gene doping definition was reworded and split into three points in agreement with the proposal of the Gene Doping Panel;
11. The stimulant methylhexaneamine, previously included in the List as a non-specified stimulant, was changed to the specified group of stimulants, because it was argued that it was frequently found in nutritional supplements;
12. The spelling of levmetamfetamine was changed to the International Non-Proprietary Name;
13. There were adjustments in the S8 section to clarify that marijuana-like substances (cannabimimetics) were included in the List;
14. Only the prohibited routes of glucocorticosteroid administration remained listed in the S9 section;
15. Modern Pentathlon (disciplines involving shooting) was removed from Alcohol at the request of the Union Internationale de Pentathlon Moderne (UIPM) and due to changes introduced in the format of the competition;
16. For clarification purposes, Skeleton, governed by Federation International de Bobsleigh et Tobogganing (FIBT), was added by name to the list of sports where beta-blockers were prohibited;
17. Gymnastics was removed from beta-blockers at the request of the Fédération Internationale de Gymnastique (FIG);
18. The HMR agreed to prohibit beta-blockers in the sport of darts at the request of the World Darts Federation (WDF).
19. Discussions by the HM&R Committee on the beta-2-agonists and the glucocorticosteroids sections of the Prohibited List reiterated the imperative of establishing thresholds for these two classes of substances.

## 3. Review and recommendation for the 2010 research projects

- Members of the HMR Committee responsible for organizing the peer-review process and WADA management 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 34 projects were selected.
- For several projects, budgetary revisions were recommended.

- Six grants from 3 different themes were considered to present extensive overlaps and therefore it was recommended that the investigators coordinate their research to avoid overlaps or establish a collaboration.
- One project was considered important but uncertain. 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.
- Two extension projects were approved with the condition that the Final reports from the previous projects were received.
- Two projects were considered important but very uncertain. A second review of the data and the grants was requested and decisions would be made based on these new set of reviews.
- One project was considered interesting but outside the realm of science and related to testing. A recommendation was made to the Standards and Harmonization Department to contact the investigators for a possible collaboration.

## 4. Report from the TUE Expert Group

- Pr. David Gerrard, Chairman of the TUE Expert Group (TUE-EG) gave an update on the TUE Subcommittee activities during 2010.
- The critical high volume of work resulted in screening TUEs for clinical "red flags"
- There was varied use of ADAMS by National Anti-Doping Organizations (NADO) and International Federations (IF).
- The TUE-EG recommended the List Expert Group to remove the request of declarations of *Use* from the List.
- There were considerations on whether long-term/lifetime TUEs could be granted for certain chronic conditions like insulin-dependent diabetes mellitus or inflammatory bowel disease. In case of recurrent medical conditions like severe asthma or anaphylaxis, the TUE-EG discussed the possibility of granting 3-year TUEs or create "stand by" TUEs. Both proposals were in the early stages of conceptualization.
- It was stressed that the Medical Information found in WADA's website was meant to assist the TUE-Committees and to standardize practice. The Guidelines demanded regular review and updates based on new medical information.
- The HMR Committee was informed that mutual recognition of TUEs granted by different Federations was an important principle. However, it was difficult to apply due to variable levels of expertise in the TUE Committees and sometimes the absence of TUE Committees in some IFs and NADOs; therefore improvements were needed in this area.

## 5. Report from the Laboratory Expert Group

- Dr. Toni Pascual, Chairman of the Laboratory Expert Group (LaEG), gave an update on the LaEG activities during 2010.
- The majority of laboratories did well in the External Quality Assessment Scheme (EQAS) program but corrective actions had to be taken in some cases.
- It was proposed to modify the number of EQAS rounds from 4 to 3 per year and to increase the number of samples per round from 5 to 6.
- The LaEG continues to review the Curriculum Vitae of proposed laboratory directors in the future.
- The Bogota (Colombia) laboratory was suspended in view of a non-compliance with the International Standard for Laboratories regarding the status of the accreditation body that granted its ISO/IEC-17025 accreditation; the laboratory's accreditation was later re-instated following its re-assessment by an ILAC full-member accreditation body .
- The Penang (Malaysia) laboratory accreditation was revoked due to recurrent analytical deficiencies and reporting mistakes.
- The Almaty (Kazakhstan) laboratory had demonstrated satisfactory performance along all the probationary phase. The UNESCO convention was ratified by Kazakhstan.

- The Buenos Aires (Argentina) laboratory pre-probationary phase was in progress; the ISO accreditation body had been contacted, new instrumentation had been acquired and a relationship had been established with the Madrid laboratory for mentoring. However, the LaEG considered that the progress of the laboratory in this period of candidacy to enter the WADA pre-accreditation phase has been too slow. The assessment of Mexico City (Mexico) laboratory to enter the pre-probationary phase was also in progress; a pre-probationary visit to the laboratory was performed by WADA Science Department and the LaEG, and the laboratory participated in a pre-probationary test. The outcomes of the visit and the results of the test are to be analyzed at the meeting of the LaEG and the laboratory will be asked to provide the applicable corrective actions for any deficiencies that may have been identified. The plan of the laboratory was to get accreditation by 2011 and a relationship had been established with the Barcelona laboratory for tutoring. It seemed unlikely that the accreditation process of the Mexico laboratory would be finished in time for the Pan-American Games in 2011.
- The Doha (Qatar) laboratory was not yet ready for the pre-probationary phase. There was a good plan to develop a laboratory by 2012 and an agreement had been established with the Barcelona laboratory for tutoring.
- The Vancouver satellite laboratory for the 2010 Winter Olympic Games had had an excellent performance during the Olympic and Paralympic Games and had already been dismantled.
- The Technical documents for: Nandrolone, Decision Limits, Minimum Required Performance Limits, Identification Criteria for Qualitative Assays, and Blood Analytical Requirements for the Athlete Biological Passport, were updated.
- The LaEG was working on a new version of the Technical Document on Endogenous Androgenic Anabolic Steroids (EAAS), including the concept of the steroid profile and the application of IRMS analysis to establish the exogenous/endogenous origin of steroids found in athletes' samples.
- The LaEG developed the Minimum Required Criteria for Satellite Haematological Laboratories that will be approved in support of the Athlete's Biological Passport (haematological module).
- The need for a B sample was considered by the LaEG. No final recommendation was made to the HMR Committee, but the pros and cons considered by the LaEG were enumerated:
  - Other fields (e.g. forensics) did not have a B sample, but the sample was not necessarily the only proof.
  - The B sample served as the back-up of the A sample if the latter broke or deteriorated with storage.
  - Not having a B sample would open the possibility of doing counter-analysis in a different laboratory.
  - Elimination of B sample would simplify the collection procedure and save money for storage and transportation.

The HMR Committee further discussed the need for a B sample later during the meeting (see below).

## 6. Report from the Gene Doping Panel

- Pr. Ted Friedmann, Chairman of the Gene Doping Panel, summarized the recommendations of the Gene Doping Panel:
  - The Panel had concluded that the molecular signatures approach may be valid but difficult. Nevertheless, all the molecular signature data generated by the WADA research projects should be analyzed through the WADA bioinformatics project at University of California San Diego (UCSD) to attempt to validate molecular candidates. Direct detection should be easier to achieve than indirect, particularly because athletes constituted a heterogeneous population subject to intense and dissimilar trainings and sport activities appeared to heavily impact on gene expression.
  - Dr Chris Evans had updated the Panel on the use of orthopedic gene therapy relevant to doping. Based on current data, Dr Evans had considered these techniques therapeutic rather than performance enhancing.

- Dr John Gearhart had updated the Panel on the use of stem cells for doping purposes. Dr Gearhart had concluded that stem cell technology was still experimental for human use and did not seem to be a concern for doping at the moment.
- Dr Kurt Zinn had given a presentation on non-invasive imaging techniques that could be useful for anti-doping i.e. Diffusion Weighted Magnetic Resonance Imaging and Sonoelastography. The Panel had shown high interest in sonoelastography and had recommended WADA to consider it for research funding if possible.
- Pr Friedmann indicated that the Panel was still not completely satisfied with the definition of Gene Doping in the Prohibited List and that they were still working on a better wording.

## 7. Athlete's Biological Passport (ABP)

- Dr Alan Vernec gave an update on the Athlete's Passport and informed that:
  - The ABP Operating Guidelines had been approved in December 2009 and they included mandatory protocols to ensure both legal solidity and scientific certainty.
  - It would be possible to use non-WADA accredited laboratories for analysing blood parameters.
  - The ABP software had been incorporated into ADAMS, allowing WADA to monitor and share the data. A group of experts in sport haematology were being identified for the data monitoring.
  - The steroid module is still under development.

## 8. Collaboration with the Pharmaceutical Industry

- Dr Olivier Rabin updated on the collaboration between WADA and the pharmaceutical industry. In the past, WADA had collaborated as needed with the pharmaceutical and biotechnology industry to develop detection techniques and exchange scientific information.
- More recently WADA had signed an agreement of collaboration with the International Pharmaceutical Manufacturers Association (IPMA), which nucleates the biggest pharmaceutical companies in the world and many national associations of pharmaceutical companies.
- WADA was also in talks with other pharmaceutical and biotechnology groups.
- The general idea was not only to work on detection methods but also to make scientists from the private sector aware that their products may be misused for doping.

## 9. Need for a B-sample

- The HMR Committee discussed the need for a B-sample based upon a position paper presented. It was noted that:
  - the main reason for the existence of a B-sample was historical, originating from the distrust between nations during the cold war. Since there was an element of suspicion when an *Adverse Analytical Finding* was reported by a Laboratory from a country in a rival block, the analysis of the B-sample in the presence of the *Athlete* or his/her representatives was meant to reassure the fairness of the procedure.
  - since the inception of doping control analyses in 1968, only in 3 instances the results from the A sample did not coincide with those reported for the B sample in the absence of satisfactory explanation (e.g degradation, manipulation, technical or reporting error).
  - B-samples existed for urinary samples but not for blood samples.
- Technical points were also discussed by the HMR Committee:
  - the A-sample would be aliquoted upon reception and one aliquot stored as a back-up for counter-analysis and to preserve the integrity of the original sample
  - less volume would be needed; therefore abolishing the B-sample would simplify collection of doping control samples and save significant costs.

- in case of an *Adverse Analytical Finding* the *Athlete* should still have the opportunity to be present for the re-analysis
- overall, the only difference in the procedure would be that the B-sample would no longer be collected; the rest would remain the same.

- The HMR Committee was in favour of discussing further the possibility of eliminating the B-sample. To this end, the Committee decided that a revised version of the position paper on the pros and cons would be issued and circulated for discussion by the end of the year. An assessment of the cost impact of maintaining the B sample collection would need to be considered. The Executive Committee would be informed of this process during their next meeting on September 18, 2010.

## 9. Next meeting

- The next HMR Committee meeting was scheduled for **September 1-2, 2011*.**
- The meeting was adjourned.

***** *Later changed to* **August 25-26 2011**