

Technical Letters 2021

Summary of Major Modifications

All WADA Technical Letters (TLs) have been revised to align with the 2021 World Anti-Doping Code (Code); the recently approved 2021 *International Standard for Laboratories* (ISL) (v.11.0); and, the other *International Standards* that are set to come into force on 1 January 2021.

All TLs have undergone formatting as well as updating of terms and definitions, where relevant.

In addition:

1. TL01 – Meclofenoxate

In this new version of the TL01, an explanatory comment regarding the pharmacokinetics of CPAHs herbicides was included in the introduction. Based on the urinary concentration of 4-CPA found for the general population, reporting levels of meclofenoxate and 4-CPA are now provided to the Laboratories in the article on Analysis and Reporting Requirements. An additional guidance for the “B” Confirmation Procedure (CP) to only confirm the presence of 4-CPA was included due to the instability of meclofenoxate in the urine. In addition, four scientific publications relevant to 4-CPA and meclofenoxate detection in human urine were included.

This TL becomes effective on 1 January 2021.

2. TL02 – Mebeverine Metabolism

In this new version of the TL02, two mebeverine specific *Metabolites* have been specified (mebeverine acid and desmethyl mebeverine acid). In addition, *p*-methoxy-ethylamphetamine, *p*-OH-ethylamphetamine and *p*-methoxy-amphetamine have been removed from the Reporting Requirements.

The Reference Materials (RM) for mebeverine specific *Metabolites* are available and the Laboratories may need to update their CP in order to include the detection of these *Metabolites* before reporting an *Adverse Analytical Finding* (AAF) for *p*-hydroxy-amphetamine.

This TL becomes effective on 1 April 2021.

3. TL03 – Zilpaterol

In this new version of the TL03, articles have been reorganized to facilitate interpretation.

This TL becomes effective on 1 January 2021.

4. TL04 – Zeranol

In this new version of the TL04, articles have been reorganized to facilitate interpretation.

This TL becomes effective on 1 January 2021.

5. TL05 – Oxilofrine

In this new version of the TL05, additional analysis and requirements were included to address whether the oxilofrine finding is consistent with the metabolization of ephedrine. Therefore, a specific minimum reporting level of 1,000 ng/mL for oxilofrine free form when detected in the presence of ephedrine has been established. Two scientific publication regarding the urinary levels of oxilofrine after the intake of therapeutic doses of ephedrine have been included for reference.

This TL becomes effective on 1 January 2021.

6. TL06 – Possible Metabolism of Proguanil into Chlorazaniil

In this new version of the TL06, articles have been reorganized to facilitate reading and interpretation. The “Scientific Background” information has been removed, and the relevant information moved into the Introduction article. A scientific publication regarding the formation of the diuretic chlorazaniil from the antimalarial drug proguanil was included as a reference.

This TL becomes effective on 1 January 2021.

7. TL07 – Andarine – Flutamide

In this new version of the TL07, the Analysis and Reporting requirements have been updated to clarify that an *AAF* for andarine shall be reported only when the presence of andarine (parent compound), and/or its glucuronic acid conjugate, and/or its deacetylated and/or hydroxylated *Metabolites*, and/or its bishydroxylated product are confirmed in the *Sample* (regardless of the presence of flutamide and/or its *Metabolite* 2-hydroxyflutamide). In addition, a comment specifying that the Laboratories shall not report an *AAF* for andarine based only on the presence of O-dephenylandarine was included.

This TL becomes effective on 1 January 2021.

8. TL08 – Use of Internal Standards

In this new version of the TL08, articles have been reorganized to facilitate interpretation.

This TL becomes effective on 1 January 2021.

9. TL09 – Oxethazaine

In this new version of the TL09, articles have been reorganized to facilitate interpretation.

This TL becomes effective on 1 January 2021.

10. TL10 – *In situ* Formation of Exogenous Compounds

In this new version of the TL10, the requirements regarding prednisolone and prednisone analysis have been removed. This TL has been updated to be aligned with the new versions of the TD2021IRMS.

This TL becomes effective on 1 January 2021.

11. TL11 – Oxymorphone

In this new version of the TL11, the Reporting Requirements now include the mandatory analysis of methylnatrexone by LC-MS before reporting an *AAF* for oxymorphone.

The RM for methylnatrexone is available and the Laboratories may need to update their CP in order to include the detection of this substance before reporting an *AAF* for oxymorphone.

This TL becomes effective on 1 April 2021.

12. TL12 – Enobosarm

In this new version of the TL12, the TL name has been updated from TL12 – Ostarine to TL12 – Enobosarm to be aligned with the SARM's nomenclature used in the *Prohibited List*. The Analysis and Reporting requirements have been updated to clarify that an *AAF* for enobosarm shall be reported only when the presence of enobosarm (parent compound), and/or its glucuronic acid conjugate are confirmed in the *Sample* (regardless of the presence of bicalutamide and/or its *Metabolites*). In addition, a comment specifying that the Laboratories shall not report an *AAF* for enobosarm based only on the presence of O-dephenylandarine was included.

This TL becomes effective on 1 January 2021.

13. TL13 – Trimetazidine

In this new version of the TL13, the Analysis and Reporting Requirements present additional guidance that the Laboratories shall consider before reporting a result as an *AAF* for trimetazidine. Therefore, the request to consult the WADA Science Department for trimetazidine suspicious findings has been removed.

This TL becomes effective on 1 January 2021.

14. TL14 – Difference in “A” and “B” *Sample* Urine Characteristics

In this new version of the TL14, articles have been reorganized to facilitate interpretation.

This TL becomes effective on 1 January 2021.

15. TL15 – Hydromorphone

In this new version of the TL15, articles have been reorganized to facilitate interpretation.

The Analysis and Reporting Requirements before reporting a result as an *AAF* for hydromorphone which may result from the permitted administration of hydrocodone were updated with the following consideration:

- The result shall be reported a Negative Finding if the concentration of total hydromorphone is lower than or equal to (\leq) the concentration of total hydrocodone or total norhydrocodone. In addition, a comment clarifying that the total concentration refers to the sum of the

concentrations of the respective free compound and its glucuroconjugated form(s) was included.

This TL becomes effective on 1 January 2021.

16. TL16 – Tretoquinol

In this new version of the TL16, the instruction to report an *AAF* for tretoquinol [Trimetoquinol] only if the *Sample* has been collected after 15 January 2019 has been removed. In addition, the instruction to record *Samples* in which the tretoquinol concentration is estimated below 20 ng/mL has been also removed.

This TL becomes effective on 1 January 2021.

17. TL17 – Detection of Tulobuterol in the Presence of Bupropion

In this new version of the TL17, articles have been reorganized to facilitate interpretation.

This TL becomes effective on 1 January 2021.

18. TL18 – Testolactone

In this new version of the TL18, articles have been reorganized to facilitate interpretation.

This TL becomes effective on 1 January 2021.

19. TL19 – Prednisone and Prednisolone

In this new version of the TL19, updates were necessary to align the TL with the new TD2021IRMS. The reference to TL10 has been removed from the Introduction and updates have been made on terms and definitions, where relevant, for consistency with the TD2021IRMS.

This TL becomes effective on 1 January 2021.

20. TL20 – Specific Substances with a Steroid Structure

In this new version of the TL20, the following substances have been included, which the Laboratories shall consider before reporting a result as an *AAF*:

- 1-epiandrosterone (3 β -hydroxy-5 α -androst-1-en-17-one);
- 7 α -hydroxy-DHEA;
- 7 β -hydroxy-DHEA; and
- 7-Keto-DHEA.

In addition, since the new TD2021IRMS does not include specific criteria for the GC/C/IRMS analysis of the substances mentioned in this TL, the recommendation to perform GC/C/IRMS analysis has been removed.

This TL becomes effective on 1 January 2021.

21. TL21 – 6-oxo and *Metabolites*

In this new version of the TL21, articles have been reorganized to facilitate interpretation.

This TL becomes effective on 1 January 2021.

22. TL22 – Ethylmorphine.

In this new version of the TL22, sections have been reorganized to facilitate interpretation.

This TL becomes effective on 1 May 2021.