Nandrolone Progress Report to the UK Sports Council from the Expert Committee on Nandrolone

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UK Sport's purpose is to lead the UK to sporting excellence by supporting:

- Winning athletes;
- World class events;
- Ethically fair and drug-free sport.

Preface

UK Sport recognises that athletes who have provided samples for the purpose of anti-doping are entitled to expect that the testing procedure is sound and that the results of the tests carried out are meaningful and completely reliable. In consequence of the increase in the number of adverse reports concerning nandrolone in the UK in 1999, UK Sport established a committee of experts to look into the issue of nandrolone. The Committee comprised a number of senior scientists with relevant experience, who in addition to considering the available information, have taken advice from other scientists, both in the UK and overseas in an attempt to gain a comprehensive and global overview of the problem.

The Committee has looked at a number of aspects, examining the analytical methods, the interpretation of results, the sample collection process as well as possible origins of nandrolone metabolites found in urine samples. The committee also looked at the rules and investigatory procedures in relation to nandrolone to consider whether any aspect needed further clarification. The Committee report to UK Sport was published in **January 2000** and made the following conclusions and recommendations which were accepted by UK Sport.

- 1. The data suggests an increase in 1999 in the number of adverse reports concerning the anabolic steroid nandrolone.
- 2. We consider that the IOC recommended sample collection procedures are satisfactory. We have examined in particular the arrangements in the UK and are satisfied that they are of a high standard. Storage and transport arrangements, together with associated chain of custody documentation should be strictly adhered to.
- The committee has examined the analytical procedures that are employed for the detection of nandrolone metabolites in urine and is of the opinion that they are satisfactory. The laboratories are accredited and approved, and employ analytical techniques and laboratory practices which are of a high standard.
- 4. We suggest that an indication of the concentration of nandrolone metabolites in a sample that is declared positive should be included in the adverse report that the laboratory issues. We recognise that this has to be done with due regard for the cost involved and that full quantification may not be necessary.
- 5. We consider that it would be helpful if the IOC would define the urine concentration of 19norandrosterone above which it considers that a doping offence may have been committed. Further studies should be carried out to investigate generally the factors influencing the endogenous production of nandrolone in human subjects.
- 6. We recommend that the IOC should publicise and make available the analytical criteria issued to laboratories (Analytical criteria for reporting low concentrations of anabolic steroids) (Appendix 4).
- 7. Some dietary supplements contain compounds similar to nandrolone or its metabolic precursors, which produce the same metabolites as does nandrolone. It may not be obvious from the label that such substances are present and are banned substances. Users of inadequately or incorrectly labelled products are at risk of unknowingly ingesting a banned substance. We therefore recommend that the sports community should be reminded they must maintain a high level of awareness of the possible hazards of using some nutritional supplements and herbal preparations.
- 8. We have not seen any evidence that suggests that a dietary substance can influence the production of nandrolone within the body.
- 9. We recommend that the availability of new nutritional supplements or substances purporting to be performance-enhancing drugs should be monitored and the rules that include the list of banned substances should be up-dated regularly in response to this information.
- 10. We are unable to assess fully the possible risk that consumption of meat may cause a notifiable urine concentration of 19-norandrosterone, but we believe that the possibility is remote from eating good quality unprocessed muscle meat from commoner animal species. It may be prudent to avoid offal from boar and horse.

UK Sport understands that governing bodies of sport, as the bodies responsible for the disciplinary procedures, should have available sufficient data to enable fair and informed decisions to be reached in hearings. Consequently, UK Sport invited the expert committee to continue to meet to consider the progress made in relation to nandrolone and the original recommendations. This report updates the information available in relation to nandrolone and has been accepted by UK Sport for publication.

UK Sport expresses its gratitude to the members of the committee (and in particular its chair Professor Vivian James) for their hard work and diligence in investigating the issues and providing expert guidance to UK Sport who are committed to taking forward the recommendations and conclusions to the international sporting community.

Richard Callicott

UK Sport Chief Executive

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Introduction

 Since the publication of the first Report of the UK Sport Expert Committee on Nandrolone in January 2000, the Committee (Appendix 1) has met on a further four occasions and has continued its enquiries, including consultation with experts external to the Committee (Appendix 2). This Report represents further conclusions and recommendations made after renewed consideration of matters relevant to the Committee's terms of reference:

"Investigate the current situation with regard to the testing of sports men and women for evidence of nandrolone abuse and to reach conclusions and make recommendations."

Incidence of adverse findings

2. The results of the UK Sport drug testing programme which includes both UK and non-UK competitors are shown in Appendix 3. In 1999 the number of positive findings which related to nandrolone was 0.29% of the total number of samples analysed. In the previous 11 years the range was 0.02% to 0.22% with an average of 0.10%. In the year 2000, the incidence declined to 0.09% of 5,406 'A' samples analysed. In 2001 and 2002, the incidence was 0.15% and 0.13% respectively. The increase during 1999 was not reflected in data from international events, although the Committee noted that with the exception of the 1999 results, the UK incidence has always been substantially less than elsewhere. It is concluded that the increase in 1999 in the UK appears to have been an exceptional occurrence, not mirrored elsewhere, and not repeated subsequently.

Contamination of supplements

3. When the Committee last reviewed the position it noted a few reports that described the contamination of "dietary supplements" with banned steroids that were not described on the label of these preparations. Since then, there have been further reports which have confirmed and extended these findings (1, 2). These show that when certain steroid preparations, herbal supplements, and nutritional supplements were examined they were found to contain undisclosed steroids

^{F1} The term "Dietary supplement" is used in this report to describe a variety of products that are marketed for the purpose of enhancing sporting performance.

- which are included within the International Olympic Committee (IOC) prohibited classes of substances (3). It has also been shown that ingestion of some of these contaminated supplements by volunteers resulted in positive urine findings (1, 2). There is as yet no explanation for the contamination, but a possible cause is cross-contamination during manufacture. In one investigation (2), it was pointed out that the manufacturer of the contaminated preparation also produced the steroids that were discovered.
- The extent of the problem is illustrated by a recent press release from the IOC (April 2002) based on the results of analysis of 634 nonhormonal dietary supplements from 13 countries by the IOC-accredited laboratory in Cologne, Germany (4). Out of the 634 samples tested, 94 (14.8%) contained prohibited anabolic-androgenic steroids. SO prohormones, not listed on any label. The data from this study confirms that the consumption of such dietary supplements may lead to positive doping tests, especially for the nandrolone metabolite 19-norandrosterone. This investigation was supported by a grant from the IOC.
- 5. The Austrian Federal Ministry for Social Security and Public Welfare, Vienna, has carried out a similar investigation of 54 supplements, of which 12 (22%) were found to contain anabolic steroids which were not declared on the packaging (5).
- These results reinforce the warning, which was given in our last report, that competitors who use dietary supplements may inadvertently put themselves at risk of producing an adverse result on testing.
- 7. One hypothesis for the cause of the above problem is possible cross-contamination during manufacture of certain supplements. UK Sport has initiated discussions with a number of suppliers in the UK in an attempt to ensure that all relevant dietary supplements offered for sale are safe with respect to steroid contamination, but to date no useful progress has been made towards resolving what is clearly a potentially serious issue for competitors who decide that they wish to use supplements. It has also been suggested that independent body might carry out analytical checks on supplements. However, independent testing would need to take account of possible between-batch variation, and would be very expensive. A high degree of purity in "safe" products is required because it has been demonstrated that only very small

amounts of contaminant are necessary to produce a positive urine test. This contamination problem requires continuing investigation to elucidate the cause(s) and the extent

Endogenous production of nandrolone

- 8. Currently, there is no definitive method for distinguishing urinary metabolites arising from administration of nandrolone (or other 19-nor androgens) from those arising from possible endogenous production. Although the use of an analytical carbon isotopic ratio measurement technique may potentially produce information which would assist with identifying the source of a metabolite in a urine sample (6, 7), the method is as yet still insufficiently refined to be to able to provide analytical results at low enough concentrations.
- 9. A paper by Le Bizec and co-workers (8) suggested that urinary 19-norandrosterone formed after nandrolone administration is exclusively conjugated to glucuronic acid whereas a proportion (~ 30%) of that produced from an endogenous source is sulpho-conjugated. Although these results are potentially of interest, the Committee noted that this was only a preliminary study and no data on the efficiency of extraction or of conjugate hydrolysis were given, the dose of nandrolone given was small (5 μg) and was administered by an oral route only and to a small number of volunteers.

Threshold reporting concentrations

10. The Committee has reconsidered the matter of threshold reporting concentrations for the urinary metabolite of nandrolone, norandrosterone. It has again been contended (9) that for sportsmen the existing threshold of 2 nanograms per millilitre of urine is too low, and principally the report (which was not peerreviewed) by Debruykere et al (10) was cited in support. The Committee has therefore again carefully reviewed all the evidence available to it. With regard to the report referred to above, it was considered that this was superseded by the subsequent publication from the same authors (11), who in referring to the values of 9, 14, and 37 nanograms per millilitre which they reported from a study of volunteer members of their laboratory staff in the paper published in 1991, commented that "although the link to contaminated meat could only be presumed at that time, as no dietary control was performed, fig 4 showing the prevalence

- of nandrolone in 1989, strengthens that presumption." On this basis, the Committee considers that the earlier high figures reported by these authors, which are completely at variance with almost all other reports, could not be considered as representative of a normal population.
- 11. A review by Kohler and Lambert (12) has also questioned the IOC threshold for reporting the presence of 19-norandrosterone in urine, on the basis that various physiological stimuli may increase the excretion of this steroid. The authors suggest that the matter is still open to debate. However, none of the relevant investigations published to date and which we consider to have been properly controlled, has indicated that conditions to which competitive athletes are exposed, such as exercise or stress, do in fact cause an increase of 19norandrosterone excretion to a concentration of current excess the threshold Nevertheless, the Committee concurs with the opinion of the authors of this review that further detailed physiological studies would be of value in defining in more detail the effect of such variables.
- 12. Reznik et al al (13) have investigated the effects of metabolic stress (hypoglycaemia), and testicular stimulation (human chorionic gonadotrophin) in ten healthy Hypoglycaemia did not significantly modify 19norandrosterone excretion, the maximum urinary concentration observed after stress being 0.19 nanograms per millilitre. After gonadotrophin administration, the urinary excretion rate of the steroid increased by 250%, but did not exceed a measured concentration of 0.43 nanograms per millilitre. Although these results must be interpreted with caution due to the limited number of volunteers, it is noted that in response to these dynamic tests, none of the subjects studied urinary 19-norandrosterone exhibited а concentration greater than 0.5 nanograms per millilitre.
- 13. The effect of exercise was chosen as the variable in a study by Saugy et al (14). A control group of 137 amateur footballers and 126 students was investigated, and prior to playing football, no detectable 19-norandrosterone (less than 0.2 nanograms per millilitre) was found in any of their urine samples. After a match, seven amateur players showed traces between 0.2 and 0.5 nanograms per millilitre and one had a concentration between 0.5 and 1 nanogram per millilitre. A group of 358 professional football players was

also examined but only after exercise; 336 showed concentrations below 0.2 nanograms per millilitre and 19 had concentrations between 0.2 and 2.0 nanograms per millilitre. Two players had concentrations after exercise of 2.2, and one of 2.5 nanograms per millilitre. Two of these samples (2.2, 2.5) though had a specific gravity greater than 1.020, indicating concentrated urines, and after allowing for this the results would have been below the appropriately adjusted IOC threshold. Thus without exercise, none of the subjects studied excreted detectable steroid, but after exercise some did do so. The study therefore confirms the observation (15) that exercise may cause an urinary concentration increase the 19-norandrosterone in some subjects, albeit in a small percentage of cases.

- 14. The Committee was uncomfortable with some aspects of the study by Saugy *et al* (14) for a number of reasons. The study was not easily interpreted because of the study design. There was an absence of controls to exclude the possibility of exogenous nandrolone administration. The protocol for the specific gravity correction had been misapplied. It therefore considered that little weight could be given to the hypothesis that the single concentration (2.2 nanograms per millilitre) above the reporting threshold was the result of endogenous production.
- 15. Some additional reports have now appeared which also relate to the basal urinary concentrations of 19-norandrosterone and the effect of exercise.
- 16. It has been suggested that a combination of the ingestion of certain dietary non-steroidal supplements and exercise could increase the endogenous production of nandrolone. No published evidence to support this claim has appeared.
- 17. Schmitt et al studied the effect of exhaustive exercise. They found basal concentrations did not exceed 0.25 ng per ml and there was no increase after exercise (16). Robinson et al (17) concluded that 6% of the footballers whom they studied showed very small amounts of 19-norandrosterone in their urine, but only after exercise. Another study (18) reported that after strenuous exercise, concentrations of up to 0.5 nanograms per millilitre were found. Le Bizec et al (19) reported a study of 385 football players before and after competition. Testosterone and LH concentrations were determined in blood to help exclude the possibility of nandrolone administration but they cannot do this completely. Urinary concentrations of 19-

- norandrosterone were generally higher after participation in a match and in the large majority of samples was less than 1 nanogram per millilitre. However, one sample had a concentration of 1.79 nanograms per millilitre.
- 18. Galan Martin *et al* (20) studied 40 healthy sports persons and 10 postmenopausal women. Four sportsmen had concentrations of 5, 6, 8 and 14 nanograms per millilitre, and a postmenopausal woman had a concentration of 22 nanograms per millilitre. The Committee considered that these findings were so completely different from all the other data available from other investigations of control subjects, that without further investigation it is difficult to accept these data as representative of a control population.
- 19. The Committee received confirmation from Dr Ueki of the data referred to in the previous Committee report (21).
- 20. A report (22) was received by the Committee from Professor Hemmersbach, Director of the IOC-accredited Laboratory in Oslo. His laboratory carried out the doping control analysis for the XVII Olympic Winter Games held in Lillehammer. A total of 524 test urine samples were analysed of which 357 came from male competitors. The samples were mainly from skiing, ice-skating and ice hockey events. Only one sample showed a concentration at or above a concentration of 2 nanograms per millilitre and this was from a female competitor who had taken an oral contraceptive containing norethisterone.
- 21. The Committee noted that some IOC-accredited laboratories are likely to have significant amounts of relevant data on urinary concentrations of 19-norandrosterone from their routine operations and felt it would be helpful if these data were to be published. The Committee also noted that there is a dearth of information on the possible amounts of urinary 19-norandrosterone excreted by non-pregnant women^{F2}, a deficiency that ought to be addressed.
- 22. Having considered all the information currently available to it, the Committee concluded that exercise may, in some cases, produce a small increase in the urinary concentration of 19-norandrosterone, but found no reason to believe this would exceed 2 nanograms per millilitre, and thus the current reporting threshold of 2

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In late pregnancy, urinary 19-norandrosterone may exceed 5 nanograms per millilitre (23).

nanograms per millilitre was regarded as appropriate for sportsmen.

Change to anti-doping code

23. The Committee noted that with effect from 1 January 2003, the IOC and the World Anti-Doping Agency have changed the Olympic Movement Anti-Doping Code, Appendix A, Prohibited Classes of Substances and Prohibited Methods, to the effect that a urinary concentration of 19-norandrosterone exceeding 2 nanograms per millilitre in a male athlete, or exceeding 5 nanograms per millilitre in a female athlete, will constitute a doping violation. Prior to this date, the onus of deciding whether a doping violation had occurred fell upon the relevant sports governing body.

Treatment of analytical uncertainty

24. In a presentation given to the International Laboratory Accreditation Co-operation/ International Accreditation Forum in September 2002 (24), it was suggested that the measurement of uncertainty employed by IOC-accredited laboratories was not made in accordance with current standards. It was pointed out to the Committee that, in fact, IOC-accredited laboratories comply with ISO 17025 and that necessitates laboratories to deal with the issue of uncertainty.

Court of Arbitration for Sport arbitral awards

25. The Committee has noted the conclusions in some recent arbitral awards in relation to 19-norandrosterone. In the case of UCI v Mason (25) the Court in considering the significance of relatively low concentrations of the metabolite had accepted the existence of a so-called "grey area" for metabolite excretion falling between 2 and 5 nanograms per millilitre of urine. The Courts written judgement stated that "within this grey zone, the likelihood that nandrolone is produced endogenously, is decreasing exponentially". Unfortunately, the award does not explain on what evidence this statement is based. In another award (26), the Court again referred to this grey zone, and commented that ".... the initiative for additional testing should lie on the side of the sanctioning body, rather than be left to the initiative of the accused athlete..." The Committee has, through UK Sport, asked the Court for evidence to support this concept and for guidance on how such further testing should be carried out, the response received explained that the Court of Arbitration for Sport (CAS) was not able to

- answer this question. We learned that an advisory opinion can only be obtain from CAS by the International Olympic Committee, an International Federation, a National Olympic Committee or an organising committee of an Olympic Games and that an advisory opinion was not binding but could be used as official reference. We were advised that "generally speaking the Court of Arbitration for Sport does not comment on an award issued by a CAS panel." (27)
- 26. In a more recent award (28), the Court has returned to the subject, and has now stated "In particular, there is <u>no</u> grey area between 2 and 5 ng/ml ... and reference to earlier decisions or statements which have made reference thereto have become irrelevant."
- 27. The Committee noted these comments and recommends that UK Sport should convey this information to sports governing bodies.

Steroid residues in food

- 28. The competent authority for veterinary residue surveillance in the UK is the Veterinary Medicines Directorate (VMD), an agency of the Department for the Environment, Food and Affairs. Rural The Veterinary Residue Committee (VRC), an independent advisory committee, oversees the residue surveillance programmes operated by the VMD and the Food Standards Agency's surveys. This committee's work includes assessing the health implications arising from the nature and concentrations of residues of authorised veterinary medicines, banned substances and contaminants detected in animals and animal products intended for human consumption in the UK. The most recent VRC annual surveillance report contains data for 2001. No evidence of nandrolone abuse was reported. Their report also notes the results of examination of fish samples (salmon and trout), which do not show detectable residues of nandrolone in muscle tissue.
- 29. Further work on the effect of ingesting edible boar tissue has been published (29). Since some boar tissues, notably liver, kidney and testicles, contain nandrolone naturally, e.g. (30), a consequence of ingesting these tissues is that 19-norandrosterone will be excreted in the urine. After consumption of a total of 310g of prepared edible boar tissue (boar kidney, heart, meat, and liver in roughly equal proportions), the resulting urinary excretion concentrations exceeded the reporting threshold but had returned to normal values (less than 0.1 nanograms per millilitre) within 24 hours (29).

30. The Committee reaffirms its view that the possibility is remote of a notifiable urine concentration arising from eating good quality meat from commoner animal species within the LIK

Laboratory procedures and reporting recommendations

- 31. Currently, IOC-accredited laboratories are required to issue an adverse report for 19-norandrosterone if the concentration in the test sample exceeds that of positive control urine. This concentration is 2 nanograms per millilitre for sportsmen and 5 nanograms per millilitre for sportswomen. The laboratory is not required to determine the concentration value.
- 32. The Committee suggested in its last report that when a laboratory issues an adverse report for 19-norandrosterone it would helpful to make available an indication of the concentration of this steroid in the sample.
- 33. This view is reaffirmed, and deemed to be of particular importance for values lying between 2 and 10 nanograms per millilitre, and it was agreed that the use of calibrants at these two concentrations was appropriate. For higher values, a concentration report is still considered helpful, albeit as an indicative value.
- 34. The Committee also agreed that for the quantification of 19-norandrosterone, peak purity is demonstrated, as described in the mass spectrometry section of the IOC document entitled "Analytical Criteria for Reporting Low Concentrations of Anabolic Steroids". The Committee also endorsed the approach currently being considered by WADA that a mathematical test (e.g. Student's t-test) should be employed to demonstrate statistically that the result is significantly greater than the reporting threshold.

Status of certain 19-norsteroids as dietary supplements

- 35. The Medicines Control Agency (MCA) has now made the following statement:
 - "The MCA has classified as medicines certain products containing 19-norsteroids (19-norandrostenedione, 19-norandrostenediol) which were on sale to the general public. Although medicine legislation does not enable 'blanket' classification of a substance, the MCA will continue to classify as medicines, products which are brought to their attention which contain steroid related compounds".

36. The Home Office has issued a letter (31) describing proposed changes to the Misuse of Drugs Act 1971 which, when brought into force, will bring these steroids within the scope of the

Specific gravity correction and expert evidence

- 37. It was noted that in a recent case dealt with by the International Amateur Athletic Federation (32) in which the urinary concentration of norandrosterone exceeded the reporting concentration, the analytical correction factor which has to be used in the case of urine samples which exceed a specific gravity of 1.020 had been misapplied. Instead of applying a correction to the positive control urine, the arbitration panel had been advised, and accepted, that the correction should be applied to the urine sample. This is at variance with the instructions that are clearly laid out in the IOC document "Analytical criteria for low concentrations of anabolic steroids". Since the CAS report refers to the fact that the Nandrolone Review Committee had approved the use of a specific gravity correction, the Committee wishes to make it clear that its statement was made on the basis that the correction is made to the positive control urine and not to the athlete's urine sample.
- 38. Disciplinary hearings, like courts of law, normally restrict witnesses to giving only factual evidence. In addition, where critical issues involve specialist knowledge and experience, as may occur in cases relating to nandrolone and other steroids, the tribunal may accept input from expert witnesses. Such people are asked to go beyond the normal limits of giving factual evidence by providing the tribunal with expert opinions.
- 39. Scientists and medical doctors normally receive no training in the role and the duties of being an expert witness and problems have occurred on this account in sports disciplinary hearings, just as they have in both civil and criminal courts. In particular, we point to the duties which expert witnesses have:
 - to act as a neutral resource for the tribunal, not allowing themselves to become advocates for either side in the proceedings, and
 - to stay within the area for which they are recognised as experts and not to offer, or allow themselves to be drawn into, giving opinions outside it.

We recommend UK Sport to address expert witness issues.

Conclusions and recommendations

- 40. The Committee makes the following comments and recommendations:
 - i) The increase in the number of adverse findings for nandrolone in 1999 appears to have been an exceptional occurrence, not subsequently repeated.
 - ii) There is further evidence that some dietary supplements contain banned steroids that are not included in the list of product ingredients.
 - iii) Competitors are again strongly advised that using dietary supplements carries the potential risk of unknowingly ingesting a banned substance.

We therefore recommend UK Sport:

- a) to encourage more manufacturers and suppliers of sports supplements to (i) strive to eliminate problem substances, and (ii) to label their products clearly to enable sport participants to avoid substances banned by the IOC.
- b) to continue its policy of encouraging and working with governing bodies, sports physicians and coaches to enhance their educational support for sport participants.
- iv) The Committee reaffirms its view that the current reporting thresholds for urinary 19-norandrosterone are satisfactory, even after exercise, and noted that the Court of Arbitration for Sport had accepted that there is no so-called "grey zone" between 2 and 5 nanograms per millilitre for this steroid for male competitors. It is recommended that this latter information be conveyed to governing bodies.

- v) It is noted that after 1 January 2003, a urinary concentration of 19-norandrosterone exceeding 2 ng/mL in a male or 5 ng/mL in a female will constitute a doping violation, as specified in the Olympic Movement Anti-Doping Code.
- vi) It is considered that the possibility is remote of a notifiable urine concentration arising from eating good quality meat from commoner species within the UK.
- vii) Recommendations are made in relation to the laboratory report, which include a suggestion that an indication of the concentration of 19-norandrosterone in the sample be reported.
- viii) The Committee considers that experts who advise governing bodies should be aware that they must offer independent advice and to present a balanced and unbiased opinion and it is recommended that UK Sport address this issue.

The Committee wishes it to be noted that this report provides an overview of the general position and not of any specific case(s), and that it expresses the opinion of the Committee at the date the report is made.

References

- Catlin DH, Leder BZ, Ahrens B, Starcevic B, Hatton CK, Green GA, et al. Trace contamination of over-the-counter androstenedione and positive urine test results for a nandrolone metabolite. Journal of the American Medical Association 2000;284:2618-21.
- Geyer H, Mareck-Engelke U, Reinhart U, Thevis M, Schanzer W. Positive dopingfalle mit norandrosteron durch verunreinigte nahrungserganzungsmittel. Deutsche Zeitschrift fur Sportsmedizin 2000;51:378-382.
- Appendix A-1. Prohibited classes of substances and prohibited methods. Olympic Movement Anti-Doping Code. Access document via http://www.olympic.org (under 'Ask a question' type 'Anti-Doping Code'). Date last accessed 12 December 2002.
- IOC nutritional supplements study points to need for greater quality control. Access web page via http://www.olympic.org (under 'Ask a question' type 'nutritional supplements' and then select the press release on 04 April 2002). Date last accessed 12 December 2002.
- 5. Forschungsberichte: "Untersuchung auf Verunreinigungen mögliche von Nahrungsergänzungsmitteln (Verzehrprodukte) mit anabolen Steroiden (chemische Analyse, gegebenenfalls toxikologische Risikobewertung)"; Seibersdorf research Bundesministerium für soziale Sicherheit und Generationen, Sektion IX - Abteilung 9, Radetzkystraße 2, 1031 WIEN. Access web page via www.dopinginfo.de then click on the title 'Institut fur Biochemie', then select 'Nahrungserganzungsmittel' followed bv 'Firmen- und Produktnamen'. Date last accessed 13 December 2002.
- 6. Desroches MC, Mathurin JC, Richard Y, Delahaut P. de Ceaurriz J. Urinary 19-norandrosterone purification immunoaffinity chromatography: application to gas chromatography/combustion/isotope ratio mass spectrometric analysis. Communications in Mass Spectrometry 2002;16:370-374.
- Mathurin JC, Herrou V, Bourgogne E, Pascaud L, de Ceaurriz J. Gas chromatographycombustion-isotope ratio mass spectrometry analysis of 19-norsteroids: application to the detection of a nandrolone metabolite in urine. Journal of Chromatography B 2001;759:267-275.

- 8. Le Bizec B, Bryand F, Gaudin I, Monteau F, Poulain F, Andre F. Endogenous nandrolone metabolites in human urine: preliminary results to discriminate between endogenous and exogenous origin. Steroids 2002;67:105-110.
- Davis S. A brief review of nandrolone doping control procedures. Web site address for article: http://ourworld.compuserve.com/homepages/SimonDavis1/Nandro.html. Date last accessed 12 December 2002.
- Debruykere G, De Sagher R, De Leenheer A, Van Peteghem C. In: Gorog S, ed. Advances of Steroid Analysis, Proceedings of the 4th Symposium on the Analysis of Steroids, Pecs, Hungary. Budapest: Akademiai Kiado, 1991:363-370.
- Debruyckere G, Vanpeteghem CH, Desagher R. Influence of the Consumption of Meat Contaminated with Anabolic-Steroids on Doping Tests. Analytica Chimica Acta 1993;275:49-56.
- 12. Kohler RMN, Lambert MI. Urine nandrolone metabolites: false positive doping test? British Journal of Sports Medicine 2002;36:325-329.
- Reznik Y, Dehennin L, Coffin C, Mahoudeau J, Leymarie P. Urinary nandrolone metabolites of endogenous origin in man: A confirmation by output regulation under human chorionic gonadotropin stimulation. Journal of Clinical Endocrinology and Metabolism 2001;86:146-150.
- 14. Saugy M, Robinson N, Cardis C, Schweizer C, Rivier L, Mangin P, et al. Nandrolone metabolites in football players: utility for in and out of competion testing. In: Schanzer W, Geyer H, Gotzmann A, Mareck-Engelke U, eds. Recent Avances in Doping Analysis (7), Proceedings of the Manfred Donike Workshop. Köln: Sport und Buch Strauss, 1999:95-108.
- 15. Le Bizec B, Monteau F, Gaudin I, Andre F. Evidence for the presence of endogenous 19-norandrosterone in human urine. Journal of Chromatography B 1999;723:157-172.
- 16. Schmitt N, Flament MM, Goubault C, Legros P, Grenier-Loustalot MF, Denjean A. Nandrolone excretion is not increased by exhaustive exercise in trained athletes. Medicine and Science in Sports and Exercise 2002;34:1436-9.
- 17. Robinson N, Taroni F, Saugy M, Ayotte C, Mangin P, Dvorak J. Detection of nandrolone metabolites in urine after a football game in

- professional and amateur players: a Bayesian comparison. Forensic Science International 2001;122:130-5.
- 18. Van Eenoo P, Delbeke FT, de Jong FH, De Backer P. Endogenous origin of norandrosterone in female urine: indirect evidence for the production of 19-norsteroids as by-products in the conversion from androgen to estrogen. Journal of Steroid Biochemistry and Molecular Biology 2001;78:351-7.
- Le Bizec B, Bryand F, Gaudin I, Monteau F, Poulain F, Andre F. Endogenous nandrolone metabolites in human urine. Two-year monitoring of male professional soccer players. Journal of Analytical Toxicology 2002;26:43-47.
- Galan Martin AM, Maynar Marino JI, Garcia de Tiedra MP, Rivero Marabe JJ, Caballero Loscos MJ, Maynar Marino M. Determination of nandrolone and metabolites in urine samples from sedentary persons and sportsmen. Journal of Chromatography B 2001:761:229-236.
- 21. Ueki M. Personal communication to Nandrolone Review Committee; Urinary concentrations of 19-norandrosterone in samples collected at the XVIII Winter Olympic Games in 1998. Doping Control Laboratory, Mitsubishi Kagaku Bio-Clinical Labs, Tokyo, Japan. Letter dated 9 April 2001.
- 22. Hemmersbach P. Personal communication to Nandrolone Review Committee; Urinary concentrations of 19-norandrosterone in samples collected at the XVII Winter Olympic Games in 1994. Hormone Laboratory, Aker University Hospital, Section for Doping Analysis, Oslo, Norway. Letter dated 20 April 2001.
- 23. Mareck-Engelke U, Schultze G, Geyer H, Schanzer W. The appearance of urinary 19-norandrosterone during pregnancy. European Journal of Sports Science 2002;2:1-7.
- 24. van der Veen AMH. Measurement of uncertainty and doping in sports: an example. ILAC/IAF Conference. Berlin, September 23-25, 2002.
- 25. Court of Arbitration Award TAS 98/212.
- 26. Court of Arbitration Award TAS 98/222.
- 27. Reeb M. Personal communication to the Nandrolone Review Committee. Acting Secretary, General Court of Arbitration for Sport. Letter dated 19 March 2001.

- 28. Court of Arbitration Award TAS 99/A/234 and 235.
- 29. Le Bizec B, Gaudin I, Monteau F, Andre F, Impens S, De Wasch K, et al. Consequence of boar edible tissue consumption on urinary profiles of nandrolone metabolites. I. Mass spectrometric detection and quantification of 19-norandrosterone and 19-noretiocholanolone in human urine. Rapid Communications in Mass Spectrometry 2000;14:1058-1065.
- 30. De Wasch K, Le Bizec B, De Brabander H, Andre F, Impens S. Consequence of boar edible tissue consumption on urinary profiles of nandrolone metabolites. II. Identification and quantification of 19-norsteroids responsible for 19-norandrosterone and 19-noretiocholanolone excretion in human urine. Rapid Communications in Mass Spectrometry 2001;15:1442-1447.
- 31. Proposed changes to the Misuse of Drugs Legislation (4 March 2002). *Access web page via* http://homeoffice.gov.uk/oicd/letter.htm and then select 'Letter'. Date last accessed 12 December 2002.
- 32. Details of the Merlene Ottey Decision (7 July 2000). Access web page via http://www.iaaf.org and then select 'News' and then 'Search' using search term 'Ottey Decision'. Date last accessed 12 December 2002.

Appendix 1: Committee membership

Chairman:

Prof VHT James, Emeritus Professor of Chemical Pathology, University of London.

Scientific Secretary:

Dr AT Kicman, Head of Research and Development, Drug Control Centre, King's College London.

Members:

Prof RV Brooks, Emeritus Professor of Chemical Endocrinology, University of London.

Prof DA Cowan, Professor of Pharmaceutical Toxicology, Director of the Drug Control Centre, King's College London.

Dr E Houghton, Senior Assistant Director and Head of Research & Development, HFL, Cambridgeshire.

Prof HS Jacobs, Emeritus Professor of Reproductive Endocrinology at University College London Medical School.

Prof HLJ Makin, Emeritus Professor of Analytical Biochemistry, University of London at St. Bartholomew's and Royal London School of Medicine. **Prof AC Moffat**, Chief Scientist of The Royal Pharmaceutical Society of Great Britain, Professor at The School of Pharmacy, University of London.

Dr P Robb, Senior Analytical Scientist, Department for Environment, Food and Rural Affairs, Central Science Laboratory, York.

Dr B Sheard, Chief Executive, HFL, Cambridgeshire (retired August 2001).

Dr AM Wallace, Consultant Clinical Scientist, Endocrine Section, Department of Clinical Biochemistry, Royal Infirmary, Glasgow.

Dr MJ Wheeler, Consultant Clinical Scientist at Guy's and St Thomas' Hospitals and Honorary Senior Lecturer, King's College, London.

Ex-officio:

Ms M Verroken, Director of UK Sports Anti-Doping Directorate, UK Sport, London.

Committee Secretariat:

Ms J Hardy, Personal Assistant to Ms M Verroken.

Appendix 2: Assistance received from experts external to the Committee

Dr H Geyer, Institut für Biochemie, Deutsche Sporthochschule, Cologne, Germany.

Prof P Hemmersbach, Scientific Director, Hormone Laboratory, Section for Doping Analysis, Aker University Hospital, Oslo, Norway.

Prof R Maughan, Department of Biomedical Sciences, University Medical School, Aberdeen, Scotland.

Prof RW Stephany, Director, EU Communities Reference Laboratory (CRL) for Residues, RIVM – National Institute of Public Health and the Environment, Bilthoven, The Netherlands.

Dr M Ueki, Doping Control Laboratory, Mitsubishi Kagaku Bio-Clinical Laboratories, Tokyo, Japan.

Appendix 3: Results of the UK Sport drug testing programme

Competitors tested within UK Sport's Testing Programme include UK competitors and non-UK competitors. Number of Findings does not indicate number of different athletes providing a positive urine sample and/or committing a doping offence. The data may also include competitors tested on more than one occasion.

Year*	Total Number of A Samples Analysed	Number of Positive Nandrolone Findings	% Positive Findings v A Samples Analysed
2002	6,009	8	0.13
2001	5,954	9	0.15
2000	5,406	5	0.09
1999	5,771	17	0.29
1998	4,669	4	0.09
1997	4,573	4	0.09
1996	4,395	3	0.07
1995	4,228	5	0.12
1994	4,435	1	0.02
1993	3,829	5	0.13
1992	4,046	1	0.02
1991	3,421	6	0.18
1990	3,708	2	0.05
1989	3,172	7	0.22
1988	2,798	2	0.07

^{*} Figures are for year ended 31 March