Summary of Major Modifications

The Technical Document on Harmonization of Analysis and Reporting of 19-Norsteroids Related to Nandrolone, TD2021NA, has been aligned with the 2021 World Anti-Doping Code (Code) and the recently approved 2021 International Standard for Laboratories (ISL); and, the other International Standards, which are set to come into force on 1 January 2021.

The main changes in the TD2021CG/LH include:

**Article 1.0 Introduction**

- A better clarification is provided (as a comment) on the possible endogenous origins of urinary 19-NA.

**Article 2.0 Initial Testing Procedure (ITP)**

- It’s been clarified that the internal standard may be labelled with isotopic labels other than deuterium.

**Article 3.0 Confirmation Procedures (CP)**

- It’s been clarified that the CP may also target the analysis of another Metabolite of 19-norsteroids (19-NE), in addition to 19-NA

**Article 3.1 Identification and Estimation of Concentration**

- A clarification is provided (as a comment) that the CP of 19-NA does not require quantification, but only to confirm the estimated concentration.

**Article 3.2.1 Conducting GC/C/IRMS Analysis**

- Includes a better description of the conditions that shall trigger GC/C/IRMS analysis of 19-NA;
- Instructions on GC/C/IRMS analysis when there are indications of $5\alpha$-reductase inhibitor activity in the Sample;
- Guidance to discriminate between oral consumption of natural sources of 19-NA and injection of norsteroid preparations based on the pharmacokinetics of 19-NA excretion, as well as on detection of 19-norsteroid preparations with a pseudo-endogenous carbon isotopic signature (which lead to negative GC/C/IRMS results);

**Article 3.2.2 GC/C/IRMS Test Method Validation Requirements**

- Guidance is provided on method validation requirements when applied to 19-NA, including the validation the use of at least two (2) endogenous reference compounds (ERCs).

**Article 3.2.3 GC/C/IRMS Analysis Requirements**
• A better description of negative and positive quality control samples, as well as the requirement to inject a blank urine sample before the Sample under GC/C/IRMS confirmation to avoid any potential contamination;

Article 3.2.4 Interpretation of GC/C/IRMS Results
• Criteria for interpretation of GC/C/IRMS results for 19-NA have been updated in accordance with the TD2021IRMS, including the mandatory use of two endogenous reference compounds (ERC) for reporting an Adverse Analytical Finding (AAF).

Article 3.3.1 Test for Norethisterone and Pregnancy
• The order of additional tests on Samples from female Athletes has been clarified, with the test for the presence of the main Metabolite of norethisterone (oral contraceptive) being done before the test for pregnancy;
• It has been clarified that Laboratories shall target the detection of the 3α,5β isomer of tetrahydronorethisterone (THNE);
• It has been clarified that for the Laboratory to conclude that the 19-NA detected in the Sample resulted from the permitted use of norethisterone-containing oral contraceptives, THNE should be detected at peak signals which are compatible with the 19-NA level.

Article 3.3.2 Test for Demethylation
• It has been clarified that the potential formation of 19-NA by in-situ 19-demethylation of androsterone (A) shall be verified by GC/C/IRMS analysis.

Article 4.0 Reporting
• A better guidance is provided for results interpretation and reporting in a tabulated form.
• The flowchart in Annex A has been updated

Article 5.0 References
• The list of scientific publications and WADA laboratory standards references has been updated

In addition:
• Formatting as well as updating of terms and definitions, where relevant;
• Footnotes have been inserted as Comments where relevant in the main text.

The TD2021NA replaces the former TD2019NA and becomes effective on 1 April 2021.