REPORTING NORANDROSTERONE FINDINGS

1. Introduction:

This document has been established to harmonize analysis and reporting of norandrosterone Adverse Analytical Findings by Laboratories.

The administration of 19-norsteroids such as 19-nortestosterone (nandrolone), 19-norandrostene-3,17-dione and 19-norandrostene-3,17-diol (delta-4 and -5 isomers) has been shown to lead mainly to the excretion of 19-norandrosterone (NA), 19-noretiocholanolone (NE) and 19-norepiandrosterone (NEA). The latter is found exclusively as its sulfoconjugate while the others are usually excreted as their glucuronide derivative. The sulfate derivatives, generally persistent, may be prevalent at the end of the excretion period.

After the i.m. administration of the long-lasting preparations of nandrolone, the metabolites may be detected for months, but metabolites formed after the oral ingestion are excreted massively in the first hours and remain detectable for only a few days. The excretion of 19-norandrosterone generally predominates that of the 5β-isomer but inversed proportions have been reported in some individuals after oral administration either at the end of the excretion period or when 5β-isomers of related norsteroids were taken (1). Norandrosterone is excreted during pregnancy and as a minor metabolite of norethisterone (2).

Special procedures such as more sensitive instrumentation, larger volumes of urine and more extensive sample clean-up were needed to detect, identify and quantify endogenous 19-norandrosterone (with limits of detection needing to be ten times lower than routine testing i.e. around 0.01 ng/mL). Under tightly controlled conditions, when 19-norandrosterone was detected in male specimens, it was found at mean values of less than 0.1 ng/mL which is well below the limit for reporting Adverse Analytical Findings (3). The physiological levels of 19-norandrosterone measured in samples collected from females are lower than 1 ng/mL, a maximum value of 0.8 ng/mL having been recorded during ovulation and correlates apparently with high levels of estrogens (4).

It appears that exercise does not increase physiological levels of 19-norandrosterone significantly and certainly not sufficiently to approach the threshold (5). A few urine specimens collected from sportsmen after the competition were reported to contain 19-norandrosterone in an amount approaching 1 to 2 ng/mL. However, these observations were made without adequate controls to exclude possible administration of norsteroids (6).
Although highly improbable, the intake of a substantial amount of non-castrated pig offal, in which the presence of norsteroids such as 19-nortestosterone has been demonstrated, could result in the excretion of 19-norandrosterone in an amount above the threshold during a few hours after ingestion (7).

Finally, the administration of some nutritional “supplements” can be the source of the presence of 19-norandrosterone in human urine samples (8).

2. Reporting requirements

The following requirements shall be applied by all Laboratories in their routine practice.

The Laboratory is to report as an Adverse Analytical Finding, any urine Sample from either a male or a female containing 19-norandrosterone (19-NA) at a concentration greater than 2 ng/mL. The specific gravity of the Sample is to be equal to or lower than 1.020 (measured in the Laboratory using an appropriate instrument). For urine Samples with a specific gravity above 1.020 a correction to the threshold is to be made.

The correction of the threshold to take into account the specific gravity of the Sample will be calculated using the following formula:

\[\text{Threshold}_{1.020} \text{ng/mL} = \left(\frac{\text{Specific gravity of the Sample} - 1}{1.020 - 1}\right) \times 2 \text{ ng/mL}\]

In addition to meeting the identification criteria (TD2003IDCR) the Laboratory must demonstrate that the concentration of 19-NA is above the threshold. The concentration of 19-norandrosterone must also be determined when it is lower than 10 ng/mL. The estimated expanded uncertainty must be considered for reporting.

More than one metabolite of administered norsteroids may be detected, but only the identification and quantification of 19-NA and its glucuronide (calculated as the total following hydrolysis of the glucuronide) is sufficient to report an Adverse Analytical Finding.

Before reporting an Adverse Analytical Finding in the urine Sample of a female, the Laboratory must take steps to ascertain that the presence of low levels of 19-norandrosterone is not due to pregnancy or to the intake of a birth control preparation or progestogen medication containing norethisterone. The Laboratory must document the absence of hCG i.e. less than 5 mIU/mL of immunoreactive hCG to exclude the possibility that an Adverse Analytical Finding had arisen because of pregnancy. The Laboratory will determine whether it is reasonable that the 19-norandrosterone was excreted in the amount measured consequent to the intake of norethisterone, by verifying that the major isomer of

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glucuroconjugated tetrahydroxysterone is present. The Laboratory will in such a case add the following phrase to the report “could be compatible with a norethisterone treatment”.

The official text of the technical document on the Reporting Norandrosterone Findings 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.

3. References:


Jeanneau T, Kintz P, Cirimele V, Ludes B. Détermination des concentrations physiologiques de la norandrostérone et de la norétilocholanolone, métabolites urinaires de la nandrolone par CPG/SM. Toxicorama 1999;XI:25-9;


Geyer H. et al., The analysis of "non-hormonal" nutritional supplements for prohormones, in Recent advances in Doping analysis, Proceedings of the 19th Cologne

