

## WADA Technical Document – TD2004EAAS

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Written by:	WADA Laboratory Committee	Approved by:	WADA Executive Committee
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### REPORTING AND EVALUATION GUIDANCE FOR TESTOSTERONE, EPITESTOSTERONE, T/E RATIO AND OTHER ENDOGENOUS STEROIDS

#### 1. Introduction:

This guide has been prepared to ensure that Laboratories can report, in a uniform way, the presence of abnormal profiles of urinary steroids resulting from the administration of testosterone or its precursors, androstenediol, androstenedione, dehydroepiandrosterone (DHEA) or a testosterone metabolite, dihydrotestosterone or a masking agent, epitestosterone. It also provides guidance to the Testing Authority on how to conduct the evaluation of *Adverse Analytical Findings* reported by the Laboratories.

It is proven that administration of these steroids alters one or more of the parameters of the urinary steroid profile. Elevated levels of urinary metabolites, which are part of the “steroid profile”, e.g. testosterone, epitestosterone, dihydrotestosterone, androsterone, etiocholanolone, DHEA as well as other specific metabolites are not consistent with normal endogenous production and result from the intake of these steroids. Increased ratios of specific pairs of steroid metabolites are also indicative of the administration of these endogenous steroids.

It is emphasized that the following requirements shall be applied by all Laboratories in their routine practice.

#### 2. Specific requirements for GC/MS measurement of T/E value, concentration of testosterone, concentration of epitestosterone:

The T/E value is given by the peak area or peak height ratio of testosterone and epitestosterone (equivalent to the glucuronide) obtained by measuring the ion at m/z 432 by GC/MS analysis in a Single Ion Monitoring mode (SIM). The T/E value is usually measurable regardless of the concentration of both steroids. Whether measured from the Screening Procedure or the Confirmation Procedure, it must be corrected using an appropriate standard (e.g. calibration curve, quality control sample(s) or authentic standard solutions of both testosterone and epitestosterone). The concentration of testosterone and epitestosterone (equivalent to the glucuronide) should be estimated but should not be used to determine the T/E value. In the case of high T/E values, the concentration of epitestosterone is frequently low and it may not always be possible to measure epitestosterone precisely. In such cases, only the concentration of testosterone (equivalent to the glucuronide) is to be determined.

The Screening Procedure which is normally conducted on a single aliquot shall be carried out including, together in the same batch, a control sample where the T/E value, concentrations of testosterone and epitestosterone are known.

Reference ranges of the various parameters of the urinary steroid profile have been described for populations of both males and females. It should be borne in mind that there is significant

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variation between individuals . A normal level for one individual may in another be elevated and be consistent with doping. The Laboratory will adapt its testing procedures to the *Sample* tested; for example, female or male, Asian or Caucasian (when the information is provided). The concentration of urinary steroids such as testosterone and epitestosterone varies greatly between individuals and also depends upon the specific gravity of the urine *Sample*; only values corrected for a specific gravity value of 1.020 can be compared.

It is recommended that a urine *Sample* in which any one of the following criteria is met during the Screening Procedure, be routinely submitted to the IRMS analysis:

- i) T/E value equal or greater than 4;
- ii) concentration of testosterone or epitestosterone (equivalent to the glucuronide) greater than 200 ng/mL<sup>1</sup>;
- iii) concentration of androsterone or etiocholanolone (equivalent to the glucuronide) greater than 10,000 ng/mL<sup>1</sup>;
- iv) concentration of DHEA (equivalent to the glucuronide) greater than 100 ng/mL<sup>1</sup>.

It is recognised that other parameters may justify a need for IRMS study and the reason should be documented.

Any result that will be used to support an *Adverse Analytical Finding* shall be confirmed and quantified.

Confirmation of elevated T/E values, concentration of testosterone, epitestosterone or any other steroid metabolite under consideration is to be performed in triplicate. The confirmation of the identity of any steroid reported with abnormal properties must be made (refer to technical document TD2003IDCR). Appropriate calibration (e.g. calibration curve, deuterated standards, quality control samples) is to be included in the protocol of the Confirmation Procedure.

Confirmed elevated concentration of steroids will be reported as such together with the value adjusted for the specific gravity of the urine *Sample* using the following formula:

$$\text{Concentration}_{1.020} \text{ ng/mL} = (1.020 - 1) / (\text{Specific gravity of the Sample} - 1) \cdot \text{Concentration measured ng/mL}$$

The urine *Sample* is not collected under sterile conditions, and where the circumstances are favourable, the microbes present in the *Sample* can cause changes to the profile of the urinary steroids. Initially there is cleavage of the glucuronides and sulfates followed by modifications of the steroids' structure by oxido-reductive reactions. To report an *Adverse Analytical Finding* of an elevated T/E value, testosterone or epitestosterone concentration or any other endogenous steroid parameters, the concentration of free testosterone and/or epitestosterone in the specimen is not to exceed 5% of the respective glucuroconjugates. Elevated amounts of 5 $\alpha$ - and 5 $\beta$ -androstan-3,17-dione in the free form also indicate microbial degradation.

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<sup>1</sup> Concentrations adjusted for a specific gravity value of 1.020

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### 3. Isotope ratio mass spectrometry:

When a parameter of the steroid profile indicates a need to further study, its  $^{13}\text{C}/^{12}\text{C}$  value expressed in delta units per mil ( $\delta^0/_{00}$ ) or that of its metabolites will be measured and compared to that of urinary reference steroids within the sample not affected by administration. Depending upon the nature of the endogenous steroid suspected to have been administered, the metabolites analysed could be testosterone, epitestosterone, androsterone, etiocholanolone, the androstane diols, DHEA, or other relevant metabolites while the urinary reference steroid usually analysed by the Laboratories is one of, pregnanediol, pregnanetriol, cholesterol, 11-hydroxyandrosterone or 11-ketoetiocholanolone. The instrumentation should be calibrated with an appropriate Reference Material.

The results will be reported as consistent with the administration of a steroid when the  $^{13}\text{C}/^{12}\text{C}$  value measured for the metabolite(s) differs significantly i.e. by 3 delta units or more from that of the urinary reference steroid chosen. In some *Samples*, the measure of the  $^{13}\text{C}/^{12}\text{C}$  value of the urinary reference steroid(s) may not be possible due to their low concentration. The results of such analyses will be reported as “inconclusive” unless the ratio measured for the metabolite(s) is below -28‰ based on non-derivatised steroid.

### 4. Reviewing and evaluating test results:

The following actions should be requested by the Testing Authority in agreement with the Laboratory:

- Isotopic ratios ( $^{13}\text{C}/^{12}\text{C}$ ) of the relevant metabolites should whenever possible be measured each time an elevated parameter of the steroid profile is estimated from the Screening Procedure or Confirmation Procedure and reported to the Testing Authority as having been determined. If the Laboratory does not have the capability to conduct such testing, the *Samples* are to be securely transferred ensuring the Chain of Custody to another Laboratory with the requisite capability.
- The results of the IRMS analysis and/or of the steroid profile measured by GC/MS shall be used to draw conclusions as to whether a doping violation may have been committed. If the IRMS study does not readily indicate exogenous administration, the result should be reported as “inconclusive” and if necessary further longitudinal studies performed.
- When available, the athlete’s previous tests on record at the Testing Authority should be accessed and the corresponding steroid profile data requested from the relevant Laboratory. These results should be examined and considered together with the existing evidence (longitudinal study).

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- If, for any reason, an IRMS analysis cannot be carried out satisfactorily (e.g. insufficient volume of urine, amount of analyte too low to enable a valid measurement) or the examination of previous test results raises suspicions due to unstable profile values, up to three further unannounced tests should be carried out, preferably within a three months period following the report of the suspicious analytical result. There should be a minimum total of three results, other than the abnormal *Sample*, of either past or post data. A *Sample* in which the elevated parameter is again measured is to be analysed by IRMS as described above. In difficult cases longer monitoring may be required.

### 5. Evaluation of longitudinal studies:

In males, the individual T/E values have been shown to vary from their mean value by less than 30% (screening values). In females, a low concentration of some urinary steroids such as epitestosterone and testosterone, close to the limit of detection using current analytical methods occurs. Normal variation of up to 60% may be expected. The individual basal T/E value should be determined from at least three test results, excluding the suspicious result under consideration. The mean, standard deviation and coefficient of variation (expressed in percent) should be calculated for those three basal values. If the suspicious test result, when compared to the basal value using appropriate statistical evaluation is found to be significantly different, that will constitute a proof of the administration of a source of testosterone. It is understood that the basal value may be calculated from previous screening test results. The comparison of screening results and confirmed results is acceptable.

The same reasoning applies to any other parameter of the steroid profile which has been estimated to be in an amount exceeding the ranges of values normally found in humans.

### 6. Other parameters:

Other parameters such as the ratio of urinary testosterone to Lutenising Hormone (T/LH) and the androsterone to testosterone ratio (A/T) may be used to provide extra information to help determine the use of some substances especially injected testosterone and many of its esters. A high T/LH ratio may be used as ancillary evidence. The A/T ratio which has markedly changed from the “normal” value found for an individual during a longitudinal study may indicate which type of substance has been used. A change to high value can indicate testosterone use and a change to low values may indicate the use of testosterone precursors such as DHEA. However, any administration of testosterone and of its precursors, androstenedione or DHEA will not necessarily alter the excretion of LH and epitestosterone glucuronide.

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### 7. Examples of specific urinary metabolites potentially altered by the administration of “endogenous steroids”;

Urinary steroid	Steroid administered
Testosterone (G)	Testosterone, androstenedione, DHEA
Epitestosterone (G)	Epitestosterone
T/E (G)	Testosterone, androstenedione, DHEA
Androsterone (G)	Testosterone, DHT, androstenedione, DHEA and androstenediol
Etiocholanolone (G)	Testosterone, androstenedione, DHEA and androstenediol
DHEA (G) (S)	DHEA
6a-OH Androstenedione (G)	Androstenedione
6β-OH Androsterone (G)	Androstenedione
6β-OH Etiocholanolone(G)	Androstenedione
6β-OH Epiandrosterone (S)	Androstenedione
7β-OH DHEA/16α-OH Androsterone (S)	DHEA
7-OH DHEA, 7 keto DHEA	7 keto DHEA

\* G indicates the glucuronide and S indicates sulphate conjugation.

The official text of the technical document Reporting and Evaluation Guidance for Testosterone, Epitestosterone, T/E Ratio and other Endogenous Steroids shall be maintained by WADA and shall be published in English and French. In the event of any conflict between the English and French versions, the English version shall prevail.

### 8. References:

Aguilera R., M. Becchi, H. Casabianca, C.K. Hatton, D. H. Catlin and B. Starcevic, *Improved method of detection of testosterone abuse by gas chromatography /combustion/ isotope ratio mass spectrometry analysis of urinary steroids*, J. Mass Spectrom. 31 (1996) 169

Aguilera, R., Catlin, D.H., Becchi, M., Phillips, A., Wang, C., Swerdloff, R.S., Pope, H.G., and Hatton, C.K. (1999). *Screening for exogenous testosterone by isotope ratio mass spectrometric analysis of one pregnanediol and two androstanediols*. J. Chromatogr.B. 727:95.

Aguilera, R., Chapman, T.E., and Catlin, D.H. (2000). *A rapid screening assay for measuring urinary androsterone and etiocholanolone  $\delta^{13}C$  (‰) values by gas chromatography/combustion/isotope ratio mass spectrometry*. Rapid Commun. Mass Spectrom.14: 2294.

Aguilera, R., Chapman, T.E., Starcevic, B., Hatton, C.K., and Catlin, D.H. (2001). *Performance characteristics of a carbon isotope ratio method for detecting doping with testosterone based on*

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*urine diols: controls and athletes with elevated testosterone/epitestosterone ratios.* Clin. Chem. 47: 292.

Aguilera R, Hatton CK, Catlin DH, *Detection of epitestosterone doping by isotope ratio mass spectrometry.* Clin Chem. 2002;48(4):629-36.

Ayotte C., Charlebois, A., Lapointe, S., Barriault D. and Sylvestre M. : *Validity of urine samples : microbial degradation. Recent advances in doping analysis.* Proceedings of the 14th Köln Workshop on Dope Analysis, Institut für Biochemie, Köln, Germany, March 17-22, 1996, W. Schänzer, H. Geyer, A. Gotzmann, U. Mareck-Engelke (editors) Sport and Buch Straub, Köln, pp 127-137 (1997).

Ayotte C., D. Goudreault, A. Lajeunesse, M. Cléroux, Y. Richard, A. Charlebois, J. -P. Couture and A. Fakirian: *GC/C/IRMS and GC/MS in “Natural” Steroids Testing*, in Recent Advances in Doping Analysis (9), Proceedings of the 19th Cologne Workshop on Dope Analysis, W. Schänzer, H. Geyer, A. Gotzmann, U. Mareck-Engelke (editors) Sport and Buch Straub, Köln (2001) p. 133

Ayotte C., *Evaluation of elevated testosterone/epitestosterone values in athletes’ urine samples*, IAF New Studies in Athletics, 12:2-3 (1997) p. 87 and reference cited

Ayotte C.: *The integrity of urine samples: the effects of temperature and bacteria on the validity of the analytical result.* Proceedings of the IAF Seminar 1995, Paris, France, October 10-11, 1995, in “ Harmonisation of Doping Issues in the IAAF ”, p. 127-138 (1997)

Baenziger J. and L. Bowers, *Variability of T/E ratios in Athletes*, Proceedings of the 11<sup>th</sup> Cologne Workshop on dope analysis, 7<sup>th</sup> to 12<sup>th</sup> March 1993, M. Donike, H. Geyer, A. Gotzmann, U. Mareck-Engelke, S. Rauth eds, Sport und Buch Strausse Edition Sport, Koln (1994) p.41

Bassindale T., D.A Cowan, S. Dale, A.J. Hutt, A.R. Leeds and A.T. Kicman, *Disposition of androstenedione and testosterone following oral administration of androstenedione to healthy female volunteers: influence on the urinary T/E ratio*, in Recent Advances in Doping Analysis (10), Proceedings of the 20<sup>th</sup> Cologne Workshop on Dope Analysis, W. Schänzer, H. Geyer, A. Gotzmann, U. Mareck-Engelke (editors) Sport and Buch Straub, Köln (2002) p. 51

Becchi M., R. Aguilera, Y. Farizon, M. M. Flament, H. Casabianca and P. James, *Gas chromatography/combustion/isotope-ratio mass spectrometry analysis of urinary steroids to detect misuse of testosterone in sport*, Rapid Commun. Mass Spectrom., 8 (1994) 304

Bosy, T.Z., Moore, K.A., and Poklis, A. (1998). *The effect of oral dehydroepiandrosterone (DHEA) on the urine testosterone/epitestosterone (T/E) ratio in human male volunteers.* J. Anal. Toxicol. 22 (6): 455.

Bowers, L.D. (1999). *Oral Dehydroepiandrosterone supplementation can increase the testosterone /epitestosterone ratio.* Clin. Chem. 45 (2): 295.

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Carlstrom K., E. Palonek, M. Garle, H. Oftebro, J. Stanghelle and I. Bjorkhem, *Detection of testosterone administration by increased ratio between serum concentrations of testosterone and 17 alpha-hydroxyprogesterone*, Clin. Chem., 38 (1992) 1779

Catlin D. H., C. K. Hatton and S. H. Starcevic, *Issues in detecting abuse of xenobiotic anabolic steroids and testosterone by analysis of athlete's urine*, Doping in Sport Symposium, Clin.Chem.,43(7) (1997) 1280

Catlin D. H., C. K. Hatton, P. W. Straus and B. Starcevic, in D. A. Cowan and A. T. Kicman (eds), *Control of Doping with Anabolic Agents*, Proceedings of the Scientific Meeting of the 4<sup>th</sup> Permanent world Conference on Anti-Doping in Sport, London (1993) p. 2

Catlin D.H., Leder BZ, Ahrens BD, Hatton CK, Finkelstein JS. *Effects of androstenedione administration on epitestosterone metabolism in men* Steroids. 2002 Jun;67(7):559-64.

Cowan D. A., A. T. Kicman, C. J. Walker and M. J. Wheeler, *Effect of administration of human chorionic gonadotrophin on criteria used to assess testosterone administration in athletes*, J. Endocrinol., 131 (1991) 147

Dehennin L. and A. M. Masumoto, *Long-term administration of testosterone enanthate to normal men: alterations of the urinary profile of androgen metabolites potentially useful for detection of testosterone misuse in sport*, J. Steroid Biochem. Mol. Biol., 44 (1993) 179

Donike M., H. Geyer, M. Kraft and S. Rauth, *Long-term Influence of Anabolic Steroid Misuse on the Steroid Profile*, in P. Belotti, G. Benzi, A. Ljungqvist eds., Doping in Sport, Monte Carlo 1989, International Athletic Foundation, Monte Carlo (1990) 107.

Donike M., K.-R. Barwald, K. Klostermann, W. Schanzer and J. Zimmermann, *Nachweis von exogenem Testosteron in Sport : Leistung und Gesundheit*, H. Heck, W. Hollmann, H. Liesen, R. Rost eds, Deutscher Arzte Verlag Koln, (1983) 293;

Donike M., S. Rauth and A. Wolansky, *Reference Ranges of urinary endogenous steroids determined by GC/MS*, Proceedings of the 10<sup>th</sup> Cologne Workshop on dope analysis, 7<sup>th</sup> to 12<sup>th</sup> June 1992, M. Donike, H. Geyer, A. Gotzmann, U. Mareck-Engelke, S. Rauth eds, Sport und Buch Strausse Edition Sport, Koln (1993) p.69

Donike M., S. Rauth, U. Mareck-Engelke, H. Geyer and R. Nitschke, *Evaluation of longitudinal studies, the determination of subject based reference ranges of the T/E ratio*, Proceedings of the 11<sup>th</sup> Cologne Workshop on dope analysis, 7<sup>th</sup> to 12<sup>th</sup> March 1993, M. Donike, H. Geyer, A. Gotzmann, U. Mareck-Engelke, S. Rauth eds, Sport und Buch Strausse Edition Sport, Koln (1994) p.33

Donike M., *Steroid Profile in Cologne*, Proceedings of the 10th Cologne Workshop on Dope Analysis, 7<sup>th</sup> to 12<sup>th</sup> June 1992, M. Donike, H. Geyer, A. Gotzmann, U. Mareck-Engelke, S. Rauth eds, Sport und Buch Strausse Edition Sport, Koln (1993) p.47

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Donike M., U. Mareck-Engelke and S. Rauth, *Statistical evaluation of longitudinal studies, part 2 : the usefulness of subject based reference ranges*, Proceedings of the 12<sup>th</sup> Cologne Workshop on Dope analysis, Koln 1995 p. 157

Falk O., E. Palonek and I. Bjorkhem, *Effect of Ethanol on the Ratio between testosterone and epitestosterone in urine*, Clin. Chem., 34(7) (1988) 1462

Flenker U. and Schanzer W., *Kinetic isotope effects during metabolism of delta-4-steroids*, in Recent Advances in Doping Analysis (9), Proceedings of the 19<sup>th</sup> Cologne Workshop on Dope Analysis, W. Schänzer, H. Geyer, A. Gotzmann, U. Mareck-Engelke (editors) Sport and Buch Straub, Köln (2001) p. 179

Leder BZ, Catlin DH, Longcope C, Ahrens B, Schoenfeld DA, Finkelstein JS. *Metabolism of orally administered androstenedione in young men.* J Clin Endocrinol Metab. 2001 Aug;86(8):3654-8.

Garle M., R. Ocka, E. Palonek and I. Bjorkhem, *Increased urinary testosterone/epitestosterone ratios found in Swedish athletes in connection with a national control program. Evaluation of 28 cases*, J. Chromatogr. B, 687 (1996) 55

Garle, M., and Palonek, E. (1998). *Androstenedione: excretion studies from single and multiple dose experiments*. In: Recent advances in doping analysis (6), Proceedings of the Manfred Donike Workshop, 16<sup>th</sup> Cologne Workshop on Dope Analysis, 15<sup>th</sup> to 20<sup>th</sup> March 1998, W. Schänzer, H. Geyer, A. Gotzmann, U. Mareck-Engelke, (Eds.), Verlag Sport und Buch Strauß, Edition Sport, p. 181. Koln, Germany.

Geyer H., U. Mareck-Engelke, W. Schanzer and M. Donike, *The Cologne protocol to follow up high testosterone/epitestosterone ratios*, in Recent advances in doping analysis (4), Proceedings of the 14<sup>th</sup> Cologne Workshop on dope analysis, 12<sup>th</sup> to 17<sup>th</sup> March 1996, M. Donike, H. Geyer, A. Gotzmann, U. Mareck-Engelke, eds, Sport und Buch Strausse Edition Sport, Koln (1997) p.139

Geyer H., W. Schanzer, U. Mareck-Engelke and M. Donike, *Factors Influencing the Steroid Profile*, in Recent advances in doping analysis (3), Proceedings of the 13<sup>th</sup> Cologne Workshop on dope analysis, 12<sup>th</sup> to 17<sup>th</sup> March 1995, M. Donike, H. Geyer, A. Gotzmann, U. Mareck-Engelke, eds, Sport und Buch Strausse Edition Sport, Koln (1996) p.95

Hemmersbach P., K. I. Birkeland, J. R. Norli and S. H. Ringertz, *Urine Storage Conditions and Steroid Profile Analysis*, in Recent Advances in Doping Analysis (4), Proceedings of the 14<sup>th</sup> Cologne Workshop on Dope analysis, 12<sup>th</sup> to 17<sup>th</sup> March 1996, M. Donike, H. Geyer, A. Gotzmann, U. Mareck-Engelke, eds, Sport und Buch Strausse Edition Sport, Koln (1997) p.99

Horning S., H. Geyer, M. Machnik, W. Schanzer, A. Hilbert and J. Oeßelmann, *Detection of Exogenous testosterone by <sup>13</sup>C/<sup>12</sup>C Analysis*, in Recent Advances in Doping Analysis (4),



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Proceedings of the Manfred Donike Workshop 14<sup>th</sup> Cologne Workshop on Dope Analysis, 17<sup>th</sup> to 22<sup>nd</sup> March 1996, M. Donike, H. Geyer, A. Gotzmann, U. Mareck-Engelke, eds, Sport und Buch Strausse Edition Sport, Koln (1997) p. 275

Kazlauskas, R., *Effects of DHEA on urinary steroids*, in Recent Advances in Doping Analysis (5), Proceedings of Koln Workshop, (1997) p. 83

Kicman A. T., H. Oftebro, C. Walker, N. Norman and D. A. Cowan, *Potential use of ketoconazole in a dynamic endocrine test to differentiate between biological outliers and testosterone use by athletes*, Clin. Chem., 39 (1993) 1798

Kicman A. T., R. V. Brooks, S. C. Collyer, D. A. Cowan, M. N. Nanjee, G. H. Southan and M. J. Wheeler, *Criteria to indicate testosterone administration*, Br. J. Sport Med., 24 (1991) 253

Lévesque J.-F. and Ayotte C. : *The oral administration of DHEA : the efficiency of steroid profiling*, in Recent Advances in Doping Analysis (7), Proceedings of the 17th Cologne Workshop on Dope Analysis, W. Schänzer, H. Geyer, A. Gotzmann, U. Mareck-Engelke (editors) Sport and Buch Straub, Köln (1999) p. 213

Lévesque J.-F. and Ayotte, C. : *Criteria for the detection of Androstenedione oral administration*, in Recent Advances in Doping Analysis (7), Proceedings of the 17th Cologne Workshop on Dope Analysis, W. Schänzer, H. Geyer, A. Gotzmann, U. Mareck-Engelke (editors) Sport and Buch Straub, Köln (1999) p. 169

Liu X., Zhang Y., Wu M. and Zhang C., *The steroid profiles after oral administration of testosterone undecanoate with different doses*, in Recent Advances in Doping Analysis (7), Proceedings of the 17<sup>th</sup> Cologne Workshop on Dope Analysis, W. Schänzer, H. Geyer, A. Gotzmann, U. Mareck-Engelke (editors) Sport and Buch Straub, Köln (1999) p. 311

Mareck-Engelke U., H. Geyer and M. Donike, *Stability of Steroid profiles*, Proceedings of the 10<sup>th</sup> Cologne Workshop on dope analysis, 7<sup>th</sup> to 12<sup>th</sup> June 1992, M. Donike, H. Geyer, A. Gotzmann, U. Mareck-Engelke, S. Rauth eds, Sport und Buch Strausse Edition Sport, Koln (1993) p.87

Mareck-Engelke U., H. Geyer and M. Donike, *Stability of Steroid profiles (4) : The circadian rhythm of urinary ratios and excretion rates of endogenous steroids in female and its menstrual dependency*, in Recent advances in doping analysis (2), Proceedings of the 12<sup>th</sup> Cologne Workshop on dope analysis, 10<sup>th</sup> to 15<sup>th</sup> April 1994, M. Donike, H. Geyer, A. Gotzmann, U. Mareck-Engelke, eds, Sport und Buch Strausse Edition Sport, Koln (1995) p.135;

Mareck-Engelke U., H. Geyer and M. Donike, *Stability of steroid profile (2) : excretion rates from morning urines*, Proceedings of the 11<sup>th</sup> Cologne Workshop on Dope analysis, Koln 1994 p. 85

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Mareck-Engelke U., H. Geyer and M. Donike, *Stability of steroid profiles (3) : ratios and excretion rates of endogenous steroids in male urines collected over 24 hours*, Proceedings of the 12<sup>th</sup> Cologne Workshop on Dope analysis, Koln 1995 p. 121

Mareck-Engelke U., H. Geyer, U. Schindler, U. Flenker, R. Iffland and M. Donike, *Influence of Ethanol on Steroid Profile Parameters*, in Recent Advances in Doping analysis (3), Proceedings of the 13<sup>th</sup> Workshop on Dope Analysis, 12<sup>th</sup> to 17<sup>th</sup> March 1995, M. Donike, H. Geyer, A. Gotzmann, U. Mareck-Engelke, Sport und Buch Strau? ?dition Sport, Koln (1996) p.143

Mareck-Engelke U., U. Flenker and M. Donike, *Stability of Steroid profiles (5) : The annual rhythm of urinary ratios and excretion rates of endogenous steroids in female and its menstrual dependency*, in Recent advances in doping analysis (3), Proceedings of the 13<sup>th</sup> Cologne Workshop on dope analysis, 12<sup>th</sup> to 17<sup>th</sup> March 1995, M. Donike, H. Geyer, A. Gotzmann, U. Mareck-Engelke, eds, Sport und Buch Strausse Edition Sport, Koln (1996) p.177

Mareck-Engelke U., U. Flenker and W. Schanzer, *Stability of Steroid profiles (6) : The influence of oral contraceptives on steroid profiles*, in Recent advances in doping analysis (4), Proceedings of the 14<sup>th</sup> Cologne Workshop on dope analysis, 12<sup>th</sup> to 17<sup>th</sup> March 1996, M. Donike, H. Geyer, A. Gotzmann, U. Mareck-Engelke, eds, Sport und Buch Strausse Edition Sport, Koln (1997) p.139

Namba O., Y. Miyachi, M. Irie and Y. Kuroda, *Urinary testosterone and epitestosterone secretion in a doping positive subject*, International Congress of Endocrinology, Kyoto, 1988, Abstract 16-22-324

Palonek E. and M. Garle, *Single Injection of Testosterone to 7 Volunteers : Results from this Study*, in Proceedings of the 10<sup>th</sup> Cologne Workshop on Dope analysis, M. Donike, H. Geyer, A. Gotzmann, U. Mareck-Engelke and S. Rauth (eds), Sport und Buch Strausse, Edition Sport, Koln, 1993, p. 131

Raynaud E., M. Audran, J. F. Brun, C. Fedou, J. L. Chanal and a. Orsetti, *False-positive cases in detection of testosterone doping*, Lancet (Letter), 340 (1992) 1468

Schweizer C., C. Cardis, M. Cauderay, L. Rivier and M. Saugy, *T/E ratio variations through puberty in male adolescents*, Proceedings of the 14<sup>th</sup> Cologne Workshop on Dope analysis, Koln 1997 p. 159

Setiawati E., Suyatna F.D., Wiria, M.S. and Ulamsari D., *Profile of urinary excretion in Indonesian volunteers after DHEA administration*, in Recent Advances in Doping Analysis (9), Proceedings of the 19<sup>th</sup> Cologne Workshop on Dope Analysis, W. Schänzer, H. Geyer, A. Gotzmann, U. Mareck-Engelke (editors) Sport and Buch Straub, Köln (2001) p. 287

Shackleton, C.H.L., Phillips, A., Chang, T., and Li, Y. (1997). *Confirming testosterone administration by isotope ratio mass spectrometric analysis of urinary androstanediols*. Steroids, 62: 379.

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Shackleton, C.H.L., Roitman, E., Phillips, A., and Chang, T. (1997). *Androstanediol and 5-androstenediol profiling for detecting exogenously administered dihydrotestosterone, epitestosterone, and dehydroepiandrosterone: Potential use in gas chromatography isotope ratio mass spectrometry*. *Steroids*, 62: 665.

Ueki, M., and Okano, M. (1999). *Analysis of exogenous dehydroepiandrosterone excretion in urine by gas chromatography/combustion/isotope ratio mass spectrometry*. *Rapid Commun. Mass Spectrom.* 13: 2237.

Uralets V. P., Gillette P.A. and Latven R.K., *Over-the-counter anabolic steroids 4-androsten-3,17-dione, 4-androsten-3,17-diol and 19-Nor-4-androsten-3,17-dione : excretion studies in men*, Recent advance in doping analysis (6), Proceedings of the Manfred Donike Workshop, 16th Cologne Workshop on Dope Analysis, 15th to 20th March 1998, W. Schanzer, H. Geyer, A. Gotzmann and U. Mareck-Engelke (eds.), Sport & Buch Strauss (1999) p. 147 ;

Uralets, V.P., and Gillette, P.A. (1999). *Over-the-Counter anabolic steroids 4-androsten-3,17-dione; 4-androsten-3,17-diol and 19-nor-4-androsten-3,17-dione: excretion studies in men*. *J. Anal. Toxicol.*, 23: 357.

Uralets V.P. and Gillette P.A. (2002). *New anabolic steroids available as nutritional supplements: 5-alpha-androstan-3,17-diol, 1,4-androstadien-3,17-dione and 5 alpha-androst-1-en-17-ol-3-one*, in Recent Advances in Doping Analysis (10), Proceedings of the 20<sup>th</sup> Cologne Workshop on Dope Analysis, W. Schänzer, H. Geyer, A. Gotzmann, U. Mareck-Engelke (editors) Sport and Buch Straub, Köln (2002) p. 73

Van Eenoo, P., Delbeke, F. R., Desmet, N., and De Backer, P. (1998). *Excretion studies with 4-androstene-3,17-dione*, Recent advances in doping analysis (6), Proceedings of the Manfred Donike Workshop, 16<sup>th</sup> Cologne Workshop on Dope Analysis, 15<sup>th</sup> to 20<sup>th</sup> March 1998, W. Schänzer, H. Geyer, A. Gotzmann, U. Mareck-Engelke, (Eds.), Verlag Sport und Buch Strauß, Edition Sport, p. 171. Koln, Germany.

Van Eenoo P., F.T. Delbeke, Desmet N. and De Backer P., *Excretion studies with 7keto-dehydroepiandrosterone*, in Recent Advances in Doping Analysis (9), Proceedings of the 19<sup>th</sup> Cologne Workshop on Dope Analysis, W. Schänzer, H. Geyer, A. Gotzmann, U. Mareck-Engelke (editors) Sport and Buch Straub, Köln (2001) p. 91

Wright F., J. P. Lafarge, J. Antréassian, M. Lagoguey and G. Péres, in P. Hemmersbach and K. I. Birkerland (eds), *Long term Study of Steroid and Peptidic Hormones in the Plasma of Healthy Young Men under Controlled Testosterone Undecanoate Therapy*, in Blood Sample in Doping Control, Second International Symposium on Drugs in Sports, Lillehammer, Norway (1993), p. 65